SYNOPSIS: ROTAVIRUS VACCINATION - WHY EUROPE IS MOVING FORWARD?

G.S.K. Symposium Faculty

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The burden of rotavirus gastroenteritis (RVGE) is considerable, impacting clinical practice, imposing costs on health systems, and acting as a source of significant morbidity.[1] Further, this burden is often underestimated.[2]

Vaccines against rotavirus (RV) were developed using some of the most comprehensive studies in vaccinology to date.[3] These live, attenuated oral vaccines were designed to mimic the protection conferred from natural infection[2] and have shown an efficacy higher than 90% in preventing severe cases of RV diarrhoea.[4] The substantial public health impact of RV vaccination has been demonstrated worldwide. Post-licensure effectiveness data from Latin America, the USA and Australia have shown that these vaccines have significantly reduced diarrhoea associated hospitalisations, outpatients and emergency department visits.[4,5] Additionally, recently published data has demonstrated the significant impact that vaccination can have in the European context.[6,7]

Despite the 2008 recommendations from the European Society for Paediatric Infectious Diseases (ESPID) and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN),[8] RV vaccination coverage in some large European countries remains low.[9] To date, only Austria, Belgium, Finland and Luxembourg have included RV vaccination in their national immunisation programmes.[9] However, the situation in Europe is slowly improving.[9] Recent data on the benefit/risk assessment of rotavirus vaccination from different parts of the world - along with a better understanding of the burden of the disease - contributed to a change in perspective.[9,10,11] The recent decision in 2012 to introduce RV vaccination into the UK schedule may indicate a growing interest in the prevention of RVGE.[12]

This symposium will allow the audience to understand how RV can be prevented and that 6 years after RV vaccine registration, Europe is moving forward.

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SYNOPSIS: ADDRESSING INVASIVE AND NON-INVASIVE VACCINE-PREVENTABLE DISEASES IN YOUNG CHILDREN

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The control of childhood infectious diseases remains the major motivation for implementing effective and durable health programmes, with paediatric vaccination schedules forming one of the major strategies. Success has been achieved with existing vaccines and vaccination programmes against pneumococcal diseases, Haemophilus influenzae type b (Hib) and meningococcal capsular group C (MenC) invasive disease, as well as pertussis, hepatitis B and poliomyelitis.[1-3] However, challenges remain including vaccine availability, adherence to schedules, the continued documentation of sustained vaccine effectiveness, and the residual burden of invasive and non-invasive disease.

The increased availability of vaccines and their inclusion in immunisation programmes has created crowding of the vaccination calendar. Combination vaccines have been a strategy to address this issue. Hexavalent vaccines, combining the diphtheria, tetanus, pertussis, hepatitis B virus, poliovirus and Hib antigens, have been developed in this context. Use of these combination vaccines has contributed to improved timeliness and adherence to childhood immunisation programs.[4] More than a decade of clinical experience with these hexavalent combination vaccines is now available.[5]Some of the highlights of this experience will be discussed within this symposium.

Bacterial meningitis remains a serious global health threat causing an estimated 170,000 deaths each year.[6] The annual incidence rate of meningococcal disease differs across countries; in 2009 the rates were 0.92/100,000 for Europe and 0.28/100,000 in the United States.[7] Meningococcal capsular groups A, B, C, X, Y and W135 are responsible for severe disease.[6] MenC monovalent conjugate vaccines are now widely used throughout Europe.[2] This success has stimulated the development of quadrivalent meningococcal conjugate vaccines, broadening the coverage to capsular groups A, W135 and Y (MenACWY). In Europe, two MenACWY vaccines are available.[8-9] This symposium will focus on the use of these vaccines in infants and toddlers.

Pneumococcal infections include serious diseases such as meningitis and bacteraemia, as well as milder but more common illnesses, such as otitis media.[10] The latest WHO report highlighted that of the estimated 8.8 million global annual deaths amongst children < 5 years of age, 476,000 were caused by pneumococcal disease, making these infections a leading cause of vaccine-preventable deaths in children worldwide.[10] Otitis media, although a less severe condition, is one of the most frequent bacterial infections for which medical advice is sought.[11-12] As a result, it places a considerable burden on healthcare resources.[11,13] Furthermore, otitis media causes significant distress for individual patients and their caregivers, and remains a major contributor to antibiotic prescriptions in young children.[12,14] Treatment of these diseases is complicated by antibiotic resistant Streptococcus pneumoniae, driven by antibiotic overuse to treat respiratory infections.[15] This symposium will focus on pneumococcal H. influenzae protein D conjugate vaccine (PHiD-CV) and the results of recently completed, large, randomised, controlled clinical trials and post-marketing studies.

GSK's hexavalent DTPa-HepB-IPV/Hib*, MenACWY-TT and PHiD-CV vaccines are an important part of GSK's contribution to global efforts in the prevention of invasive and non-invasive diseases.

*Diphtheria and tetanus toxoids, acellular pertussis, hepatitis B, inactivated poliovirus and H. influenzae type b.

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UPDATE ON VECTOR BORNE DISEASES: EHRLICHIOSIS, BABESIOSIS, ROCKY MOUNTAIN SPOTTED FEVER AND LYME

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Background: “Vector-borne disease" is the term commonly used to describe an illness caused by a pathogen that is transmitted to people by blood-sucking arthropods. The arthropods, either insects or arachnids include blood sucking insects such as mosquitoes, fleas, lice, biting flies and bugs, and blood sucking arachnids such as mites and ticks. The term “vector” refers to any arthropod that transmits a disease through feeding activity. This abstract will focus on the Tick associated vector illnesses.

Methods: Similar to other vector-borne diseases, temperature accelerates the ticks' developmental cycle, egg production, population density, and distribution. Data on tick vector, pathogen, and presentation and treatment guidelines were reviewed.

Results: The vector for each of these illnesses has been identified. All illnesses have been recorded worldwide. Diagnosis for these pathogens is dependent on suspicion of illness at presentation and may include rash, signs and symptoms of CNS illness and may mimic symptoms seen in viral illnesses. Treatment is indicated in all cases of presumed RMSF (doxycycline), and acute severe anemia in Babesiosis (atovaquone plus azitromycin), but in not emergent in Lyme (amoxicillin or doxycycline) and can often wait confirmation of infection. Treatment of asymptomatic illness in case of Babesia and Ehrlichia is not indicated.

Conclusions: Vector borne infections are worldwide in presentation. Diagnosis is often driven by suspicion of disease at time of clinical presentation, and confirmatory laboratory assessments are available. Treatment is simple and results in clinical cure of illness.

4

SAFETY AND IMMUNOGENICITY OF A MENC BOOSTER DOSE IN ADOLESCENTS

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The main purpose of vaccination is achieving long-term individual (and herd) immunity. For many infectious diseases, this requires a booster vaccination in addition to primary vaccination. As has been shown previously, immunity against Meningococcal serogroup C disease (MenC) wanes after several years in infants and toddlers, indicating that also for MenC a booster vaccination might be necessary. Young children between 0-5 years of age are most vulnerable to invasive MenC disease. Vaccination at a young age is therefore most appropriate but does not lead to long term protection.

Since teenagers aged between 12-18 years are also at risk for developing invasive MenC disease, a booster MenC vaccination during or prior to adolescence can be considered. Determining the appropriate age for this booster vaccination is a challenge as a booster vaccination during late adolescence probably leads to more prolonged individual (and herd) protection, but leaves the young adolescents at risk.

In an attempt to determine the optimal age for a booster (second) vaccination, a study is currently conducted in The Netherlands (TIM study). In the Dutch immunization program, MenC is administered at the age of 14 months as a single dose vaccination. For the TIM study, three age groups (10, 12 and 15 years) are vaccinated with the same vaccine that was as used in the routine immunization program.

The results so far from this study will be discussed.

5

VALUE OF MONOVALENT MEN-C VACCINES IN RELATION TO CONJUGATED MEN-ACYW135- AND OTHER COMBINATED VACCINES

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Serogroup C polysaccharide-protein conjugate vaccines were introduced over a decade ago and are now used successfully throughout the world. Recently multivalent meningococcal conjugate vaccines for serogroups A, C, W-135, and/or Y became available in some countries and protein-based Men B vaccines have just been licensed. In light of these developments there is an emerging debate which vaccination strategy can provide best preventive measurements.

Obviously there is not one single solution. The incidence and epidemiology of meningococcal disease vary geographically and over time. Differences in invasive capsular serogroups and potential effects of ongoing vaccination programs influenced the epidemiology of infection and disease. Serogroups B, C, and Y are responsible for the majority of cases in Europe, the Americas, and Oceania; serogroup A has been associated with highest incidence in Africa and Asia; serogroups W-135 and X have caused major disease outbreaks in sub-Saharan Africa.

In addition, vaccine-related issues have to be addressed: Durability of protective immune response and optimal timing of booster immunizations need to be established for every vaccine as well as costs and benefits of Men-ACWY conjugate vaccines in comparison to monovalent MenC conjugate vaccines. The value of providing protection against each disease-causing serogroup might differ for countries, depending upon country-specific disease burden, changes in epidemiology or potential for local outbreaks with non-predominant serogroups. Especially for countries with high incidence of MenC-disease and low infection rates with MenA, W and Y continuing with established MenC-vaccination programs might be a wise choice, also leaving room for future implementation of MenB-vaccines.

6

IS A SINGLE DOSE OF MENC IN THE FIRST YEAR OF LIFE ENOUGH?

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In 1999, the UK introduced meningococcal serogroup C conjugate (MCC) vaccines at 2,3,4 months of age with a single dose for children 1-18 years. In 2006, the schedule was refined to 3, 4, 12 months of age. The potential of a single MCC priming dose in infancy has been demonstrated.

A UK study provided evidence for reducing the priming doses of MCC-TT together with the positive correlation of lower quantity of antigen and SBA levels post-primary but a higher magnitude of the booster response. The results of clinical trials investigating a reduced infant MCC schedule, will be discussed. A UK study, demonstrated one dose of MCC-TT or MCC-CRM 197 at 3 months to give comparable responses (SBA titres ≥8) both post-primary vaccination and post-booster Hib/MCC-TT at 12 months. However, the magnitude of the SBA GMT was higher in the MCC-TT primed post-booster. A single priming dose of MCC-TT (at 4 or 6 months) compared to two doses (2 and 4 months) gave high SBA titres in all groups, post-primary and post-booster at 12-13 months, with the highest SBA responses observed in the 4 month single dose group. A study in Malta, comparing one dose of MCC-TT or MCC-CRM197 at (3 months) versus two doses of MCC-CRM197 (3 and 4 months), showed a high proportion of subjects achieving SBA titres ≥8 following a single dose.

These studies show that a single-dose priming vaccination in infancy can be considered. The UK Joint Committee on Vaccination and Immunisation has recommended the use of a single priming dose at 3 months with the move of the second infant dose to adolescence.

7

MENC SEROSTATUS IN THE POPULATION AND THE PREDICTION OF FUTURE EPIDEMIOLOGY

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There is an increasing thinking that Men C vaccination schedule has to be modify. In order to maintain an appropriate level of herd immunity, it seems to be important to have high level of seroprotection in adolescents and young adults.

In Valencia, in spite of a vaccination program with catch up until 19 years of age (y.o.a.), the incidence in the unvaccinated population did not decrease until 2009, which is in contrast to other countries with massive catch-up programs (e.g. UK, The Netherlands).

We conducted a seroepidemiological study in which we assessed the MenC seroprotection rates in different age groups, and also estimated the vaccine coverage by means of reviewing the vaccine registry of Valencia. Multiple imputation was applied for those not included in the registry.

Persistence of antibodies depend on the age of immunization. Five years after receiving one vaccine dose in the second year of life 30% are seroprotected and 24% at age 11. When a catch up is given at age over 8 y.o.a., the persistence of antibodies is higher.

In 2011, 30% of the Valencian population 3 to 29 y.o.a. were seroprotected, with the highest proportion in subjects 17 to 29 years old (47%). Before vaccination, MenC carriage occurred in this age group, and therefore, having them protected is needed to maintain herd protection. Ideally this should not increase the cost of the program and a reduction of the number of vaccines given in the first year of life should be considered.

SYNOPSIS: ADOLESCENT VACCINATION: CHALLENGES FOR IMPLEMENTATION OF EFFECTIVE IMMUNISATION PROGRAMMES

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Over the years, vaccination of young children has become a real success; however, when it comes to adolescent vaccination, some progress still needs to be achieved.

Indeed, adolescence is a time of increased independence, resulting in a larger and more diverse social network, and behaviours that may increase the chances of exposure to infectious diseases.[1] Many adolescents also begin to spend more time apart from caregivers, reducing the chance that infectious diseases like meningococcal meningitis, which progresses rapidly and can be fatal if not treated, will be recognised.[1]

Outbreaks of meningococcal disease and pertussis among adolescents can cause substantial disease and can also increase the risk of exposure for others with whom they come in contact.[1,2] This could be of particular concern for babies and infants who have yet to be immunised and are particularly vulnerable to severe morbidity from such diseases.[3] However, booster doses can help maintain the immunity acquired from prior childhood vaccinations, such as those against pertussis, and can allow 'catch-up' for missed doses.[4,5]

Human papillomavirus (HPV) infection is typically contracted during adolescence soon after sexual debut and virtually 100% of cervical cancer cases are caused by oncogenic HPV types.[6,7] However, the time from HPV infection to disease development is long, resulting in cervical cancer and precancerous diseases typically occurring at a later age. Primary vaccination for adolescent girls against HPV may, therefore, help to protect against cervical cancer and precancerous lesions of the cervix.[6,8,9] Furthermore, treatment of cervical diseases can lead to obstetrical complications, such as preterm delivery, that may adversely affect newborns.[10,11] This further indicates that vaccination against HPV may help reduce various aspects of the disease burden related to cervical cancer.[6,12]

In order to be effective, immunisation should be timely and coverage should be high. However, in practice, in European countries[13,14] and in the US,[15] many adolescents are not up-to-date with the recommended vaccines for their age group. Reasons for this low uptake of vaccines include poor awareness among adolescents and their caregivers about infectious diseases, vaccines and the public health rationale for immunisation programmes.[1,16] Adolescents tend to reduce their contacts with healthcare professionals, thereby reducing the number of immunisation opportunities.[17] Adolescent immunisation rates are also hampered by negative perceptions of vaccination among adolescents, their parents and healthcare providers, including social and cultural sensitivities about the age at which adolescents are likely to start engaging in risky behaviours.[1] Strategies to overcome these barriers, such as educational campaigns, improved tracking of adolescent healthcare visits, and delivery of vaccines at both schools and other non-traditional settings, could help improve adolescent immunisation rates.[1,18]

Vaccine-preventable diseases such as invasive meningococcal disease, pertussis and those caused by HPV, especially cervical cancer, cause healthcare burden in the adolescent population, and can have even greater effects in the longer term, through transmission to others in society, or through effects such as predisposition to cancer (in the case of HPV).[1] The challenges for successful implementation of immunisation programmes targeted to this age group are balanced by the potential benefits for adolescents themselves, for their families and their society, and even for future generations.

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AN UPDATE ON VACCINES TO PREVENT RESPIRATORY ILLNESSES IN CHILDREN

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Because of the large burden of influenza in children, preventive vaccines remain a high priority. While the live vaccines are more efficacious, their reaction profile has restricted licensure in the youngest children. More recent pediatric studies of adjuvanted seasonal influenza vaccines have demonstrated them to be highly efficacious. However, concerns remain about their safety in children. To reduce the need for yearly administration of influenza vaccine, the development of universal influenza vaccines is also being actively pursued and will be discussed.

Early attempts at generating a formalin inactivated respiratory syncytial virus (RSV) vaccine were marked by immune mediated reactions, resulting in some fatalities. In spite of these setbacks, attempts at RSV prevention remain very active. Passive RSV antibody administration to young children at high risk for complications from RSV is widely utilized in many developed countries; supporting the concept that antibody will prevent RSV infection. Active immunization using either subunit or biologically or genetically engineered live attenuated RSV vaccines is being tested in ongoing clinical trials. In addition, the use of live attenuated parainfluenza virus (PIV) vaccines as vectors for both PIV and RSV antigens is being pursued. With many vaccine candidates for study, it is hoped that new and promising vaccines will emerge for the routine administration in young children to reduce the large impact of viral respiratory infections.

10

HOW TO MANAGE PEDIATRIC MENINGITIS

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Bacterial meningitis is still an important cause of mortality and morbidity despite advances in antimicrobial therapy. Apart from antibiotic treatment supportive therapy including dexamethasone is widely used. In children with H. influezae meningitis dexamethasone was shown to significantly prevent hearing loss. In contrast, there is increasing evidence that the therapy with dexamethasone might not be as beneficial especially in pneumococcal meningitis as previously reported. The usage of clinical tools such as the bacterial meningitis score may help to differentiate between acute bacterial meningitis and aseptic meningitis and eventually to determine the correct diagnosis. Furthermore, biomarkers like procalcitonin may also be more suitable than C-reactive protein to distinguish between acute bacterial meningitis and aseptic meningitis. However, in very young children such as preterm babies and neonates diagnosing meningitis remains still a challenge. The performance of lumbar punctures with consequent culture for meningitis causing pathogens remains the mainstay of diagnostics especially in this young age group.

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HOW TO MANAGE PEDIATRIC MENINGITIS

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Bacterial meningitis is one of the most serious infections in infants and children, with considerable morbidity and mortality. Despite the spreading of conjugated vaccines against Haemophilus influenzae type b (Hib), the most important pneumococcal serotypes and serogroup C meningococcus has reduced the incidence of this infection in developed countries, it still remains a global public health problem and an important cause of mortality and disability. Recent guidelines and recommendations based on the best available evidence on the management of bacterial meningitis in infants and children are clear and conform about diagnostic procedures, management in pre-hospital settings and secondary care and in the use of targeted antibiotics. Instead, whether corticosteroids should be used as a complementary therapy to antibacterials is still not clear because of the disparate findings from clinical trials and clinical evidence. In high-income countries dexamethasone has shown good results to prevent hearing loss in Hib meningitis if administered before or at the same time as the first dose of antibiotics. Dexamethasone should be evaluated in pneumococcal meningitis: it may be less beneficial in children with delayed presentation to medical attention and may be unfavourable in case of cephalosporin-resistant pneumococci. On the contrary, there is no evidence to recommend the use of corticosteroids in meningococcal meningitis. Further studies that take into account the epidemiologic changes of recent years, consider enrolment based on the onset of symptoms and evaluate outcomes such as hearing loss and neurologic sequelae with advanced techniques are urgently needed.

12

DIFFERENCES IN PREVALENCE OF PARASITES IN STOOL SAMPLES BETWEEN TWO DISTINCT ETHNIC PEDIATRIC POPULATIONS IN SOUTHERN ISRAEL, 2007-2011

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Background and aims: Intestinal parasite infections cause significant morbidity worldwide, particularly in developing populations. Two populations reside in southern Israel: the Jewish population (comparable to a Western population) and the Bedouin population, formerly desert nomads, transitioning to a western lifestyle (comparable to a developing population). Our aim was to compare total and parasite-specific positive samples proportions in stool exams between two ethnic pediatric populations in southern Israel.

Methods: A retrospective, laboratory, population-based surveillance. Stool ova and parasites (O&P) tests examined between 2007 and 2011 were included. Nearly all region residents are being treated by one hospital, and most O&P tests sent from hospitalized and community patients are performed by the hospital parasitology laboratory.

Results: 45,978 samples (1 per patient/month) were examined. 16,317 parasites were identified in 12,325 (26.8%) positive samples. Total positive (≥1 parasite/stool) stool samples proportion was higher in Bedouin compared with Jewish children, both in < 5 years (3,797/12,931, 29.4% vs. 850/8,927, 9.5%, respectively, P< 0.001), and in 5-19 years (5,933/14,423, 41.1% vs. 1,745/9,697, 18.0%, respectively, P< 0.001). Blastocystis hominis and Entamoeba species predominated in Bedouin children 5-19 years, while Giardia lamblia and Hymenlopis nana predominated in Bedouin children < 5 years, compared with Jewish children.(**Table 1**)

	<5 years			5-19 Years		
Parasite	N, % Bedouin children (N=12,931)	N, % Jewish children (N=8,927)	Relative risk (range, 95% CI)	N, % Bedouin children (N=14,423)	N, % Jewish children (N=9,697)	Relative risk (range, 95% CI)
Blastocystis hominis	850 (6.6%)	230 (2.6%)	2.6 (2.2-2.9)	3,329 (23.1%)	1,013 (10.4%)	2.2 (2.1- 2.4)
Giardia lamblia	2,768 (21.4%)	500 (5.6^)	3.8 (3.5-4.2)	1,590 (11.0%)	349 (3.6%)	3.1 (2.7-3.4)
Entamoeba coli	407 (3.1%)	78 (0.9%)	3.6 (2.8-4.6)	1,720 (11.9%)	381 (3.9%)	3.0 (2.7-3.4)
Entamoeba species	295 (2.3%)	110 (1.2%)	1.9 (1.5-2.3)	1,071 (7.4%)	381 (3.9%)	1.9 (1.7-2.1)
Other protozoa	33 (0.3%)	6 (0.1%)	3.8 (1.6-9.1)	93 (0.6%)	52 (0.5%)	1.2 (0.9-1.7)
Hymenolepis nana	250 (1.9%)	11 (0.1%)	15.7 (8.6-28.7)	450 (3.1%)	73 (0.8%)	4.1 (3.2-5.3)
Other helminths	30 (0.2%)	20 (0.2%)	1.0 (0.6-1.8)	63 (0.4%)	164 (1.7%)	0.3 (0.2-0.3)
Total	4,633 isolates in 3,797 (29.4%) samples	955 isolates in 850 (9.5%) samples	3.1 (2.9-3.3)	8,316 isolates in 5,933 (41.1%) samples	2,413 isolates in 1,745 (18.0%) samples	2.3 (2.2-2.4)

[Proportions of parasites prevalence in stool]

Conclusions: Bedouin children were characterized by higher rates of total and positive stool O&P testing, compared with Jewish children, probably reflecting higher intestinal parasitic disease rates. This may be associated with lifestyle differences between the two populations living in the same region.

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A PREDICTIVE SIGNATURE GENE SET FOR DISCRIMINATING ACTIVE FROM LATENT TUBERCULOSIS IN WARAO AMERINDIAN CHILDREN

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Background: Blood transcriptional profiling has improved our understanding of disease pathogenesis of tuberculosis (TB) in adults and may offer future leads for diagnosis and treatment. It is unknown whether the existing signature gene sets based on adult cohorts are applicable to childhood cohorts.

Methods: Twenty-seven HIV-negative Amerindian children with TB (n=9), latent TB infection (LTBI, n=9) and healthy controls (HC, n=9) were selected for gene expression profiling of whole blood. Identified signature genes were validated by quantitative real-time PCR in an additional cohort of 54 children with LTBI, HC and non-TB pneumonia.

Results: We identified a 116-gene signature set and a minimal gene set of only 9 genes that showed an average prediction error of 11% for TB vs. LTBI in our dataset. Furthermore, the minimal set showed a significant discriminatory value for TB vs. LTBI in all previously published adult studies with average prediction errors between 17% and 23%. To identify a robust representative gene set that would perform well in genetically distinct populations, we selected ten genes that were highly discriminative between TB, LTBI and HC in all literature datasets as well as in our dataset. Functional annotation of these genes highlights a possible role for genes involved in calcium signaling as biomarkers for active TB.

Class comparison. Columns represent selected gene biomarker sets in the literature sets as well as in our dataset. Rows represent the studies on which the gene biomarker sets displayed in the columns were tested.	Signature gene set	This study				Berry et al. (Nature 2010;466:973-977)		Maertzdorf et al. (Genes Immun 2011;12:15-22)	
	Study	116 gene set	Minimal TB-LTBI set	Minimal TB-LTBI-HC set	Robust 10 gene qPCR set	86 gene set	393 gene set	11 gene set	5 gene set
TB vs. LTBI	Berry et al.	20.1	19.4	not determined	not determined	12.5	11.1	13.0	16.3
	Maertzdorf et al.	19.1	16.9	not determined	not determined	11.3	10.1	10.2	10.1

	This study	11.1	11.1	not determined	not determined	50.0	50.0	33.0	50.0
TB vs. LTBI average prediction error		16.8	15.8	not determined	not determined	24.6	23.7	18.7	25.5
TB vs. LTBI vs. HC	Berry et al.	27.6	not determined	23.9	34.9	20.1	14.1	27.3	30.4
	Maertzdorf et al.	25.6	not determined	25.6	48.9	17.8	21.3	26.2	32.8
	This study	11.1	not determined	14.8	14.8	66.7	74.1	74.1	70.4
TB vs. LTBI vs. HC average prediction error		21.4	not determined	21.4	32.9	34.9	36.5	42.5	44.5

[Performance of signature gene sets]

Conclusions: Our data justify the further exploration of our signature set as biomarkers for potential childhood TB diagnosis. As the identification of different biomarkers in ethnically distinct cohorts is apparent, it is important to cross-validate newly identified markers in all available cohorts.

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SEVERE MALARIA IN A DISTRICT HOSPITAL IN RURAL BURKINA FASO: RELEVANCE OF NEUROLOGICAL SYMPTOMS

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Background and aim: Malaria is the leading cause of death in children under 5 in sub-Saharan Africa. Aim of this study was to evaluate epidemiological data of malaria with a special focus on neurologic symptoms in children admitted to a distric hospital in rural Burkina Faso (BF) where prevalence of malnutrition is high.

Methods: Retrospective study of paediatric malaria cases - positive smear or rapid diagnostic test - admitted between December 2011 and November 2012 to Saint Camille Hospital, Nanoro (BF) was carried out. Informations including epidemiological, clinical and outcome data were analyzed.

Results: We reviewed 521 cases (58% male; 52%< 2 years). The majority (92%) were diagnosed during the high malaria transmission season. All were P.falciparum, (mean parasite density: 61370 trophozoites/µL). 90% fulfilled WHO criteria for severe malaria. Mean hemoglobin and platelet count were 6.5g/dL and 201K/µL. Neurological symptoms were evident in 15.93% (83/521) and in 20.54% (107/521) malaria was associated with moderate to severe malnutrition. Mortality was 5.57% (29/521). Highest parasitaemias were found in infants ($p< 0.05$). Neurological symptoms and mortality were both associated with higher parasitaemia ($p=0.01$ and $p< 0.0001$). Fatal outcome was associated with neurological symptoms (OR:3.2; 95% CI:1.2-9.0; $p< 0.05$) and borderline associated with age, malnutrition and thrombocytopenia. Malnutrition was associated with neurological symptoms (OR:2.4; 95% CI:1.1-5.2; $p< 0.05$).

Conclusion: Severe malaria was highly prevalent in our setting. Neurological symptoms were the main predictor of mortality and were more prevalent in malnourished children. Cerebral malaria and death were both associated with higher parasite load.

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EXTENSIVE PARASITE SEQUESTRATION IS NOT A UNIFORM REQUIREMENT FOR SEVERE P. FALCIPARUM MALARIA IN GAMBIAN CHILDREN

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Background and aims: Intravascular sequestration of parasitized red blood cells (pRBC) is believed to cause severe Plasmodium falciparum malaria (SM) but sequestered parasite burdens have not previously been compared between children with different manifestations of SM and a control group with uncomplicated malaria (UM).

Methods: In a nested-case control study, sequestered P. falciparum parasite biomass was compared between Gambian children with UM and children with one or more features of SM (prostration (SP), cerebral malaria (CM), severe anemia (SA), or hyperlactatemia (LA)). Circulating parasite biomass was calculated from blood film parasitemia, total parasite biomass was estimated from the plasma concentration of P. falciparum histidine rich protein 2 (PfHRP2) using a mathematical model, and sequestered parasite biomass was calculated from the difference between the two.

Results: Circulating- and total-, but not sequestered-, parasite biomass estimates were significantly greater in children with SM (n=169 (57.1%)) than in those with UM (n=127 (42.9%)). Sequestered biomass in patients with LA or SP was similar to those with UM, whereas sequestered biomass was higher in patients with SA or CM, and fatal cases. Blood lactate concentration correlated with circulating- and total-, but not sequestered parasite biomass. These findings were robust after controlling for age, prior antimalarial treatment and clonality of infection, and over a realistic range of variation in model parameters.

Conclusions: Extensive sequestration of pRBCs is not associated with LA or SP. The pathophysiological mechanisms that initiate SM may differ between SM syndromes, and different therapeutic strategies may be required.

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DETERMINANTS FOR TUBERCULOSIS INFECTION AMONG CHILDREN INVESTIGATED WITH INTERFERON GAMMA RELEASE ASSAYS AND HAVING CONTACT WITH ADULT TUBERCULOSIS CASES

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Background and aims: The predictive factors of latent tuberculosis infection (LTBI) among children remain irresolute. The study evaluated the determinants associated with LTBI among children having contact with adult index cases.

Methods: A cross-sectional study was conducted among 223 children (mean age±SD:7.8±4.7 years) evaluated for LTBI. Participants were assessed concomitantly with the tuberculin skin test and QuantiFERON-TB Gold-In-Tube (QFT-IT) assay. Children with indeterminate QFT-IT findings were excluded. LTBI was defined among children with positive QFT-IT.

Results: Among the study sample (n=223), QFT-IT results were negative in 59.6% (n=133), positive in 37.7% (n=84), and indeterminate in 2.7% (n=6) children. Children with LTBI did not differ from their non-infected counterparts with respect to age (p=0.147), gender (p=0.850), or ethnicity (p=0.220). The proportion of adult cases among whom the laboratory isolation of M. tuberculosis was confirmed was similar between groups (p=0.320). LTBI children did not differ from their non-infected counterparts with respect to living conditions and/or socioeconomic indicators. Following controlling for confounding factors, the multivariate regression analysis indicated that LTBI was independently associated with lack of prior BCG immunization (adjusted odds ratio, AOR:4.17; 95% CI:1.33-12.55), patient age (AOR:1.23; 95% CI: 1.09-1.39), and origin from a TB endemic country (AOR:3.33; 95% CI:1.45-7.69).

Conclusions: Lack of prior BCG immunization was proximally associated with LTBI among children having contact with adult cases. Additional determinants included greater age and origin from a TB endemic country. Public health interventions aimed at deterring LTBI among children should account for the identified risk factors for TB infection.

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PERFORMANCE OF QUANTIFERON TB GOLD ASSAY IN THE DIAGNOSIS OF MYCOBACTERIUM TUBERCULOSIS INFECTION IN CHILDREN

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Background and aims: QuantiFERON-TB Gold assay (QFT-IT) have been developed to replace tuberculin-skin-test for the detection of latent tuberculosis infection (LTBI), showing promising results in adults. Its performance in children is debated, since it has been suggested that their immune system may not be properly mature to respond to antigenic stimuli. Purpose of this study was to evaluate the performanceof QFT-IT in children with suspected tuberculosis.

Methods: Retrospective study on children aged 0-14 years evaluated for tuberculosis infection and tested with QFT-IT assay from January 2007 through July 2010 at Catholic University of Rome.

Results: Of 623 children evaluated, 59 children (9.5%) scored positive, 532 (86.3%) negative and 26 (4.2%) indeterminate results. Percent of positivity ranged from 7,59% for the 25-36 months group to 10,94% for the 37-48 months group.

Among the positive results, 21 cases of active TB and 38 cases of LTBI were detected. The sensitivity of QFT-IT in children with active TB was 80%, ranging from 62.5% in children 25-36 months to 100% in children > 49 months. No statistically significant effect of age on the magnitude of the immune response as assessed by the amount of IFN-g secreted following RD1 antigens restimulation was found. No differences were observed in the ability of children of different age to respond to the mitogenic stimuli.

Conclusion: Our study indicate that children < 5 years of age are capable of properly responding to RD1 antigens and mitogen included in QFT-IT, supporting its usefulness in the diagnosis of LTBI/tuberculosis in children.

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EXTRA-PULMONARY TUBERCULOSIS IN CHILDREN

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Extra-pulmonary tuberculosis is a much more frequent presentation in childhood TB compared with adult TB and has a wide spectrum of clinical manifestations and levels of severity.

My presentation will review the more unusual presentations and explore possible reasons for why this form of TB might be more commonly found in younger children and in the immunocompromised.

I will describe immunological clues, the role that different strains of mycobacteria might play and discuss the general management from diagnosis to treatment.

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NEW TESTS FOR TB DIAGNOSIS

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Childhood tuberculosis accounts for a considerable part of the total disease morbidity and mortality burden. Microbiological confirmation of TB diagnosis among children is the exception rather than the rule due to the difficulty to obtain adequate specimens and also due to the paucibacillary nature of the disease. The diagnosis is commonly based on clinical and radiological findings which are often non-specific. The recently developed interferon gamma release assays (IGRAS) have comparable sensitivity but higher specificity compared to tuberculin skin test (TST). Therefore, they can be used in a complementary fashion to increase the accuracy of TB diagnosis. Similar to the TST the IGRAs cannot differentiate between latent tuberculosis infection and active disease. Microbiological confirmation of TB diagnosis and drug susceptibility testing is important for the effective treatment of TB in children. Recent advances include new methods for sample collection, optimization of smear microscopy and modified culture techniques to shorten detection time. The new nucleic acid amplification tests (NAATs) have lower sensitivity in childhood TB which is usually smear negative due to its paucibacillary nature. The recent development of the Xpert MTB/RIF assay (Cepheid) is a remarkable advance in TB diagnosis. It is a real-time PCR technique that detects DNA of Mycobacterium tuberculosis and rifampicin resistance. Within less than 2 hrs and with minimal sample handling this assay detects 2-3 times more cases compared to smear microscopy. It has somewhat lower sensitivity compared to culture in children since it detects almost all smear positive and about two thirds of smear negative samples with repeated testing. Newer promising methods based on the detection of mycobacterial antigens or volatile organic compounds have relatively low to moderate sensitivity among adults and they have not been studied in children. Novel holistic approaches including proteomics and transcriptomics are now being explored to identify new biomarkers and biosignatures specific for active disease and latent TB infection. Despite the recent advances there is an urgent need for a rapid, simple, inexpensive point -of-care test for the diagnosis of tuberculosis in children.

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ANTIMICROBIAL RESISTANCE PROFILES VARY BETWEEN AGE GROUPS AND WARD TYPES IN EUROPEAN CHILDREN LESS THAN 2 YEARS OF AGE

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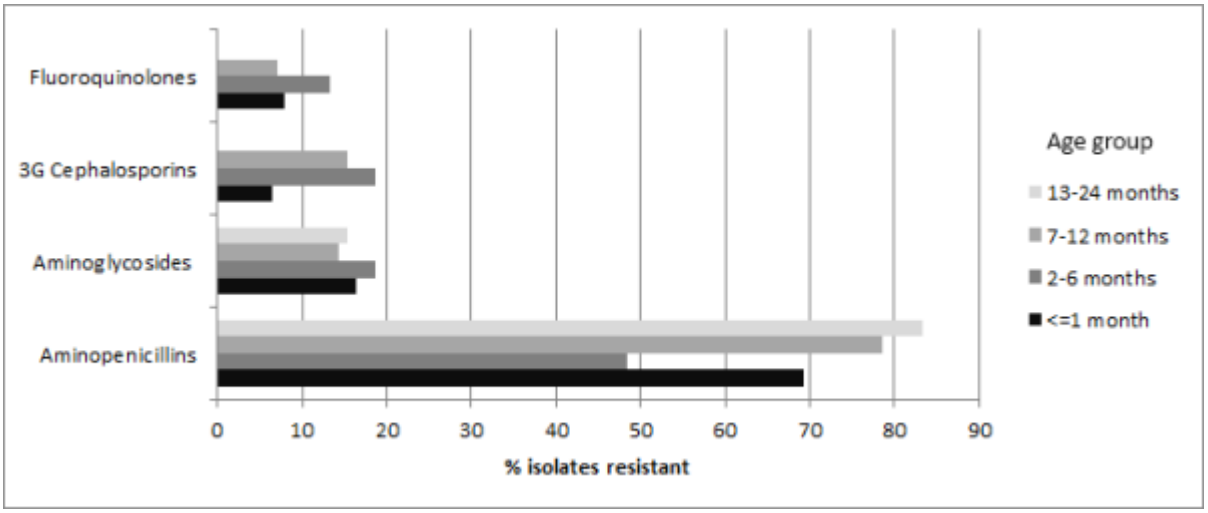
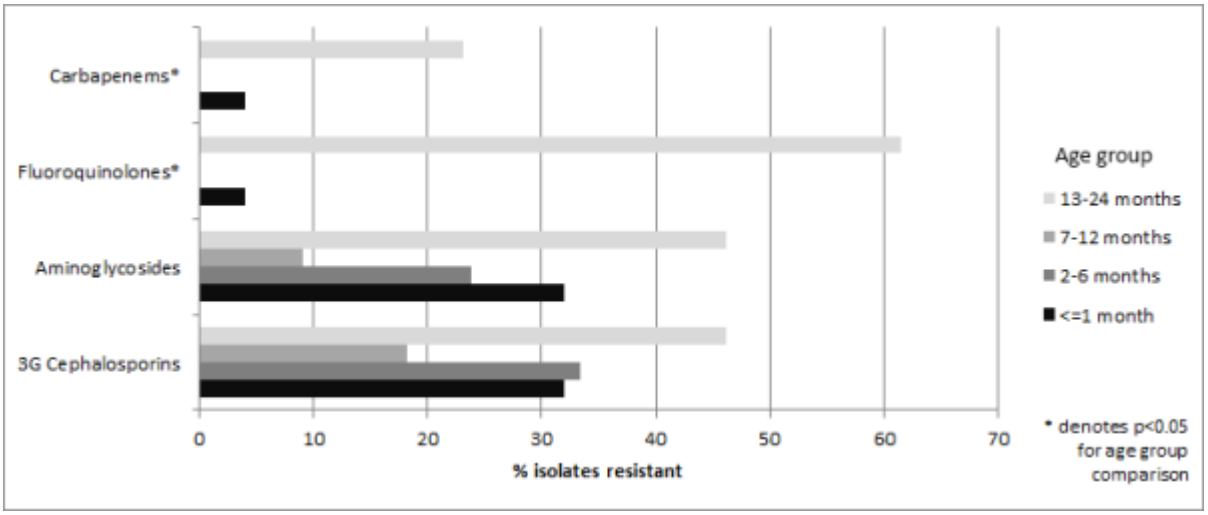
Background/aims: The Antibiotic Resistance and Prescribing in European Children (ARPEC) project aims to evaluate accurate and reliable surveillance methodology for bacteraemia antimicrobial resistance (AMR) in neonates and children. The aim of this analysis was to determine the added value of capturing age and patient location for young children.

Methods: 2011 routine bacteraemia data for 7 key pathogens as defined by the European Centre for Disease Prevention and Control (ECDC) were collected retrospectively from 15 participating paediatric centres in 12 European countries. Antimicrobial sensitivity results for specified bug/drug combinations were reported and prevalence of AMR in children under 2 years of age determined for E.coli and K.pneumoniae. This was compared by age group and location using $\chi 2$ or Fisher's exact tests.

Results: Out of 755 isolates, 533 came from children ≤ 2 years of age. 244 (45.7%) were E.coli, K.pneumoniae or P.aeruginosa. 121/244 were from infants ≤1 month of age. The resistance profiles of E.coli and K.pneumoniae isolates are shown in figures 1 and 2.

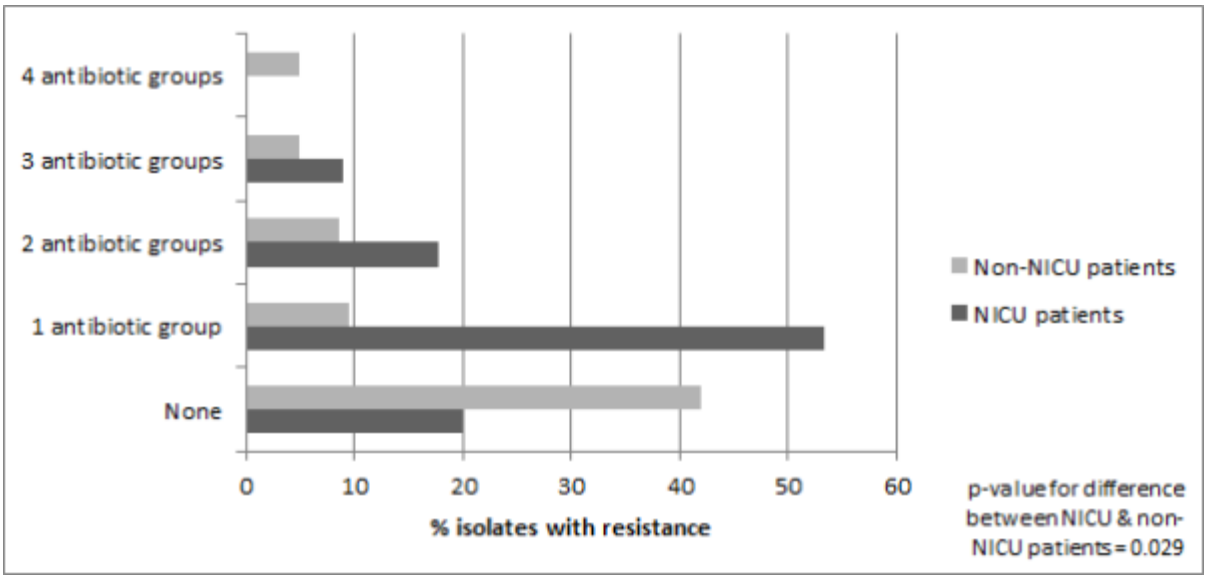


[% resistant E.coli isolates]



[% resistant K.pneumoniae isolates]

Combined resistance in E. coli against the 4 bug/antibiotic group combinations considered for NICU and non-NICU patients is shown in figure 3.



[Combined resistance for NICU vs. non-NICU isolates]

Conclusions: There is substantial AMR variability in young children. To capture AMR more accurately it may be necessary to record more detailed age and ward location information than is presently possible through EARS-Net.

Age group	Aminopenicillins %	Aminoglycosides %	Third generation	Fluoroquinolones %

	(x/n)	(x/n)	Cephalosporins % (x/n)	(x/n)
<=1 month	69.33 (52/75)	16.44 (12/73)	6.58 (5/76)	7.89 (6/76)
2-6 months	48.39 (15/31)	18.75 (6/32)	18.75 (6/32)	13.33 (4/30)
7-12 months	78.57 (11/14)	14.29 (2/14)	15.38 (2/11)	7.14 (1/14)
13-24 months	83.33 (10/12)	15.38 (2/13)	0 (0/12)	0 (0/13)
p-value	p=0.074	p=0.980	p=0.127	p=0.634

[% E. coli resistant to antibiotic group]

Age group	3rd generation Cephalosporins % (x/n)	Aminoglycosides% (x/n)	Fluoroquinolones* % (x/n)	Carbapenems* % (x/n)
<=1 month	32 (8/25)	32 (8/25)	4 (1/25)	4 (1/25)
2-6 months	33.33 (7/21)	23.81 (5/21)	0 (0/21)	0 (0/21)
7-12 months	18.18 (2/11)	9.09 (1/11)	0 (0/10)	0 (0/10)
13-24 months	46.15 (6/13)	46.15 (6/13)	61.54 (8/13)	23.08 (3/13)
P-value	p=0.56	p=0.245	p<0.001	p=0.041

[% K.pneumoniae resistant to antibiotic group]

Combined resistance	NICU patients (% isolates with resistance)	Non NICU patients (% isolates with resistance)
None	20	41.98
1 antibiotic group	53.33	9.51
2 antibiotic groups	17.78	8.64
3 antibiotic groups	8.89	4.94
4 antibiotic groups	0	4.94
P-value: 0.029	Total n isolates = 45	Total n isolates = 81

[Combined resistance in E.coli isolates by ward]

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RELATIONSHIP BETWEEN PREVALENCE OF ANTIMICROBIAL RESISTANCE AND CLINICAL BURDEN OF RESISTANCE IN CHILDHOOD BACTERAEMIA IN EUROPE

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Background and aims: Antimicrobial resistance (AMR) surveillance programmes usually report resistance prevalence. This may lead to biased conclusions about the overall burden of resistance. We compared the pattern of childhood bacteraemia AMR in Europe using prevalence and rate statistics.

Methods: Childhood bacteraemia AMR surveillance data collected retrospectively for 2011 from 11 European centres was analysed to identify AMR and MDR prevalence and isolation rate per 100,000 occupied bed days (OBD) for E.coli, K.pneumoniae, P.aeruginosa, E.faecalis, E.faecium and S.aureus. Standardised definitions of MDR were applied. Prevalence and rates were compared for Northern (Estonia, France, Germany, Lithuania, Netherlands, Switzerland, UK) and Southern (Greece, Italy, Slovenia, Portugal) countries.

Results: Results are presented in table 1.

Region	% any AMR (95%CI)	% MDR (95%CI)	N isolates/ 100,000 OBD (95%CI)	N isolates with any AMR/ 100,000 OBD (95%CI)	N MDR isolates/ 100,000 OBD (95%CI)
North	43.0 (36.3-49.9)	13.0 (9.0-18.4)	53.3 (46.3-61.1)	22.9 (18.5-28.2)	6.9 (4.6-10.0)
South	50.6 (45.2-56.0)	22.5 (18.3-27.4)	84.5 (75.7-94.1)	43.0 (36.6-49.7)	19.0 (15.0-23.8)

[Prevalence & rate of resistant BSI in EU countries]

Although the overall prevalence of AMR is high (43.0% and 50.6% in Northern and Southern countries, respectively), childhood AMR burden is relatively low (22.9 and 43.0 resistant isolates/100,000 OBD in the North and South, respectively). AMR prevalence is relatively similar in Northern and Southern European centres. However, the rate of AMR isolation differs substantially, which may be explained through higher MDR prevalence and a higher isolation rate for the surveyed pathogens in Southern countries.

Conclusion: The statistics currently in common use for AMR surveillance help to identify regional and temporal trends in AMR development. However, they may provide little information on the burden of AMR disease for clinical management.

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SERUM SOLUBLE ST2 AS DIAGNOSTIC MARKER OF BACTERIAL SIRS IN CHILDREN

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Background and aims: Early diagnosis of bacterial vs non-bacterial infections in children with systemic inflammatory response syndrome (SIRS) still remains a hard challenge. In the contest of new biochemical markers research, we explored the possible role of the soluble secreted form of ST2 (sST2).

Methods: The study was conducted in a tertiary care paediatric hospital in Rome. It was a prospective, obsvervational study including all patients aged 0-12 years fulfilling criteria for SIRS with suspected infective aetiology, hospitalized between July 2011 and October 2012. Blood samples were collected at the time of the enrolment and the sST2 measurement was carried out by Enzyme-linked immunosorbent assay (ELISA) and compared with Procalcitonin values.

Results: Overall, 64 patients with SIRS diagnosis were included. Among them, 41 were classified as bacterial and 23 as non-bacterial infections. The median value of sST2 resulted 1327.0 pg/ml in the bacterial cohort, 209.1 pg/ml in non-bacterial SIRS, and 108.0 pg/ml in the control group ($p< 0,05$). ROC curve analysis revealed that both sST2 and PCT resulted in significant area under the curve (AUC) (0.9 for sST2, 95% CI: 0.8-0.96, $p< 0.0001$; 0.89 for PCT, 95% CI: 0.77-0.96, $p< 0.0001$).

Conclusion: Our findings demonstrate that children with SIRS associated with bacterial infection present significantly increased levels of sST2 compared to non-bacterial SIRS and healthy children. Noteworthy, ROC curve analysis indicated that sST2 has a significant diagnostic performance in early identification of bacterial-SIRS, similar to PCT. Therefore, sST2 level may prove useful in distinguishing between bacterial and non-bacterial SIRS in children.

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ARE C-REACTIVE PROTEIN AND PROCALCITONIN BOTH NEEDED FOR DETECTING SERIOUS BACTERIAL INFECTIONS IN FEBRILE CHILDREN? VALIDATING AND IMPROVING THE LAB-SCORE

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Background: The Lab-score, including C-reactive protein (CRP), procalcitonin (PCT), and urinalysis, is a powerful, validated tool to assess the risk of serious bacterial infection (SBI) in febrile children.(Galetto-Lacour 2010) Kinetics of inflammatory markers suggest a potential differentiating role of duration of disease

Aim: Validating the Lab-score and updating the Lab-score with duration of fever; constructing a clinical algorithm to minimize diagnostic testing.

Methods: Previously healthy children with fever, aged 1 month to 16 years, attending the emergency departments of the Erasmus MC-Sophia university children's hospital and the Maasstad teaching hospital (Rotterdam, the Netherlands) between 2009 and 2012 were eligible. Standardized clinical signs and symptoms, CRP, PCT, and urinalysis were collected prospectively. Lab-Score: CRP ≥40 mg/L, 2 points; ≥100 mg/L, 4 points; PCT ≥0.5 ng/mL, 2 points; ≥2.0 ng/mL, 4 points; positive urine dipstick, 1 point (range 0-9 points). Logistic multivariable regression analysis was used to calculate diagnostic performance and to determine added value of duration of fever.

Results: 1,055 children were included, median age was 1.6 years (IQR: 0.8-3.5), 170 children (16%) had SBI. The Lab-score validated well (ROC area 0.79, 95% CI 0.71-0.87); Lab-score ≥3 points was useful to identify children with SBI (positive LR: 4.13, 95% CI: 3.37-5.07). Duration of fever had no added value to the Lab-score. PCT did not alter post-test probabilities substantially in children with elevated CRP levels.

CRP ≥40 mg/l	2 points
CRP ≥100 mg/l	4 points
PCT ≥0.5 ng/ml	2 points
PCT ≥2.0 ng/ml	4 points
Urinalaysis: positive dipstick	1 point

[Table 1. Original Lab-score (range 0 - 9 points) (]

Conclusion: The Lab-score performed well in a prospective cohort of febrile children. Depending on clinical risk thresholds, diagnostic testing can be limited to CRP in febrile children.

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ROLE OF PROPHYLACTIC ANTIBIOTICS IN PREVENTING SEPSIS IN NEONATES BORN THROUGH MECONIUM STAINED AMNIOTIC FLUID(MSAF)- A RANDOMIZED CONTROLLED TRIAL

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Background: Most newborns with MSAF receive antibiotics as meconium has been incriminated to increase incidence of both intraamniotic and postnatal sepsis. Due to rising concerns about inadvertent overuse of antibiotics, this practice needs to be systematically evaluated.

Aims: To evaluate the role of prophylactic antibiotics on occurrence of neonatal sepsis in term neonates born through MSAF.

Methods: Out of 359 eligible neonates, 109 were excluded based on exclusion criteria and remaining 250 randomized to Study (Antibiotic group - receiving first line antibiotics for 3 days), and Control (No Antibiotic) group. Both the groups were evaluated for sepsis on clinical and laboratory parameters. All neonates were monitored for complications related to MSAF. After discharge babies were followed up for sepsis till 28 days of life.

Results: 121 babies were randomized to Antibiotic group and 129 to No Antibiotic group. Of the total 250 neonates, 24 (9.6%) developed suspected sepsis, 8 in Antibiotic (6.6%) and 16 in No Antibiotic group (12.4%) (p= 0.12,OR 0.5, 95% CI: 0.21-1.22). Culture proven sepsis occurred in 12 babies (4.8%), 5 in Antibiotic and 7 in No Antibiotic group (4.13% vs. 5.42%, p= 0.63, OR 0.75, 95% CI: 0.23-2.43).The incidence of mortality (2.5% vs. 2.3%), meconium aspiration syndrome.

(18.2% vs. 15.5%, p=0.57) and other complications like air leaks, PPHN and intracranial hemorrhage was comparable between the two groups.

Conclusions: Prophylactic antibiotics in neonates born through MSAF do not reduce the incidence of sepsis. Hence, empiric use of antibiotics without documented evidence of infection should be avoided.

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TRENDS IN ANTIBIOTIC PRESCRIBING BY MORBIDITY GROUP AND ANTIBIOTIC CLASS. A REPORT FROM THE ROYAL COLLEGE OF GENERAL PRACTITIONERS DATABASE

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Background and aims: Antibiotic resistance and excessive prescription of antibiotics are major problems. Most antibiotic prescriptions are issued in primary care and much publicity has been given to reduce prescribing. The RCGP Research Centre conducts weekly surveillance of antibiotic prescribing by diagnosis age and antibiotic class, which has been validated against national dispensing data (PACT). We used the accumulated database to examine trends since 2007.

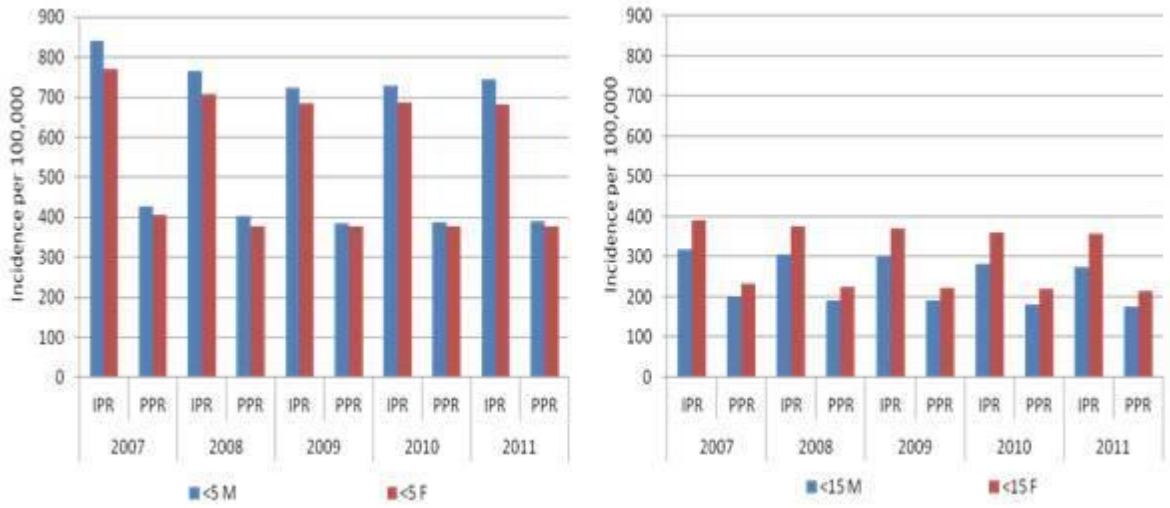
Methods: Annual age specific (0-4,5-14) person and antibiotic Item prescribing rates per 1000 persons (PPR and IPR) were calculated and examined for trend in morbidity linked group and antibiotic class.

Results: There is no secular trend in PPR and IPR for total antibiotics(figure1). More males than females 0-4 experience RTI and receive antibiotics. PPR are approximately twice IPR indicating each child has an antibiotic prescription twice per year.

Average annual PPR and IPR for antibiotic prescriptions 2007-2011

a) 0-4 age group

b) 5-14 age group

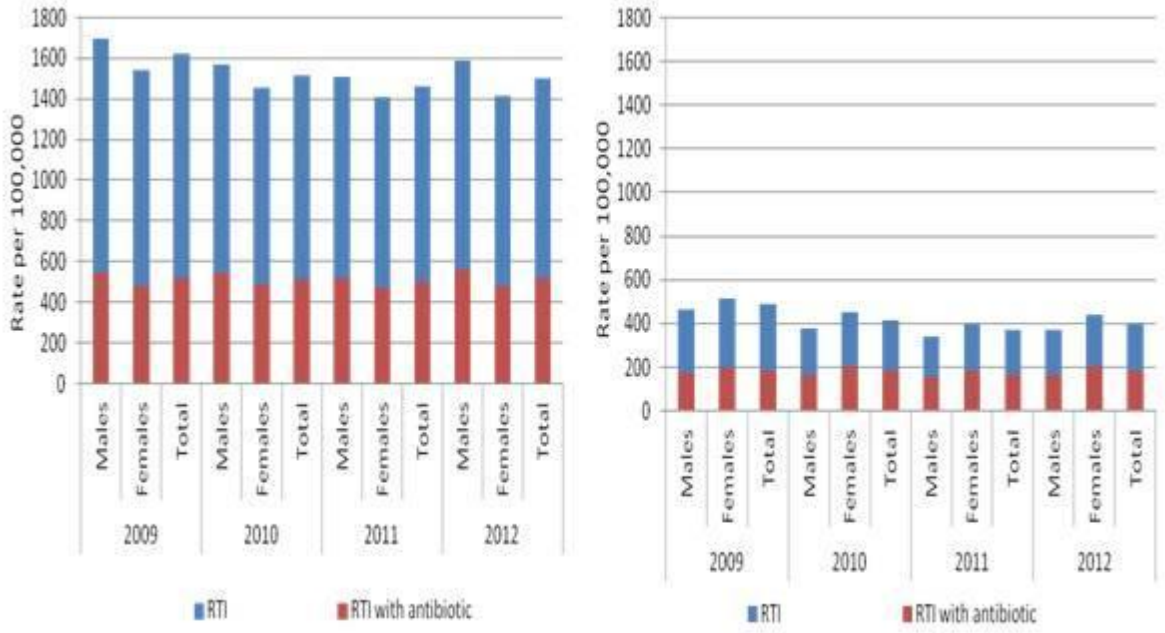


[Figure 1]

The average incidence of RTI in each year and the RTI plus prescription

a) 0-4 age group

b) 5-14 age group



[Figure 2]

Figure 2 includes RTI annual incidence rates per 100,000 and incidence rates of antibiotics linked to RTI. 33% of children 0-4 and 4% age 5-14 were prescribed an antibiotic for RTI.

Conclusions: There have been no substantial changes in the numbers of children receiving antibiotics nor in the proportions receiving them for RTI over the last 6 years.

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NEURODEVELOPMENTAL OUTCOME OF PRETERM INFANTS WITH POSTNATALLY ACQUIRED CYTOMEGALOVIRUS INFECTION

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Introduction: Long-term sequelae of postnatal CMV infection in preterm infants are insufficiently evaluated. The aim of this study was to assess whether postnatally acquired CMV infection in preterm infants affects their neurodevelopmental outcome.

Methods: Preterm infants (< 32 weeks) treated in our NICU between January 2007 and December 2010 were included. Postnatal CMV infection was diagnosed at term-equivalent age, using CMV PCR in urine. Congenital CMV infection was excluded. Clinical, demographic and neuro-imaging data were collected. Neurodevelopmental outcome was assessed using Griffiths Mental Developmental Scales (GMDS) at 16 months and 24 months corrected age (CA), respectively, and Bayley Scales of Infant and Toddler Development-III (BSITD-III) at 24 months CA, as well as age of independent walking. Differences in neurodevelopmental outcome between infected and non-infected infants were calculated.

Results: CMV status was determined in 449 infants of whom 390(87%) and 326(73%) were assessed at 16 months and 24 months CA, respectively. Sixteen % of studied infants had postnatal CMV infection. Infected infants had significantly lower gestational age, were more frequently born from non-native Dutch mothers and more often developed lenticulostriate vasculopathy compared to non-infected infants. At 16 months CA, infected infants performed better on the GMDS locomotor scale (p=0.049). They were also significantly younger able to walk unaided (p=0.026). Multivariable linear regression analysis showed that this difference was related to ethnicity. There were no differences between infected and noninfected infants at 24 months CA.

Conclusion: Postnatal CMV infection in preterm infants does not adversely affect neurodevelopmental outcome at two years CA.

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IMPACT OF SEPSIS ON NEUROLOGICAL OUTCOME AT 2 YEARS' CORRECTED AGE IN PRETERM INFANTS

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Background and aims: Neonatal sepsis causes high mortality and morbidity in preterm infants, but less is known regarding the long-term outcome after sepsis. This study aimed to determine the impact of sepsis on neurodevelopment at 2 years' corrected age in extremely preterm infants.

Methods: Infants born between 2004 and 2008 at 24 $^{6/7}$ to 32 $^{0/7}$ weeks' gestational age were included in the study. Neurological outcome was assessed with the Hammersmith Infant neurological examination.

Results: Of 215 infants, 61 (28.4%) had proven sepsis, 41 (19.1%) had suspected sepsis, and 113 (52.6%) had no signs of infection. Cerebral palsy (CP) occurred in 10 of 61 (16.39%) infants with proven sepsis compared with 5 of 113 (4.42%) uninfected infants (odds ratio [OR]: 4.23 [95% confidence interval (CI): 1.376-13.042]; p=0.011).

Multivariable analysis confirmed that proven sepsis independently increased the risk of CP (OR: 1.52 [95% CI: 1.09-3.4]; p=0.02). In contrast, suspected sepsis was not associated with the increased risk of CP. The presence of pathologic brain ultrasonography, birthweight, and gestational age increased the risk of CP (p=0.012, p=0.04, p=0.045, respectively)

Conclusions: Proven sepsis significantly increases the risk of CP in preterm infants, independent of other risk factors. Better strategies aimed at reducing the incidence of sepsis in this highly vulnerable population are needed.

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TRENDS IN HEALTHCARE ASSOCIATED BLOODSTREAM INFECTIONS (HABSI) IN A NEONATAL INTENSIVE CARE UNIT (NICU) OVER A 20-YEAR PERIOD (1992-2011)

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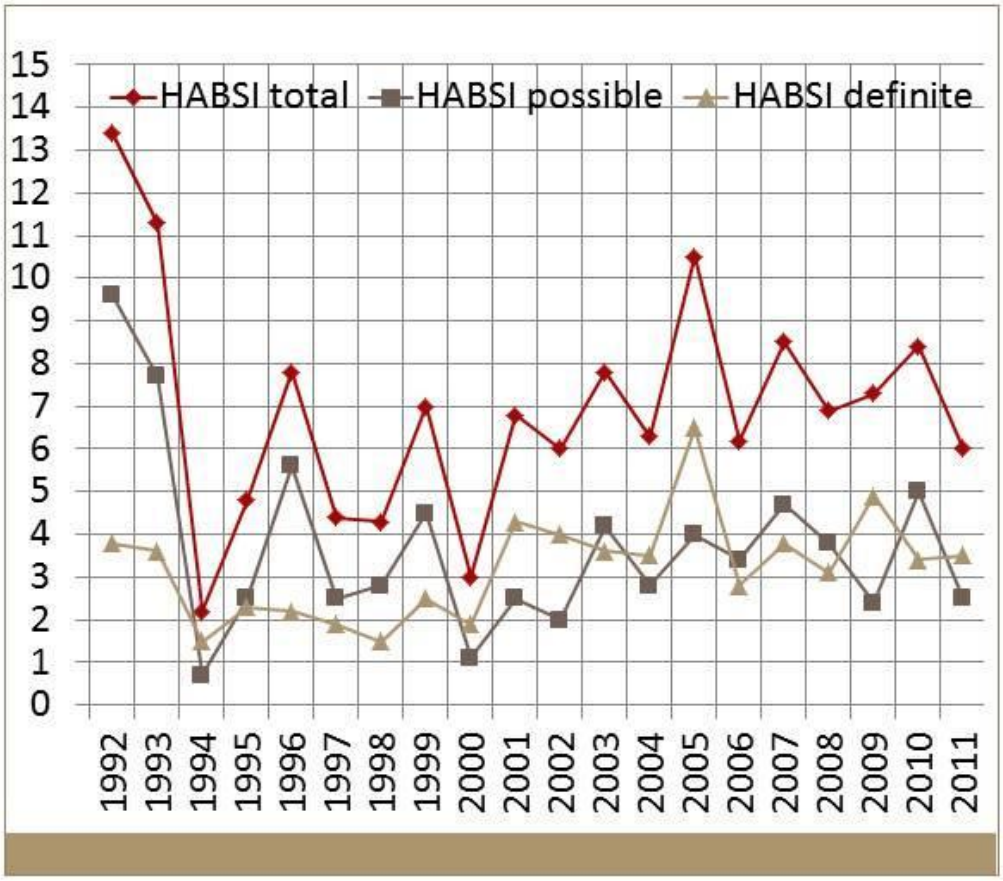
Background and aims: HABSI is the most frequent infectious complication in NICU's. Given favorable trends in survival, it is expected that a higher proportion of NICU patients is at risk for HABSI. Previous studies report prevalence rates from 5 till 32%. We evaluated trends in prevalence of HABSI over a 20 year period.

Methods: Since 1992 a hospital-wide prospective surveillance of HABSI is organized at Ghent University Hospital. HABSI, either possible or definite, are defined according to NICHD criteria. Neonates who died < 48h after birth are excluded. Trends in prevalence are expressed as number of HABSI/100 NICU admissions (%).

Results: Over the study period 682 episodes of HABSI occurred in 9829 admissions (6.9%). HABSI rates are shown in the figure and ranged between 2.2% (1994) and 13.4% (1992). No trend was observed. HABSI were mostly caused by coagulase-negative Staphylococci (62.9%) and Enterobacteriaceae (15.5%). Pseudomonas and Candida species are rare. An increase in S. aureus was observed in more recent years albeit the prevalence of S. aureus HABSI remains low: 20/5449 admissions (0.4%) in 1992-2003 vs. 53/4380 admissions (1.2%) in 2004-2011. No other trends in species distribution were observed.



[% Habsi NICU Ghent UH]

Conclusion: Prevalence of HABSI remained stable over the past two decades and is in line with the results of other researches. Nevertheless, a 7% prevalence on average indicates that HABSI remains an issue in neonates and stresses the need for vigorous application of evidence-based prevention measures.

29

15 YEARS PROPSECTIVE SURVEILLANCE FOR NEONATAL HSV IN AUSTRALIA INDICATES DECLINING MORTALITY, INCREASING HSV1 DISEASE, AND OVERREPRESENTATION OF YOUNG MOTHERS

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Background: Neonatal herpes simplex virus (HSV) infection is uncommon and can be lethal. National surveillance has been undertaken in Australia since 1997 over which time recommended antiviral doses have increased and sensitive molecular diagnostic techniques have become available.

Objectives: To describe the epidemiology, management and mortality of neonatal HSV infection in Australia over the 15 year period (1997-2011).

Methods. Prospective surveillance was undertaken through the Australian Paediatric Surveillance Unit. De-identified clinical, demographic and management data were obtained from notifying child health clinicians and compared with population norms where applicable.

Results: 130 confirmed cases of neonatal HSV disease were identified in 15 years from 261 notifications (94% response rate)(reported incidence of 3.33 cases/100,000 live births). The incidence was stable whereas the mortality rate signficantly declined over the study period (25% to 18.5%, F=4.21, p=0.042). Young mothers (< 20 years) were overrepresented in the series compared to the Australian population (18.4% vs 4.0% ; P < 0.001). HSV-1 accounted for 61% of cases, and the rate of HSV-1 infection significantly increased compared to HSV-2 over the study period. High dose parenteral acyclovir (60mg/kg/day) was prescribed the majority of infants from 2002.

Conclusions: Mortality from neonatal HSV disease in Australia remains high but has declined over the last 15 years. Changes in HSV serotype, prescribing practices and diagnostic techniques may account for this change. HSV-1 is the major serotype causing neonatal disease in Australia, particularly in offspring of adolescent mothers with genital herpes, who represent an important group to target for prevention.

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GBS MENINGITIS IN BABIES < 90 DAYS OF AGE: A UK AND REPUBLIC OF IRELAND PROSPECTIVE STUDY

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Background and aims: Group B streptococcus (GBS) is the leading bacterial cause of meningitis in neonates. A United Kingdom (UK) and Republic of Ireland (ROI) study in 2000-1 reported an incidence of 0.15/ 1000 live births with a case fatality rate (CFR) of 12%. We aimed to define the current incidence and outcome.

Methods: Between 1 July 2010 and 31 July 2011, we identified cases of GBS meningitis in babies < 90 days through a comprehensive prospective surveillance system.

Results: 151 cases were identified (incidence 0.16/ 1000 live births [95% CI: 0.13-0.19]). 78 (52%) male, 31/136 (23%) preterm (< 37 weeks) and the median age of disease was 14 days (range 0-88). The majority (99, 66%) were late onset (>6 days of life) at presentation and most babies (90, 66%) were at home when clinical features first developed. Presenting features were non-specific (poor feeding (74%), lethargy (71%), irritability (70%), fever (55%), respiratory distress (55%), poor perfusion (52%). Overall CFR was 5% and 32 (25%) had a significant complication at discharge.

Conclusion: The incidence of GBS meningitis has not changed in the UK and the ROI over the last 12 years although the CFR has fallen significantly (p=0.01). An effective GBS vaccine is required to prevent this condition

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GRAM-NEGATIVE NEONATAL SEPSIS: A SIX YEARS ANALYSIS FROM THE NEONIN SURVEILLANCE NETWORK (NEONIN)

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Background and aims: Gram-negative infection (GNS) is a major cause of morbidity and mortality in neonates. The aim of this study was to characterise responsible organisms for neonatal GNS in a UK neonatal infection network.

Methods: NeonIN is a web-based, infection surveillance database capturing data on culture proven neonatal infections. For the purposes of this analysis data on GN cases from 2005-2011 were extracted. Early-onset (EOS) and late-onset (LOS) sepsis were defined as cases occurring within 48hrs and after 48hrs of birth respectively. Repeatedly positive cultures from the same baby were classified as a single episode if they occurred within 7 days of each other.

Results: 754 episodes of GNS (involving 462 infants) were identified from 17 neonatal units; representing 16% of all infections (30% if CoNS excluded). Overall incidence was 2.4/1000 live-births and 21.4/1000 NNU-admissions. 55% were males. Median gestational-age (GA) was 26 wks (22-41 wks) and median birth-weight (Bwt) 830g (410-4430g). Multiple episodes of GNS occurred in 31% of infants, more likely to occur in the smaller GA and Bwt group ($p< 0.01$). 11% of GNS was EOS (median-GA 29.5 wks; median-Bwt 1200 g); the majority due to E.coli (70%) followed by H. influenzae (11%). LOS-GNS (median-GA 25 wks; median-Bwt 800 g) was most commonly due to Klebsiella spp. (29%), E. coli (26%) and Enterobacter spp (17%).

Conclusions: GNS is an important problem, especially in preterm infants. Whilst E.coli is responsible for most EO GNS cases, Klebsiella spp are a relatively more frequent cause of LO GNS.

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PNEUMOCOCCAL CARRIAGE IN ELEMENTARY SCHOOL CHILDREN, 12-36 MONTHS AFTER INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINES TO THE NATIONAL IMMUNIZATION PROGRAM (NIP)

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Background/aims:

1) To determine pneumococcal nasopharyngeal carriage (Pnc-CAR) rates and colonization density, among 6-10yrs old elementary school children 12-36m post implementation of 7-valent PCV (PCV7; July 2009) and 13-valent PCV (PCV13; November 2010) into the NIP;

2) to compare Pnc-CAR dynamics between Jewish children (JC; resembling Western population), and Bedouin children (BC; largely resembling developing populations).

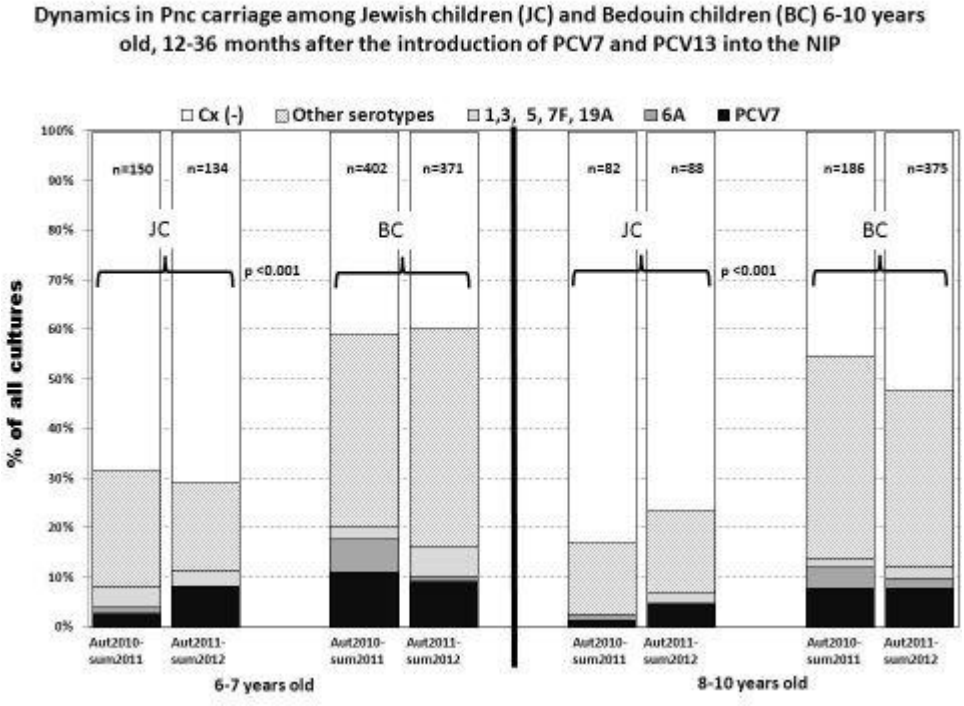
Methods: The study was initiated 1yr after NIP introduction. Nasopharyngeal swabs were obtained in 2 BC and 2 JC schools in summers, autumns and winters of 2010-12. Density was determined by semi-quantitative culture using 4-quadrant dilutions. Density was graded as 1+ (lowest), 2+, 3+, and 4+ (highest).

Results: Overall, and VT7/VT13 serotype Pnc-CAR rates were higher among BC than JC ($p < 0.001$) (**FIGURE**). No significant reduction in overall and PCV7/PCV13 serotypes (7VT/13VT) carriage was observed in JC and BC during the study period. Larger proportion of BC had higher colonization density (3+/4+) than JC for 7VT, 13VT and non-PCV serotypes (p-values adjusted for age, season and antibiotics in last month 0.049, 0.023, and < 0.001, respectively).

Conclusions:

1) 12-36m after 7PCV/13PCV introduction, PCV serotype carriage rates among children 6-10yrs were still not negligible;

2) 7VT/13VT prevalence and density among BC were significantly higher than among JC. Elementary school children may become an important vaccine type pneumococcal reservoir which could negatively affect indirect protection through herd effect.



[Figure]

33

UNIVERSAL VACCINATION WITH PCV7 VS. PCV13: CHANGES IN INVASIVE PNEUMOCOCCAL DISEASE (IPD) INCIDENCE RATES BY CLINICAL PRESENTATION AND CHILDREN AGE

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Background and aims: In 2006 PCV7 was introduced for universal vaccination in Madrid (6 million inhabitants) and on May 2010 PCV13 replaced PCV7. This study analyses, per- clinical presentation and per- children age, incidence rates of pediatric IPD in May2007-April2010 (PCV7 period) vs. May2011-April2012 (PCV13 period).

Methods: A prospective, culture and/or PCR-confirmed surveillance of all IPDs requiring hospitalization was performed in all hospitals with Pediatric department in Madrid. Incidence rates (IR) were calculated as no. cases/100,000 inhabitants using population data on children in Madrid from the Spanish Instituto Nacional de Estadistica.

Results: A total of 499 IPDs in the PCV7 and 79 IPDs in the PCV13 periods were identified**.** Table shows IR of clinical presentations (BP: bacteremic pneumonia, PE: parapneumonic empyema, PB: primary bacteremia, M: meningitis) by children age (months) in PCV7 / PCV13 periods.

	<12m.	≥12 - <24m.	≥24 - <60m.	≥60m.	Total
BP	5.79 / 4.08	9.04 / 2.66	12.27 / 2.70*	2.63 / 0.76*	5.51 / 1.56*
PE	1.78 / 1.36	13.57 / 2.66*	13.81 / 8.55	2.36 / 1.53	5.72 / 3.12*
PB	15.58 / 10.88	5.88 / 3.99	1.07 / 0.00	0.27 / 0.00	2.05 / 1.07
M	16.02 / 5.44*	4.52 / 2.66	0.77 / 0.45	0.66 / 0.46	2.16 / 0.97*
Total	47.62 / 27.20*	40.24 / 14.63*	29.00 / 12.61*	6.25 / 3.05*	17.09 / 7.70*
*p<0.05 vs. PCV7 period					

[IR of clinical presentations by age group]

Conclusions: The significant decrease in IR of overall IPD in the PCV13 period was due to significant decreases in IR of BP (in global, and in children ≥24m.), PE (in global, and in children ≥12-< 24m.) and meningitis (in global, and in children < 12m.).

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CHANGES IN INCIDENCE OF SEROTYPE-SPECIFIC PRESENTATIONS OF INVASIVE PNEUMOCOCCAL DISEASE FOLLOWING SWITCH FROM PCV7 TO PCV13 FOR UNIVERSAL VACCINATION

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Background and aims: In 2006 PCV7 was introduced for universal vaccination in Madrid and on May-2010, PCV13 replaced PCV7. This study analyses, per-serotype specific presentations, incidence rates (IR) of IPD in children ≤15 years in May2007-April2010 (PCV7 period) vs. May2011-April2012 (PCV13 period).

Methods: A prospective, culture and/or PCR-confirmed surveillance of all IPDs requiring hospitalization was performed in all hospitals with Pediatric department in Madrid. IRs were calculated as no.cases/100,000 inhabitants using population data.

Results: Table shows IR of presentations (BP: bacteremic pneumonia, PE: parapneumonic empyema, PB: primary bacteremia, M: meningitis) by serotype in PCV7 / PCV13 periods (*:p< 0.05 PCV13 vs. PCV7 period).

	BP	PE	PB	M	Total
PCV7	0.24 / 0.00	0.24 / 0.00	0.10 / 0.00	0.07 / 0.00	0.72 / 0.19
1	2.23 / 0.97*	2.26 / 1.17*	0.10 / 0.00	0.07 / 0.10	4.79 / 2.53*
3	0.14 / 0.10	0.51 / 0.49	0.07 / 0.00	0.03 / 0.00	0.89 / 0.58
5	0.89 / 0.00*	0.55 / 0.00	0.21 / 0.00	0.14 / 0.00	1.88 / 0.00*
7F	0.55 / 0.10	0.31 / 0.39	0.31 / 0.10	0.14 / 0.00	1.44 / 0.58
19A	0.72 / 0.00*	0.89 / 0.00*	0.75 / 0.29	0.62 / 0.00*	3.77 / 0.49*
PCV13	4.76 / 1.17*	4.76 / 2.05*	1.58 / 0.39*	1.16 / 0.10*	13.49 / 4.38*
Non-PCV13	0.75 / 0.39	0.96 / 1.07	0.48 / 0.68	0.99 / 0.88	3.60 / 3.31
TOTAL	5.51 / 1.56*	5.72 / 3.12*	2.05 / 1.07	2.16 / 0.97*	17.09 / 7.70*

[IR of clinical presentations by serotype]

IR of serotype 6A-IPDs were: 0.17 (PCV7 period), 0.00 (PCV13 period).

Conclusions: IR reduction of total IPDs (and of BP, PE and M) in PCV13 period was due to reductions in IPDs by serotypes 1, 5, 19A and PCV13. IPDs by non-PCV13 serotypes did not increase.

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INDIRECT IMPACT OF 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV10) AGAINST INVASIVE PNEUMOCOCCAL DISEASE (IPD) AMONG UNVACCINATED CHILDREN IN FINLAND

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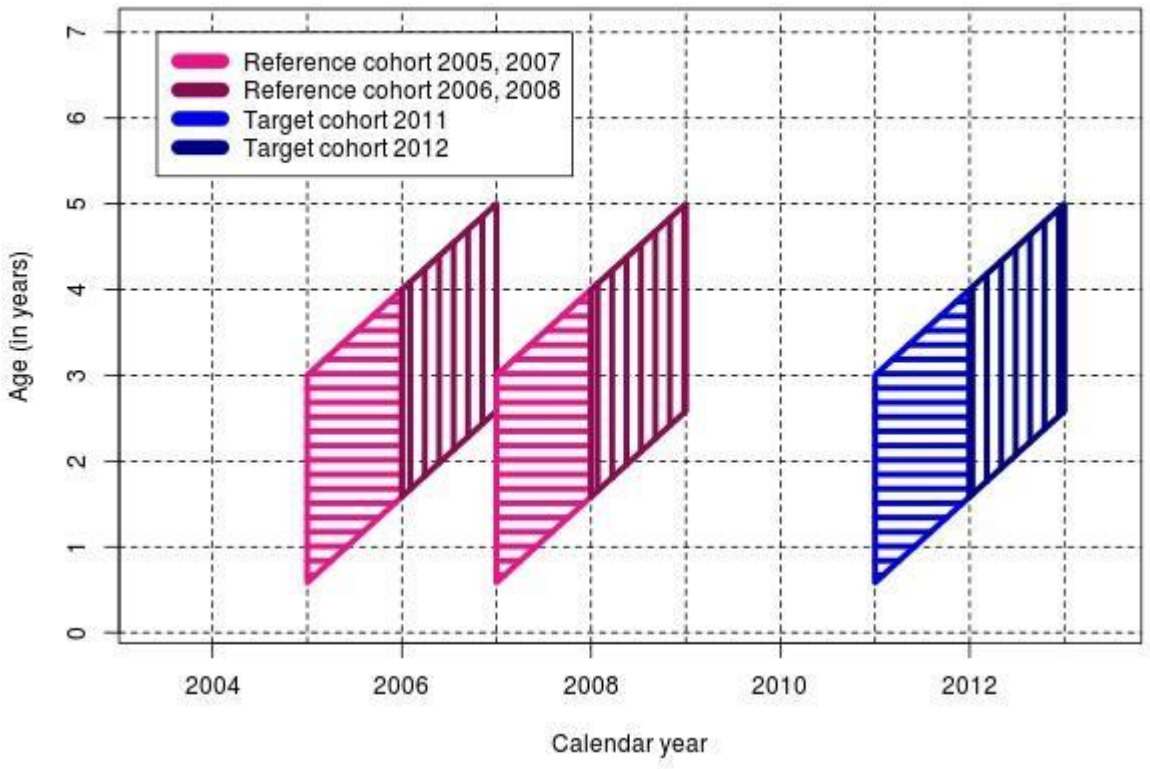
[1]Department of Vaccination and Immune Protection, [2]Department of Infectious Disease Surveillance and Control, National Institute for Health and Welfare, Helsinki, [3]Department of Vaccination and Immune Protection, National Institute for Health and Welfare (THL), Tampere, [4]Ministry for Social Affairs and Health, Helsinki, [5]University of Tampere Medical School, Tampere, Finland

Background: PCV10 was introduced into Finnish National Vaccination Programme (NVP) for children born after May 2010. Indirect effects of PCV10 have not been reported previously. We evaluated the herd impact against IPD among unvaccinated children two years after the NVP-introduction.

Methods: We conducted IPD surveillance during 2011-2012 in the target cohort (N=116,672) of children ineligible for NVP (Born Jan´2008 to May´2010). Children vaccinated with PCV10 in a clinical trial during 2009-2010 (N=30,972) were excluded. Comparative data were collected for years 2005-2006 and 2007-2008 with two age- and season-matched reference cohorts born from Jan´2002 to May´2004 (A, N=140,555) and from Jan´2004 to May´2006 (B, N=143,424) (Figure). National Infectious Disease Register data were used for calculating culture-confirmed overall, PCV10 and PCV10-related (i.e. serotypes belonging to the same serogroup as PCV10) IPD-rates in these unvaccinated cohorts.



[Cohorts for comparing the indirect impact of PCV10]

Results: Table shows the IPD-rates/100,000 person-years (N cases) by cohort and year of observation, and the

relative rate reduction in 2011 and 2012 compared with calendar-time and age-matched periods before NVP-introduction.

Cohort	Reference cohort A: Born January 2002 - May 2004 (N=140,555)		Reference cohort B: Born January 2004 - May 2006 (N=143,424)		Target cohort: Born January 2008 - May 2010 (N=116,672)		Relative rate reduction % (95%CI)	
Year of observation	**2005**	**2006**	**2007**	**2008**	**2011**	**2012**	**2011 vs 2005&2007**	**2012 vs 2006&2008**
Any culture-confirmed IPD	44.9 (62)	21.0 (29)	51.6 (73)	23.3 (33)	40.1 (49)	10.7 (13)	17 (-14, 41)	51 (15, 74)
PCV10 and PCV10-related serotypes	41.3 (57)	20.2 (28)	51.2 (71)	19.7 (28)	35.2 (43)	9.9 (12)	23 (-7, 46)	50 (11, 75)

[IPD in unvaccinated cohorts before and after NVP]

Conclusions: By 2012, the overall and PCV10&PCV10-related serotype IPD-rates were significantly lower among children in the target cohort compared with those in the reference cohorts. These data suggest herd protection against IPD among unvaccinated children.

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EFFECTS OF 3 YEARS OF IMMUNIZATION WITH HIGHER VALENT PNEUMOCOCCAL CONJUGATE VACCINES IN GERMAN CHILDREN

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Objectives: A general recommendation for vaccination with pneumococcal conjugate vaccine (PCV) was issued for German children ≤2 years in July 2006. In 2009, higher-valent PCVs were licenced in Germany: PCV10 (April), PCV13 (December). Here, we present data on IPD-cases sent in for serotyping in the seven years following the start of PCV-vaccination, focusing on the effect on the new serotypes in PCV10 (1,5,7F) and PCV13 (1,3,5,6A,7F,19A).

Methods: Pneumococcal isolates recovered from children with invasive pneumococcal disease (IPD) were sent to the GNRCS. Serotyping was performed using the Neufeld-Quellung-reaction.

Results: In 2011-2012, a total of 77 cases of IPD in children < 2 years were reported. Cases with PCV7 serotypes had decreased by over 90% (n=4), while cases with non-PCV7 serotypes almost doubled. Particularly, the six new serotypes increased after PCV7 introduction but decreased after higher-valent vaccine introduction. In 2011-2012 only 28 cases (PCV13nonPCV7) were reported, as compared to 47 in 2009-2010, representing a 41% reduction. Reduction was observed for serotypes 1(78%), 3(50%), 7F(53%) and 19A(70%). Serotype 5 is very rare in Germany, and serotype 6A has already almost disappeared because of cross-protection from serotype 6B. Interestingly, of the 28 cases in 2011-2012 with PCV13 serotypes, 17(61%) were not vaccinated.

Conclusions: Seven years after the general vaccination recommendation reported cases caused by PCV7 serotypes have almost disappeared. Three years after the introduction of higher valent PCVs strong effects are visible, among children < 2 years due to the additional six serotypes. The reduction of 19A serotype cases was 70%.

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EFFICACY OF MF59®-ADJUVANTED INACTIVATED INFLUENZA VACCINE AGAINST LABORATORY-CONFIRMED INFLUENZA IN CHILDREN, BY SEVERITY OF ILLNESS

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Background and aims: In follow-up to a previously-reported phase 3, multi-centre, observer-blind study (PIDJ. 2011; 30: 1081-5) comparing efficacies of unadjuvanted inactivated influenza vaccine (IIV) and MF59-adjuvanted IIV (aIIV) in previously unvaccinated 6-71 month-old children, we re-analysed the database for respective efficacies against PCR-confirmed clinically-diagnosed lower respiratory tract illness (LRTI).

Methods: Subjects in the trial had been tested for influenza infection if they reported symptoms consistent with CDC-defined influenza-like illness (ILI) which requires fever ≥ 37.8° C. In reporting those illnesses, investigators categorized LRTI as tracheitis, bronchitis, or pneumonia and graded them as clinically mild, moderate, or severe, without a formal case-definition. We calculated vaccine efficacies (VEs) of the two interventions against any and serious LRTI endpoints.

Results: Of 110 PCR-confirmed influenza cases, 33 were diagnosed as LRTI: 30 bronchitis, 17 serious; 3 tracheitis or tracheobronchitis, 1 serious; and 0 pneumonia.

Clinical Diagnosis	Vaccine	VE (95% CI)	Number Needed to Treat
ILI	aIIV	86% (74-93)	27
ILI	IIV	43% (15-61)	61
Any LRTI	aIIV	80% (50-92)	77
Any LRTI	IIV	62% (17-83)	101
Serious LRTI	aIIV	94% (98-99)	133
Serious LRTI	IIV	41% (-54-77)	336

[VE against PCR-confirmed influenza]

Conclusions: VEs of aIIV against ILI, LRTI, and serious LRTI were similar, perhaps because the ILI endpoint itself requiring fever indicated a serious degree of illness. The analysis was limited by the imprecision of the clinical endpoints.

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IMMUNOGENICITY AND SAFETY OF 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE (PHID-CV) IN HEALTHY FINNISH INFANTS AND TODDLERS

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Background and aims: Immunogenicity and safety of PHiD-CV (GlaxoSmithKline Vaccines) was assessed in children in a cluster-randomized, double-blind trial in Finland (NCT00839254), nested within a large invasive pneumococcal disease (IPD) effectiveness study (NCT00861380).[1]

Methods: Healthy children (enrolment age 6 weeks [W] to 18 months [M]) received PHiD-CV or a control vaccine (Hepatitis B < 12M, Hepatitis A ≥12M) according to a 3+1 or 2+1 infant schedule (6W-6M; N=5093), a 2+1 catch-up schedule (7-11M; N=445) or a 2-dose catch-up schedule (12-18M; N=639). Routine paediatric vaccines such as DTPa-IPV/Hib and human rotavirus vaccine were co-administered. Safety was assessed in all vaccinated children, immunogenicity in a subset.

Results: Seropositivity rates and geometric mean concentrations (GMCs) for anti-pneumococcal antibodies are shown below. GMCs were higher after the 3- than after the 2-dose primary infant schedule; these differences diminished post-booster.

Table 1: Percentages of PHiD-CV-vaccinated children with serotype-specific pneumococcal antibody concentrations ≥0.2 µg/mL (according-to-protocol cohort for immunogenicity)

	Infant schedules				Catch-up schedules		
	3+1 6W–6M		2+1 6W–6M		2+1 7–11M		2 doses 12–18M
	Post-primary N=209	Post-booster N=189	Post-primary N=205	Post-booster N=193	Post-primary N=151	Post-booster N=137	Post-vaccination N=167
Vaccine serotypes							
1	100	100	98.0	100	98.7	100	99.4
4	99.5	100	99.0	100	100	100	100
5	100	99.5	98.5	100	100	100	100
6B	79.3	94.7	66.3	96.9	60.3	90.5	86.2
7F	100	100	98.5	100	100	100	100
9V	99.5	100	98.0	100	96.7	100	99.4
14	100	100	98.5	99.5	100	100	100
18C	99.0	98.9	99.0	100	99.3	100	100
19F	98.6	100	97.6	99.5	97.4	99.3	100
23F	84.1	94.7	77.1	97.4	77.5	97.8	94.0
Cross-reactive serotypes							
6A	38.5	76.7	28.1	77.7	37.3	82.5	63.5
19A	41.3	84.0	42.2	86.5	62.3	93.4	95.8

[Table 1]

Table 2: Serotype-specific pneumococcal geometric mean antibody concentrations in PHiD-CV-vaccinated children (µg/mL) (according-to-protocol cohort for immunogenicity)

	Infant schedules				Catch-up schedules		
	3+1 6W–6M		2+1 6W–6M		2+1 7–11M		2 doses 12–18M
Sero-type	Post-primary N=209	Post-booster N=189	Post-primary N=205	Post-booster N=193	Post-primary N=151	Post-booster N=137	Post-vaccination N=167
Vaccine serotypes							
1	1.86	2.13	1.37	1.91	1.96	2.62	1.87
4	2.47	3.61	1.87	3.16	5.85	5.45	5.28
5	2.73	3.27	1.97	2.82	2.40	4.11	3.45
6B	0.51	1.43	0.32	1.43	0.27	1.06	0.69
7F	2.90	4.25	1.76	3.62	3.61	5.44	3.95
9V	2.23	3.98	1.38	3.88	1.42	2.81	1.60
14	5.00	6.40	3.31	4.84	3.81	8.38	6.04
18C	6.51	10.43	3.38	10.60	10.03	19.87	21.27
19F	5.91	8.04	3.40	7.41	6.64	11.73	12.10
23F	0.68	2.30	0.54	2.18	0.55	2.04	1.27
Cross-reactive serotypes							
6A	0.13	0.53	0.09	0.50	0.11	0.70	0.32
19A	0.15	0.95	0.13	0.89	0.33	1.98	2.61

N, maximum number of children with available results; post-primary, 1 month post-primary vaccination; post-booster, 1 month post-booster vaccination; post-vaccination, 1 month post-dose 2; W, weeks; M, months. Antibody concentrations were measured using GlaxoSmithKline's 22F-ELISA.

[Table 2]

4 serious adverse events (SAEs) in the infant PHiD-CV 3+1 group (sepsis, pyrexia, 2 convulsion cases) and 2 in the infant control groups (petit mal epilepsy, pyrexia) were considered as vaccination-related. 1 fatal SAE (sudden infant death, not considered vaccination-related) was reported in the infant PHiD-CV 2+1 group.

Conclusions: PHiD-CV administered according to different age-appropriate schedules had an acceptable safety profile and was immunogenic. This information, together with opsonophagocytic activity responses currently being analysed, will be valuable when long-term serotype-specific protection against IPD will be evaluated.

Funding: GlaxoSmithKline Biologicals SA.

[1]Palmu, Lancet 2012.

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IMPROVEMENT IN HOSPITAL QUALITY OF CARE AFTER THE INTRODUCTION OF ROTAVIRUS VACCINATION: A PILOT STUDY IN BELGIUM

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Background and aims: Rotavirus gastro-enteritis has its peak during winter periods as other child diseases such as influenza, RSV, pneumococcal diseases, etc... Rotavirus vaccination has been reimbursed in Belgium since November 2006. This study aimed to establish a method that could determine whether hospital quality of care during winter epidemic seasons was improved after the introduction of rotavirus vaccination.

Methods: From a pediatric ward in one hospital in Belgium, nine variables were selected: hospitalization, bed-day occupancy, bed turnover, nosocomial infection, deaths, unplanned readmission, full-time equivalent, sick leaves, and overtime work. Factor analysis was used to extract latent variables or factors and their summary scores were calculated per day. The average scores per annual epidemic period were evaluated to assess an eventual difference between pre- and post-vaccination periods in hospital pattern and personnel management, using a two-sided t-test. Lower score indicates better condition.

Results: Two factors were extracted and 6 out of the 9 variables were selected. Factor-1 and Factor-2 represent hospital pattern and personnel management, respectively. The average pre-vaccination period score was 0.52 for Factor-1 and 0.15 for Factor-2. A significant reduction in both Factors is seen post-vaccination, with an average score difference of 1.03±0.60 (standard error) and 0.23±0.72 ($p < 0.05$). The score analysis per Factor and per day allows identifying stress periods, mainly seen in the pre-vaccination period.

Conclusions: It is possible to measure hospital Quality of Care using Factor Analysis. Changes in the scores over time indicate an improvement in quality of care after rotavirus vaccination introduction.

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THE RELATIONSHIP BETWEEN SPECIFIC ANTIBODY TITRES AT BIRTH AND RESPONSE TO PRIMARY IMMUNISATION

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Background and aims: Maternal immunisation increases infant antibody levels, reducing vulnerability to infection in early infancy. However, there are concerns this reduces response to primary immunisation. We examine the relationship between specific antibody titres to pertussis, Haemophilus Influenzae type b (Hib), tetanus and pneumococcus in mother-infant pairs at birth and following infant primary immunisation.

Methods: Healthy mother-infant pairs were recruited from a UK maternity unit (March 2011-January 2012). Peripheral blood samples from mothers and infants were obtained within 72 hours of delivery and repeated 5 months later, following infant vaccination according to the UK schedule. Specific antibody levels were determined using standard commercial enzyme-linked immunosorbent assays. Pertussis antibody titres >50FDA U/ml (defined as “positive” by the manufacturer), Tetanus antibody titres >0.1 IU/ml and Anti-Hib antibody titres >1.0mg/l were regarded as protective.

Results: 99 mother-infant pairs were recruited, 61 completed follow-up. Maternal and infant antibody levels at birth to Hib and pertussis were low. Only 33% and 43% of infants had protective titres to pertussis and Hib respectively. Fold-change in infant antibody level post-immunisation was inversely correlated with antibody level at birth (rs Hib -0.7; pertussis -0.7; tetanus -0.9; pneumococcus -0.8; all $p< 0.0001$); however most infants still developed protective antibody levels post-vaccination (Hib 66%; pertussis 90%; tetanus 96%).

Conclusion: Two-thirds of infants lacked protective antibody titres to pertussis at birth. Although higher levels of passively acquired antibody at birth were correlated with lower vaccine response, most infants still attained protective antibody levels. This supports maternal pertussis immunisation in the UK.

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THE KNOWLEDGE OF POSTPARTUM WOMEN ABOUT PERTUSSIS AND INFLUENZA. POSSIBILITY TO PREVENT THE DISEASE IN THEIR BABIES THROUGH MATERNAL VACCINATION

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Background: Pertussis remains a major cause of morbidity and mortality around the world. The main objective of this study is to describe the knowledge of recent mothers on pertussis and indirect protection of her newborn through their own immunization. The secondary objective is to evaluate the vaccination coverage against influenza.

Method: Prospective study, with a epidemiological inquiry applied in 300 patients hospitalized during the immediate post-natal period, in a hospital in the city of São Paulo, Brazil. The following variables were evaluated: knowledge about pertussis and its prevention through vaccination and the indirect protection of the newborn as well as assess vaccination coverage against influenza.

Results: Most of recent mothers, 255 (85.0%) reported knowledge about pertussis, but 246 (82.0%) of them were unaware about the most susceptible age group to acquire the disease. Almost half (137/45.6%) knew about the existence of a vaccine, but only 16 (5.3%) believed that the vaccine could be applied in adolescents and adults. 269 (93.4%) would agree to receive the vaccine in order to protect indirectly their newborn and 272 (90.6%) would accept receiving the vaccine during hospital stay if available. Influenza vaccination in the 2011 season were reported by 241 (80.3%) women, smaller rate than the one reported in the post pandemic season - 2010 (287/300, 95.6%), with statistical significance ($p < 0.0001$ IC 92.69% -97.6%).

Conclusions: The ignorance about pertussis prevention by post partum women is still high, but their interest about getting vaccine and protecting themselves and their babies is very high.

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EFFECTIVENESS OF PNEUMOCOCCAL VACCINATION IN CHILDREN < 5 YEARS DURING TRANSITION ERA FROM PCV7 TO PCV13 IN ITALY, 2010-2013

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Background and aims: In May 2010 PCV13 replaced PCV7 in universal vaccination for infants introduced since January 2006 in Puglia (Italy). A catch-up dose was recommended for children up to 5 years. PCV13 vaccination coverage was 91% in the 2010 birth cohort.

Our study aimed at estimating the overall vaccine effectiveness (VE) for pneumococcal vaccination during and after the change in the immunization schedule.

Methods: Since May 2010 to the present, a prospective, laboratory-confirmed surveillance for IPD in hospitalized children 0-59 months (≈60,000) has been implemented involving 28 paediatric wards in regionwide.

Identification and serotyping were performed on sterile sites by PCR. We calculated the proportion of cases vaccinated (PCV) by vaccine type and the proportion of the population vaccinated (PPV) as vaccination coverage in general population. We estimated VE (only PCV7; PCV7+PCV13 transition schedule; only PCV13) using the screening method.

Results: We identified 148 suspected IPD; 46% were < 2 years. Fifthy-nine/148 were sepsis, 5/148 meningitis, 70/148 pneumonias; 14 other diagnosis. According to children´s age, 44.6% received the full PCV7 schedule and 18.2% was vaccinated also against the 6 additional serotypes in PCV13. Thirty children were partially vaccinated and 25 did not receive any dose.

Serotype 9V (pneumonia) was isolated in 2 children adequately vaccinated with PCV7; serotype 3 (meningitis) in one non-vaccinated; serotype 15B/C (meningitis) in one vaccinated with PCV13 series. The overall VE was 90.1%.

Conclusions: Three/4 IPD were by PCV13 circulating serotypes. PCV13 is expected to have a large impact on IPD among young children.

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FUNCTIONAL ANTIBODY RESPONSES TO 13-VALENT VERSUS 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13; PCV7): A RANDOMIZED, DOUBLE-BLIND TRIAL

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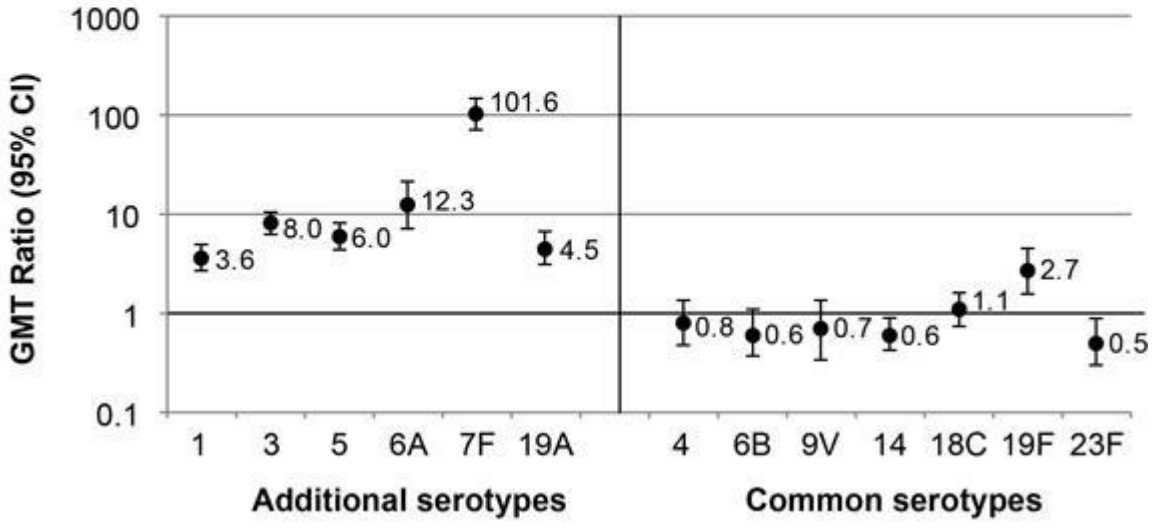
Background and aims: A randomized, double-blind trial in healthy infants in Israel showed that PCV13 elicited significantly higher immune responses measured by ELISA than PCV7 for the additional PCV13 serotypes (1, 3, 5, 6A, 7F, 19A), and for common serotype 19F, with similar or lower responses for the remaining serotypes. Consistent with the IgG responses, PCV13 significantly impacted nasopharyngeal colonization of the additional serotypes when grouped, as well as serotypes 6C and 19F, with no differences between vaccine groups for remaining common serotypes. We present a post hoc analysis of functional antibody responses measured by opsonophagocytic activity assays (OPA) to further understand the relationship between vaccine immunogenicity and carriage.

Methods: PCV13-serotype OPA titers were determined for a randomly selected subset of subjects (n=100 in each vaccine group) in sera obtained 1 month post infant series (2, 4, 6 months) and toddler dose (12 months).

Results: Post infant series PCV13 showed significantly higher OPA responses than PCV7 for the PCV13 additional serotypes and for serotype 19F; responses for the remaining common serotypes were similar or lower **(Figure)**. A similar response pattern was observed post toddler dose. In the PCV13 group, OPA correlated positively with IgG responses for all 13 serotypes and in the PCV7 group for all 7 common serotypes and additional serotype 6A.

Figure 1: Geometric Mean Titer (GMT) Ratios After the Infant Series: PCV13 vs PCV7



[Figure]

Conclusions: Functional antibody OPA responses for PCV13 compared with PCV7 recipients were similar to those with anticapsular IgG-binding antibody, supporting a relationship between immune responses and nasopharyngeal colonization.

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SAFETY AND IMMUNOGENICITY OF AN INVESTIGATIONAL MATERNAL TRIVALENT VACCINE TO PREVENT PERINATAL GROUP B STREPTOCOCCUS (GBS) INFECTION

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Background: GBS is a leading cause of neonatal sepsis and meningitis. In the absence of a licensed vaccine, 2 studies were conducted to investigate safety and immunogenicity of the Novartis investigational trivalent (serotypes Ia, Ib and III) GBS CRM197-glycoconjugate vaccine, first in non-pregnant and then in pregnant women.

Methods: Dosage (5 or 20 µg of each glycoconjugate), formulation (unadjuvanted or with $Al(OH)_3$) and schedule (1 or 2 injections) were first evaluated in non-pregnant Belgian women. Results guided a subsequent study in 320 pregnant South African women examining 5, 2.5 or 0.5 µg dosages (vs placebo) for safety and immunogenicity (ELISA) at baseline and at delivery.

Results: Vaccines were well tolerated with no vaccine-related SAE. All dosages and formulations were immunogenic. Day 61 GMC (µg/ml; combining data across groups) showed no added benefit from 20 vs 5 µg dosage (11.6 vs 14.4 µg/ml); from 2 vs 1 injection (11.8 vs 14.1 µg/ml) or adjuvant vs no adjuvant (10.4 vs 16.0 µg /ml). Accordingly, pregnant women received 1 injection of unadjuvanted vaccine at dosages ≤ 5 µg. Responses to 0.5 µg trended lower than those to 2.5 or 5 µg for all serotypes. Among pregnant women with undetectable Ia-specific Ab at baseline, highest Ab responses occurred after 5 µg (6.5 µg /ml) vs 2.5 µg (3.2 µg /ml) or 0.5 µg (2.43 µg /ml; serotype Ia) dosages.

Conclusions: Data support advancement of a single injection of 5 µg (each glycoconjugate) of unadjuvanted trivalent vaccine to larger scale studies in pregnant women.

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ECONOMIC ANALYSIS OF 2-DOSE VARICELLA VACCINATIONS - COMPARISON OF THE MODELLING RESULTS IN THE POLISH AND HUNGARIAN ENVIRONMENTS

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Background and aims: This study aims to assess the impact of co-financed varicella vaccination in Poland and Hungary (birth cohorts are 389,000 and 90,000), where 130,000 and 40,000 varicella cases are reported yearly.

The cost effectiveness and reduction in cases and complications are estimated and compared.

Methods: An age-structured dynamic model which includes both varicella and zoster diseases was used to simulate the evolution of varicella over a 30-year time period from payer perspective in both countries. The conservative assumption on exogenous immunity boosting on zoster incidence was taken into account.

Three scenarios were determined according to coverage and level of reimbursement: 50% reimbursement of vaccination for children in the 2nd year of life with 35% coverage (Scenario1); 50% reimbursement of vaccinations for children in the second year of life and catch-up vaccination in the 10th years of age - with 35% coverage for both cohorts) (Scenario2); universal routine vaccination programme for children in the second year of life with 98% coverage (Scenario3).

Results: The ICERs (EUR/QALY), the approximate number of varicella cases and number of varicella complications avoided by the different scenarios for the two countries are the following:

Payer perspective, 30-year time period	Scenario1		Scenario2		Scenario3	
	Poland	Hungary	Poland	Hungary	Poland	Hungary
ICER (EUR/QALY)	7 615	7 532	7 803	5 861	22 310	16 157
Varicella cases avoided (approx)	3 664 000	764 000	3 867 000	1 060 000	9 060 000	2 200 000
Varicella complications avoided (approx)	176 000	4 600	184 000	7 300	395 000	17 000

[Results on ICERs,cases and complications]

Conclusion: The predictions of the model show that co-financing of varicella vaccination in both countries under the assumed scenarios is likely to be cost-effective. The scenarios show benefits in terms of varicella cases and costs avoided.

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PREDICTING THE FUTURE: PROJECTING VACCINATION EFFECTS FROM PRE-ROTAVIRUS VACCINE GASTROENTERITIS EPIDEMIOLOGY IN A LARGE UK PAEDIATRIC EMERGENCY DEPARTMENT

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Background and aims: Rotavirus vaccine will be introduced into the UK immunisation schedule in September 2013. Active prospective rotavirus surveillance is needed to provide a clear understanding of pre-vaccine epidemiology. Here we report the first season of our ongoing surveillance and predict likely initial vaccine effects.

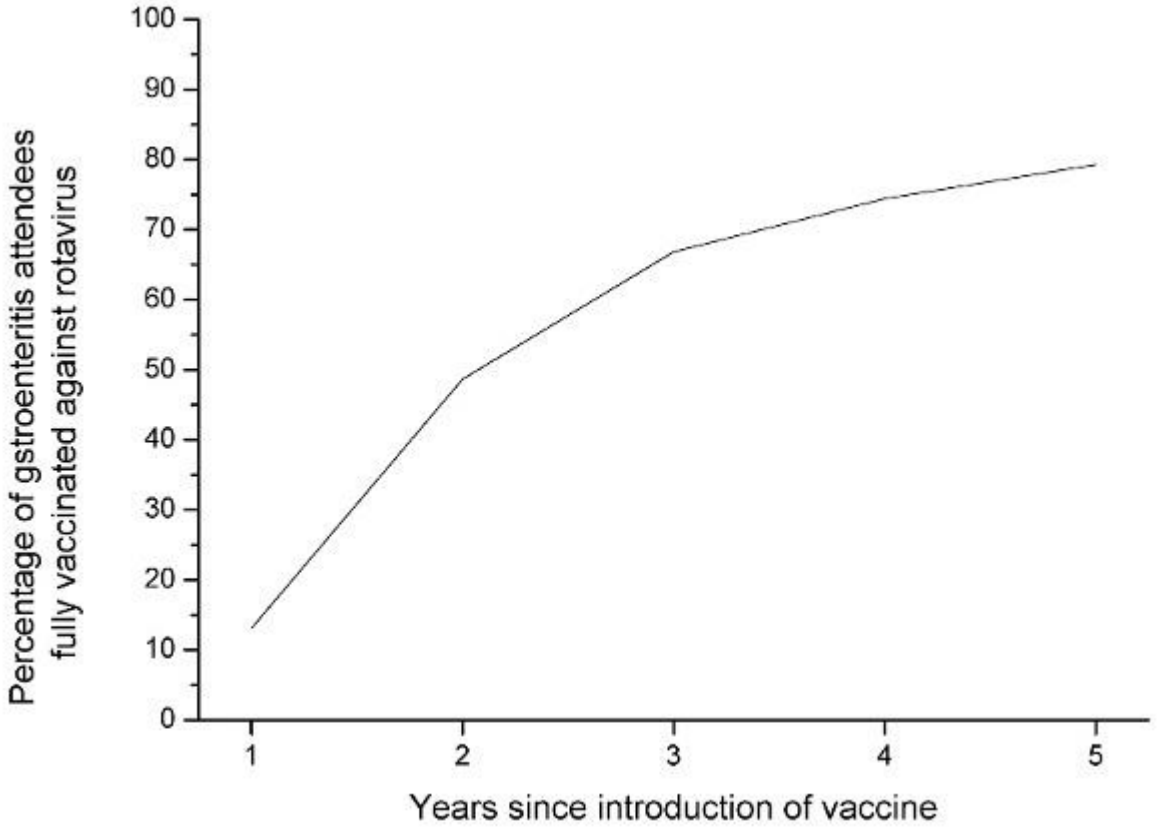
Methods: During the 2012 rotavirus season (February-July) all children attending Bristol Children's Hospital Emergency Department with acute gastroenteritis (AGE) (>2 loose stools and/or >1 episode of forceful vomiting in the last 24hours) were asked to provide a stool specimen and had their symptoms and outcomes prospectively recorded. Samples were tested for rotavirus, adenovirus, astrovirus, sapovirus and norovirus using realtime-PCR.

Results: There were 1355 AGE attendances (table 1). 32% presented with just vomiting. 34% of those with diarrhoea provided stool samples. Rotavirus was detected in 54% of samples.

Age	0-6m	>6m-1y	>1y-2y	>2y-3y	>3y-4y	>4y-5y	>5-10y	>10y
Percentage of cohort (number)	15.1 (204)	21.6 (293)	27.7 (376)	11.0 (149)	6.9 (93)	4.4 (59)	9.2 (124)	4.2 (57)

[Table 1: Gastroenteritis population breakdown]

Conclusions: From the age distribution of this cohort, only 13% would have been eligible to complete routine vaccination in the first year of the programme. We predict only a minor impact on the 2014 rotavirus season. By 2015 49% of cases would have been eligible for vaccine. With no catch-up campaign, the observed effect will be crucially dependent on the threshold of vaccination coverage at which indirect protection is seen in our population.



[Graph 1: Predicted vaccine coverage]

Acknowledgements: This study was supported by an unrestricted investigator led grant from GlaxoSmithKline.

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DIVERSE KINETICS OF IGM AND IGG B-MEMORY CELLS POST IMMUNIZATION WITH THE 13-VALENT PNEUMOCOCCAL POLYSACCHARIDE VACCINE (PCV13) IN ASPLENIC B-THALASSEMICS

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Background: Memory B cells(MBCs) have been associated with establishment of immunological memory and antibody persistence. However, the kinetics of IgM and IgG MBCs in response to vaccination have not been fully investigated. We studied the kinetics of the serotype-specific IgM and IgG MBCs and IgG antibodies after immunization with PCV13 in asplenic β-thalassemics.

Methods: Thirty seven adults(20male,mean age35.7years) were vaccinated with PCV13. All patients had received 1-4 doses of the 23valent pneumococcal polysaccharide vaccine(PPV23) in the past and one PCV7 seven years earlier. Blood samples for cell and sera isolation were taken at baseline and 28 days after PCV13. Serotype-specific MBCs were quantified by ELISpot and serum PS-specific antibodies to 3,19A,19F,9Vand23F by ELISA.

Results: Prior to vaccination, all subjects had detectable IgM and IgG MBCs against all tested serotypes. Post-PCV13, IgG MBCs increased significantly($p \leq 0.001$ for 9V,19F,23F,3;$p=0.018$for19A) whereas IgM MBCs remained at baseline levels for all serotypes tested. Serotype-specific IgG antibodies were high at baseline and increased significantly one month post-PCV13($p=0.014$ for3;$p \leq 0.001$ for19A,9V,19Fand23F). There was a strong correlation between IgG MBCs at baseline and IgG antibody titers one month post-PCV13($p< 0,001$ for19A,19F,23F;$p=0,036$ for9V;$p=0,079$ for3).

Conclusion: Detectable MBCs at baseline demonstrate the establishment of immunological memory at a cellular level, following immunization with PCV7(PCV7 serotypes) or natural exposure(non-PCV7 serotypes). Baseline IgG MBCs could predict the antibody response to secondary immunization providing further evidence for the association of immunological memory with antibody response. IgM and IgG MBCs diverse kinetics post vaccination, reveal the distinct immunological characteristics of the different MBC subsets.

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CHANGING EPIDEMIOLOGY OF EMPYEMA FOR CHILDREN IN HONG KONG AFTER THE LAUNCHING OF CONJUGATED PNEUMOCOCCAL VACCINES

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The annual incidence of hospitalized children with empyema was found to be increasing (2008-2012) in Hong Kong despite of the introduction of conjugated pneumococcal vaccine to the Childhood Immunization Program (CIP) with evidence of serotype replacement.

Background: Streptococcus pneumonia is the most common cause of pneumonia and empyema. Although conjugated pneumococcal vaccine has decreased the incidence of pneumococcal disease, their effectiveness in reducing empyema is unclear with conflicting evidence. In Hong Kong PCV7, PCV10 and PCV13 were introduced to CIP in September 2009, October 2010 and December 2012 respectively with good coverage.

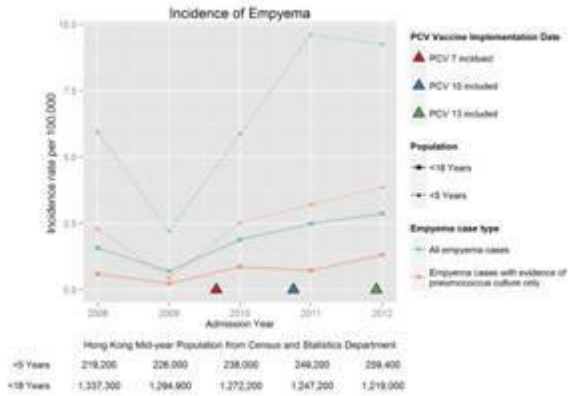
Aims: To study the annual incidence of hospitalized children with empyema.

Methods: We studied all children admitted to public hospitals with empyema attributable to pneumococcal infection in Hong Kong (2008-2012). The annual incidence was calculated using the census data. Logistic regression was used to study the time trend.

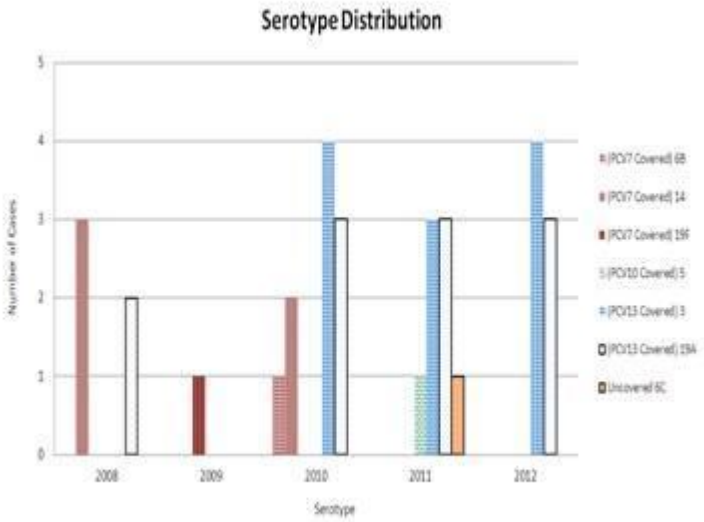
Results: The incidence increased over years for children aged < 5 and < 18 years which were statistically significant. (Table 1 and Fig 1) Empyema was more likely to be caused by non-vaccine serotypes after launching of conjugated pneumococcal vaccine to CIP. (Fig2)

Year	Age <5 years				Age <18 years			
	Empyema (All except those caused by organisms other than pneumococcus)		Empyema with positive pneumococcal culture		Empyema (All except those caused by organisms other than pneumococcus)		Empyema with positive pneumococcal culture	
	Count	Incidence (per 100,000)	Count	Incidence (per 100,000)	Count	Incidence (per 100,000)	Count	Incidence (per 100,000)
2008	13	5.93	5	2.28	21	1.57	8	0.6
2009	5	2.21	1	0.44	9	0.7	3	0.23
2010	14	5.88	7	2.94	24	1.89	12	0.94
2011	24	9.63	8	3.21	31	2.49	9	0.72
2012	24	9.25	10	3.86	35	2.87	16	1.31
Logistic Regression	Std=0.22, P=0.0077		Std=0.31, P=0.0222		Std=0.23, P=0.0004		Std=0.26, P=0.0152	

[Table 1. Incidence of Empyema (2008-2012)]



[Fig 1. Incidence of Empyema (2008-2012)]



[Fig 2. Serotype Distribution of Empyema]

Conclusion: Active surveillance of empyema should be conducted to monitor the changing epidemiology of empyema after launching of conjugated pneumococcal vaccines.

Acknowledgement: Colleagues in CHP for data retrieving.

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AETIOLOGY, RISK FACTORS AND OUTCOME OF INVASIVE BACTERIAL AND FUNGAL INFECTIONS IN PAEDIATRIC ONCOLOGY PATIENTS IN SOUTH WEST LONDON

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Aims: This study aimed to describe the pathogens, risk factors and outcomes for serious bacterial and fungal infection (BFI) in south west London (SWL) hospitals over a 3 year-period.

Methods: Case notes of all children aged 1 month to 15 years with cancer who had a positive blood or cerebrospinal fluid (CSF) culture at any of five SWL hospitals during 2009-11 were used to complete standardised web-based questionnaires. Positive cultures were considered significant if the child received intravenous antibiotic therapy directed towards that pathogen.

Results: During 2009-11, 119 children had 259 and 4 positive blood and CSF cultures, respectively, during 150 admissions to hospital. Blood culture isolates included 127 (49.0%) coagulase-negative staphylococci (CoNS), 40 (15.4%) other Gram-positive, 58 (22.4%) Gram-negative, 19 (7.3%) fungi/yeasts and 15 (5.8%) mixed/other pathogens.

Most admissions (145/150, 96.7%) were in children with an indwelling venous catheter or ventriculo-peritoneal shunt. Neutropenia (< 1.0 $x10^9$/L) within 48 hours was recorded in 61 (41.0%) admissions and was associated with increased fungal/yeast infections (11.1% vs 1.1% isolates; P=0.003). Sixty-nine children (58.0%) had haematological malignancy and 50 (42.0%) solid tumours; CoNS were the main pathogens in both groups (50.3% vs 52.1%), followed by Gram-negative (28.7% vs 20.0%; P=0.11) and other Gram-positive (15.5% vs. 17.0%) organisms. Six patients died, including three who died from their infection.

Pathogen (n=259)	Number	%
Coagulase-negative Staphylococci	127	49.0
Other gram-positive organisms	40	15.4
Gram-negative organisms	58	22.4
Fungal/yeast	19	7.3
Mixed/not specified	15	5.8

[Table 1: Bacterial pathogens isolated from blood]

Discussion: In children and adults, central-line associated CoNS infections were responsible for half the infections in children with cancer. Interventions to reduce line-related-infections could have a significant impact in reducing BFI in children with cancer.

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INCREASED RISK OF INVASIVE PNEUMOCOCCAL DISEASE AND PNEUMONIA IN CHILDREN WITH CHRONIC MEDICAL CONDITIONS

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Background: Asthmatic children are known to be at increased risk for pneumococcal disease (PD), but PD risk attributable to other common chronic medical conditions in children has not been well-defined. We report the largest study to date of PD risk among children with chronic medical conditions including asthma, diabetes and neurologic disorders.

Methods: Data were obtained from two large independent healthcare claims databases. The study population included all children < 18 enrolled in participating health plans during 2007-2010, and was stratified by presence of selected "at-risk" or "high-risk" conditions. Chronic medical conditions and PD (invasive pneumococcal disease [IPD], pneumococcal pneumonia [PP], and all-cause pneumonia [PNE]) were ascertained from diagnosis, procedure, and drug codes. Incidence rate ratios (RR) were used to compare PD incidence between children with at-risk and high-risk conditions to PD incidence in age-matched "healthy" counterparts.

Results: During 16.2 million person-years of observation, incidence of IPD, PP, and PNE was higher among children with at-risk conditions (especially those with ≥ 2 conditions) or high-risk conditions compared with age-matched healthy counterparts (Table).

Table. Rates of disease per 100,000 person-years and rate ratios in US children by presence of underlying chronic medical conditions

	IPD Rate	IPD RR	PP Rate	PP RR	PNE Rate	PNE RR
Healthy	2.6	--	19	--	570	--
At-Risk (≥1 at-risk condition)*	6.5	2.5	53	2.8	1,793	3.1
Asthma	4.1	1.6	52	2.8	1,697	3.0
Diabetes	3.7	1.4	26	1.4	783	1.4
Neurologic/Seizure disorders	14.7	5.7	105	5.6	2,553	4.5
≥2 at-risk conditions	12.6	4.8	185	9.9	5,740	10.1
≥3 at-risk conditions	32.8	12.6	434	23.3	13,184	23.1
High-Risk**	48.9	18.8	156	8.3	3,752	6.6

*Includes asthma, diabetes, heart/lung/liver disease, Down's syndrome, neuro/seizure disorders, short gestational age/low birth weight
**Includes functional/anatomic asplenia, HIV, renal failure, chronic immunosuppressant use, malignancies, congenital immunodeficiency, diseases of white blood cells, and cochlear implant

[Table]

Conclusions: Risk of PD was elevated among children with a spectrum of medical conditions compared to the risk in healthy children, especially those children with ≥2 at-risk conditions or a high-risk condition.

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SEVEN-FOLD RISE IN LIKELIHOOD OF PERTUSSIS TEST REQUESTS IN A STABLE SET OF AUSTRALIAN PRIMARY CARE ENCOUNTERS, 2000-2011

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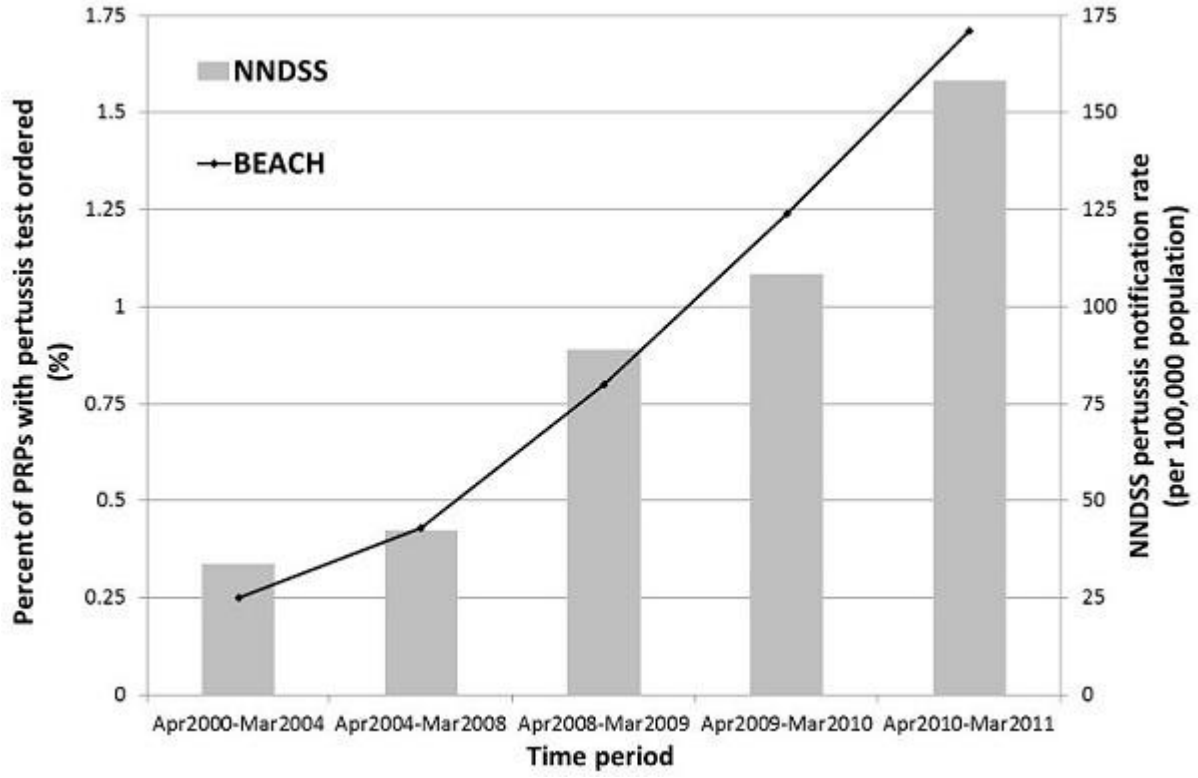
Background: Since 2008 pertussis notifications have been increasing in Australia: this may be due to a true increase in disease, an increase in testing, or a combination of both.

Methods: The Bettering the Evaluation and Care of Health (BEACH) program is a continuous cross-sectional national study collecting details of Australian primary care encounters. We identified 13 problems most likely to result in a pertussis laboratory test request - pertussis-related problems (PRPs) from 2000-2011.

Results: PRPs captured 86-96% of pertussis-test requests annually. The proportion of these encounters resulting in a pertussis-test request increased from 0.25% in Apr2000-Mar2004, to 1.71% in Apr2010-Mar2011 (odds ratio: 7.0; 95% CI: 5.5-8.8).

Comparison with national disease notification data revealed that the two datasets were highly correlated (r=0.99), with the increasing notification data mirroring increased likelihood of a pertussis test request in the primary care setting.

Fig.1: Percent of BEACH PRPs for which a pertussis test was ordered, and annual (2008-2009, 2009-2010, 2010-2011) or averaged annual (2000-2004, 2004-2008) rate of national pertussis notifications, Apr2000-Mar2011, Australia.



[Figure 1]

Conclusion: Increasing likelihood of being tested over the study period may largely be due to expanded availability and use of polymerase chain reaction (PCR) testing amplifying detection of recent pertussis activity.

It is important to analyse changes in infectious diseases using a range of surveillance systems. Using laboratory-confirmed notification data in the PCR era as the only monitoring source for pertussis increases the possibility of inappropriate public health concern or action.

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PERTUSSIS EPIDEMIC IN ISRAEL, 2010-2012, INCREASED LABORATORY DETECTION DESPITE TWO ADDITIONAL DTAP BOOSTER DOSES

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Background: Despite the addition of two booster dTap doses in 2005 and 2008, the Israeli ministry of health surveillance data reveals a marked increase in the incidence rate of pertussis between 2010 and 2011, 15.9/100,000 vs. 28.8/100,000 respectively.

Objective: To assess the recent change in the rate of pertussis-positive real time PCR and culture at a Pertussis reference laboratory.

Methods: Real time PCR and culture data were available for 1.1. 2010-2.12.2012. For the entire study period, the same laboratory technique was used with the detection of Bordetella pertussis based on the amplification of the Insertion Sequence 481.

Results: There was an increase in the detection rate of positive pertussis PCR during the study period, 40/408 (9.8%), 66/491 (13.4%) and 111/504 (22%), for the years 2010, 2011 and 2012, p=0.001, respectively. A similar trend was also evident for positive- culture specimens, 19/362 (5.2%), 29/356 (8.14%) and 45/416 (10.8%) for the years 2010, 2011 and 2012, p=0.02, respectively. All culture positive cases were PCR positive.

Conclusion: The increase in pertussis laboratory detection may be due to:

1) The lower effectiveness of dTap compared to the whole cell vaccine

2) More pronounced waning immunity with dTap vaccine,

3) Improved collection techniques resulting in enhanced sensitivity, and

4) Increased awareness among health- care providers of pertussis´ role in cough illnesses with subsequent increased testing of patients with pertussis who would not have been sampled in the past.

Our findings suggest the need for studies utilizing designs aimed at testing these alternative explanations.

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COMPLEX TIMING OF BLOODSTREAM INFECTIONS IN RELATION TO IN-PATIENT HOSPITAL ADMISSION DATE IN CHILDREN IN ENGLAND, 2010-11

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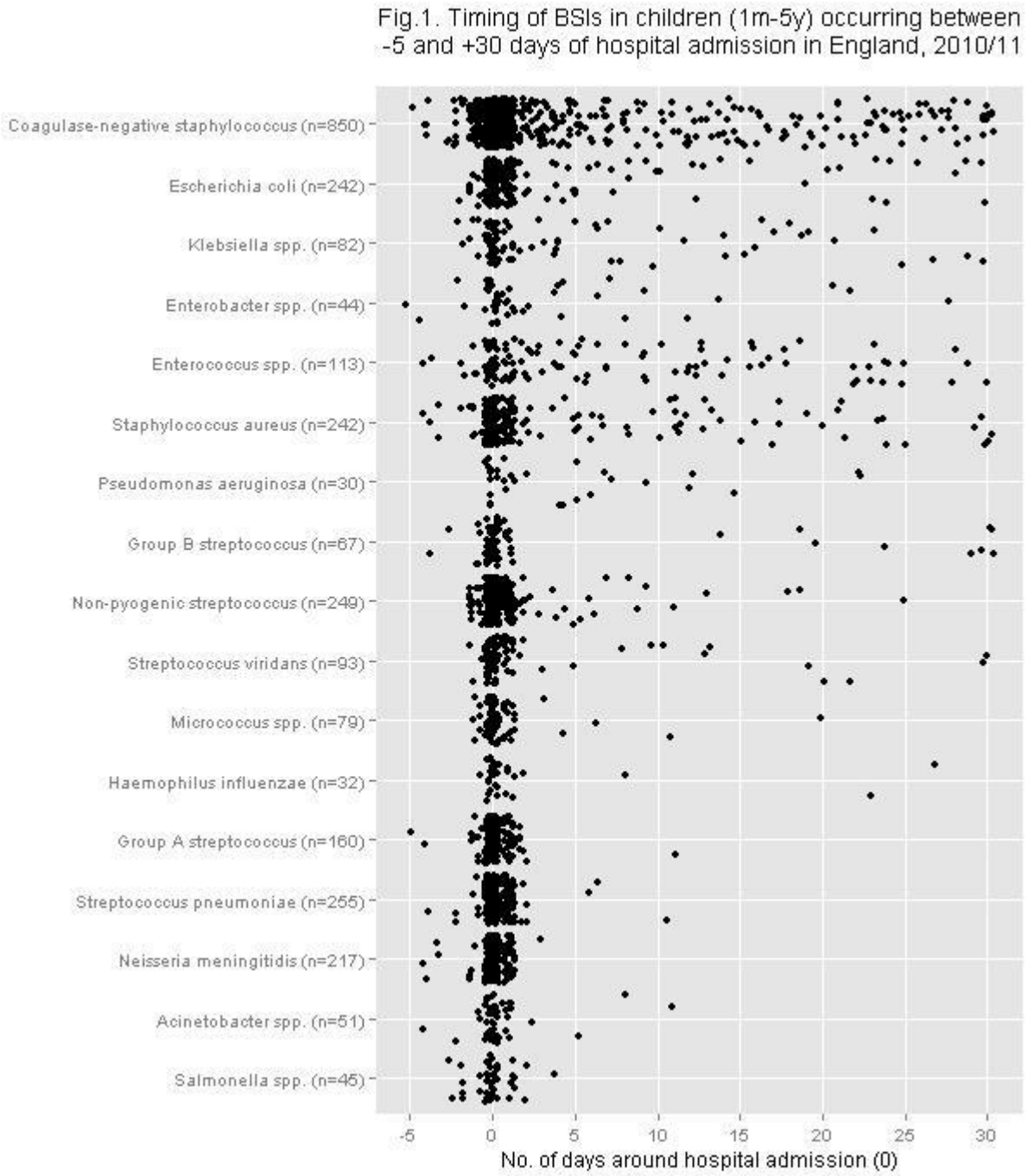
Background and aims: Bloodstream infections (BSIs) are an important cause of child morbidity and mortality, frequently requiring targeted empiric antibiotic therapy. As empiric therapy is often determined by timing of BSI relative to hospital admission (community-acquired [CA] vs. hospital-acquired [HA] infection), we investigated the distribution of timing of BSI onset by different organisms for paediatric in-patient hospital stays in England.

Methods: We probabilistically linked 1 year (2010/11) of hospital microbiology data on BSI in children aged 1month-5years in England, to hospital administrative data (Hospital Episode Statistics [HES]) using Python. We used STATA and R for analysis.

Results: 5,185 BSIs were reported, of which 84% linked to HES. Of these, 93% (n=4,028) BSIs occurred between 5 days before hospital admission and 3 days after hospital discharge; 90% (n=3,616) of these were for the 17 commonest organisms. 79% (n=2,851) occurred between -5 and +30 days after admission (Fig.1.), with the majority (87%) occurring between -5 and +3 days; 15% (n=537) between 31 and 400 days after admission; 6% (n=228) between 1 and 3 days after discharge.



[Figure 1]

Conclusions: We found no clear-cut separation between CA- and HA-BSI in children, where typical HA-BSI bacteria may present in the community and CA-BSI bacteria may present during admission. These findings suggest that timing of infection alone is not a useful basis for empirical antibiotic therapy as previously thought, and may be better informed by knowledge of co-morbidity, recent healthcare contacts and procedures.

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H.INFLUENZAE OR S. PNEUMONIAE INVOLVED IN ACUTE OTITIS MEDIA: CHARACTERISTICS AND OUTCOMES AFTER 7 VALENT PNEUMOCOCCAL CONJUGATE VACCINE IMPLEMENTATION

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Objectives: S. pneumoniae (Sp) and H. influenzae (Hi) are the main bacterial species involved in acute otitis media (AOM). 7valent pneumococcal conjugate vaccine implementation has changed the composition of nasopharyngeal flora (NP) and the epidemiology of AOM. Because NP is the reservoir of bacteria implicated in AOM, if only one otopathogen is isolated in the NP flora, there is a high probability that this species is involved in the episode of AOM diagnosed. Our aim was to compare the clinical and epidemiological characteristics of AOM and outcome of children carrying only Sp or Hi.

Methods: NP samples were collected in 6 to 24 months old children with AOM. Children carrying only Sp or Hi were followed during one month after the beginning of the episode.

Results: Between 2007 and 2010, among the 3535 children with AOM enrolled, 23.5% carried Sp (11.8%) or Hi (11.7%) alone.

N (%) **Characteristics**	**Hi alone** **(n = 415)**	**Sp alone** **(n = 417)**	**p**
Mean age ±SD (months)	14.1± 5.4	12.8± 4.9	0.0002
Day care attendance (%)			
Day care center	38.9	30.2	0.03
Home	26.6	29.7	
Childminder	34.5	40.1	
History of AOM	58.6	48.9	0.01
Otitis prone children	20.1	13.5	0.03
ATB use 3 months before (%)	51.1	39.3	0.001
Fever and otalgia (%)	35.4	50.1	<0.0001
Conjunctivitis (%)	60.2	10.8	<0.0001
Outcome day 10/14	319	341	
Failures	68 (21.3)	44 (12.9)	0.004
Outcome 1 month	134	172	0.003
Recurrences	33 (24.6)	20 (11.6)	

[table]

Conclusion: After PCV7 implementation, we found an equal proportion of children with AOM carrying in NP, Hi and Sp as single otopathogen. Clinical and epidemiological profiles of AOM due to Sp or Hi remain different for several characteristics.

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THE EPIDEMIOLOGY OF CHILDHOOD ACUTE BACTERIAL MENINGITIS IN ENGLAND AND WALES: 2004-2011

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Introduction: Acute bacterial meningitis (ABM) remains a major cause of childhood morbidity and mortality worldwide. This population-based study aimed to describe the incidence and aetiology of ABM in England and Wales over an 8-year period

Methods: Electronic reports by NHS microbiology laboratories of positive cerebrospinal fluid cultures or blood cultures with a clinical diagnosis of meningitis in < 15 year-olds during 2004-2011 were extracted from LabBase2 and analysed.

Results: There were 2525 childhood ABM cases reported (incidence 3.3/ 100,000; 95% CI, 3.2-3.4). Most cases (1733 [69%]; incidence 32/100,000) were reported in infants, followed by 1-4 years-olds (522 [21%], 2.5/100,000) and 5-14 year-olds (270 [11%]; 0.5/100,000). Overall, Gram-negative and Gram-positive pathogens were equally likely to cause ABM. Four bacteria accounted for 68% of all pathogens: Neisseria meningitidis (n=895, 35%), Streptococcus pneumoniae (n=406, 16%), group B streptococci (n=301, 12%) and Escherichia coli (n=136, 5%). In infants, N. meningitidis (n=533, 31%) was the most common, followed by group B streptococci (n=299, 17%) and S. pneumoniae (n=246, 14%). Among 1-4 year-olds, N. meningitidis (n=362, 46%) was followed by S. pneumoniae (n=160, 20%).

Conclusion: N. meningitidis, S. pneumoniae and group B streptococci remain the most important pathogens causing childhood ABM in England and Wales. Effective broad-spectrum meningococcal and group B streptococcal vaccines could significantly reduce the incidence of childhood ABM.

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MICROBIOLOGY OF ACUTE OTITIS MEDIA WITH EFFUSION AND NASOPHARYNGEAL CARRIAGE OF CHILDREN FROM A BARCELONA'S COUNTY (HERMES STUDY 2011-12)

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Background and aims: The 13-valent pneumococcal conjugated vaccine (PCV13) was marketed in Barcelona in 2010 as private market. This study aimed to compare the otopathogens in Acute Otitis Media with Effusion (OME) with the microbiology of concomitant nasopharyngeal (NP) colonization in children in the Valles Occidental County (400,000 inhabitants).

Methods: An epidemiological, prospective and active multicentric study was performed in 10 Primary Care Centres and 2 Hospitals. Nasopharyngeal and middle ear swabs were collected from all children (2m - ≤8y) with OME (< 48h) attended in any Centre and sent to a Central Laboratory for isolation by culture. All pneumococcal isolates (for serotyping) and culture-negative ear swabs (for PCR detection of S. pneumoniae or H. influenzae) were further characterized at Hospital Clínico.

Results: 238 cases (mean age: 32.2 months; 54.6% males) were included. The Table shows the distribution of cases by pathogen at middle ear and nasopharynx and the relevant medical history. Serotype 19A was the most prevalent pneumococcal serotype isolated both at middle ear (15%) and nasopharynx (11%) followed by Serotype 3 (10% and 2.7%) and 19F (10% and 5.5%, respectively). 67% of 19A isolates were multidrug resistant strains.

DISTRIBUTION BY PATHOGEN IN MIDDLE EAR AND NASOPHARYNX AND RELEVANT MEDICAL HISTORY

AOM by pathogen	SP	HI	SP+HI	Spy	SA	PA	CN	Others	Total
N	33	40	9	32	12	9	80	23	238
Non previous AOM history (%)	54.5	12.5*	33.3	40.6	41.7	44.4	37.5	34.8	36.1
≥ 4 previous AOM episodes (%)	18.2	42.5*	22.2	15.6	0	0	17.5	26.1	21
Isolation at nasopharynx									
SP	20	8	1	0	4	3	0	26	69
HI	2	9	0	0	0	3	1	12	33
SP+HI	2	13	6	0	0	0	5	16	43
Spy	1	0	0	0	24	1	0	3	29
CN	8	7	2	0	3	2	1	18	47

SP: *S. pneumoniae*; HI: *H. influenzae*; Spy: *S. pyogenes*; SA: *S. aureus*; PA: *P. aeuruginosa*; CN: culture-negative. *: p<0.05 vs other pathogens.

[TableHermesfinal]

Conclusions: As it has been described, OME caused by H. influenzae was particularly associated with recurrent disease. The role of Serotype 19A and 3 in the current OME episodes supports the potential benefit of the early protection with PCV13.

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SURVEILLANCE OF INVASIVE DISEASE CAUSED BY STREPTOCOCCUS PNEUMONIAE, HAEMOPHILUS INFLUENZAE OR NEISSERIA MENINGITIDIS IN CHILDREN (< 5 YEARS) IN INDIA

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Background and aims: Burden of childhood pneumococcal pneumonia is very high in India. The ASIP study aimed to determine burden of pneumococcal disease, serotype prevalence, and antimicrobial susceptibility pattern of S. pneumoniae in India.

Methods: ASIP network (2011-2012) included 18 tertiary care centers/teaching institutes, 59 sentinel pediatricians and 10 local laboratories. Children < 5 years with clinical suspicion of pneumonia, meningitis or bacteremia were enrolled based on study specific inclusion criteria. Blood, cerebrospinal fluid (CSF), or other normally sterile body fluids were cultured. All pneumococcal isolates were serotyped by Quellung and antimicrobial susceptibility determined by E test method.

Results: 3132 subjects were enrolled. Of 183 (5.84%) culture positives,165 were S. pneumoniae , 15 Haemophilus influenzae and 3 Neisseria meningitidis. Pneumonia was the major clinical presentation (54%) among the study subjects. Among S. pneumoniae culture positives, 40% were from < 1 year of age. Mortality among study subjects was 7%.

Overall, 62% (n=102) of S.pneumoniae isolates belonged to serotypes 14, 5, 1,19F and 6B. Types 19A and 23F occurred among 3% (n=5) each. Penicillin and cefotaxime non-susceptibility was 7% and 4%.. Resistance to cotrimoxazole and erythromycin was 70% and 33% respectively.

Conclusion: ASIP has helped to establish invasive pneumococcal surveillance across multiple Indian institutions and sentinel sites. In India, it is early to assume if any particular serotype (19A, 6A, 6B) or antimicrobial resistance is increasing. Around 70% of serotypes isolated in India are included in the licensed and available pneumococcal vaccines.

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TUBERCULOSIS IN CHILDREN IN LONDON 2009-2011: ARE OPPORTUNITIES FOR PREVENTION BEING MISSED?

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Background: Tuberculosis in children in London may be preventable. We aimed to estimate the size of that problem and identify socio-demographic factors associated with failure to prevent.

Methods: We interviewed parents/guardians of children (0-15 years) with TB over 28 months to identify missed opportunities for prevention. We referred to an algorithm reflecting national guidance in the UK. Socio-demographic factors, potentially associated with failing to be vaccinated or contact traced appropriately, were analysed using chi-square or Fisher's exact tests and uni- and multivariable logistic regression.

Results: There were 405 children with TB. Response rate was 36% (145/405). Of 26 (18%) who did not get BCG vaccine, 16 were UK-born. Of these eight (6% overall) should have received vaccine. Eight were ineligible as they were not in a risk group and born in an area of London with a selective policy. There was a known TB contact in 71 children (49%; 71% in 0-1 years vs. 30% in 11 - 15 years old), of whom 64 (91%) were diagnosed through contact tracing. Six (4% overall) children should have been contact traced and all were of black ethnic origin with index cases among extended family members (within their household) or relatives or family friends from abroad. No particular factor was associated with missed opportunity to vaccinate or contact trace.

Conclusion: Overall few missed opportunities for prevention occurred. However, universal neonatal BCG might be a pragmatic approach for London and we recommend increased rigour when contact tracing any case where a child is exposed.

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QUANTIFERON TO DIAGNOSE INFECTION BY MYCOBACTERIUM TUBERCULOSIS: PERFORMANCE IN INFANTS AND OLDER CHILDREN

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Background and aims: Despite an increasing number of pediatric studies, QuantiFERON Gold In Tube (QF-TB-IT) value in young children remains debated. Heterogeneity in the studied populations increases controversies. This is the first study that simultaneously assessed QF-TB-IT sensitivity, specificity and rate of indeterminates in a large series of immunocompetent children that were stratified according to age and to associated clinical conditions.

Methods: QF-TB-IT reactivity was analysed in 226 immunocompetent children (0-15 years old). 31 were uninfected despite Tuberculosis (TB) contact. 51 presented TB-disease. 39 had Latent TB (LTB). 105 had TB disease suspected but alternative diagnosis (TB-excluded).

Results: QF-TB-IT specificity was 100% in TB-excluded. In TB-disease, low sensitivity of QF-TB-IT in infants (40%) increased with aging (77% in 1-< 5 years and 82% in 5-< 15 years old subgroups). In LTB, agreement between TST and QF-TB-IT was 0% in infants, 40% in 1-< 5 years and 57% in >5 years old children. In children >1 year old, combining QF-TB-IT and TST contributed to diagnose TB disease in two cases and LTB in one case. Finally, the incidence of indeterminate results was high (24%) in < 5 years old children with TB excluded especially with non-TB pneumonitis (61%) but low (0-6%) regardless age groups in TB-disease, LTB and uninfected contact cases.

Conclusions: QF-TB-IT has high specificity, good sensitivity and low rate of indeterminates in immunocompetent children exposed to TB since 1 year of age. Combining both TST and QF-TB-IT since 1 year of age improved diagnosis of TB infection.

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PARAPNEUMONIC PLEURAL EFFUSIONS (PPE) CAUSED BY STREPTOCOCCUS PNEUMONIAE SEROTYPE 3 IN CHILDREN IMMUNIZED WITH 13-VALENT CONJUGATED PNEUMOCOCCAL VACCINE (PCV13)

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Background and aims: In 2010, PCV13 was introduced in Greece for immunization of infants and children against pneumococcal infections. We investigated S. pneumoniae serotypes associated with PPE following PCV13 introduction.

Methods: During 2012, pleural fluid specimens from patients ≤14 years old with PPE were sent to the National Meningitis Reference Laboratory for molecular identification by the use of three multiplex PCR assays: one species-specific, for identification of S. pneumoniae, and two for serotype identification (1, 3, 4, 6B, 14, 18C, 19A, 19F, 23F). Patients' pneumococcal immunization history was recorded.

Results: In total 20 pleural fluid specimens were studied. Among 9 serotypes investigated, serotype 3 was identified in 15 specimens (75%), followed by serotypes 19A and 14 in 3 (15%) and 1 (5%) respectively. Among 15 children with serotype 3 infection, 5 (33%) had been previously immunized with PCV13 according to the national immunization schedule: 4 had received one dose of PCV13 each, at the age of 24, 27, 32 and 54 months respectively. The fifth patient had received two doses, at the age of 21 and 25 months. Notably, none of these patients had received ≥3 doses of PCV13.

Conclusions: Serotype 3 is currently the most frequent S. pneumoniae serotype causing PPE in Greece. One third of the children with PPE caused by S. pneumoniae serotype 3 had been previously vaccinated with PCV13 according to the national immunization schedule. This finding warrants close monitoring and further investigation in order to evaluate the protection afforded by PCV13 against this serotype.

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TUBERCULOSIS IN PEDIATRIC PATIENTS WHO ARE RECEIVING ANTI-TNFA AGENTS

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Background and aims: Adult patients receiving anti-TNFα treatment are at increased risk for developing tuberculosis (TB). We describe the occurrence of latent tuberculosis infection (LTI) and TB in children and adolescents treated with anti-TNFα agents.

Methods: Cohort observational study including pediatric patients receiving anti-TNFα agents in a tertiary-care pediatric hospital. LTI is ruled out by the implementation of anti-TNFα drugs by tuberculin skin test (TST) and, from March 2012, QuantiFERON Gold-In Tube® test (QTF). Along treatment, patients are evaluated every 6 months for TB using history and physical examination, but TST/QTF are not systematically repeated.

Results: The final cohort consisted of 214 patients (55.1% female), of whom 49.7%/29.6%/20.7% treated with etanercept/adalimumab/infliximab, respectively, for a variety of rheumatic diseases (71.5%), inflammatory bowel disease (23.4%) and inflammatory eye diseases (5.1%).The mean(SD) age at diagnosis of the primary condition was 7.1(4.7) years and the duration of the disease before implementing the anti-TNFα agent was 2.9(3.3) years. The total follow-up time under anti-TNFα treatment was 541 patients-year; mean(SD) time per patient: 2.5(2.1) years.

LTI was diagnosed in 2 adolescent girls (prevalence rate: 0.9%; 95% CI: 0-2.2) affected with juvenile idiopathic arthritis, who received isoniazid chemoprophylaxis and were later treated with anti-TNFα, without incidences. QTF tested positive in both patients, while TST was positive in only one of them. No incident cases of TB were observed.

Conclusions: In our study, the prevalence of LTI (0.9%) was similar to that reported in population screening studies in Spain and no incident cases of TB were observed.

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INVASIVE ACINETOBACTER INFECTIONS IN A PEDIATRIC HOSPITAL IN SÃO PAULO, BRAZIL

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Background and aims: Invasive Acinetobacter infections are important cause of mortality in children and of increasingly importance in health care-associated infections, due to it´s extended antimicrobial resistance patterns. Bloodstream infections in a Pediatric Unit were analysed to determine risk factors and antimicrobial susceptibility.

Methods: Data from children with positive blood cultures for Acinetobacter spp. from January, 2010 to January, 2013 was collected. Patient's age, sex, antimicrobial susceptibility, underlying condition, need of PICU, length of hospitalization prior to specimen collection, and patient outcome were analysed.

Results: Fifty-two pediatrics patients with non-duplicate Acinetobacter spp. isolates were identified during the study, fifty-one (98%) of them as A. baumannii and one as A. lwolfii (2%). Fifty-two percent were male and 48% were female, with the mean age 5,5 years. Base comorbidities were seen in 49 patients (94,2%), of which cardiopathy (19,2%), prematurity (15,4%), gastrointestinal/hepatic disorders (13,5%) and oncologic/hematologic diseases (11,5%) were the most prevalent. Ten children (19,2%) needed invasive procedures. Crude mortality rate was 30,8%, with higher rates among those with multidrug-resistant isolates (75%) than those with susceptible isolates (25%). The median hospitalization time was 52 days, during wich 88,5% needed PICU. Isolates were resistant to amikacin (34,6%), ciprofloxacin (42,3%), ampicillin+sulbactam (36,5%) and meropenem (42,3%). Twenty-two patients (42,3%) had multidrug-resistant isolates, from which 13 (59%) of them died.

Conclusions: Acinetobacter spp is an emerging and difficult-to-treat pathogen in pediatric hospitalized patients, especially in PICU. Risk factors for A. baumannii infections were presence of base comorbidity, need of invasive procedures and long periods of hospitalization.

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NECROTIZING PNEUMONIA IN CHILDREN: REPORT OF 41 CASES BETWEEN 2006 AND 2011

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Necrotizing pneumonia (NP) is a rare but severe complication of community-acquired pneumonia (CAP) in children. Our aim is to describe the initial clinical, biological, microbiological and radiological features of patients hospitalized for NP, as well as their management and outcome.

Children hospitalized for NP between May 2006 and April 2011 at the pediatric teaching Hôpital Robert Debré were retrospectively included.

During this period, 4859 patients consulted for CAP in the Emergency department, 635 (13%) were hospitalized and 41 (0.8%) had NP with a median age of 14 months (1 month-16 years). The rate of NP doubled during the 2 years following the H1N1 pandemia. Pleural empyema was associated in 26 (63%) cases. Microbiological diagnosis was obtained in 21 cases (51%) including 13 Staphylococcus aureus, 7 Streptococcus pneumoniae and 1 Fusobacterium nucleatum. All the S. aureus strains encoded the Panton-Valentine leucocidin (PVL) with only one methicillin-resistant strain. Cases of S. pneumoniae NP had significant higher C-reactive protein and higher incidence of empyema at admission compared to patients with S. aureus NP. One patient with S. aureus NP developed an acute respiratory distress syndrome preceded by haemoptysis and leukopenia. All the patients had favourable outcomes without surgical treatment. Median times for apyrexia and hospital stay were respectively of 7 days (1-25 days) and 16 days (7-43 days).

In our series, NP represent 6% of hospitalized CAP. S. aureus and S. pneumoniae must be considered in the antibiotic treatment for NP. The presence of PVL was rarely associated with severe outcome.

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PNEUMOCOCCAL, MENINGOCOCCAL AND HAEMOPHILUS INFLUENZAE MENINGITIS IN BABIES < 90 DAYS OF AGE: A UK AND REPUBLIC OF IRELAND STUDY

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Background and aims: Studies from the 1990s in England and Wales reported that Streptococcus pneumoniae (Spn, 6%), Neisseria meningitidis (NM, 3%) and Haemophilus influenzae (Hi, 1%) together accounted for 10% of all neonatal bacterial meningitis. Infant immunisation against some of the main serotypes/serogroups (ST/SG) of all three pathogens have since been introduced. We aimed to define the proportion and outcome of meningitis caused by these bacteria in < 90 day-olds in the UK and Ireland.

Methods: Out of all reported cases of bacterial meningitis between 1 July 2010 and 31 July 2011, we identified those caused by Spn, NM and Hi in < 90 day-olds through a comprehensive prospective surveillance system.

Results: Of 304 confirmed bacteria causing meningitis, 55 (18%) were Spn (n=28, 9%), NM (n=24,8%) or Hi (n=3, 1%). Median ages at presentation were 39 (Spn), 58 (NM) and 55 (Hi) days; 15 (28%) presented in the neonatal period. ST/SG data were available for 22 Spn isolates (82% covered by PCV13), all NM (92%: serogroup B) and all Hi (n=1: Hib). Case fatality was 5/26 (19%, Spn), 2/3 (67%, Hi) and 0% (NM), with 9/21 (43%, Spn) and 4/20 (20%, Nm) developing sequelae. In a multivariate analysis of all bacterial meningitis Spn, had the highest case fatality and accounted for 20% of all deaths.

Conclusion: Spn and Nm remain important causes of meningitis in infants < 90 days of age. Vaccines with broader coverage and new strategies are required to reduce disease in this vulnerable age group.

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PAEDIATRIC PARAPNEUMONIC EMPYEMA (PPE) IN CHILDREN IN GERMANY - RESULTS ON THERAPEUTIC MANAGEMENT FROM A NATIONWIDE SURVEILLANCE STUDY

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Background: The treatment of PPE and especially the superiority of either non-operative or surgical treatment is still under discussion.

Methods: From September 2010 to June 2012, surveillance of PPE has been conducted in all 472 German paediatric departments using the German Surveillance Unit for Rare Paediatric Diseases (ESPED).

Results: Of 400 children with PPE, 111 (28%) were treated solely with antibiotics. Non-surgical drainage (NSD) was used in 190 (48%), surgical debridement (SD) in 99 (25%) children, either by VATS (n=69) or thoracotomy (n=30). Eighty-four (85%) of the 99 children with SD stayed at PICU, compared to 115 (61%) of 190 children with NSD ($p< 0.001$). 22% of these children received surgery within 3 days after hospitalisation (early SD; median 1 IQR 1-2) and 78% after day 3 (late SD; median 12, IQR 7-17). Children with early SD were older (median 10 years (IQR 5-15) vs. 3 years (IQR 3-7), $p=0.001$) and hospitalization was shorter (15 days (IQR 11-26) vs. 25 days (IQR 20-38), $p=0.001$). Of the children with late SD, 70% had previous NSD at a median of 9 days (IQR 5-15) before SD.

Discussion: Timing of SD in children with PPE was either done early or late in the course of disease. Late SD was clearly associated with young age, often after unsuccessful conservative treatment, whereas early SD (VATS) was mainly done in older children. This may be either due to a more conservative approach in younger children or a more severe initial presentation of PPE in older children.

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EPIDEMIOLOGY OF PAEDIATRIC VARICELLA AND HERPES ZOSTER, ONTARIO, CANADA, 1992-2011: REDUCTION IN SEVERE VARICELLA AFTER INTRODUCTION OF IMMUNIZATION PROGRAM

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Background and aims: Publicly-funded varicella vaccine (VV) was introduced in Ontario, Canada in 2004 (population 13.5 million); children born since 2000 are eligible. We sought to determine the impact of VV on varicella zoster (VZ [chickenpox]) and herpes zoster (HZ) in children (< 18 years), including hospitalizations for complicated VZ (intensive care unit [ICU] admissions and VZ-associated skin and soft tissue infectious [SSTIs]).

Methods: We extracted population-based, universal-healthcare data on VZ and HZ hospitalizations from the Canadian Institute for Health Information's Discharge Abstract Database, and on emergency room [ER], office visits, and VZ ICU admissions from physician billing, between April 1992 to March 2012 (Fiscal years [FYs] 1992-2011). Due to data limitations, ER visits were studied FY1992-2010 and SSTIs FY2002-2011. We examined trends using Poisson regression and Chi-square test. The pre- and post-VV periods were FY1992-FY2003 and FY2004-FY2011, respectively.

Results: Omparing the periods, Table 1 shows annualized incidence rates of VZ/HZ-related outcomes. All decreased, except HZ ER visits. Rates of VZ hospitalizations decreased (p< 0.01) among all ages, including those too old and young for publicly-funded immunization. HZ office visits decreased in < 12 year-olds (p< 0.01) but were stable among 12-17 year-olds. HZ ER visits were stable among < 12 year-olds but increased in 12-17 year-olds (p< 0.01).

VZ/HZ-related outcome	Pre-VV, 1992-2003 (per 100,000/year)	Post-VV, 2004-2011 (per 100,000/year)	p-value
VZ hospitalizations	13.2	4.3	< 0.01
VZ ICU admissions	0.5	0.3	< 0.01
VZ-associated SSTI	2.4	0.7	< 0.01
VZ office visits	1507.2	504.0	< 0.01
VZ ER visits	139.6	52.5	< 0.01
HZ hospitalizations	1.7	1.5	<0.05
HZ office visits	130.4	109.0	< 0.01
HZ ER visits	14.8	15.2	>0.05

[Table 1. Incidence of medically-attended VZ and HZ]

Conclusions: Our data suggests Ontario's VV program has reduced medically-attended VZ, including complicated VZ, among program eligible and ineligible children, suggesting herd immunity. Changes in HZ varied by clinical setting.

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ENTEROVIRUS GENOTYPES CAUSING HAND FOOT AND MOUTH DISEASE IN SHANGHAI, CHINA: A MOLECULAR EPIDEMIOLOGICAL ANALYSIS

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Background and aims: A rapid expansion of hand, foot, and mouth disease (HFMD) outbreaks has occurred and caused deaths in China in recent years, but little is known about the other etiologic agents except enterovirus 71 (EV71) and coxsackievirus A 16 (CA16). The objective of this study is to determine the genotype compositions of enterovirus causing HFMD in Shanghai and identify any associations between enterovirus types and clinical manifestations.

Methods: Stool specimens were collected from patients hospitalized for treatment of HFMD, from May 2010 to April 2011. Enterovirus was detected by reverse transcription PCR and directly genotyped by sequencing the PCR products. Phylogenetic analysis was based on the VP1 partial gene.

Results: Of 290 specimens, 277 (95.5%) tested positive for enterovirus. The major genotypes were EV71 (63.8%), CA10 (9.0%), CA6 (8.3%), CA16 (6.9%), CA12 (2.4%), and CA4 (1.4%). The EV71 strains belonged to the C4a subtype and CA16 belonged to the B subtype. CA6 was closely related to strains detected in Japan, Taiwan and China, and CA10, CA12 and CA4 were phylogenetically similar to other strains circulating in China. Mean hospital stays and the prevalence of complications in patients with EV71 infection were higher than those in patients in CA6, CA10 or CA16 infection ($P < 0.05$ for all comparisons). Children with CA12 infection were the youngest, and most likely have the highest risk of complications when compared to the other non-EV71 infection groups.

Conclusions: This study demonstrated a diversified pathogen compositions attributing to HFMD and clinical symptoms differing in enterovirus genotypes.

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LOW VARICELLA DISEASE BURDEN IN THE NETHERLANDS IN PRIMARY CARE DATA

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Background: In the Netherlands, a relatively low varicella disease burden is observed within routine surveillance. To gain insight in possible underreporting, we estimated the disease burden of varicella using The Integrated Primary Care Information (IPCI) database.

Methods: Potential varicella patients in the period 2006-2008 were identified within the electronic medical records of IPCI by the International Classification of Primary Care (A72) and free text in the medical journal. All potential patients were manually validated and categorized as 'varicella' or 'probable varicella' cases. The incidence of GP-consultations and hospitalizations due to varicella was calculated, standardized by the Dutch population 2006-2008.

Results: We identified 1881 varicella cases (2348 including probable cases) in the period 2006-2008, 14 patients were hospitalized. The overall incidence of GP-consultations due to varicella per 100,000 person-years was 281 (95%CI 268-294), and was highest in the age groups < 5 year. If probable cases were included the incidence increased to 354 (95%CI 340-369). The overall incidence of hospitalizations per 100,000 person-years was 2.0 (95%CI 1.2-3.4).

Conclusions: The incidence of GP-consultations due to varicella in 2006-2008 is slightly higher than according to routine surveillance (267 per 100,000), whereas the number of hospitalizations is comparable (1.7 per 100,000 or 2.4 including side diagnoses). These results confirm the somewhat lower disease burden due to varicella in the Netherlands compared to other countries, probably related to the young age of infection. This is important information for the decision making process whether or not to introduce routine childhood varicella vaccination in the Netherlands.

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NOROVIRUS BURDEN OF DISEASE AS IMPORTANT AS ROTAVIRUS AMONG CHILDREN IN EUROPE

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Background: Norovirus has been recognized as the most important viral cause of acute gastroenteritis across all age groups. A new vaccine against norovirus-related disease has shown its potential to prevent norovirus illness in a challenge study. We compare the burden of disease caused by norovirus to the burden historically caused by rotavirus, for which vaccination is recommended in many countries.

Methods: We reviewed the recent literature to estimate the total burden of disease of norovirus among children in Europe.

Results: Published studies on the burden of norovirus disease in Europe are sparse and heterogeneous in their design. Based on available data, the incidence of acute gastro-enteritis due to norovirus leading to a medical visit or hospitalization among European children < 5 years can be estimated at 26.9/1000 person-years, and 2.8/1,000 person-years, respectively. Thus, approximately 0.7 million medical visits and 70 thousand hospitalizations among children < 5 in the EU every year can be attributed to norovirus. Compared to rotavirus, this represents a similar number of outpatient visits and approximately 75% as many hospitalizations. Since numbers of norovirus cases are continuously rising over recent years an expansion of disease burden has to be expected. Very limited information still is available on mortality attributable to norovirus infection.

Conclusion: The burden of disease caused by norovirus among children in Europe is considerable and comparable to the burden caused by rotavirus before the introduction of vaccination. Norovirus and rotavirus are capable of causing severe gastroenteritis in children.

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NEWLY DISCOVERED RESPIRATORY VIRUSES CAUSE SEVERE ACUTE RESPIRATORY TRACT INFECTIONS IN PREVIOUSLY HEALTHY CHILDREN

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Background: Respiratory viruses are a well-known cause of severe acute respiratory tract infections (ARTI) in children. However to which extent the newly discovered human bocavirus, human coronaviruses (NL63/HKU1), and human metapneumovirus contribute to severe ARTI's in healthy children remains a matter of debate. Especially in the light of underlying disease and/or (bacterial) co-infections, which are often thought to be the primary reason for severe illness.

Aim: To study whether recently discovered respiratory viruses can cause severe ARTI's in previously healthy children.

Methods: Patients (0-18 years) of whom respiratory tract samples were screened for 15 respiratory viruses were retrospectively identified in our department's diagnostics database. We subsequently selected those admitted to the ICU for further analysis. Patients admitted for disease not linked to viral infection were excluded. Clinical and lab parameters were extracted from the electronic medical records of the selected patients.

Results: A total of 2071 patients were identified in our database, of which 3269 samples were taken (mainly nasal washes). Infection with a single virus was shown in 171/735 patients, who were admitted to the ICU. 42 of those 171 had a bacterial infection (Group 1), 96 patients had a medical history (Group 2), and 33 were previously healthy children until admission (Group 3). Primary reason for admission was severe ARTI (±75%). For detailed virological data see Table 1.

Conclusions: Newly discovered viruses are detected as sole pathogen in previously healthy children admitted to the ICU for severe ARTI's.

Table 1. Virus detection in samples study group 1, 2 and 3.

Viruses	Group 1 (n = 42)	Group 2 (n = 96)	Group 3 (n = 33)
Human bocavirus 1	3 (7.1)	11 (11.5)	4 (12)
Human coronavirus NL63	1 (2.4)	1 (1)	1 (3)
Human coronavirus OC43	2 (4.8)	3 (3)	-
Human coronavirus 229E	-	-	1 (3)
Human metapneumovirus	3 (7.1)	5 (5.2)	1 (3)
Influenza A virus	2 (4.8)	11 (11.5)	3 (9)
Influenza B virus	-	2 (2)	-
Parainfluenza virus 1	3 (7.1)	2 (2)	2 (6)
Parainfluenza virus 2	-	-	-
Parainfluenza virus 3	1 (2.4)	2 (2)	-
Parainfluenza virus 4	-	3 (3)	-
Rhinovirus	12 (28.6)	30 (31.2)	3 (9)
Adenovirus	5 (11.9)	9 (9.4)	2 (6)
Respiratory syncytial virus	10 (23.8)	17 (17.7)	16 (48.5)

Data are presented as the number (percentage) of patients.

[Table 1.]

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HUMAN PARECHOVIRUS MENINGITIS - OLD FOE OR NEW ADVERSARY?

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Background and aims: Human parechoviruses (HPeV), particularly type 3, are known central nervous system pathogens, causing serious infections in infants. The association for HPeV 3 as significant pathogen was only reported in 2008. There is still limited understanding of HPeV. The aims:

- To examine the clinical course of HPeV meningitis in affected infants.
- To determine if cerebrospinal fluid (CSF) counts were a predictor for infection.

Methods: All CSF samples which tested positive for HPeV from January 2011 to December 2012 were included. CSF samples were tested as part of meningitis screen by real-time PCR. A Retrospective review of clinical signs of paediatric cases was performed.

Results: In total, 17 patients were diagnosed and all were admitted to hospital during the 2 year period (9 female and 8 male). All were typed as HPeV3. Median age on admission was 19 days. Complications included apnoeas (n= 3), coagulation defects (n = 3), hypotension (n = 1) and seizures (n = 2). 1 infant had signs of white matter damage on a follow-up MRI. 15% of children admitted required intensive care. The disease process was life threatening in over 10%. 9 were followed up as part of normal medical paediatric review, without specific guidance. There was an absence of CSF pleocytosis.

Conclusions: HPeV3 caused significant infection in infants less than 3 months old. PCR testing is required to diagnosis infections. As a result of the severity of infection there is need for understanding of disease process and guidance for long-term follow up.

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OUTCOMES AND RISK FACTORS OF DENGUE VIRAL INFECTION-CAUSED ACUTE LIVER FAILURE

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Background and aims: There are few published cohort studies on acute liver failure (ALF) in children with severe DVI. This study was undertaken to examine the outcomes and risks of ALF in children with severe DVI.

Methods: The medical records of patients age < 15 years hospitalized during 1989-2010 with severe DVI [dengue hemorrhagic fever (DHF) grades III-IV or DVI with complications including active bleeding or DVI-associated organ failure (respiratory, liver, and kidney)] were reviewed. ALF was defined by severe acute liver injury with prothrombin time ≥1.5x the control and encephalopathy in a patient with no history of liver disease.

Results: ALF was found in 32/144 (22.2%) patients with severe DVI. The mean age of DVI with ALF was lower (7.0 ± 4.1 vs 8.6 ± 3.5 years, p=0.03) and the median (interquartile range) weight standard deviation score (WSDS) [0.75 (0.12 to 2.02) vs 0.10 (-0.13 to 1.1), p < 0.001] was higher in patients with ALF. Multivariate analysis found that WSDS >1 SD, age < 5 years, and DHF grade IV were the major risk factors of ALF with odds ratios and 95% confidence intervals of 8.4 (1.8-39.4), 3.8 (1.2-11.5), and 13.1 (4.6-37.2), respectively. Respiratory failure, massive bleeding, renal failure, and mortality were found in 90.6%, 62.5%, 81.3% and 75.0% of ALF cases, respectively.

Conclusion: DVI-caused ALF has a grave prognosis. DHF grade IV, WSDS >1SD, and age younger than 5 years are risk factors for developing ALF.

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HUMAN PARECHOVIRUS AND KLASSEVIRUS INFECTION IN CHILDREN HOSPITALIZED WITH MENINGITIS AND SEPSIS-LIKE ILLNESS

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Background: The human parechoviruses (HPeV) have recently been recognized as important viral pathogens causing sepsis and meningitis in children, but data is limited in Korea. Klassevirus is known to be an etiologic agent of acute gastroenteritis,but its role in meningitis is unclear.

Objectives: To understand the epidemiology of HPeV and Klassevirus in sepsis-like illness and meningitis through detection and typing of the virus in cerebrospinal fluid specimens(CSF).

Methods: One hundred and eighty-three CSF samples collected from 183 patients ranging in age from 1 day to 15 years were tested using a RT-PCR assay for HPeV, EV and klassevirus. Amplification products of the VP1/VP3 and 3D region of HPeV genome were sequenced to identify the parechovirus type.

Results: Twelve HPeV positive specimens(6.5%) were identified from 183 CSF samples. Altough enteroviruses were detected in 39 patients (21%); echovirus 25 and CVA6 being frequently found, mixed infection of HPeV and EV was not detected.Klassevirus was not detected in the study population. Most of HPeV positive patients were under 3 months of age. All twelve samples were typed as HPeV3 and detected mostly in the summer season. The VP1/VP3 gene of the twelve Korean strains clustered most close to the Japan Strain (AB759192).

Conclusions: To our knowledge, this is the first report of HPeV detection in CSF in Korea. Routine testing of HPeV in young infants will improve the detection of etiologic agents of sepsis-like illness, but klassevirus could not still be considered as having a role in these illness.

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SOCIOECONOMIC IMPACT OF INFLUENZA IN CHILDREN IN THE COMMUNITY IN SHANGHAI

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Background and aims: Influenza is a common cause of outpatient visits in childhood. The objective of this study is to understand the epidmiology of influenza in children in Shanghai and the socioeconomic impact of influenza.

Methods: We carried out a prospective surveillance of influenza among children visiting outpatient clinic for influenza-like illness (ILI) between June 2009 and May 2012. Influenza viruses were detected and subtyped using RT-PCR.

Results: Out of 3475 enrolled cases, influenza was virologically confirmed in 978 (28.1%) otherwise healthy children; 577 were influenza A positive (A/H3N2: 341, pandemic A/H1N1: 219, seasonal A/H1N1: 4, and untyped: 10), and 421 (43.0%) were influenza B positive; 451 (46.1%) were < 3 years old and 527 (53.9%) were ≥ 3 years old; 489 (50%) had close contact with persons suffering from simialr diseases, of whom, 299 (61.2%) contacts were family members. The outbreaks of A/H3N2, pandemic A/H1N1 and influenza B took place in fall, winter and spring, alternatively. A total of 199 children with influenza during the 2011-2012 season were followed up. The mean cost of influenza were 736 CYN. Influenza-related hospitalization occurred in 4.0% of cases. Household diseases similar to that of the infected child were reported in 24% of cases.

Conclusion: The annual outbreak of influenza led to a high rate of outpatient visits among children in Shanghai. Household members were the main disseminators to spread influenza among children. Influenza imposes a significant socioeconomic burden on children and their families.

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HUMAN BOCAVIRUSES IN STOOLS OF CHILDREN ARE NOT ASSOCIATED WITH ACUTE GASTROENTERITIS

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Background and aims: Human bocaviruses (HBoVs) are suggested to be divided in to respiratory (HBoV1) and enteric (HBoV2-4) viruses. We studied HBoV types in children with acute gastroenteritis (AGE) and with acute respiratory tract infection (ARTI) as well as children with symptoms of both AGE and ARTI. We particularly wanted to assess if there was an association of HBoV2 in AGE.

Methods: PCR was used to detect HBoVs from 999 stool samples, 1534 nasal swabs and 439 blood samples collected in Tampere University Hospital. Antibodies specific for HBoV1-3 were determined using competition EIAs.

Results: HBoV1 was found in stools of 5.6% of patients with ARTI and 7.1% of patients with symptoms of both ARTI and AGE but only in 1.1% with AGE only. HBoV2 was found equally in stools of patients with AGE (5.8%), ARTI (5.0%) and symptoms of both (5.6%) and so was HBoV3; 0.5%, 1.1% and 0.8%. In nasal swabs HBoV1, HBoV2 and HBoV3 were found in 69, three and zero cases, respectively.

Sera of 37 HBoV DNA- positive cases were available, only five of these were seronegative for all three viruses, and 13 had IgM antibodies, specificities of which will be determined.

Conclusions: HBoV2 and HBoV3 may primarily multiply in gastrointestinal rather than respiratory tract but were not associated with AGE in children in this study. HBoV1 is a respiratory virus but is commonly found also from stool samples during respiratory tract infection.

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TWO YEAR'S PROSPECTIVE STUDY OF HAND, FOOT AND MOUTH DISEASE AND HERPANGINA THROUGH A CITYWIDE SENTINEL SYSTEM, CLERMONT-FERRAND, FRANCE

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Background and aims: Hand foot and mouth disease (HFMD) and herpangina are usually benign illnesses associated with species A enteroviruses. Since 1998, large epidemics of HFMD were reported in Asia and China and associated with enterovirus 71 (EV-71). This emerging type is responsible for rare fatal neurological complications with cardio-pulmonary involvement. This epidemiological pattern justifies reinforcing the surveillance and investigation of HFMD in Europe..

Methods: Throat and buccal swabs of children presenting with HFMD and/or herpangina along with a standardized report form were obtained and tested prospectively for enterovirus molecular detection and genotyping.

Results: From April, 1st 2010 to December, 31st 2012, a total of 571 children were enrolled; 384 (67%) presented with an enterovirus infection. Herpangina was the predominant clinical presentation (230, 60%). Typical HFMD was observed in 157 (41%) and atypical rash localisation in 111 (28.9 %). No neurological complication was reported. Enterovirus infections occurred each year in two epidemic waves in summer and the late autumn. Predominant serotypes, coxsackievirus (CV-) A6 (35%), A10 (26%), and A16 (20%) displayed different seasonal distribution. EV-71 represented only 3% of cases.

Conclusions: This is the first study reporting prospective clinical and epidemiological characteristics of HFMD/herpangina in a European country. These syndromes are frequent and usually arose during epidemic waves, but EV-71 is a rare occurrence. It is unclear if the increased frequency of CV-A6 infections in Europe and USA over the last four years results from increased clinical attention to HFMD or from the emergence of new virus variants.

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MEASLES-RELATED HOSPITALIZATIONS IN THE PEDIATRIC POPULATION IN ITALY IN 2006-2010: CROSS SECTIONAL STUDY UTILIZING NATIONAL HOSPITAL DISCHARGE DATABASE

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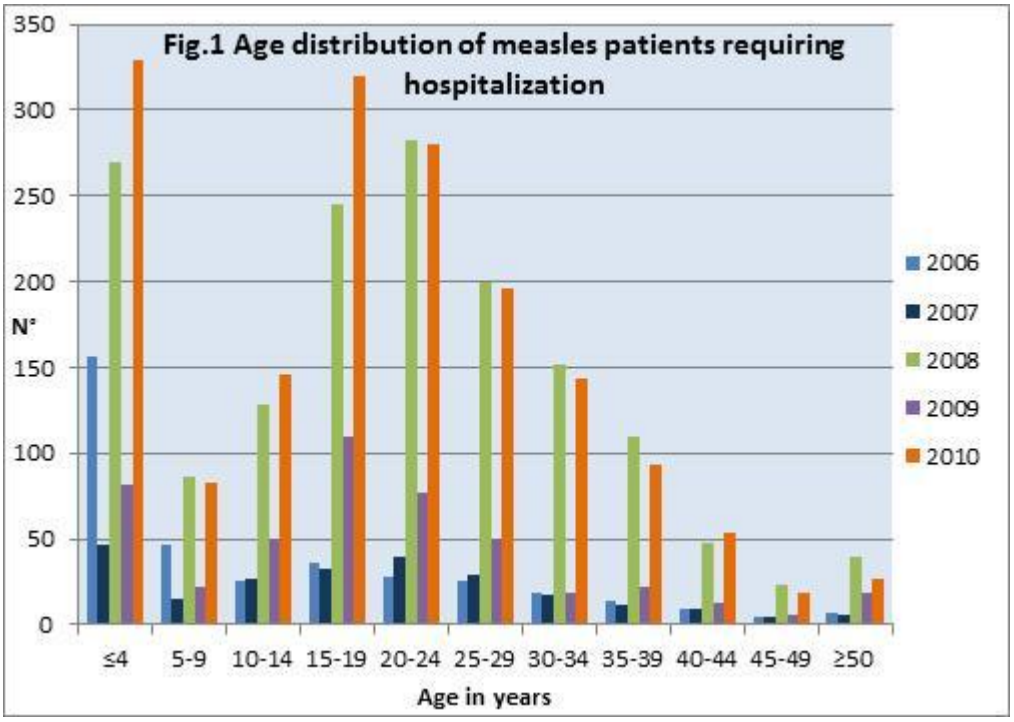
Background and aims: The primary objective was to estimate the frequency of hospitalization for measles in Italy for the period 2006-2010 in children aged 0-14 years, and to analyze hospitalization rates (HR) for geographical location.

Methods: Hospital discharge abstract data for measles-related hospitalizations in 2006-2010, was obtained from the National-Discharge-Database held by the Ministry of Health. Data were analyzed to obtain number and rates of measles hospitalizations per 100,000 population, by age group, and geographical area (North, Centre, South and Islands), using population for each study year published by the National Institute of Statistic (ISTAT) website.

Results: A total of 4,347 hospitalizations for measles were identified,1,512 (34,8%) of which occurred in children < 15 years of age. Patient age distribution showed two peaks: ≤4 years and 15-24 years (figure 1). The following HR were recorded: 0,63/100,000 inhabitants in 2006, 0,4/100,000 in 2007, 2,65/100,000 in 2008, 0,77/100.000 in 2009 and 2,79/100,000 in 2010. Most hospitalizations occurred in northern Italy (33,5%) but the greatest HR was in Islands in 2010 (9,8/100,000 residents). 955(63,2%) patients aged < 15 had main discharge diagnoses of measles without complications,109(7,2%) patients had pneumonia, 9(0,6%) had encephalitis, 4(0,3%) had conjunctivitis, and 6(0,4%) had otitis media.



[measles graph]

Conclusions: Substantial progress has been made towards the national elimination targets, improving coverage rates in children by 2 years and 5-6 years of age, but in the over-14 years age group, due to suboptimal coverage rates, a large proportion of individuals still remains susceptible to measles.

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PARENTAL AWARENESS OF RESPIRATORY SYNCYTIAL VIRUS (RSV) DURING INFANCY: A MULTINATIONAL SURVEY ASSESSMENT

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Background: RSV is a common cause of lower respiratory tract infection (LRTI) hospitalizations during infancy. This study sought to evaluate awareness of RSV in parents whose infants were hospitalized for severe RSV.

Methods: Data was obtained from a multinational Parent Burden Study. Parents with infants (< 1 year) hospitalized for LRTI were asked to complete a survey upon their infant's discharge from hospital. Parents reported their prior knowledge of RSV and their knowledge of the associated risk factors. Descriptive statistics were applied to determine the percentage of parents with prior RSV awareness; how the knowledge was acquired; and their awareness of RSV risk factors. Results were stratified by mother and father respondents.

Results: A total of 250 infants had confirmed RSV, of which 247 mother surveys and 167 father surveys were completed. Among mothers, 84 (34.0%) had awareness of RSV. This knowledge was most commonly acquired from the healthcare system (38.8%), media (15.3%) and family/friends (11.8%). 74 (30.0%) mothers reported awareness of RSV risk factors. Of the risk factors, born premature (52.0%), smoking exposure (36.0%) and daycare (34.0%) were most commonly known. 33 (19.8%) fathers were aware of RSV. Knowledge was most commonly derived from the healthcare system (42.4%), family/friends (30.3%) and media (9.1%). 29 (17.4%) fathers reported an awareness of RSV risk factors. Born premature (35.0%), siblings (35.0%) and daycare (30.0%) were most commonly known.

Conclusion: Parents with infants at risk of severe RSV infection seem to lack relevant knowledge. Strategies to improve awareness and knowledge of RSV are needed.

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GENOME CHARACTERIZATION OF ENTEROVIRUSES 117 AND 118: A NEW GROUP WITHIN HUMAN ENTEROVIRUS SPECIES C (HEV-C)

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Background and aim: Two new HEV-C (EV-C117 and EV-C118) were identified in the Community-Acquired Pneumonia Pediatric Research Initiative (CAP-PRI) study, and the present study describes the characterisation of the complete genome of one EV-C117 strain (LIT22) and two EV-C118 (ISR38 and ISR10) strains.

Methods: Complete genome sequencing was obtained using degenerate primers designed by means of the multiple alignment of the EV-C104 and EV-C109 genomes available in GenBank, and additional primers designed on the basis of the first and subsequent rounds of sequencing in accordance with the primer walking method.

Results: The EV-C117 and EV-C118 5'UTR sequences were related to those of EV-C104, EV-C105 and EV-C109, and were slightly shorter than those of other HEV A-D species. Similarity plot analyses showed that EV-C117 and EV-C118 have a P1 region that is highly divergent from that of the other HEV-C, and phylogenetic analyses highly supported a monophyletic group consisting of EV-C117, EV-C118, EV-C104, EV-C105 and EV-C109 strains. Phylogenetic, Simplot and Bootscan analyses indicated that recombination was not the main mechanism of EV-C117 and EV-C118 evolution, thus strengthening the hypothesis of the monophyletic origin of the coding regions. Phylogenetic analysis also revealed the emergence of a new group within HEV-C that is divided into two subgroups.

Conclusion: Our findings characterise the complete genome of two new HEV-C. Nucleotide and amino acid identity in VP1 sequences have been established as useful criteria for assigning new HEV types, but analysis of the complete P1 region improves the resolution of their identification and characterisation.

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CLINICAL FEATURES OF INFLUENZA A AND B INFECTIONS IN CHILDREN 1-3 YEARS OF AGE

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Background and aims: It is generally thought that influenza A viruses cause more severe illnesses than influenza B viruses. However, this conventional concept may be seriously confounded by age because in most studies children with influenza B have been substantially older than those with influenza A. We compared the clinical presentation of influenza A and B infections in homogeneous groups of outpatient children 1-3 years of age.

Methods: We followed cohorts of pre-enrolled children (n=1185) throughout two consecutive influenza seasons.

The children were examined at our study clinic whenever they had fever or signs of respiratory infection. During each visit, the signs and symptoms were recorded on a structured form, and nasal swabs were obtained for virological analyses.

Results: Of 127 children diagnosed with influenza, 92 had influenza A and 35 had influenza B. The mean highest temperatures were 38.9°C in children with influenza A and 38.7°C in children with influenza B infections; 40% of children with influenza A and 34% of children with influenza B had fever ≥39.0°C (both differences statistically not significant). No significant differences were observed in the frequencies of rhinitis, cough, gastrointestinal symptoms, impaired general condition, laryngitis, wheezing, conjunctivitis, or tonsillar exudates between children with influenza A and B. Acute otitis media developed in 30% of children with influenza A and in 26% of those with influenza B (difference not significant).

Conclusions: The clinical presentation and severity of influenza A and B infections appear to be comparable in children 1-3 years of age.

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CHARACTERISTICS AND OUTCOME OF SEVERE HUMAN PARECHOVIRUS INFECTIONS FROM THREE LONDON TERTIARY UNITS BETWEEN 2008-2012

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Background and aims: Human Parechoviruses (HPeVs) cause a spectrum of disease ranging from self-limiting illness to meningitis, multi-organ failure and death. Sixteen serotypes have been identified. Clinical characteristics and outcomes of infected children in three tertiary units in London are described.

Methods: Cases of HPeV between 2008-2012 were identified through an electronic search of NHS and private virology databases and patient discharge databases. Relevant data were extracted from patient clinical notes.

Results: HPeV was identified in 55 children; 54% were male, 85% under 6 months of age and 56% required admission to PICU. Of the infants < 6 months, the majority was unwell at presentation (72%) with poor feeding (98%), fever (82%), irritability (66%), mottling (56%), lethargy (56%), prolonged capillary refill time (49%), rash (37%), apnoeas (30%), abdominal distension (28%), diarrhoea (27%) and seizures (17%) the most common signs.

Liver function and coagulation tests were the most frequently abnormal results on admission. The median hospital stay was 5 days (1-47 days). Brain MRI was abnormal in 10/13 patients. Neurodevelopment was impaired in 6 of 18 children at follow up (secondary to HPeV infection in 3). No cases from neonatal units were reported.

Conclusions: HPeV can cause severe disease and long term neurological sequelae in young infants. Infants presenting with HPeV infection are unwell at presentation and may mimic those with significant bacterial infections therefore a high index of suspicion is essential. Further research is needed to improve early diagnosis of this infection and to develop effective antiviral therapy.

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ROTAVIRUS GENOTYPE DISTRIBUTION IN BELGIUM: CONTINUED HIGH PREVALENCE OF G2, 6 YEARS AFTER VACCINE INTRODUCTION

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Background: In 2006 and 2007 respectively, Rotarix™ and RotaTeq™ were introduced in the national immunization program of Belgium. This has led to a dramatic decline in rotavirus gastroenteritis in children below 5. Although both vaccines are available in Belgium, Rotarix™ is by far the most used.

Methods: Since the 2007-2008 rotavirus season a national rotavirus surveillance system has been implemented, collecting approximately 600 rotavirus positive samples each season. Rotavirus positive samples were G- and P-genotyped by partially sequencing VP7 and VP4.

Results: In the first 5 seasons after vaccine introduction G2 was the most prevalent genotype, except for the 2010-2011 season. Preliminary data for the 2011-2012 rotavirus season show that the most prevalent genotype in Belgium was G2 (37.9%), followed by G9 (19.9%), G1 (18.0%), G3 (16.5%), G12 (4.0%) and G4 (3.1%). Interestingly, we also found 2 G6P[5] strains. Both strains have a different origin: one G6 clustered very closely with RotaTeq™ and was probably vaccine-derived, while the other G6 was only distantly related to RotaTeq™ and most likely represents a ruminant-to-human interspecies transmission.

Conclusions: After vaccine introduction the G2 genotype was the most prevalent in five out of six rotavirus seasons. In addition, in all rotavirus seasons after vaccine introduction the relative proportion of G2 genotypes was higher than in seasons before vaccine introduction, most likely due to selective vaccine pressure. However, there is still fluctuation in the genotype distribution indicating that other factors besides vaccination also play a role.

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BACTERAEMIA DUE TO MULTIDRUG-RESISTANT GRAM-NEGATIVE BACILLI IN THE NEONATAL INTENSIVE CARE UNIT PATIENTS: RISK FACTORS, ANTIBIOTIC TREATMENT AND OUTCOMES

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Objective: To assess the risk factors, antibiotic therapy and outcomes of multidrug-resistant Gram-negative bacilli (MDRGNB) bacteraemia in the neonatal intensive care unit (NICU) patients.

Methods: Episodes of MDRGNB bacteraemia were compared with a susceptible control group in an 8-year cohort study.

Results: Of 1106 bacteraemias, 393 (35.5%) were caused by a Gram-negative bacilli (GNB). Seventy (18.6%) were caused by a MDR strain. The most frequent mechanism of resistance was extended-spectrum β-lactamase (ESBL) production (67.1%), mainly by Klebsiella pneumoniae (59.6%). Previous antibiotic exposure to 3rd generation cephalosporin [odds ratio (OR) 5.97; 95% confidence interval (CI) 2.37-15.08, P < 0.001] and carbapenem (OR 3.60; 95% CI 1.26-10.29, P=0.017) and underlying renal disease (OR 7.08; 95% CI 1.74-28.83, P=0.006) were identified as independent risk factors for MDRGNB acquisition. Patients with MDRGNB bacteraemia more likely received inadequate initial antibiotic therapy (72.9% versus 7.8%, P< 0.001), had a higher rate of infectious complication (21.4% versus 10.5%; P=0.011), and a higher overall case-fatality rate (28.6% versus 10.5%; P < 0.001). Independent risk factors for overall mortality were presence of infectious complications after bacteremia (OR 3.16; 95% CI 1.41-7.08, P=0.005) and underlying secondary pulmonary hypertension with/without cor pulmonale (OR 6.19; 95% CI 1.88-20.31, P=0.003).

Conclusions: MDRGNB accounted for 18.6% of all neonatal GNB bacteremia, especially in those with previous broad-spectrum antibiotic therapy and underlying renal disease. The most frequent mechanism of resistance was ESBL production. Neonates with MDRGNB more frequently received inadequate empiric antibiotic therapy and presented poorer outcomes with a higher overall case-fatality rate.

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DOES GANCICLOVIR TREATMENT OF CONGENITAL CMV SELECT FOR RESISTANCE?

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Background and aims: Congenital Cytomegalovirus (cCMV) is the commonest known congenital infection. It is a leading cause of sensorineural hearing loss which often presents for the first time and/or progresses months after birth. Ganciclovir (6mg/kg twice daily IV for 42 days) has been shown in a randomised controlled trial to prevent hearing deterioration in babies born with CNS symptoms if started within the first month of life (Kimberlin DW et al, 2003). Ganciclovir is initially phosphorylated by the HCMV UL97 kinase towards its active triphosphate form. We examined the incidence of UL97 mutations in cCMV infected newborns treated with ganciclovir.

Method: Serial clinical samples were obtained from eight newborns at days 0, 21, 42 of treatment and 7days post. Codons 439 - 645 within the UL97 gene were examined for mutations associated with ganciclovir resistance using a modified published method (Castor J et al, 2007).

Results: 20 blood, 24 urine and 24 saliva samples with CMV viral loads detectable >2.5 $\log_{10}$ were amplified. The sequencing showed that all samples were wild type at baseline and none developed resistance mutations within the UL97 region during treatment.

Conclusion: These results indicate that evidence-based treatment with 42 days IV ganciclovir does not frequently select for resistance mutations in UL97. Reports from other groups would suggest that these results should not be extrapolated to longer treatment courses.

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UREAPLASMA VACCINE TO PREVENT NEONATAL INFECTION

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Background: Ureaplasma infection causes neonatal sepsis, pneumonia, meningitis and bronchopulmonary dysplasia. High colonization rate, antibiotic resistance, and diagnostic difficulty make antibiotic treatment difficult. Ureaplasma multiple banded antigen (MBA) appears important in virulence and attachment.

Objective: Develop an Ureaplasma vaccine utilizing the conserved region of the MBA.

Design and methods: Adult female mice were injected with saline or an Ureaplasma (parvum, serotype 6, clinical strain) rDNA (386 bp) MBA conserved region vaccine, and serum collected for 9 months for activity against Ureaplasma species (parvum, serotype 14; urealyticum, serotype 8; and diversum, serotype A). We measured: total IgG, IgG subclasses, IgA, IgM by ELISA; pathogen specific IgG and IgA by ELISA; bacterial killing by in-vitro neutralization; survival and bacteremia of vaccinated dam pups following infection at birth.

Results: rDNA vaccinated dams demonstrated significant: serum pathogen specific IgG ($p < 0.001$) involving multiple subclasses; serum pathogen specific IgA ($p < 0.005$); serum neutralizing antibody

(with < 0.31 % serum); prevention of sepsis and death in their pups for multiple (three) consecutive pregnancies ($p < 0.002$). This activity was present against all Ureaplasma species tested.

Conclusions: An Ureaplasma MBA rDNA vaccine adminstered to mice prior to pregnancy was effective in preventing Ureaplasma sepsis related death in pups for multiple pregnancies against multiple species, and the mechanism appeared in part related to pathogen specific antibody. This suggests the vaccine has a broad range of efficacy and long lasting impact. We speculate that a vaccine targeting the conserved region of the MBA would be effective in preventing neonatal Ureaplasma infection.

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CONGENITAL CYTOMEGALOVIRUS INFECTION SCREENING PROGRAM IN PREMATURE NEWBORNS: PRELIMINARY RESULTS FROM A SINGLE SPANISH TERTIARY HOSPITAL

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Background and aims: Serological screening for cytomegalovirus (CMV) during pregnancy is not recommended. Universal hearing screening (HS) do not identify all children with congenital CMV (cCMV). We evaluated a urine screening in premature newborns to optimize screening strategies.

Methods: Prospective study of premature infants from December 2009-December 2011: cCMV infection screening was performed using a shell vial urine culture assay (Vircel®) during the first week of life. HS was performed using evoked otoacoustic emissions. Premature newborns were classified according to gestational age (GA) and birth weight (considering SGA when birth weight was below 10th percentile for GA). During study period, CMV culture was also performed in SGA full-term infants.

Results: A total of 830 premature newborns (51.3% male) were tested. Median GA: 33.5 weeks (range 23.7-37). Mode: 34 weeks. Average birth weight: 1778.6 g (SD 603.4). Two hundred sixty-seven (32.1%) were very low birth weight infants (< 1500 g) and 10% infants were SGA. According to GA, 45% were born between 34-37 weeks.

Prevalence of cCMV infection among preterm infants was 0.36% (3 asymptomatic premature infants detected -1 was SGA- with normal neonatal hearing screening evaluation).

Also 87 SGA full-term infants were tested, 2 were positive. Prevalence of cCMV infection among all SGA infants was 1.8%. HS was performed in all premature newborns, 5% did not pass. None had cCMV infection.

Conclusions: Prevalence of cCMV infection in our premature infants is low. Screening might be restricted to SGA newborns (regardless of gestational age) and very low birth weight infants.

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INCIDENCE OF SEPSIS IN LATE PRETERM BABIES BORN FROM PREGNANCIES COMPLICATED WITH PPROM

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Background: Preterm Premature Rupture of Membranes (PPROM) complicated 3% of all pregnancies and is associated with 40% of preterm birth. Optimal management of PPROM pregnancies between 34 until 37 weeks is not welldefined.

Objectives: The aim of our study was to determine the incidence of neonatal sepsis in late preterm born from mothers with PPROM between 34 until 37 weeks of gestation, and to assess the effect of planned early birth compared with expectant management for those pregnancies .

Material and methods: The study was prospective, from March 2008 until October 2011. It included 307 pregnant women with PPROM between 34 until 37 weeks of gestation. Patients were randomized, 157 of them to planned early birth, and 150 patients to expectant management.

The primary outcome measure was neonatal sepsis. Secondary outcome was respiratory morbidity, and mode of delivery.

Results: Primary outcome: neonatal sepsis was diagnosed in 5 newborns(3.1%) in planned early birth group, and in 6 newborns(4%) in expectant management group (RR 0.74). Secondary outcomes had no significant differences: RDS was seen in 12 newborns(7.6%) of early planned birth group versus 9 newborns(6%) of expectant management group. Mode of delivery: Cesarean section was seen in 12.7% in early planned birth group versus 14 % of expectant management group.

Conclusion: The incidence of sepsis in late preterm babies born from PPROM pregnancy is low and it does not influenced by early planned birth or expectant management of these pregnancies.

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RESPIRATORY COLONIZATION BY GENITAL MYCOPLASMA IN PRETERM NEONATES AND INCIDENCE OF THE BRONCHOPULMONARY DYSPLASIA

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Background and aims: Over the past three decades, survival of premature neonates has improved significantly. The result of this increased survival is more infants at risk of morbidity from conditions such as bronchopulmonary dysplasia (BPD). The etiology of BPD is likely to be multifactorial. However, there is growing inferential and experimental evidence linking genital Mycoplasma infection with lung disease in preterm neonates. The aim of our study was to investigate the influence of respiratory colonization by genital Mycoplasma on the incidence of DPB.

Methods: We conducted a retrospective and monocentric study on preterm neonates nasopharyngeal or tracheal samples, on which a U. urealyticum and M. hominis search was realized between 2002 and 2009.

Results: Among the 180 preterm neonates enrolled 26 (14,4%) had a positive sample either for U. urealyticum, or for M. hominis. For these, (i) the BPD was significantly more elevated at 36 weeks, 64.5% vs 31.5% ($p< 0.001$); (ii) the invasive ventilation and the duration of hospitalization were prolonged ($p< 0.05$); (iii) preterm labor ($p=0.001$), spontaneous rupture of membrane ($p< 0.001$) and spontaneous vaginal delivery ($p< 0.005$) were more frequent.

Conclusions: This retrospective study showed a significant link between respiratory colonization by U. urealyticum and/or M. hominis and BPD at 36 weeks of corrected age in the enrolled preterm neonates. It will be interesting to confirm these results by a prospective study only on extremely premature, who are more susceptible to be colonized by genital Mycoplasma and to have an immature pulmonary tract.

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THE NEONATAL AND PAEDIATRIC ANTIMICROBIAL WEB-BASED POINT PREVALENCE SURVEY IN 24 EUROPEAN AND 18 NON-EUROPEAN COUNTRIES IN 2012

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Background and aims: The 2012 Point Prevalence Survey was conducted as part of the Antibiotic Resistance and Prescribing in European Children (ARPEC) Project. We aimed to collect representative national antimicrobial prescription data to determine variation in quantity and quality of antimicrobial use; and to create an international database for scientific research and hypothesis formulation.

Methods: Data collection was completed during October-November 2012 using the validated and standardized ARPEC-PPS method for data collection, entry and reporting.

Results: There were 11825 European and 5503 non-European inpatients reported for in total 169 EU and 54 non-EU hospitals. 34.3% EU (range: 16.7% for Malta; 86.2% for Romania) and 40.4% non-EU (range: 21.8% for Australia; 81.1% for Gambia) inpatients received at least one antimicrobial. Antimicrobial proportions were higher for paediatric wards (EU: 40.6%; non-EU: 43.0%) than in NICUs (EU: 29.8%; non-EU: 37.1%). From the 10923 reported antimicrobials, 84% were antibacterials for systemic use. Among neonates (≤29 days), mainly gentamicin (EU and non-EU: 23%) and (mostly in combination with) ampicillin (EU: 13%; non-EU: 22%) was prescribed. Cefotaxime was prescribed in 9% of EU and 8% of non-EU neonates. High variation in antibiotic prescribing for children is observed with highest use of co-amoxiclav in EU (10%; versus 2% in non-EU) and ceftriaxone in non-EU (11%; versus 7% in EU) countries. Overall, 4% of neonates and 6.5% of paediatric inpatients received meropenem.

Conclusion: The standardized PPS method supplied representative country data providing a tool for analysis, target setting and further collaborative research at national and international level.

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BREASTFEEDING PATTERN AND THE RISK OF NEONATAL ILLNESSES AMONG URBAN POOR IN LUCKNOW, NORTHERN INDIA: A PROSPECTIVE FOLLOW-UP STUDY

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Objective: To assess the newborn feeding patterns and associated risks of occurrence of neonatal illnesses among urban poor in Lucknow, northern India.

Methods: The study was conducted at two urban public-hospitals at Lucknow. Neonates were enrolled within 48 hours of birth and followed-up once at six weeks at the outpatients' clinic or home to assess neonatal illnesses and voluntary breastfeeding pattern. Association of established breastfeeding patterns with neonatal illnesses was studied using multivariate logistic regression, adjusting for potential confounders.

Results: 1020 neonates were enrolled from March 2007-April 2008. Among those followed-up (n=937), 46% presented with any illness, with 20.2% reported with at least one Integrated Management of Neonatal and Childhood Illnesses (IMNCI) danger sign of severe illness.

Partially breastfed neonates were significantly more likely to develop any illness (Adj. OR= 7.3; 95% CI= 4.4 to 12.0, p< 0.001) as well as IMNCI illnesses (Adj. OR = 6.4; 95% CI= 3.1 to 13.1, p< 0.001) as compared to exclusively breastfed. Similarly, predominantly breastfed neonates were significantly more likely to develop any illness (Adj. OR= 3.4; 95% CI: 2.0 to 5.9, p< 0.001) as well as IMNCI illnesses (Adj. OR= 2.7; 95% CI= 1.1 to 6.2, p=0.02) as compared to exclusively breastfed. The strength and consistency of these associations remained similar on refitting the model with term, singleton, and normal birth weight neonates.

Conclusion: Exclusive breastfeeding during neonatal period was significantly protective against any illness as well as illnesses mentioned in the IMNCI program, as compared to predominant or partial breastfeeding.

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AN AUSTRALIAN POPULATION BASED COHORT STUDY OF CEREBRAL PALSY SUGGESTS CONGENITAL CYTOMEGALOVIRUS INFECTION LINKED WITH SEVERE DISABILITY

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Intrauterine (congenital) cytomegalovirus infection (cCMV) can result in poor neurological outcomes including cerebral palsy (CP).

Aims: To describe the incidence, clinical profile and co-morbidities of CP cases attributed to cCMV in the Australian CP Register.

Methods and subjects: Cases (birth years 1993-2003) were drawn from three state CP registers (South Australia, Victoria, and Western Australia) with population level ascertainment for CP (a rate ≥1.5 per 1000 live births). Clinical and demographic data were extracted from CP cases where cCMV was reported as the attributed cause and compared with data from CP cases where cCMV status was negative/unknown.

Results: Children with cCMV (n=36) accounted for 1.6% of CP cases in this series (rate of 3.1 per 100,000 live births; 95%CI: 2.1-4.1).When compared with the negative/unknown cCMV group, the cCMV group had proportionally more cases of spastic quadriplegia (75% v 22%, χ^2=51.7, $_{df}$=1, p< 0.001), wheeled mobility dependence (76% v 26%, χ^2=22.2, $_{df}$=1, p< 0.001), epilepsy (68% v 29%, χ^2=25.1, $_{df}$ = 1, p < 0.001), bilateral deafness (56% v 10%, p < 0.001), functional blindness (16% v 5% ,χ^2=17.7, $_{df}$=1, p< 0.001) and severe communication impairment (64% v 21%,χ^2=29.4, $_{df}$=1, p< 0.001).

Conclusions: Thus, cCMV is associated with severe disability for cases recorded in the Australian CP register. In the absence of newborn screening, the true incidence of cCMV in CP in Australia is not known. Congenital cytomegalovirus is an important, potentially preventable causal pathway to severe forms of CP.

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COMPARISON OF HIGH-SENSITIVE C-REACTIVE-PROTEIN, C-REACTIVE-PROTEIN, PROCALCITONIN, AND INTERLEUKIN-8 IN THE DIFFERENTIAL DIAGNOSIS OF TRANSIENT TACHYPNEA OF NEWBORN AND PNEUMONIA

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Background: In neonatal care units, transient tachypnea of newborn (TTN) and pneumonia are the most frequent causes of respiratory distress. All patients with respiratory distress are treated with antibiotics at the beginning of symptoms to prevent any delay in pneumonia treatment, because of difficulty in differential diagnosis of TTN and pneumonia.

Aim and method: We compared the use of high-sensitive (hs) C-reactive protein (CRP) with CRP, procalcitonin (PCT), and interleukin (IL)-8 in differentiating TTN and pneumonia in newborns.

Results: Fifty-seven neonates with a gestational age of >35 weeks admitted to a university hospital due to respiratory distress within 4-6 hours of life. Fifty-two patients were treated with antibiotics until the diagnosis were definite. Twelve (21%) and 45 (79%) neonates were diagnosed as pneumonia and TTN, respectively. Thus 40 neonates with TTN have received unnecessary antibiotic treatment for at least 3-5 days.

Conclusions: In this study, hs-CRP, CRP, PCT, and IL-8 are thought not to be helpful within 4-6 hours of life for the differential diagnosis of pneumonia and TTN. Unlike the samples drawn at 4-6 hours of life, the blood samples collected at the 24th hour of life, hs-CRP, CRP, PCT, and IL-8 levels were significantly higher in neonates with pneumonia. PCT was the most sensitive (86%) and specific (73%) and the earliest-rising marker. hsCRP was the second most sensitive and specific marker. These two parameters can be clinically useful for the early (after 4-6 hours of life) diagnosis of pneumonia.

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BACTERIAL COLONIZATION IN NEONATES AND RESPIRATORY SYMPTOMS DURING THE FIRST YEAR OF LIFE - A PROSPECTIVE BIRTH COHORT STUDY

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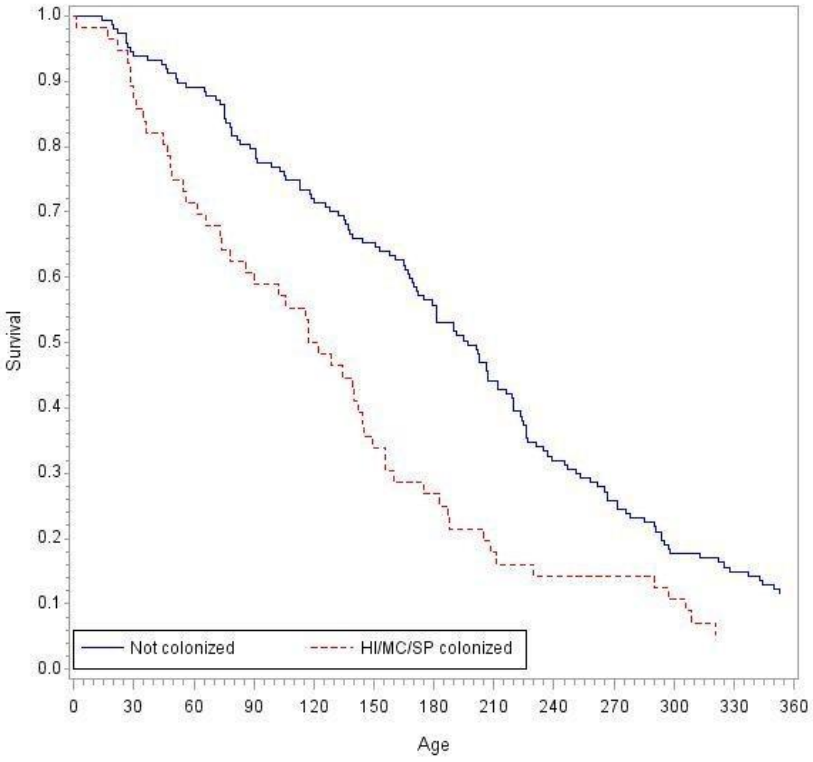
Background and aims: A recent study has found that children born to asthmatic mothers and who were colonized with H. influenza (HI), S. pneumoniae (SP) or M. cattharalis (MC) at one month of age, had an increased risk of subsequent wheezing and asthma at age five. The aim of this study was to investigate whether bacterial colonization in unselected healthy infants is associated with respiratory symptoms during the first year of life.

Methods: HI, SP and MC were detected by real-time polymerase-chain reaction of nasal swab specimens obtained from one-month-old healthy children followed in the community from birth to one year of age during 2004-2006. Respiratory episodes were defined as three consecutive days of respiratory symptoms (diary cough or wheezing). Time to first respiratory episode was modelled with Cox regression. Confounders were chosen a priori as gender and presence of older siblings.

Results: Nasal samples were available for 203 (84%) of 242 included children. Colonization to HI, MC or SP was present in 56 (27.6%) children. Almost all children experienced a respiratory episode within the first year of life (n=184, 91%). Adjusted for the chosen confounders, we found an increased risk of episodes if the child was colonized, HR 1.82 [1.25-2.67]; p=0.002. Figure 1 presents the Kaplan-Meier survival plot for time to first respiratory episode by bacterial colonization.

Conclusions: Neonatal colonization with HI, SP or MC is associated with cough and wheezing episodes during the first year of life.



[Figure 1]

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DIAGNOSIS OF SEPTICAEMIA IN EXTREMELY PRETERM INFANTS

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Background and aims: Neonatal septicaemia is one of the leading causes of morbidity and mortality in neonatal intensive care units (NICU). The early diagnosis is still difficult and represents a significant clinical problem in the early diagnosis of septicaemia ,especially in extremely preterm infants. The aim of the study was to assess biological markers such as C-reactive protein (CRP) level, white blood cell (WBC) count and platelet count together with clinical signs in diagnosis of neonatal septicaemia.

Material and methods: 176 infants were enrolled in this retrospective study. They were less than 28 weeks of gestational age (GA) and hospitalized in the NICU in Lund and Malmö between 2002-2011.Criteria for septicaemia were positive blood cultures or U-Arabinitol quota>5.Diagnosis was clinically compatible with biological markers of infection (CRP>8mg/l, total WBC>15000 or< 5000, platelet count< 100000u/L).

Results: Out of 176 infants 36,4% (95%CI 29,6-43,7%) were identified as infants with septicaemia. The median GA and birth weight (BW) was 26 weeks+1day and 810g respectively. The biological markers of infection most often were an increase of CRP 83%(95%CI 71,8-90,1%),followed by thrombocytopenia 44%(95%CI 32,3-55,9%), leukocytosis 9%(95%CI 4,4-19,1%) and leukopenia 5%(95%CI 1,6-13,1%).The most frequent clinical signs were cardiopulmonary: apnea 44%(95%CI 32,3-56,1%) and bradycardia 31%(95%CI 21,2-43,4%), abdominal distention 31%(95%CI 21,2-43,4%), respiratory distress 16%(95%CI 8,7-26,4%), hyporeactivity 9%(95%CI 4,4-19,1%) and vomiting 9%(95%CI 4,4-19,1%).

Conclusions: C-reactive protein is a good marker for the detection of septicaemia, response to therapy and development of complications. The most frequent clinical sign was apnea.

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SUCCESSFUL ELIMINATION OF EXTENDED SPECTRUM BETA-LACTAMASE (ESBL) PRODUCING NOSOCOMIAL BACTERIA AT A NEONATAL INTENSIVE CARE UNIT

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ESBL-producing bacteria are an emerging problem in Neonatal Intensive Care. Since we could not reach a major decrease in the number of ESBL-colonized and infected neonates, a multiple step project was started in September 2011, which resulted in the decrease and long-term elimination of ESBL bacteria from our NICU.

We conducted a retrospective (between January and September 2011) and prospective (between September 2011 and October 2012) analysis of bacterial cultures of neonates and samples from the ward. Multiple hygienic steps included isolation and separate nursing of colonized patients, a change of antibiotic protocol, increase of the frequency of hygienic surveillance, educational program to increase the efficiency of hand washing and provisional change of the place of care.

Both Enterobacter cloaceae (predominantly EbC052 pulsotype) and Klebsiella pneumoniae (predominantly Z-pulsotype) were found at the ward. The major source of infection was a water bed wich served for the warming of nutriments of neonates. The consumption of antiseptic fluids increased significantly ($p < 0.01$). There was a significant decrease in the number of either colonized or infected neonates between the 1st and 2nd 5-month-long periods of the prospective study (10 infections, 35 colonizations /86 admissions versus 3 infections, 20 colonizations /75 admissions. The last confirmed colonization was registered in June 2012.

ESBL-colonization in the NICU could be succesfully treated by several interventions and with close collaboration with the hygienic team. Continuous surveillance and the maintenance of interventions is vital, since ESBL bacteria may be imported and spread within the ward at any time.

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OUTBREAKS OF HEALTHCARE-ASSOCIATED INFECTION (HCAI) IN NEONATAL UNITS (NNUS) IN ENGLAND - AN IMPORTANT AND UNDER RECOGNISED PROBLEM

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Background and aims: HCAI outbreaks in NNUs are associated with substantial morbidity, mortality and cost to the healthcare system. The number, size and causative organisms of HCAI clusters in English NNUs, were estimated for 2011.

Methods: Data from Health Protection Agency's voluntary-laboratory reporting, national-reference laboratories systems, and an incident-reporting tool, were searched to identify NNU clusters occurred in 2011. The analysis was limited to the most likely causative organisms for HCAI on NNUs. Clusters were defined as:

(i) any cluster or outbreak reported;

(ii) laboratory reports of at least 2 isolates from the same hospital, sharing the same strain-type, with at least one case below the age of 28-days, in a maximum of 14-days between cases,

(iii) 2 or more reports, of the same infection in the same hospital in a 14-day period. Cross linkage of the 3 sources was attempted.

Results: 116 neonatal clusters including both colonisation and invasive disease were identified, involving 666 neonates. 43.4% of the clusters were MRSA, followed by MSSA (26%), E.coli (13%), Enterobacter (12%), and Pseudomonas (10%). There were 9.2 clusters/month (range 0-14). There was a median of 3 babies/cluster (range 2-80). When only bacteraemia samples were considered, E.coli was the most common organism (57% of clusters). It was not always possible to confirm the clusters as outbreaks due to data limitations.

Conclusions: This analysis identified a high number of HCAI clusters in English NNUs, suggesting NNU HCAI outbreaks are an important problem. Systematic European reporting, prevention and management are required.

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NEONATAL SEPSIS: A EUROPEAN NEONATAL INFECTION SURVEILLANCE NETWORK

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Background and aims: Infection is a major cause of neonatal mortality and morbidity. Infections due to Gram-negative (GN) organisms are increasing, although the epidemiology may differ across Europe. The aim of this study was to compare organisms causing neonatal infection in UK and Greek units.

Methods: NeonIN is a web-based, surveillance database capturing information on culture proven neonatal infections. Data from 2012 were extracted. Early-onset (EOS) and late-onset (LOS) sepsis were defined as cases occurring within 48hrs and after 48hrs of birth respectively.

Results: 389 episodes of BSI (involving 280 infants) were identified from 12 NNUs in UK vs 44 episodes (involving 32 infants) from a single tertiary unit in Greece. Incidence was 8.6/1000 live-births and 68.8/1000 NNU-admissions vs 6.2/1000 live-births and 118/1000 in UK and Greek units respectively; 55% were male in UK and 65% in Greece. Median gestational-age (GA) was 29wks (24-40wks) and median birth-weight (Bwt) 908g (518-3631g) in UK vs 33wks (26-39wks) and 1730 gr (890-3995g) in Greece. GN pathogens accounted for 17% of all infections and 86% of LOS in UK vs 30% and 92% respectively in Greece. The most frequent GN pathogens were E.coli in the UK and Klebsiella spp in Greece.

Conclusions: Continuous surveillance and monitoring of neonatal infections is a cornerstone for improving outcomes. With the recent addition of Estonian neonatal units, neonIN is now a European neonatal surveillance network.

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MATERNAL SERUM VITAMIN D LEVELS DURING PREGNANCY CORRELATE WITH PNEUMOCOCCAL ANTIBODY LEVELS IN THEIR NEWBORN INFANTS

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Background and aims: Published data show that pneumococcal antibody levels are often low in newborn infants, particularly in infants of HIV infected mothers. Interestingly, robust antibody responses are seen in HIV exposed uninfected infants following routine vaccination. Invasive pneumococcal disease (IPD) is a leading cause of morbidity and mortality in childhood. Infants are particularly at risk before vaccination. The aim of this study was to identify whether maternal vitamin D status affects protective pneumococcal antibody levels of newborn infants.

Methods: A community-based cohort study was undertaken in Khayelitsha, S.Africa, between March 2009, and April 2010 of 109 HIV-infected and uninfected women and their infants. Serum samples were collected from 104 women and 100 infants at birth and from 93 infants at 16 weeks. Pneumococcal vaccine specific antibody levels were determined by enzyme-linked immunosorbent assays. Maternal 25OH-VitD levels were estimated using liquid chromatography/tandem mass spectrometry (LC-MS-MS).

Results: 31% (32/104) of women had sufficient 25OH-VitD levels. HIV positivity appears to be associated with a lower 25OH-VitD. Median 25OH-VitD in HIV positive women = 38nmol/L (IQR 28.5-52.5nmol/L), and 57nmol/L (IQR 30.75-65.25nmol/L) in HIV -ve women (p=0.07). Maternal 25OH-VitD levels appear to be associated with infant pneumococcal specific antibody levels at birth (Spearman r =0.33, p=0.002). This association is particularly obvious in HIV exposed infants (Spearman r=0.40, p=0.006).

Conclusions: Routine vitamin D supplementation during pregnancy may aid transplacental transfer of pneumococcal specific antibody and reduce infant morbidity and mortality from IPD where it is difficult to vaccinate against numerous strains.

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PEDIATRIC HOSPITALIZATIONS DUE TO LOWER RESPIRATORY TRACT INFECTIONS (LRTI) IN BRITISH COLUMBIA (BC): PRE-, POST- AND DURING THE H1N1 PANDEMIC

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Introduction: Pediatric LRTI hospitalizations are a significant burden on patients, families and healthcare systems. In June 2009, the WHO declared the start of an influenza pandemic which remained in effect until August 2010. During this pandemic, there was increased implementation of public health strategies. This study describes all LRTI inpatient admissions for pediatric patients (< 19 years of age) during fiscal years 2008/09, 2009/10 and 2010/11 in any acute-care hospital in British Columbia and compares its hospitalization pattern to hospital admissions due to H1N1.

Methods: Pediatric LRTI admissions between 2008 and 2011 were extracted from the BC Discharge Abstract Database using ICD-10 diagnosis codes and summarized by diagnosis and fiscal year. H1N1 admissions were also extracted using ICD-10 codes. The pandemic was declared in the fiscal year 2009/2010.

Results: During the study timeframe, 7239 pediatric LRTI hospitalizations were identified: 2498 in 2008/09; 2090 in 2009/10 and 2651 in 2010/11. Respiratory syncytial virus (RSV) (defined as J210; J121; J205) was the highest known specified viral cause for pediatric LRTI hospitalization across all three timeframes: 858 in 2008/09; 495 in 2009/10 and 739 in 2010/11. This can be compared to pediatric hospitalizations for H1N1 (defined as J09): 3 in 2008/09; 362 in 2009/10 and 7 in 2010/11.

Conclusion: Results highlight that RSV hospitalizations are an ongoing public health concern. RSV admissions did decrease during the time of the H1N1 pandemic; however RSV remained a primary cause of pediatric LRTI hospitalizations in acute-care facilities in British Columbia.

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CHARACTERISATION OF ACUTE RESPIRATORY INFECTIONS AT A UK PAEDIATRIC HOSPITAL FOLLOWING H1N1 PANDEMIC (ASSESSING H1N1 IMPACT ON PREDOMINANT VIRAL PATHOGENS)

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Background/aims: According to the WHO, H1N1 influenza has moved into the post-pandemic phase, but there were still high numbers of infections occurring in the UK in 2010-11. It is therefore important to examine the burden of acute respiratory infections at a large paediatric hospital to determine patterns of seasonality and severity of illness during this period.

Methods: This was a retrospective study of respiratory virus aetiology in acute admissions to a paediatric teaching hospital in the North-West of England between 1st April 2010 and 31st March 2011. Patient demographics and data regarding severity of illness, presence of co-morbidities and respiratory virus sampling method were retrieved from case notes. Seasonality was compared to data collected over a 10 month period from June 2009 to March 2010.

Results: 645 patients were admitted between 1/4/2010 and 31/3/2011. 82 (12.7%) patients were positive for H1N1, of whom 24 (29.3%) required PICU admission, with 7.32% mortality rate. In children under 1 year, there was no difference between proportions of patients with co-morbidity presenting with H1N1 infection versus those with other viruses. In all other age groups, H1N1 was commonest in children with no co-morbidities. Presence of H1N1 did not influence prevalence of other viral pathogens.

Conclusions: H1N1 is still prevalent in the UK and occurs frequently in otherwise healthy children, but is also capable of causing severe disease in those with existing co-morbidities. It is therefore important to remain vigilant and to adhere to guidelines on seasonal influenza immunisation programmes, even during the post-pandemic phase.

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AUSTRALIAN AND NSW STATE-BASED DATASETS INDICATE DECLINING CHILDHOOD ENCEPHALITIS MORTALITY BUT A HIGH PROPORTION WITH UNKNOWN CAUSE

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Introduction: Encephalitis is a complex neurological syndrome caused by inflammation of the brain. For most cases, a cause is not found. Australia has unique wildlife and vectors, and potentially unique causes of encephalitis.

Objectives: To examine trends in encephalitis mortality in Australian children and review the rate and causes of childhood encephalitis-associated hospitalisations in New South Wales (NSW).

Methods: Mortality data was collected from the National Mortality Database from 1979-2004, and hospitalization data collected from NSW Inpatient Statistics Collection (2001-11). Children < 14 years were included if their cause of death or hospitalization was attributed to encephalitis. Data were analysed by age, gender, Aboriginality, year, geography and cause.

Results: 238 encephalitis-associated deaths were identified in the Australian paediatric population over a 26 year period (average rate 0.24/ 100,000 £14 years). Significant declines in the mortality rate were noted from 1979 to 2004, particularly associated with HSV, SSPE and post measles encephalitis. Hospitalisation rates varied over the study period (average 3.2/100,000). Children < 1 year had the highest proportion of encephalitis-associated deaths nationally (23% all cause, 43% of HSV), and admissions. The cause was 'unspecified' for the majority (56.4%) of cases, more so in older children.

Conclusion: Although deaths from childhood encephalitis have decreased, encephalitis remains an important cause of hospitalization, particularly in children < 1 year of age. The proportion of cases with 'unspecified' cause remains high. National surveillance and systematic diagnostic testing is required to prospectively identify the emergence of novel infectious diseases and identify opportunities for prevention.

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ACUTE MENINGITIS IN A PEDIATRIC POPULATION

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Background and aim: Meningitis is a medical emergency which require an appropriate antimicrobial therapy can be initiated. A confirmed diagnosis require a lumbar puncture and the analysis of cerebrospinal fluid (CSF). Aim of the study was to analyze the epidemiology of meningitis in a paediatric population.

Methods: We retrospectively reviewed the medical records of children 0-18 years old hospitalized at Infectious Diseases Unit, Bambino Gesù Hospital, Rome, Italy, for a laboratory confirmed meningitis between 1st January 2001 and 1st January 2013.

Results: We reviewed 214 cases of meningitis. The mean age was of 4,5 years (range 5 days-17.3 years); out of them 9 were neonates. The incidence of cases was significantly higher in males than in females (70,6 % and 29,4%, respectively). In 105 patients (49%) a pathogen was isolated from CSF samples. The distribution of etiologies was as follows: N. meningitidis (36,2%), S. pneumoniae (21%), S. agalactiae (10,4%), H. influenzae (8,5%), Enterovirus (7,6%), tuberculosis (3,8%), HSV (2,8%), E.coli (2,8%), HHV6 (1,9%), S.pyogenes (1%). S.aureus (1%), parvovirus (1%), Klebsiella (1%), HHV7 (1%). Referring to neonates, S.agalactiae was found out in 4 cases, E.coli in 2 cases, Enterovirus in 2 cases and Klebsiella in 1 case.

Conclusions: S.agalactiae and Escherichia coli and are the most common organisms causing bacterial neonatal meningitis. Streptococcus pneumoniae and Neisseria Meningitidis are the most common cause of bacterial meningitis in infants and children older than one month of age. As for viral meningitis, enteroviruses are the most frequent detached microrganisms.

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EXSEROHILUM INFECTIONS: REVIEW OF 17 PAEDIATRIC CASES BEFORE THE US OUTBREAK

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Objective: Exserohilum species are environmental fungi rarely identified as human pathogens. The recent outbreak of Exserohilum meningitis in the USA has stimulated interest to this fungus. Our objective was to systematically review all paediatric cases of Exserohilum spp. infections published before the outbreak.

Methods: Exserohilum infections of 0-18 year-old patients were retrieved by searching PUBMED using terms “Exserohilum”, “Drechslera halodes”, “Drechslera longirostrata”, “Drechslera rostrata”, “Bipolaris halodes”, “Bipolaris rostrata”, “Helminthosporium halodes”, “Helminthosporium rostrata”, “Luttrellia rostrata” and “Setosphaeria rostrata”. Demographic data, underlying conditions, microbiology, clinical manifestations, therapy and outcome were recorded and analyzed.

Results: We studied 17 paediatric cases with median age 10 (range, 0.07-18) years and 10:7 male:female ratio. The majority were reported from USA (59%), Israel (24%) and less frequently from India, Canada and South Africa (6%). All infections with Exserohilum species identification (10/17, 58.8%) were due to Exserohilum rostratum. They occurred in patients with hematological malignancies (29%), aplastic anemia (18%), asthma (12%), allergic rhinitis (6%) and hemophagocytic lymphohystiocytosis (6%). Cases included sinus (59%), cutaneous (30%), invasive (23%), corneal (6%) and multifocal infections (29%). Antifungal treatment mainly consisted of amphotericin B (65%), alone or combined with an azole. Surgery was used in 53% of patients. Outcome was unfavorable in 3 (17.6%) cases.

Conclusion: Paediatric Exserohilum spp. infection reports are scant. Sinusitis is the predominant manifestation and haematological disorders the most frequent underlying condition. The most appropriate antifungal therapy remains to be established and surgical intervention, when indicated, may improve outcome.

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INTESTINAL PARASITIC INFECTION PREVALENCES IN INDIGENOUS AND RURAL NON-INDIGENOUS POPULATIONS OF VENEZUELA

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Background: Venezuela is characterized by a rich cultural display with climatic and biogeographical differences between regions. Possibly, parasitic infection prevalence rates are associated with these differences.

Methods: Stool samples from 388 Venezuelan children between 4 and 15 years from three Venezuelan regions were collected for direct parasitic examinations.

[Location of study sites in Venezuela]

Results:

	Carabobo State (n=93)	Orinoco River Delta (n=148)	Amazon State (n=147)	P value

Giardia lamblia (%)	23	15	16	0.20
Ascaris lumbricoides (%)	37a	29ab	15c	<0.01
Hymenolepis nana (%)	0a	8b	0a	<0.01
Trichuris trichiura (%)	39a	40a	25b	0.010
Hookworm (%)	5a	5a	64b	<0.01
Strongyloides stercoralis (%)	0a	5b	16c	<0.01

[Prevalence rates of parasitic infections]

The prevalence of helminths infecting the host through skin penetration, Hookworm and Strongyloides stercoralis, was highest in children from the Amazon rainforest that play naked in soil while children from the mountainous area of Carabobo State wear clothes. In the Orinoco Delta, children play on wooden platforms along the river lacking soil. Prevalence of other nematodes was highest in the Orinoco Delta and Carabobo where children defecate close to their homes.

Age of included children did not significantly differ by region. Median age in children with Strongyloides stercoralis was lower compared to uninfected children (8.5 vs. 9.8 years, p=0.036).

Conclusion: The observation that helminth prevalence in Venezuela differs significantly by region suggests that this is determined by behavioural characteristics and sanitation practices.

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DEFINITIONS AND OUTCOME MEASURES FOR TRIALS ASSESSING NUTRITIONAL INTERVENTIONS IN CHILDREN WITH RESPIRATORY INFECTIONS

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Background: A subgroup of the Consensus group on Outcome Measures Made in pediatric Enteral Nutrition clinical Trials (COMMENT) aimed at defining criteria for assessing key outcomes in pediatric nutrition trials in the field of respiratory infections.

Methods: We critically reviewed clinical trials studying the impact of nutritional interventions on upper (URTI) and lower (LRTI) respiratory tract infections. We focused on definitions, key outcomes, settings and confounding factors.

Results: After application of inclusion criteria, 47 papers were included (44 on prevention and 3 on treatment). Nutritional interventions ranged from enriched formulas to micronutrient given for a broad ranges of time. Most trials were focused on prevention of influenza-like-syndrome and URTI in children up to 6 years. The definitions of respiratory infections were highly heterogeneous. In 10/47 trials, URTI or LRTI were diagnosed by pediatricians (eg.pharyngitis,otitis, flu,bronchiolitis,pneumonia). In 30 trials, definitions were less detailed and based on symptoms reported by families or field-workers (eg.cough, sore throat, tachypnea). Seven trials did not provide a specific outcome definition. Incidence was the most common outcome measure in prevention trials. Duration and illness severity were the main outcomes considered in trials on treatment.

Conclusions: Because clinical trials usually involve large populations monitored by parents or field workers, well-defined and easy-to-monitor parameters should be used. Respiratory symptoms with fever during influenza season may represent a “practical outcome” for future prevention trials. Secondary outcomes may be antibiotic consumption, workdays lost and hospitalizations. However, controls should be included and adjusted for age, setting, risk factors and comorbidities.

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CORONARY COMPLICATIONS IN RECURRENT KAWASAKI DISEASE AND RELATED RISK FACTORS

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Background: The clinical features of and risk factors of recurrent Kawasaki disease (KD) remain unclear.

Methods: We conducted a retrospective review of consecutive cases of KD from 2002 to 2010 in our hospital. Demographic, clinical, laboratory and echocardiographic data were recorded. Risk factors for recurrent KD identified by a univariate analysis were applied in a logistic regression analysis.

Results: The incidence of recurrent KD was 1.88%, and the average interval between the initial episode and the recurrence was 12 months, and females were more likely to suffer a recurrence

(9 males vs. 13 females, 1:1.4). On the initial onset of recurrent KD, children who went on to suffer recurrent KD had longer durations of fever, higher levels of alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), and lower hemoglobin levels than single episode KD. Multivariate logistic regression analysis showed that long fever durations, high AST levels and reduced hemoglobin levels were significantly associated with recurrent KD. Ten of 22 recurrent children had coronary artery complications during the initial onset, and 6 (60%) of them had coronary complications at recurrence. Only 2 of 12 children without coronary complications in initial onset developed complications during the recurrence ($P = 0.035$).

Conclusions: Children who may be at an increased risk of recurrent KD could be identified by longer durations of fever, lower hemoglobin levels and higher AST levels. coronary artery complications complications are more likely to occur in recurrent KD if they were present during the initial episode.

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HUMAN PAPILLOMAVIRUS (HPV) AND CHLAMYDIA TRACHOMATIS (CT) INFECTIONS IN SEXUALLY ACTIVE YOUNG GIRLS, NORTHERN ITALY

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HPV and Ct are the cause of two of the most common STIs affecting especially young women, but few data are available on the prevalence of these infections in teenagers.

This study aimed at evaluating the molecular epidemiology of HPV and Ct infections in sexually active young women aged 13-19 years in Northern Italy.

157 cervical brushes were collected from asymptomatic girls aged 13-19 years (median age 18 years): 50 samples from girls aged 13-17 years and 107 from those of 18-19 years. HPV-DNA and Ct-DNA were detected by PCR amplification of a 450bp segment of ORF L1 and of a 150pb segment of cryptic plasmid, respectively.

Overall, the girls with at least one of the two infections were 29.3% (95%CI:22.6-36.8); in particular 42% (95%CI:28.9-55.9) in the group of adolescents 13-17 years and 23.4% (95%CI:16.1-32.1) among those of 18-19 years ($p< 0.05$).

The prevalence of HPV-DNA in the population studied was 27.4% (95%CI:20.8-34.8): 38% and 22.4% in girls aged 13-17 years and 18-19 years respectively ($p< 0.05$). The prevalence of Ct-DNA was 7% (95%CI:3.7-11.9): 12% in girls aged 13-17 years and 4.7% in those of 18-19 years. 8 girls (5%, 95%CI:2.4-9.4) showed an HPV/Ct co-infection, with a higher prevalence in the girls aged 13-17 (8% vs 3.7%).

The high prevalence observed in this preliminary study underlines the great vulnerability to STIs of subjects at risk for sexual risk behaviours and early sexual debut, such as young women. Particular attention must therefore be paid to appropriate preventive measures.

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IMPACT OF UNIVERSAL VARICELLA VACCINATION ON HOSPITALISATION IN CHILDREN UNDER 15 YEARS IN TUSCANY REGION, ITALY

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In Italy, the implementation of universal varicella vaccination is postponed until 2015, when data from Regional vaccination pilot programs will be available. Tuscany introduced a universal immunization program against varicella with measles- rubella-mumps-varicella (MMRV) vaccine in children 13-15 months old since July 2008. The aim of our study was to evaluate the impact of this program on hospitalisations in young subjects in Tuscany in order to help the Italian decision makers on the future national adoption.

Data on hospital discharge (hospitalisation year, age at discharge, costs) due to varicella diseases in subjects < 15 years were collected from the Tuscany Region database. Hospitalisation data were analysed for two three-year periods: pre-vaccination (2005-2007) and vaccination period (2009-2011), excluding 2008 (transition year).

The high vaccine coverage (82,2% in 2011) obtained quickly in Tuscany resulted in a relevant decline of varicella cases in subjects under 15 years from 18,793 (2005-2007) to 10,246 (2009-2011). The number of children hospitalised for varicella decreased from 245 (pre-vaccination period) to 174 (vaccination period). The reduction was evident in all age groups. The total number of hospitalisation days decreases also from 1,192 to 880, with a saving amount of 146,102 Euro.

The introduction of universal varicella vaccination with MMRV in Tuscany has resulted in a significant reduction of varicella-related hospitalisations and related costs already after three years of implementation. Particularly, hospitalised cases resulted greatly reduced among younger subjects (involved in the vaccination program), although a positive effect of vaccination on hospitalisations is evident also in older children.

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VITAMIN D SUPPLEMENTATION DECREASES PRIMARY CARE VISITS FOR ACUTE RESPIRATORY INFECTIONS DURING INFANCY: A RANDOMISED CONTROLLED TRIAL

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Aims: To determine whether vitamin D supplementation prevents primary care visits for acute respiratory infections (ARI) during infancy.

Methods: We performed a randomised, double-blind, placebo-controlled trial in Auckland, New Zealand (latitude 36ºS). Pregnant mothers, from enrolment at 28 weeks gestation to birth, and then their infants, from birth to age 6 months, were assigned to receive placebo, or one of two dosages of daily of oral vitamin D_3 . The enrolled woman/infant pairs were randomised to: placebo/placebo, 1000IU/400IU, or 2000IU/800IU.

We audited the primary care records (blind to group allocation) of enrolled infants to age 12 months, identified all acute visits and categorised these as visits for an ARI, skin infection, other infection or a non-infectious consultation.

Results: 260 pregnant women were enrolled and randomised to placebo (n=87), lower dose (n=87) or higher dose (n=86) vitamin D. In comparison with the placebo group (84%), ARI visits were less frequent among infants randomised to the lower dose (71%, p=0.046) and the higher dose (66%, p=0.007) of vitamin D. The number (median, interquartile range) of visits for ARIs also supported a dose-response relationship; placebo group (4, 0-5), lower dose (3, 0-5, p=0.04) and higher dose (2, 0-8, p=0.03).

The proportion of infants taken to their general practitioner, and the number of visits made, for skin infections, other infections, or non-infectious causes did not differ between the three randomly assigned groups.

Conclusions: Vitamin D supplementation during pregnancy and infancy reduces primary care visits for ARIs during infancy.

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EMERGING INFECTIOUS DISEASES: PARASITIC INFESTATIONS IN INTERNATIONALLY ADOPTED CHILDREN

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Background and aims: Parasitic infestations (PIs) are a primary problem in internationally adopted children, especially those coming from developing countries.

Our aim was to determine the prevalence of extra-intestinal and intestinal PIs in adopted children.

Methods: Internationally adopted children referred to Regina Margherita Children's Hospital, Turin, Italy, from 2009 to 2012 were included. Patients were evaluated within a few weeks of arrival in Italy. Extra-intestinal PIs were diagnosed through serologic or direct tests, while intestinal PI were identified by at least one positive stool specimen.

Results: 296 children were studied. One hundred thirty-four patients (82 M, 52 F) presented at least one PI (45.2%): 59 came from Sub-Saharan Africa, 31 from Asia, 26 from Eastern Europe and 18 from Latin America. Mean age was 5.3 ± 3.2 years. Twenty-two children had both intestinal and extra-intestinal PIs.

110 children (37%) had intestinal PIs, with 29 of them having multiple isolated parasites. Among protozoa, Entamoeba hystolitica (57) and Giardia intestinalis (39) were prevalent pathogens. Hymenolepis nana was the most frequently identified helminth (8). Six children had a recurrent disease after antiparasitic treatment.

41 children (14%) had extra-intestinal PIs: 38 developed toxocarasis, three schistosomiasis and two malaria by Plasmodium falciparum.

We recorded also a Larva migrans cutaneous infestation.

Conclusions: This study confirms that PIs are among the most relevant infectious disease in internationally adopted children. A complete medical evaluation of adopted children, especially those coming from endemic areas, is an important tool to ensure long term wellness and prevent disease dissemination among contacts.

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VITAMIN D (VD) SUPPLEMENTATION REDUCES THE RISK OF NEW EPISODES OF ACUTE OTITIS MEDIA (AOM) IN OTITIS-PRONE CHILDREN

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Background and aim: VD could modulate bacterial and viral infections. The aim of this study was to evaluate whether VD hypovitaminosis could be associated with an increased risk of recurrent AOM (rAOM) and VD supplementation could be effective in limiting the number of new AOM episodes in otitis-prone children.

Methods: A total of 116 children with a history of rAOM (defined as ≥3 or ≥4 episodes in the preceding 6 or 12 months, respectively) were randomized to receive VD 1,000 IU/day by mouth for 4 months or placebo. Episodes of AOM were monitored for six months and two blood samples (one at enrollment and one at the end of VD supplementation) were obtained in order to determine serum VD concentration.

Results: A total of 58 children were treated with VD and 58 received placebo. The number of children who experienced at least one AOM was significantly lower in VD group than among placebo (26/58 vs 38/58; p=0.03). The mean number of AOM episodes globally diagnosed in VD group was significantly lower than in placebo (0.7 ± 0.8 vs 1.4 ± 1.4; p=0.003). A significant reduction of AOM episodes was found when serum VD level was higher than 30 ng/mL.

Conclusion: VD hypovitaminosis is associated with an increase in the incidence of AOM, particularly when VD serum levels remain < 30 ng/mL. Administration of VD at the dose of 1,000 IU/day is associated with a significant reduction of the risk of AOM, suggesting this kind of prophylaxis in children with rAOM.

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RECURRENT COMMUNITY-ACQUIRED PNEUMONIA (RCAP) IN PEDIATRIC AGE: A CASE-CONTROL STUDY

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Background and aim: RCAP is an increasing problem in pediatric age, but literature on this topic is few. The aims of this study were to describe the clinical profile of children affected by rCAP and identify the factors associated to recurrence.

Methods: This case-control study involved 146 otherwise healthy children (73 males; mean age ± SD, 7.9±4.5 yrs) with a history of rCAP (defined as ≥2 CAP in one year or ≥3 CAP at any time frame) and 146 age- and sex-matched healthy controls without a history of rCAP. Study population was evaluated for demographic characteristics, living conditions and predisposing factors (i.e., immune disorders, atopy/allergy, rhinosinusitis, nasal ciliary function, gastroesophageal reflux, tuberculosis, reactive airway diseases, right middle lobe syndrome).

Results: Significant risk factors for rCAP resulted history of rhinosinusitis (OR 59.33, 95% CI 24.48-144.97; p< 0.001), wheezing (OR 32, 95% CI 10.14-100.96; p< 0.001), asthma diagnosis (OR 10.50, 95% CI 3.77-29.28; p< 0.001), atopy/allergy (OR 7.44, 95% CI 3.71-14.93; p< 0.001), recurrent upper respiratory infections (OR 6.75, 95% CI 3.68-12.37; p< 0.001) and low birth weight (OR 3.57, 95% CI 1.54-8.28; p< 0.001). Highly-recurrent rCAP were associated with a history of asthma diagnosis (OR 3.46, 95% CI 1.48-8.08; p=0.0001), right middle lobe syndrome (OR 3.02, 95% CI 1.36-6.71; p=0.001) and atopy/allergy (OR 2.20, 95% CI 1.10-4.42; p=0.005),.

Conclusion: Pediatric patients with rCAP do not usually have a serious predisposing disease and with a limited number of examinations at least one clinical factor potentially associated with recurrences can be identified.

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INCIDENCE OF CANDIDA SPP INVASIVE INFECTION, IN SPAIN PEDIATRIC INTENSIVE CARE UNITS

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Introduction: Invasive fungal infection (IFI) has a high morbidity-mortality in immunosuppressed and critically ill patients. IFI incidence seems to increase, especially by Candida and Aspergillus pathogens. Candida spp represents the 70-90% of all IFI and C. albicans is the etiology in the 50%.

Aim: To describe the incidence of IFI and of invasive Candidiasis (IC), in Spain Pediatric Intensive Care Units (PICU).

Patients and method: Epidemiological, prospective and multicenter study, from October 2010 to december 2011. Inclusion criteria: patients younger than 18 years, with lengh of stay > 72 hours, admitted at Spain PICUs (36 units). The preliminary estimated incidence was 0.7%, so that the calculated number of patients required results in 742 (precision of 0.6 and statistically significance 0.05).

Results: There were recruited 1.075 patients from 36 PICUs. Were males 58.4%, with mean age of 3.4±4.3 years (55.7% younger than 2y). Principal diagnosis at admission: respiratory disease (34.5%), general surgery (33%), cardiac surgery-congenital malformation (15.2%), oncological (5.2%). The mean of Pediatric Risk Mortality Score was 6.4 ±5.62, median 5 (p25:2, p75:10) (min 0, max 39) points.

Fifty-tree from the 1.075 patients had IFI (4.9%), due to IC in 45 cases (4.2%). C. albicans was the etiology in 26 patients (2.4%) and C. parapsilosis in 15 (1.4%). IFI localization: sepsis 44.1%, urinary 28.3%, catheter infection 19.7%, respiratory 15%, other 14.2%. IC rate was 1.1 cases/1.000 patients/year.

Conclusions: IC incidence was relatively low in Spain PICUs, but surveillance is necessary due to the severity of this infection.

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MICROBIOLOGY OF INVASIVE FUNGAL INFECTIONS IN A TERTIARY PEDIATRIC HOSPITAL DURING A 6-YEARS PERIOD

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Background and aims: Invasive fungal infections (IFI) are an important cause of morbidity, increased hospitalization and healthcare costs in critically ill or immunocompromised children. The purpose of this study was to investigate the microbiology of IFI in our hospital.

Methods: Microbiology records of children hospitalized and diagnosed with IFI at “Aghia Sophia” Children's Hospital, the major tertiary Pediatric Hospital in Greece, from January 2007 to December 2012, were retrospectively analyzed. Only children with blood fungemia were included in the analysis. Identification of isolates was done conventionally and by PCR-sequencing. MICs were measured using gradient MIC method (Liofilchem, MIC Test Strips).

Results: Fungemia was diagnosed in 101 patients 0-14 years of age. Candida albicans was isolated in 48 children (47.5%), Candida parapsilosis in 27 (26.7%), Candida glabrata in 5 (5%), Candida famata in 2 (2%), Candida rugosa in 2 (2%), Candida lusitaniae in 3 (3%), Candida guilliermondii in 2 (2%), Saccharomyces cerevisiae in 5 (5%) and Candida kefyr, Candida tropicalis, Candida zeylanoides, Cryptococcus terreus and Malassesia furfur in 1 (1%) children. C. albicans strains were 97.9% sensitive to amphotericin, 81.2% to fluconazole and 97.9% to caspofungin and 100% to voriconazole. C. parapsilosis strains were 92.6% sensitive to amphotericin and fluconazole and 100% to caspofungin and voriconazole. C. glabrata strains were 100% sensitive to amphotericin, caspofungin and voriconazole, 20% Susceptible Dose Depended (SDD) to fluconazole and itraconazole and 20% resistant to itraconazole.

Conclusions: A significant number of non-Candida albicans invasive infections were identified in our area with different sensitivities to antifungal medications.

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RAPID DETECTION OF NOROVIRUS PSEUDO-OUTBREAK BY USING REAL-TIME SEQUENCE BASED INFORMATION

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Background and aims: Sequence based information is increasingly used in the surveillance of viruses, not only to provide insight in viral evolution, but also to understand transmission during outbreaks. However, sequence analysis is not yet incorporated in laboratory routine, hindering the use in clinical practice. We show that sequence based information, available immediately after detection of the virus, is able to guide infection control measures.

Methods: During the second half of January 2013, a rise in norovirus infections was detected among patients and personnel on the children's hospital oncology ward. Clinical and epidemiological information was collected. Noroviruses were characterized by sequence analysis of the ORF1 region within three days after detection.

Results: Norovirus infection was detected in seven children and two health care workers. Six of seven patients had a nosocomial infection. After notification of the first two patients, additional infection control measures were taken. Despite these measures, again three patients with norovirus infection were notified. Norovirus sequence analysis results became rapidly available in 5/7 patients. Four different genotypes were detected, providing evidence for multiple introductions of different norovirus strains with few secondary cases rather than ongoing nosocomial transmission. This strengthened us to maintain the already implemented infection control measures without closure of the ward.

Conclusion: Sequence based information available in real-time is essential for the understanding of norovirus transmission in the hospital during a season where admission of infected patients occurs frequently. This makes it possible to focus the massive outbreak infection control measures.

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METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS OF NASAL CARRIAGE: A NEW MULTIPLEX PCR TO DETECT SCCMEC TYPES

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Introduction: Methicillin-resistant Staphylococcus aureus (MRSA) is the main pathogen involved in healthcare-associated infections and the nasal colonization is an important risk factor to the development of these infections.

Objectives: The aim of this study was to evaluate a new multiplex PCR to detect SCCmec types of MRSA isolates from nasal source starting from a bacterial culture in oxacillin selective broth (OSB).

Methods: Swabs (n=147) collected from anterior nares of patients attended in a dermatologic pediatric ambulatory and their relatives were plated on mannitol-salt agar (MSA) followed by classical tests for MRSA identification. Following, the same swab was inoculated into OSB tubes with Mueller-Hinton broth supplemented with 7% NaCl and 2ug/ml of oxacillin. After incubation the DNA was liberated by boiling and the PCR multiplex was carried out using eight primers: SA1 and SA2 (S. aureus species-specific), MRS1 and MRS2 (mecA gene), and MECIP3 and MECIP2, and DCS R1 and DCS F2, that are able to distinguish between the SCCmec types II, III and IV.

Results: PCR multiplex method identified 29 (19,7%) MRSA isolates, being 3 (10.3%) type II, 2 (6.9%) type III, 21 (72.4%) type IV and 3 (10.3%) non-typable cassettes.

Conclusions: The new PCR multiplex showed to be a quick and reliable method to detect MRSA isolates recovered from nasal swabs, even community isolates, which frequently are more susceptible to antimicrobials and present resistance to oxacillin closer to breakpoint. In addition, the rapid detection of the SCCmec types could help in control and prevention policy of MRSA infections.

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A NATIONAL POINT-PREVALENCE SURVEY OF PEDIATRIC INTENSIVE CARE UNIT- HEALTH CARE ASSOCIATED INFECTIONS IN TURKEY

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Introduction: This study aimed to determine the epidemiology of the Health care associated infections (HCAIs) in a pediatric intensive care unit (PICU) in a developing country and to define the risk factors associated with HCAIs.

Methods: PICU HCAI Study Group (n = 50 hospitals) participated in a point-prevalence survey on September 27, 2012. Data collected for all PICU in patients included demographics, infections, therapeutic interventions, and outcomes.

Results: There were 327 patients in 50 PICUs. The median age was 48 ± 57 months (range 1-216 months). One hundred twenty two patients had 1 or more HCAIs corresponding to a prevalance of %37. The most frequently reported sites were lower respiratory tract (n=77, 23,5%), blood-stream (n=38, 11,6%) and urinary tract (n=10, 3%). The most frequent pathogens were Pseudomonas aeruginosa (in 30 infections, 42%), Acinetobacter spp. (in 18 infections, 25%) and Candida spp. (in 9 infections, 12%). Hospital type (research and education or university hospital were found to be independent risk factor for HCAIs. Most frequently administered antimicrobials were third generation cephalosporins (19%), carbapenems (14%) and glycopeptides (9%). According to a 4-weeks follow up, 43 (13%) patients died, 28 (8%) of whom died from healthcare-associated infections. Mechanic ventilation and development of HCAIs were found to be independent risk factors for death.

Conclusion: This national multicenter study documented the high prevalence of healthcare associated infections. Preventing these infections should be a national priority.

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BORDETELLA PERTUSSIS INFECTION IN PAEDIATRIC HEALTHCARE WORKERS

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Background: Healthcare workers (HCW) are at increased risk for acquiring pertussis and may transmit the infection to high-risk patients and colleagues.

Objective: To assess the incidence of recent pertussis infection in HCW of pediatric care areas.

Methods: A cross-sectional study was conducted in a Paediatric Department of a tertiary-care referral center, from October to December of 2011, in which HCW (physicians, nurses and nursing assistant) were invited to participate provided they had not been vaccinated against pertussis in the previous twelve months. A self-completed questionnaire was used to record demographic characteristics and previous vaccination history. Serum Pertussis Toxin IgG antibodies were assessed by ELISA. Antibodies above 62.5IU/mL were considered suggestive of infection in the past year.

Results: 388 HCW were included in this survey: 51.8% physicians, 16.5% nurses and 31.7% nursing assistants. The overall incidence of B. pertussis infection was 6.4% (physicians, 7.5%; nurses, 6.3%; nursing assistants, 4.8%). Multivariate analysis demonstrated that medical residents (OR 4.15; 95% CI: 1.42-12.14; p= 0.009) and HCW from Emergency setting and Pediatric Intensive Care Unit (OR 2.49; 95% CI 0.90-6.89; p=0.08) had an increased risk of pertussis infection. Working more than 40 hours a week also increased risk of pertussis infection (OR 3.29; 95% CI 1.17-9.26; p=0.024). By contrast, male gender was associated with lower risk of infection (OR 0.13; 95% CI 0.02-1.01; p=0.051).

Conclusions: Incidence of recent pertussis infection was high among paediatric HCW. Among them, medical residents are at increased risk and should be considered a target group to receive vaccine.

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DURATION OF GASTROINTESTINAL COLONIZATION BY EXTENDED-SPECTRUM B-LACTAMASE (ESBL)-PRODUCING ENTEROBACTERIACEAE AMONG YOUNG CHILDREN DISCHARGED FROM THE NEONATAL INTENSIVE CARE UNIT

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Background and aims: Isolates of Klebsiella pneumoniae and Escherichia coli (Enterobacteriaceae) can become multi-drug resistant by production of extended-spectrum β-lactamases (ESBL´s). In recent years, outbreaks of ESBL-producing Enterobacteriaceae infection and colonization have been reported in neonatal intensive care units (NICU´s). However, there is little information regarding the duration of colonization by ESBL-producing bacteria. The aim of this study was to investigate the length of gastrointestinal colonization by ESBL-producing Enterobacteriaceae in young infants.

Methods: A retrospective cohort study of infants discharged from NICU carrying ESBL+ isolates between 2007-2011. Rectal swabs were taken repeatedly from participants in 2011-2012 and demographic and clinical data collected. ESBL+ isolates were compared by species and antibiograms to original NICU colonizing strains. Infection rates with ESBL+ isolates were examined.

Results: Of 210 children acquiring ESBL+ colonization in the NICU, 65 (31%) aged 1-51 months participated, with at least one rectal swab. The mean gestational age, birth weight, and length of NICU stay were 31 weeks, 1620 grams, and 39 days respectively. Rectal colonization was observed to the age of 6 months. No differences were found in clinical and demographic parameters (such as length of NICU stay and complications) between children under 6 months carrying ESBL+ isolates (n=10) and those who were no longer carriers (n=8). Although 48% of children were readmitted, none were infected with ESBL+ strains. Six (9%) children carried non-NICU ESBL+ isolates.

Conclusion: Rectal ESBL+ carriage after discharge from the NICU is short with no clinical significance. There was evidence of community-acquisition of ESBL+ Enterobacteriaceae.

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DIAGNOSIS OF CONGENITAL CYTOMEGALOVIRUS INFECTION ON DRIED BLOOD SPOTS: ALL PCR'S ARE NOT EQUAL!

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Background and aims: Cytomegalovirus (CMV) infection is the most common congenital infection and the leading cause of non-genetic congenital hearing loss. Within two weeks after birth, infection can be diagnosed by culture or PCR on urine, thereafter by CMV PCR on dried blood spots (DBS) usually collected within one week after birth for newborn screening. Since 2006, Quality Control for Molecular Diagnostics (QCMD) organizes yearly proficiency testing for CMV DNA detection on DBS. We analyzed the performance of the participants over the last 5 years within the context of clinically relevant CMV DNA viral loads.

Methods: Descriptive analysis of proficiency testing on DBS over the past five years in relation to previous results of DBS testing in a population screening setting and in children with bilateral hearing loss.

Results: We reported previously that the median viral load in 35 CMV-DNA positive DBS samples from 6,500 newborns was 5,000 cps/ml (range 400 - 160,000 cps/ml). The viral load in QCMD proficiency samples for CMV-DNA detection on DBS usually ranges between 100,000 and 500 cps/ml. Approximately 90 % of participants were able to detect CMV in samples with ≥ 5000 cps/ml, but only 50 % in samples with 200 to 5,000 cps/ml.

Conclusions: Although the disease burden of congenital CMV is increasingly acknowledged, the use of DBS for diagnosis is still limited. The highly variable and sometimes alarmingly poor performance of some laboratories may be part of the reason. However, the approach has clear potential as shown by a number of laboratories.

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ACOUSTIC REFLECTOMETRY PERFORMED BY TRAINED NURSES IN DETECTING ACUTE OTITIS MEDIA IN YOUNG SYMPTOMATIC OUTPATIENTS

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Background and aims: Spectral gradient acoustic reflectometry (SG-AR) is an adjunctive diagnostic tool for pneumatic otoscopy to detect the presence or absence of middle ear effusion. Since the incidence of acute otitis media (AOM) is high in young children, reliable ear examination performed by nurses would save physicians' time. Our aim was to determine whether trained nurses can use SG-AR as a diagnostic tool to detect AOM in young symptomatic children.

Methods: In outpatient setting, we trained 3 nurses to perform SG-AR. These nurses performed SG-AR on 284 symptomatic children aged 6-35 months. The proportions of 5 manufacturer-recommended SG-AR levels were compared with pneumatic otoscopy performed by the study physician.

Results: The nurses performed a total of 782/892 (88%) successful SG-AR examinations. When SG-AR showed level 1 (angle value >95°) result, AOM was diagnosed in 10/159 (6%) of otoscopic examinations. With level 2 (70-95°) and level 3 (60-69°) results, AOM was diagnosed in 33/245 (13%) and 32/109 (29%) of examinations, respectively. With level 4 (49-59°) and level 5 (< 49°) results, AOM was diagnosed in 40/110 (36%) and 94/159 (59%) of otoscopic examinations, respectively.

Conclusions: Performed by trained nurses, SG-AR level 1 result seems to exclude AOM in young symptomatic children. However, even SG-AR level 5 result does not reliably indicate AOM. Therefore, pneumatic otoscopy is needed to make the accurate diagnosis.

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HIGH PREVALENCE OF ACUTE RESPIRATORY TRACT INFECTIONS IN EÑEPA AMERINDIANS IS POSITIVELY ASSOCIATED WITH STREPTOCOCCUS PNEUMONIAE CARRIAGE

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Background: High prevalences of acute respiratory tract infections (ARTIs) and acute otitis media (AOM) have been observed in Latin American indigenous populations. The aetiology of ARTIs and AOM in these geographically isolated populations is poorly understood.

Methods: A total of 82 Eñepa Amerindian children, of which 40 suffered from an ARTI, were included in a case-control study. Nasopharyngeal and oropharyngeal samples of children and their mothers were collected and the presence of Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus and Moraxella catarrhalis was investigated by bacterial culture. In addition, the presence of 17 distinct respiratory viruses, Mycoplasma pneumoniae and Chlamydophila pneumoniae/psittachi was screened by real-time PCR.

Results: S. pneumoniae (75%), M. catarrhalis (27%), H. influenzae (21%), S. aureus (21%), rhinovirus (10%), enterovirus (7%), influenza virus A H1N1 (6%), human bocavirus (3%), adenovirus (1%), human metapneumovirus (1%), respiratory syncytial virus (1%) and Chlamydophila pneumoniae (1%) were detected in children. Bacterial colonization rates in mothers were extraordinary high; 52% carried at least one bacterial pathogen. S. pneumoniae carriage was significantly higher in childhood cases of ARTI and AOM compared to controls (resp. $p< 0.01$ and $p=0.018$). When at least one bacterial pathogen was detected, co-infection with enterovirus was significantly associated with a higher risk of AOM compared to no detection of enterovirus ($p=0.037$).

Conclusions: This study shows a positive association between S. pneumoniae carriage and ARTI and AOM in Amerindian children under 11 years of age. In the presence of bacterial carriage, enterovirus appears to play a significant role in AOM development.

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QUALITY CARE IMPROVEMENT APPROACH TO REDUCE INFECTIONS IN CHILDREN WITH ACUTE LEUKEMIA

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Background and aims: Patients with acute leukemia have high risk of severe infections. We applied a Quality care Improvement (QCI) approach to reduce the incidence of infectious episodes and central-line blood stream infections (CLABSI) in children with acute leukemia.

Methods: A multidisciplinary team of physicians and nurses reviewed local procedures and identified the main gaps between evidence-based recommendations and current clinical practice. Baseline infection rate/1000 patients-at-risk-days and CLABSI/1000 CVC-days were considered as main outcome measures. After a 27-month retrospective and prospective observation, we carried out a multifaceted intervention based on up-to-date of CL management procedures and personnel education. Baseline data were compared with those obtained for 3 months after the intervention.

Results: 139 infections were recorded in 70 children. Mean duration of fever and hospitalization was 4.06 and 18.38 days, respectively. Most episodes occurred in children with acute lymphoblastic leukemia, but patients with acute myeloid leukemia had a higher risk of recurrence (OR=5.19,95%CI:2.8-9.5). The QCI approach included the following major interventions based on identification of local failures and barriers: promotion of Maximal Sterile Barrier Precautions, replacement of povidone-iodine with chlorhexidine, antibiotic-resistance monitoring, introduction of checklists for device management. Infections rate results are in the table.

Outcome measures	Baseline	At 3 months after multifaceted intervention
Infection rate/1000 patient at risk-days (95%CI)	23.6(0-62)	17.5(0-57)
CLABSI/1000 device-days (95%CI)	9.17(0-36)	6.88(0-31)

[Infection rates before and after interventions]

Conclusion: Update of procedures and presence of an infection control system are key steps to reduce infections in high-risk patients. A multifaceted QCI process may reduce infections in children with leukemia.

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THE EFFECT OF A SACCHAROMYCES BOULARDII ON THE DURATION OF DIARRHEA IN CHILDREN WITH ACUTE DIARRHEA IN TURKEY (PROBAGE STUDY)

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Background: Systematic review and meta-analysis of the efficacy of Saccharomyces boulardii concluded that there is strong evidence that this probiotic has a clinically significant benefit in the treatment of acute infectious diarrhea in children.

Methods: In this multicenter, randomized, prospective, controlled, single blind clinical trial which was performed in children with acute watery diarrhea, we aim to evaluate the effect of S. boulardii in children requiring hospitalization, requiring emergency care unit (ECU) stay and outpatient settings. The primary endpoint was the duration of diarrhea (in hours). Secondary outcome measures were duration of hospitalization (days, if available), diarrhea at the 3rd day of intervention.

Results: In total, data from 337 children could be evaluated (190 S.boulardii and 147 controls). The clinical characteristics and severity of gastroenteritis did not differ; stool frequency during the 24 hours prior to admission was similar. The duration of diarrhea was significantly reduced in the S.boulardii group in hospital, ECU and outpatient settings ($p< 0.001$, $0< 0.01$,$p< 0.001$, respectively). The number of stools per day was significantly lower in the S.boulardii group after 48 and 72 hours. The percentage of children that was diarrhea-free was significantly larger after 48 and 72 hours in all settings. Mean length of hospital stay and ECU stay was shorter in the S.boulardii group than the control group ($p< 0.001$and $p< 0.01$,respectively).

Conclusion: S.boulardii is a very effective probiotic in acute gastroenteritis, reducing both the duration of acute diarrhea in hospitalized and outpatients as well as reducing the hospital stay.

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AN APPROPRIATE INSERTION BUNDLE CAN MINIMIZE THE INCIDENCE OF CATHETER-RELATED BACTEREMIA IN A PEDIATRIC INTENSIVE CARE UNIT

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Background and aims: Catheter-related blood stream infections (CRBSI) are associated with a significant mortality and morbidity, particularly in critically ill children. In our Pediatric Intensive Care Unit (PICU), we have recently adopted a specific ´bundle´ of recommendations for the insertion of central venous catheters (CVC), aiming to minimize such complication.

Methods: We reviewed all CVC inserted in our PICU in the last 20 months, excluding PICCs and emergency CVCs. In this time period, elective CVCs were inserted according to this ´bundle´:

(1) hand washing and maximal barrier precautions;

(2) skin antisepsis with 2% chlorhexidine;

(3) ultrasound guided venipuncture;

(4) tunneling of the catheter so to obtain an exit site in the infraclavicular area;

(5) sealing of the exit site with glue;

(6) securement with sutureless device;

(7) coverage with transparent semipermeable dressing.

Results: We inserted 183 CVC in 165 patients (15 aged < 1 month, 70 aged 1-12 months, 80 aged 1-6 years). All CVCs were inserted by supraclavicular approach, in the brachio-cephalic vein (n=167), or internal jugular vein (n=10), or subclavian vein (n=3), or external jugular vein (n=2). We had no insertion failures and no puncture-related complcations. In 85% of cases, the vein was punctured at first attempt. The average dwelling time was 16±9 days. We had two episodes of CRBSI (0.6 episodes per 1000 catheter days), diagnosed by delayed time to positivity after paired blood cultures from the CVC and from a peripheral vein.

Conclusion: An appropriate insertion bundle minimizes CRBSI even in critically ill pediatric patients.

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HERD EFFECT RELATED TO ROTAVIRUS VACCINATION: OBSERVED DATA VERSUS MODEL PROJECTIONS

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Background and aims: Quantifying the indirect effect of vaccination is challenging because of the difficulties to design a proper study. Modelling is often used to estimate both direct and indirect effects. Therefore checking against real-life data is needed and more important for rotavirus vaccination. We estimate the accumulated and time-specific herd effect of rotavirus vaccination by comparing model severe rotavirus-gastroenteritis cases with observed hospitalization data over 5 years post-vaccination in Belgium.

Methods: Using Belgian coverage, a static model was used to estimate the direct effect and a dynamic model was used to estimate both direct and indirect effects of rotavirus vaccination in children ≤5 years. Both model estimates were compared to observed data.

Results: Comparing the observed yearly data of vaccine impact with the direct effect modelling results shows that the vaccine indirect effect is high in the 1st year (13.5%) and low in the 5th year post-vaccine introduction (4.6%). The estimated accumulated indirect effect after 5 years was 7.3% for an 86%-vaccine coverage. When dynamic model was compared with observed data, the total effect (direct and indirect) was lower in the 1st year (-3.8%) and higher in the 5th year (+10.8%), while the 5-year accumulated total effect was +8.5%. Literature reports an indirect effect between 4-10% of vaccine effectiveness depending on the vaccine coverage rate (70-90%).

Conclusions: Static model underestimated full effect of vaccination, while dynamic model somewhat overestimated it after first year. However initial herd effect could be large and consequently critical where vaccine uptake is limited.

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ASSESSMENT OF PCR AS SCREENING METHOD FOR INVASIVE ASPERGILLOSIS IN PEDIATRIC CANCER/ALLOGENEIC HSCT PATIENTS

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Background: Invasive aspergillosis (IA) remains difficult to diagnose at an early stage. We analyzed the predictive value of an Aspergillus-specific polymerase chain reaction (PCR) assay in blood as sceening method for IA in children and adolescents with cancer and/or allogeneic HSCT.

Methods: 95 patients (median: 9.5, range: 0.5 to 20.5 years; hematological malignancies, 55%, solid tumors, 28%, non-malignant hematological disorders, 17%; 11 patients s/p allogeneic HSCT) were included over a period of 3 years. Using a validated 2-step PCR method, we analyzed 253 unselected episodes with signs and symptoms of infection (i.e., fever with or without granulocytopenia, resulting in a microbiological work up and antimicrobial treatment).

Results: 38 patients (56 episodes) had possible IA whereas none of the patients fulfilled EORTC/MSG criteria of probable/proven IA. 97/984 PCR analyses (9,9 %) were positive for Aspergillus-specific nucleic acid sequences. Sensitivity, specificity, positive and negative predictive values of the PCR per episode were 34%, 78%, 31%, and 81%, respectively, using possible IA as endpoint. Multivariate analysis revealed significant correlations of positive PCR signals with antineoplastic and antifungal chemotherapy, but not with the presence of pulmonary infiltrates, detection of galactomannan antigen, prior IA, granulocytopenia, diagnosis of leukemia, s/p allogeneic HSCT, GVHD, immunosuppressive therapy, and mortality at 3 months.

Conclusions: The results suggest that an undirected screening by PCR in peripheral blood is of little diagnostic value. Further efforts to harness PCR for early diagnosis of IA should be directed at focussed analyses in high-risk patients in clinical situations where IA needs to be excluded.

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USE OF NASOPHARYNGEAL STREPTOCOCCUS PNEUMONIAE (SP) LOAD TO DEFINE PNEUMOCOCCAL ETIOLOGY OF COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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Background and aim: Pneumococcal CAP is frequently associated with chest X-ray findings suggesting alveolar involvement. Recently, it has been reported that determination of nasopharyngeal Sp load could be useful for the identification of pneumococcal etiology in CAP. However, no data are available about the association between nasopharyngeal Sp load and alveolar CAP as well as the relevance of viral coinfections in conditioning bacterial load.

Methods: On nasopharyngeal secretions of 386 children aged < 5 years with radiographically-confirmed CAP, the presence of 17 respiratory viruses and of Sp was evaluated by means of Luminex xTAG Respiratory Virus Panel Fast assay and by specific real-time polymerase chain reaction (PCR) for LytA and wzg (cpsA) Sp genes. Nasopharyngeal Sp load was calculated and analyzed according to chest X-ray characteristics.

Results: A total of 209 children (54.1%) were found positive for Sp and 309 (80.0%) for viruses. In alveolar CAP cases, both positivity for Sp and nasopharyngeal bacterial load were significantly more common (59.2% vs 44.8%; p = 0.0076) and higher (4.13 ± 1.41 vs 3.63 ± 1.55 log10 copies/mL; P = 0.025) than in children with non alveolar CAP. Children with viral coinfection(s) had similar Sp load than children without (3.94 ± 1.37 vs 4.01 ±1.52 log10 copies /mL; P = 0.75).

Conclusion: Higher nasopharyngeal Sp load is more common in children with alveolar CAP suggesting that determination of this variable can contribute to the definition of pneumococcal etiology of CAP. Viral coinfections do not influence bacterial load.

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OPTIMIZATION OF THE ETIOLOGY OF VIRAL ACUTE GASTROENTERITIS - PROSPECTIVE MULTICENTER STUDY

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Background and aims: Our aim is reduce the number of Acute gastroenteritis(AGE) episodes without etiology, using reverse transcription-polymerase chain reaction(RT-PCR) and verify if ESPGHAN/ESPID recommendations are followed.

Methods: Prospective multicenter study that includes individuals under eighteen years, with AGE, attending ER of four main Minho hospitals, between April 2011 and March 2012. Questionnaire, concerning epidemiological/clinical findings and treatment was filled, stool samples were collected and tested by RT-PCR for rotavirus(RV), noroviruses(NV), adenovirus(AdV) and enterovirus(Echo).

Results: Questionnaire were answered by 518(Males:320) and 250(Males:152) stool samples collected. Median age was 21(range:1-215) months. RV was detected in 15.6%(39/250), NV in 13.2%(33/250), AdV in 2.5%(13/250) and Echo in 1.9%(10/250). There were 2 co-infections RV/NV, 1 NV/AdV and 1 Echo/Adv. From RV positive samples 2 children were vaccinated. Twenty eight(89.7%) cases of RV positive samples and 29(87.9%) of NV occurred under 5 years. Viral AGE(VAGE) was predominant in March(88.9%,8/9), followed by January(75%,6/8) and February(68.8%,11/16). Most cases of RV happens in April(43.6%,17/39) and NV in May(21.2%,7/33). NV was most prevalent VAGE in October(83.3%,5/6) and represented 36.3% of all VAGE. Sixty two children were hospitalized and 103 remained under observation. After discharge 15.7%(68/433) were advised to change diet, 1.4%(6/420) stop feeding>4h and 6.1%(26/427) to use special formula. ORS was recommended to 78.1%(335/429). Antibiotic weren`t prescribed.

Conclusion: This is the first multicenter study in Portugal with research of NV. RV was most frequent viruses isolated but closely followed by NV. The conduct on AGE was mostly based on ESPGHAN/ESPID recommendations, however still seems necessary emphasize these recommendations.

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BACK TO THE FUTURE: A SYSTEMATIC METHODOLOGICAL REVIEW OF EMERGING APPROACHES FOR DETECTING RENAL SCARRING IN PEDIATRIC UTI

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Background: Despite continuing debate, attention is moving from VUR to scarring, the most clinically relevant end-point, associated with worse renal outcomes in early adulthood. Selective approaches for UTI investigations reduce cost and distress, but misdiagnosis of the fewest possible patients with significant conditions remains the fundamental objective. We aimed to systematically review decision algorithms available.

Methods: Systematic review of such decision algorithms.

Results: The top-down approach yielded a 75-96 % sensitivity and a 52-60% specificity for VUR. Renal US was not very sensitive for acute pyelonephritis (APN), dilating VUR, neither scarring (sensitivity: 46-63%), but offered a better specificity (62-93). Interestingly, ureteral dilation yielded a higher sensitivity (75%) with a 60% specificity. CRP yielded a 53-82% sensitivity for APN, VUR or scarring, with a 62-75% specificity for APN but a 28-56% for VUR and scarring. All Oostenbrink's, Wang's and Preda's algorithms combined Renal US with CRP: Oostenbrink yielded a 100% sensitivity for dilating VUR but with a validation 3% specificity, Wang's rule better predicted VUR (sensitivity: 86%, specificity: 79%), Preda's algorithm offered 85% sensitivity and 59-65% specificity for VUR and scarring. Procalcitonin offered a 65-92% sensitivity with 30-85% specificity for all three outcomes, which was not improved when combining with renal US.

Conclusion: Renal US and VCUG alone are not reliable. Scores failed to confirm promising predictive value. Biomarkers provide an interesting alternative, endorsing translational proteomic strategies. Future algorithms may therefore focus more on scarring, with less emphasis on VUR, and possible incorporation of proteomic tools, to provide optimal individualized nephroprotection.

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EFFECTIVENESS OF A HANDWASHING PROGRAMME IN THE PREVENTION OF SCHOOL ABSENTEEISM DUE TO RESPIRATORY INFECTIONS

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Background: Respiratory infections are an important cause of school absenteeism. The aim of the study was to assess the effectiveness of a hand-washing programme using hand sanitizer in the prevention of school absenteeism due to upper respiratory infections.

Methods: A cluster, randomised, controlled and open study of a sample of 1,341 children aged 4-12 years old, attending 5 Public Schools in Almería (Spain), with eight months follow-up. The experimental group (EG) washed their hands with soap and water, complementing with the use of hand sanitizer, and the control group (CG) followed the usual hand-washing procedure. Rates of absenteeism due to upper respiratory infections were compared between the two groups through Poisson Regression Analysis. Multiple regression analyses were done to study the socio-demographic factors related to school absenteeism due to upper respiratory infections

Results: 1,271 cases of school absenteeism due to respiratory infections were registered, including those who required medical attention (68%). The schoolchildren from the EG had a 38% lower risk of absenteeism due to respiratory infections (IRR: 0,62, CI 95%: 0,55-0,70); 0,72 (0,64-0,69%), a decreases absenteeism of 0.45 episodes/ child/ academic year (0.72 vs 1.17/episodes/child/academic year) and decrease in the duration of each episode of absence by 0.75 days (2.41 of GC vs 1.66 of GE; $p< 0.001$); NNT= 2,21 (CI95: 2,13 - 2,31).

Conclusions: The use of hand sanitizer and the dissemination of educational messages play an important role to improve hygienic practice in the hand-washing of school children, reducing the school absenteeism caused by respiratory infections.

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A FLUORESCENT MULTIPLEXED MICROSPHERE IMMUNOASSAY (FMIA) FOR QUANTITATION OF IGG AGAINST STREPTOCOCCUS PNEUMONIAE, HAEMOPHILUS INFLUENZAE AND MORAXELLA CATARRHALIS PROTEIN ANTIGENS

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Background and aims: Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis are pathogens commonly associated with infectious diseases in childhood. This study aimed to develop a new fluorescent multiplexed microsphere immunoassay(FMIA) using recombinant proteins for the quantitation of antibodies against these bacteria.

Methods: Eight pneumococcal proteins(PcpA,PhtD-supplied by Sanofi-Pasteur; Ply,CbpA,PspA1,PspA2-supplied by St.Judes Children's Research Hospital,Memphis,TN and University of Alabama,Birmingham,AL; SP1732-3 and SP2216-1), 3 proteins of H. influenza(NTHi-Protein-D,NTHi0371-1,NTHi0830) and 5 proteins of M. catarrhalis(MC-Omp-CD,MC-RH4-2506, MC-RH4-1701,MC-RH4-3729-1,MC-RH4-4730) were used to develop bead-based immunoassay with Luminex xMAP®Technology. Correlations determined from linear regression analysis of the Mean Fluorescence Intensity(MFI) values obtained in singleplexed and multiplexed assays were evaluated. Inhibition-of-binding studies were conducted to confirm the specificity. Comparison with ELISA was performed using samples previously assayed for anti-Ply,-CbpA,-PcpA and -PhtD. Reproducibility was evaluated by determining the intra-assay and inter-assay(day-to-day) variation, and the variation produced by 2 technicians.

Results: The FMIA was specific, reaching>92% homologous inhibition for all specificities and there were six cases of heterologous inhibition. Correlation between the singleplexed and multiplexed assay was excellent, with R≥0.978 for all antigens. Comparison with ELISA demonstrated good correlation(R=0.89 for Ply;R=0.828 for CbpA;R=0.952 for PcpA;R=0.842 for PhtD). The reproducibility was good; with averages of intra-assay variation≤10.5%, day-to-day variation≤9.7% and variation between technicians≤9.1% for all antigens.

Conclusions: The developed FMIA was sensitive, specific, reproducible and economic, using small amounts of recombinant proteins and sera to detect antibodies against S. pneumoniae, H. influenzae and M. catarrhalis. The assay would be suitable for studies for etiological diagnosis and vaccine trials.

Acknowledgements: We thank Intercell for supplying:SP1732-3,SP2216-1,NTHi-Protein-D,NTHi0371-1,NTHi0830,MC-Omp-CD,MC-RH4-2506, MC-RH4-1701,MC-RH4-3729-1and MC-RH4-4730.

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NEONATAL SEPTICEMIA IN A TERTIARY LEVEL MATERNITY AND NEONATAL UNIT

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Introduction: Neonatal infection being an important cause of morbidity and mortality, surveillance is necessary for monitoring changes over time.

Design: Prospective study in a tertiary level neonatal unit.

Participants: Newborns admitted in NICU between 2009-2012 staying for more than 3 days with positive blood culture and treated with antibiotics.

Outcome measure: Incidence, pathogens, demographic data, mortality due to sepsis and antibiotic susceptibility profiles.

Results: 6524 babies born during the study period, among which 1206 were admitted to NICU. Total 763 babies met the inclusion criteria. The incidence of neonatal infection was 0.5% of live births and 4.6% of neonatal admissions. Majority of infections (77 %) occurred in babies < 34 weeks gestation of which 44.4% occurred in babies < 28 weeks. Gram negative pathogens (65%), Klebsiella and Serratia were the two most common organisms followed by gram positive (35%) bacteria, Staphylococcus Aureus and Enterococcus. Neonatal mortality rate was 3.6% (24 of 6524) of live births. Death due to sepsis was 8.3% (2 out of 24) of live births. Amikacin used in our unit covered 95% of the gram negative organisms isolated.

Conclusions: Lower rates of sepsis and decreased mortality can be achieved by simple, effective measures of sterilization. Gram negative infections are still the most common cause of sepsis in NICU. But there is emergence of new infections with Serratia and Burkholderia. Our data showed that Cephalosporin/ Amikacin combination can be used as second line antibiotic followed by Vancomycin/ Meropenem as reserve drug and emerging pathogens showed similar susceptibility.

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EFFECTIVENESS OF THE 10-VALENT PNEUMOCOCCAL HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE (PHID-CV10) AGAINST HOSPITAL-DIAGNOSED PNEUMONIA IN INFANTS- FINIP TRIAL

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Background and aims: FinIP trial was designed to evaluate vaccine effectiveness (VE) of PHiD-CV10 (GlaxoSmithKline) against several disease endpoints associated with S. pneumoniae and non-typeable H. influenzae.

Methods: In this nationwide cluster-randomized, double-blind trial, children enrolled < 19 months received PHiD-CV10 in two thirds or hepatitis vaccines as control in one third of clusters according to 3+1 or 2+1 schedules (infants < 7 months) or catch-up schedule (age 7-18 months). This preliminary analysis included subjects enrolled in FinIP and the nested acute otitis media trial from February 2009 onwards in 78 clusters and followed from each subject's first vaccination to December 31, 2011. Outcome data were collected from the National Care Register covering all care provided in Finnish hospitals. Hospital-diagnosed pneumonia (HDP) was any register-based event with pneumonia ICD10-diagnosis: J10.0, J11.0, J12 to J18, J85.1 or J86. Hospital-treated primary pneumonia (HTPP) was HDP resulting in inpatient hospitalization with pneumonia as the primary discharge diagnosis. VE was calculated against all pneumonia episodes, new episode starting if >90 days had elapsed from the beginning of the previous one.

Results: Incidences of HDP and HTPP in infant control group were 13.2 and 6.0/1000 person-years, respectively. VE in infant 3+1 and 2+1 schedules and catch-up groups are summarized below.

Pneumonia endpoint	Infant schedule 3+1	Infant schedule 2+1 (N total = 15 313)	Catch-up schedule (N total= 15 447)
HDP	25.2 % (2.6 - 42.6 %)	27.6 % (5.5 - 44.6 %)	27.1 % (8.8 - 41.8 %)
HTPP	24.6 % (-2.2 - 44.3 %)	29.5 % (3.9 - 48.3 %)	33.5 % (5.3 - 53.3 %)

[VE (95% CI) of PHiD-CV10 against pneumonia]

Conclusions: PHiD-CV10 provided remarkable protection against pneumonia in both 3+1 and 2+1 schedules.

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IMMUNOGENICITY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ADMINISTERED ACCORDING TO 4 DIFFERENT PRIMARY IMMUNISATION SCHEDULES IN HEALTHY INFANTS: THE PIM STUDY

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Introduction: Immunization schedules for PCV differ largely between countries with respect to number of doses, interval between doses, and age at first dose. To assess the optimal primary schedule, we performed an open-label parallel-group randomized controlled trial in the Netherlands to compare immunogenicity of PCV13 in four different immunization schedules.

Methods: We randomly assigned 400 healthy infants to receive PCV13 at 2-4-6 months, 3-5 months, 2-3-4 months or 2-4 months with a booster dose at 11 months. All infants received DTaP-IPV-Hib vaccine at 2-3-4-11 months. Blood samples were collected 1 month after primary series, at 8, 11 and 12 months. Primary outcome measure was IgG antibody level against PCV-13-included serotypes at 12 months measured by multiplex immunoassay.

Results: After the booster, virtually no differences in GMC levels were observed and seroprotection levels were similar for all schedules (94%-100%). Post-primary series, the 2-4-6 schedule was found superior to the 3-5, 2-3-4 and 2-4 schedules for 3, 9 and 10 serotypes, respectively. Likewise, the 3-5 schedule was superior to the 2-3-4 and 2-4 schedules for 5 and 11 serotypes, respectively. The 2-3-4 schedule was superior to the 2-4 schedule for 5 serotypes.

Conclusions: Optimal timing proved to be more important than number of doses preferring the 2-4-6 and the 3-5 over the 2-3-4 and 2-4 schedules. However, the optimal primary schedule based on effectiveness of the immune responses has to be weighed against the need for early protection depending on country-specific pneumococcal epidemiology, especially in the absence of established herd protection.

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IMPACT OF 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV10) AGAINST INVASIVE PNEUMOCOCCAL DISEASE (IPD) AMONG VACCINE-ELIGIBLE CHILDREN IN FINLAND

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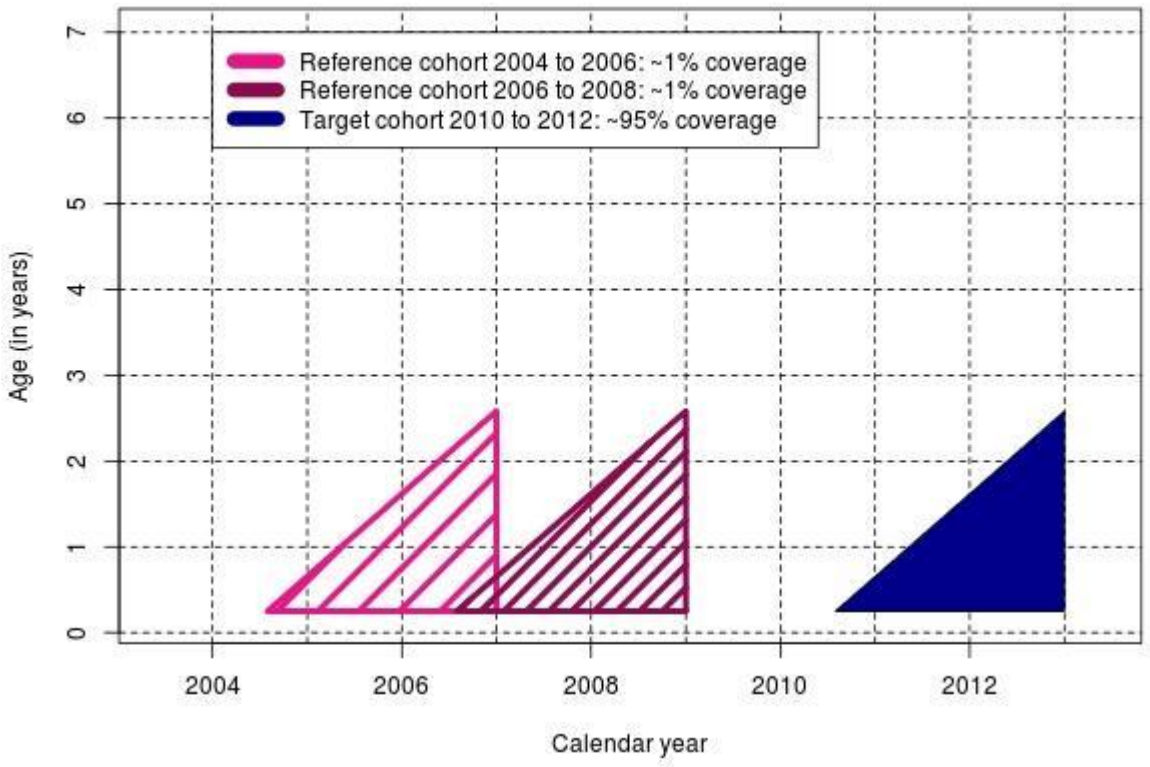
Background: PCV10 was introduced into Finnish National Vaccination Programme (NVP) in September 2010 using a 2+1 schedule (3,5,12 months). We evaluated the impact of PCV10 against IPD among vaccine-eligible children two years after the NVP-introduction.

Methods: The target cohort eligible for NVP (children born 06/2010-09/2012) was compared with two calendar-time and age-matched (3-29 months) cohorts before NVP-introduction (Figure). Period 01/2009-08/2010 was excluded because of PCV10-trial conducted in Finland. National Infectious Disease Register data were used for calculating culture-confirmed serotype-specific IPD-rates in these cohorts.



[Cohorts for comparing PCV10-impact in vaccinated]

Results: By 12/2012, no PCV10 or PCV10-related (i.e. serotypes belonging to the same serogroup as PCV10) IPD cases were reported among children >5 months in the target cohort who had received >1 dose of PCV10. Table shows the IPD-rates/100,000 person-years (N cases) by cohort, and the relative rate reduction in the target cohort compared with the combined reference cohorts.

	Reference cohort 2004-2006 (N=135,987)	Reference cohort 2006-2008 (N=138,489)	Reference cohorts combined	Target cohort 2010-2012 (N=142,206)	Relative rate reduction % (95%CI): Target vs. reference cohorts
PCV10 serotypes	56.3 (89)	42.2 (68)	49.2 (157)	6.7 (11)	87 (76, 93)
PCV10-related serotypes	5.7 (9)	8.1 (13)	6.9 (22)	0 (0)	100 (91, 100)
19A (PCV10-related)	2.5 (4)	4.3 (7)	3.4 (11)	0 (0)	100 (79, 100)
Non-PCV10 or non-related serotypes	5.1 (8)	2.5 (4)	3.8 (12)	3.6 (6)	3 (-209, 70)
Undefined	2.5 (4)	1.2 (2)	1.9 (6)	1.8 (3)	3 (-422, 82)
Any culture-confirmed IPD	69.5 (110)	54.0 (87)	61.7 (197)	12.1 (20)	80 (69,88)

[Rates of IPD in reference and target cohorts]

Conclusions: We observed a significant reduction in IPD-rate among vaccine-eligible children after NVP introduction. PCV10 appears to provide cross-protection also against PCV10-related IPD in the vaccinated children.

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ANTIBODY PERSISTENCE TO PRE-SCHOOL YEARS FOLLOWING IMMUNISATION AT 2, 4 AND 12 MONTHS WITH 7-VALENT AND 13-VALENT PNEUMOCOCCAL GLYCOCONJUGATE VACCINES

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Background/Aims: In a previous UK multi-centre study, children were randomised to receive 7-valent (PCV-7) or 13-valent (PCV-13) pneumococcal conjugate vaccine at 2, 4 and 12 months of age. At 13 months >90% of these children had opsonophagocytic activity (OPA) titres ≥8, for the serotypes against which they had been immunised.

Methods: 108 children who had participated in the original study were enrolled again at 3.5 years of age. Serum OPA titres were determined before and after a PCV-13 booster.

Results: Before the PCV-13 booster >71% of participants had OPA ≥8 for the 'shared' serotypes except for serotypes 4 (PCV-13 group: 30%; PCV-7 group: 29%), 18C (52%; 57%) and 19F (PCV-13 group: 63%). For the 6 'additional' serotypes, OPA ≥8 were observed in >74% of PCV-13 group participants for serotypes 3, 6A, 7F and 19A, but were lower for serotypes 1 (27%) and 5 (35%). In the PCV-7 group, >45% of participants had OPA ≥8 for serotypes 3, 6A, 7F and 19A; 4% for serotype 1 and 0% for serotype 5. Following the PCV-13 booster, 100% of participants from both groups had OPA ≥8 for all serotypes. These results are consistent with previously reported ELISA IgG data.

Conclusions: This is the first study assessing persistence of functional antibody following infant pneumococcal vaccination. Despite some decline in antibody from 13 months of age, these data suggest children receiving PCV-13 at 2, 4 and 12 months are unlikely to require a further booster as the majority maintain protective levels until the pre-school years.

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CLINICAL SIGNIFICANCE OF CO-INFECTIONS WITH VIRUSES AND BACTERIA

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Community-acquired pneumonia (CAP) in children is a leading cause of childhood morbidity and mortality, mainly in the developing world. Prompt etiological diagnoses is still limited by inadequate clinical, radiological and laboratory methods.

Streptococcus pneumoniae, is still the main pathogen of CAP at children under the age of 5. Respiratory viruses are implicated in CAP, respiratory syncitial virus being a leading pathogen.

Rhinoviruses and influenza are shown to play an important role. In recent years several reports have underlined that almost one quarter to one third of the CAP are due to viral-bacterial coinfection.

The viruses seem to pave the way for airway colonising bacteria. Studies have shown that the optimal timing for bacterial infection to develop into CAP is around the 4^{th} day of the viral infection. These findings were measured by different inflammatory parameters and also demonstrated by electron-microscopy and fluorescence microscopy.

RSV and influenza viruses can enhance the adherence of S. pneumoniae to respiratory epithelial cells.

RT-PCR is a new diagnostic tool that may enhance the accuracy of diagnostic and treatment at children with CAP. The clinical outcome, for coinfection versus single infection, has been shown to be different and worse, calculated in hospitalization days compared to single infection.

The clinical implication of mixed viral bacterial coinfection is far from being resolved.

Treatment and prevention options of CAP in children should include modalities for viral etiologies such as anti influenza drugs along with vaccination against S. pneumoniae, H. influenzae and against viral etiologies such as Influenza.

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GENE EXPRESSION PROFILE AND CORRELATION WITH SEVERITY OF ILLNESS AMONG CHILDREN WITH ACUTE HEMATOGENOUS OSTEOMYELITIS CAUSED BY METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS

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Background and aims: Gene expression of children with invasive Staphylococcus aureus infections is characterized by elevated neutrophil activity and diminished adaptive immunity. Our aim was to assess gene expression of children with acute hematogenous osteomyelitis (AHO) from methicillin-resistant Staphylococcus aureus (MRSA) and the correlation of gene expression with illness severity.

Methods: 10 children with AHO, culture positive for MRSA, were consecutively evaluated to calculate a severity of illness score. Whole blood was drawn within 48 hours of admission for subsequent gene expression analysis. Amplified biotin-labeled cRNA was hybridized to Illumina Sentrix BeadChips. Gene expression and modular analyses were performed and compared to healthy controls. Statistical correlation with severity of illness scores was assessed with logistical regression analysis.

Results: 23,023 transcripts were compared between the children with MRSA osteomyelitis and healty, age-matched control subjects. After hierarchical and condition clustering, 269 transcripts were significantly different between groups ($p < 0.05$) (Welch t-test with Benjamini and Hochberg False Discovery). Modular analysis demonstrated over-expression of neutrophil response and under-expression of lymphocyte and cytotoxic T cell response. Ultimately 58 transcripts were over-expressed in the MRSA cohort. Severity of illness scores ranged from 4 to 10 among the MRSA cohort. However, there was no correlation between clinical severity of illness and relative magnitudes of gene over-expression.

Conclusions: Children with MRSA osteomyelitis demonstrate enhanced neutrophil response and diminished adaptive immunity by gene expression during the acute phase of illness. The magnitude of gene expression does not correlate with clinical severity of illness score.

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EFFECT OF FEEDING TYPE ON THE COMPOSITION OF THE NASOPHARYNGEAL MICROBIOTA IN INFANTS

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Background and aims: Breastfeeding has shown to reduce episodes of respiratory infections in infancy. Several compounds in breastfeeding might contribute to this protective effect, nevertheless the exact mechanisms are unclear. Breastfeeding has shown to induce a more beneficial microbiome profile of the gut. We therefore hypothesized that breastfeeding might influence respiratory health by influencing bacterial colonization patterns, i.e. the microbiota, of the upper airways. We therefore compared the microbiota of the nasopharyngeal region of breastfed with formula-fed children.

Methods: From a well-characterized Dutch collection, nasopharyngeal swabs from 87 exclusively breastfed (until 6 months of age) and 101 formula-fed infants collected at the age of 6 weeks and 6 months were analyzed by 16s based sequencing.

Results: We observed age-related effects on microbiota composition with higher microbial diversity and differences in bacterial composition at 6 weeks compared to 6 months of age. Nasopharyngeal microbiota profiles of breastfed children were significantly different from formula-fed children (nMDS, p=0.001) with significant increased abundance of clusters of Corynebacterium spp (RR=7.3, p=0.001) and Dolosigranulum (RR 14.9, p=0.003) and decreased abundance and/or presence of a large cluster of Streptococcal species and anaerobes like Prevotella and Veillonella. In 6-month-old infants, this difference had merely disappeared.

Conclusions: Our data strongly suggest an effect of breastfeeding on bacterial colonization of the upper respiratory tract in 6-week-old infants. Observed differences in microbial profile may contribute to the protective effect of breastfeeding on respiratory infections in early infancy.

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APPLICATION OF JAPANESE SCORES TO DETERMINE CANDIDATES TO INMUNOGLOBULIN AND METILPREDNISONE TREATMENT IN SPANISH PEDIATRIC PATIENTS WITH KAWASAKI DISEASE

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Backgrounds and aims: Kawasaki disease patients (KDP) refractory to initial treatment with gammaglobulin and AAS often develop coronary lesions. The RAISE study (Kobayash etal), showed that combination therapy (gammaglobulin, AAS, methylprednisolone), improves clinical response and decreases the coronary lesions in KD patients at high risk, identified by Kobayashi score. These scores have been proved useful in Western countries. The aim is to determine the reliability of Kobayashi and Egami scores (KES) in detecting patients at high risk of resistance to initial treatment or developing coronary lesions in a third level Spanish hospital.

Methods: We reviewed the medical records over a period of 10 years (January 2002 - December 2011) of patients with KD refractory to treatment (persistent fever >37.5ºC, 48h after the beginning of infusion of Gammaglobulin and ASA). We selected two controls for each case: previous and following patient.

Results: Twenty refractory KDP were recorded. Two were excluded because of insufficient data. 18 cases and 36 controls were analysed. 17 refractory KDP received a second dose of 2g/kg gammaglobulin, one took oral prednisone. (table1) KES ≥4 points showed low sensitivity detecting refractory cases to initial treatment. However, both scores showed high sensitivity and specificity detecting patients with future coronary aneurysms (Table 2).

	Refractory KD	Non refractory KD
Number of patients	18	36
Median Age (months)	29	28
Male %	22%	33%

[Table 1]

	Refractory KD to initial treatment		Persistent coronary dilatations after 2 months		Coronary Aneurysm	
Score	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Kobayashi ≥4	50%	72%	62%	73%	80%	72%
Egami ≥4	44%	89%	50%	86%	80%	87%

[Table 2]

Conclusion: KES have shown good sensibility and specificity for detecting refractory KD and coronary aneurysms. These scores can be used to select candidates to combination therapy.

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HBSAG QUANTITY STRONGLY CORRELATES WITH PLASMA LEVELS OF MIRNAS ABERRANTLY EXPRESSED IN HBEAG POSITIVE AND HBEAG NEGATIVE CHILDREN WITH CHB

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Background: miRNA control has emerged as a critical regulatory principle in chronic infections. Our group has recently identified a panel of miRNAs aberrantly expressed in HBeAg positive and HBeAg negative children with chronic hepatitis B (CHB). Hepatitis B virus produces high quantities of subviral surface antigen particles (HBsAg) which circulate in the blood. Interestingly, HBsAg was recently shown to carry hepatocellular miRNAs and may thus function as a transporter of miRNAs between cells.

Aim: To describe the levels of HBsAg and selected plasma miRNAs over time in a cohort of children with CHB.

Patients and samples: In all, 35 treatment-naïve children with CHB were recruited (HBeAg positive, n=21, HBeAg negative, n=14). From each child 3-5 blood samples were collected sequentially with minimum intervals of half a year over a 1-7 year period. Total: 150 samples.

Methods: Plasma HBsAg was quantified using ARCHITECT® HBsAg assay and plasma miRNA levels were measured by RT-qPCR.

Results: Plasma levels of both HBsAg and all the miRNAs analysed were significantly higher in HBeAg positive children compared with in HBeAg negative children ($p < 0.001$). Interestingly, plasma levels of HBsAg and of the majority of miRNAs declined over time. A strong correlation was observed between quantity of HBsAg and plasma levels of miRNAs ($p < 0.001$).

Conclusion: We are the first to investigate the correlation between HBsAg quantity and plasma levels of selected miRNAs in children with CHB. Our results may advance understanding of the complex interaction between hepatitis B virus and host.

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THE FIRST NOROVIRUS BIVALENT GI.1/GII.4 VIRUS-LIKE PARTICLE (VLP) VACCINE IN MAN

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Noroviruses are highly infectious and easily spread in all ages. We conducted a randomized, double-blind, placebo-controlled study to evaluate safety and immunogenicity of a bivalent norovirus virus-like particle (VLP) vaccine given by the intramuscular (IM) route. The vaccine included GI.1 VLP and consensus GII.4 cVLP adjuvanted with Monophosphoryl Lipid A (MPL; GlaxoSmithKline) and aluminum hydroxide. Adults 18-49 (n=64), 50-64 (n=19) and 65-85 (n=19), received two doses of vaccine or saline (days 0 and 28). Solicited, unsolicited, and serious adverse events (SAEs) were evaluated. Serum Pan-Ig, IgG, and IgA ELISAs, histo-blood group antigen blocking, and hemagglutination-inhibition antibodies were measured on days 0, 7, 21, 28, 35, 56, 180 and 365.

Prior to vaccination, all 102 adults were seropositive for both VLPs by Pan-Ig ELISA and most adults were seropositive by other assays. Antibody responses to each VLP increased at day 7 after the initial dose, the first time point measured. The second dose did not boost titers significantly. Seroresponse-rates (4-fold rises) and geometric-mean-fold rises to GI.1 were higher than to GII.4. For both VLPs, antibodies were significantly increased and response patterns were similar. Elevations in antibody persisted at one year. Injection site pain and tenderness were the most common symptoms. No subjects reported fever or vaccine-related SAEs.

Conclusions: These data with a Norovirus bivalent vaccine candidate support that a single dose of this investigational vaccine given IM was generally well tolerated and immunogenic. Future studies will continue to explore responses to the vaccine in adults, older children and naïve infants.

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MAJOR REDUCTION OF ROTAVIRUS BUT NOT NOROVIRUS GASTROENTERITIS FOLLOWING UNIVERSAL IMMUNIZATION WITH ROTATEQ VACCINE IN FINLAND

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Universal rotavirus (RV) vaccination is expected to reduce hospitalizations for acute gastroenteritis (GE) of children by eliminating most of severe RVGE, but not to have any effect on norovirus (NV), the second most common causative agent of GE in children.

After introduction of RV vaccine into the National Immunization Programme (NIP) of Finland in 2009, we conducted a prospective study of GE in children either as outpatients or inpatients at Tampere University Hospital, and compared the results with a similar two-year survey conducted prior to NIP in the years 2006-2008. In 2009-2011, 330 stool specimens were collected and analyzed by RT-PCR and sequencing to detect RV, NV and/or sapovirus.

Compared with the pre NIP two-year period, in 2009-2011 hospitalizations for RVGE were reduced by 76% and outpatient clinic visits by 81%. NVGE showed a slight decreasing trend, and accounted for 34% of all cases of GE seen in hospital as compared to 26% (down from 52%) for RV. On the GE cases admitted to hospital ward, RV accounted for 28% and NV for 37%. The impact of RV vaccination was reflected as a 57% decrease in all hospital admissions and 62% decrease in all outpatient clinic visits for GE of any cause.

RV vaccination in NIP has led to a major reduction of hospital admissions and clinic visits due to RVGE, but has had no effect on NVGE. After 2 years of NIP NV has become the leading cause of acute GE in children seen in hospital.

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LYME DISEASE

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Lyme disease is caused by spirochetes of the Borrelia burgdorferi complex and is transmitted by tick bites. In Europe at least five species (B. afzelii, B. garinii, B. burgdorferi, B. spielmanii, B. bavariensis) are known to cause human disease.

It is the most frequent tick-transmitted disorder and causes a multi-organ infection with early and late clinical manifestations. Early manifestations are erythema migrans, borrelial lymphozytoma, early neurological manifestations with lymphocytic meningitis, periphereal facial palsy, and other cranial nerve abnormalities. Carditis, radiculitis, or ocular involvement is observed only in a few paediatric cases. The most frequent late manifestation is arthritis, whereas acrodermatitis chronica atrophicans or chronic neuroborreliosis is reported only in very few case reports.

Erythema migrans can be diagnosed without supporting laboratory test. For other presentations of Lyme borreliosis the mainstay of laboratory diagnosis is a two tier serological testing using first a sensitive enzyme linked immunosorbent assay and second if positive separate IgM and IgG immunoblots. Positive tests should be interpreted in the view of high background rates of seropositivity. For diagnosis of neuroborreliosis tests for intrathecal antibodies are required.

For early localized dermatological manifestations doxycycline is recommended for children 9 years of age and older and amoxicillin for younger children. Children with lymphocytic meningitis should be treated with third-generation cephalosporins. Children younger than 9 years of age with persistent or recurrent arthritis should be treated intravenously with third-generation cephalosporins. In older children oral doxycycline is an alternative. Antimicrobial therapy for asymptomatic seropositivity is discouraged.

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SAFETY OF THE 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE AND ITS EFFECT ON MORTALITY: A RANDOMIZED STUDY

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Background and aims: The Clinical Otitis Media and PneumoniA Study (COMPAS, NCT00466947) evaluated the efficacy and safety of the 10-valent pneumococcal non-typeable Haemophilus influenzae protein D conjugate vaccine (PHiD-CV).

Methods: In this double-blind study, healthy infants in Colombia, Argentina, and Panama were randomized (1:1) to receive primary vaccination with either PHiD-CV and DTPa-HBV-IPV/Hib (PHiD-CV group) or hepatitis B vaccine and DTPa-IPV/Hib (Control group) at 2, 4, and 6 months of age, followed by a booster dose of PHiD-CV or hepatitis A vaccine, both co-administered with DTPa-IPV/Hib, at 15-18 months of age. Serious adverse events (SAEs) and mortality rates were assessed during a mean follow-up period of 33 months post-dose 1.

Results: No differences between groups were observed in terms of the total number of reported SAEs (relative risk [PHiD-CV over Control group]: 0.95, 95% confidence interval [CI]: 0.90-1.00). No SAEs were considered related to PHiD-CV vaccination (Table 1). There were fewer fatalities in the PHiD-CV than in the Control group (PHiD-CV efficacy against all-cause mortality: 27.0%, 95% CI: -31.8-59.6), mainly apparent in the first year of life (9 versus 17 fatalities, respectively). The number of fatalities plausibly attributable to pneumococcal infections was lower in the PHiD-CV than in the Control group.

Table 1. SAEs reported during the entire study period (total vaccinated cohort)

SAE	PHiD-CV group (N=11798) n (%)	Control group (N=11799) n (%)
Any SAEs	2534 (21.5)	2668 (22.6)
SAEs considered related to study vaccination	0 (0.0)	1 (0.0)
Fatal SAEs	19 (0.16)	26 (0.22)
Gastroenteritis	553 (4.7)	497 (4.2)
Pneumonia	478 (4.1)	557 (4.7)
Bronchiolitis	473 (4.0)	518 (4.4)
Dehydration	463 (3.9)	438 (3.7)
Asthmatic crisis	192 (1.6)	210 (1.8)
Bronchial obstruction	127 (1.1)	141 (1.2)
Bronchitis	124 (1.1)	129 (1.1)
Febrile convulsion*	95 (0.8)	135 (1.1)

**febrile convulsions were solicited after booster vaccination; Only most frequently reported SAEs are included; N, total number of participants; n (%), number (percentage) of participants in the specified category; SAE, serious adverse event*

[Table 1]

Conclusions: In this multinational study, no safety concerns were identified in children receiving PHiD-CV and the overall mortality rate was lower than in the Control group.

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IMPACT OF A QUADRIVALENT CONJUGATE (MENACWY-CRM) OR A SEROGROUP B (4CMENB) MENINGOCOCCAL VACCINE ON MENINGOCOCCAL CARRIAGE IN ENGLISH UNIVERSITY STUDENTS

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Background: Serogroup C meningococcal conjugate vaccination programs had a significant impact on oropharyngeal carriage. With multivalent (ACWY) conjugate vaccines available and recent EMA approval of a serogroup B meningococcal vaccine, we investigated the effect of these vaccines on carriage in university students (NCT01214850).

Methods: This phase III study enrolled 2968 students in 10 universities across England from September-December 2010 to receive either one dose of a licensed quadrivalent meningococcal conjugate vaccine, MenACWY-CRM (Menveo®; n = 956) followed by saline placebo, or two doses of either meningococcal serogroup B vaccine, 4CMenB (Bexsero®: n = 932) or Japanese Encephalitis vaccine (Ixiaro®; n = 948). Oropharyngeal samples were taken before vaccination and at 5 subsequent visits over one year.

Results: Prior to vaccination, 947 (33%) of 2836 evaluable samples yielded Neisseria cultures, mostly (98%; n=930) N. meningitidis, mainly of serogroups B and Y. Primary analysis at one month after the vaccination series did not reveal significant impact of either vaccine. Across the cumulative later timepoints, MenACWY-CRM was associated with a carriage-reduction efficacy of 32.7% (95% CI: 12.0−48.6) against serogroup ACWY strains; 4CMenB was associated with a modest decrease in N.meningitidis carriage (16.5% [95%CI: 1.5−29.2]), especially among students enrolling within 30 days of the academic year (34.7% [95%CI: 15.3−49.7%]).

Conclusion: In secondary analyses, MenACWY-CRM and 4CMenB both showed evidence of carriage impact during the 12 month post-vaccination period. These results raise the possibility of an impact on individual carriage, which may translate into greater herd protection in settings where the vaccines are implemented broadly.

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MEASLES AND RUBELLA OUTBREAKS IN EUROPE: HOW TO ELIMINATE THEM?

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Background: The widespread and long-standing use of measles and rubella vaccines has resulted in substantial progress being made in the World Health Organization (WHO) European Region towards reaching the goal of measles and rubella elimination. However, some countries still reported high incidence rates and outbreaks of these diseases in 2012.

Objective: We assessed the epidemiology of measles and rubella in the WHO European Region in relation to the goal and key strategies of the elimination plan.

Methods: We analysed surveillance data for 2012 on measles and rubella for age-group, diagnosis confirmation and vaccination.

Results: For 2012, there were 23,871 measles cases and 29,361 rubella cases reported in the Region, mostly among unvaccinated persons. In a few countries, widespread outbreaks or continued indigenous transmission of measles persisted in 2012. While most countries of the Region have controlled rubella, a small number still reported a high incidence and outbreaks. Four countries did not have national rubella surveillance systems to enable reporting of cases from the total population. Almost one in three patients with measles and one in five patients with rubella, in the Region, were aged 20 years and older.

Conclusion: The large number of cases reported in 2012 necessitates stronger political will and efforts, particularly in high incidence countries, to achieve and maintain the required high vaccination coverage of at least 95% in the population. The accumulation of susceptible populations of different ages over time is most probably a result of vaccination coverage levels that may have fluctuated over the years. To close these immunity gaps, opportunities for vaccination should be provided to those individuals who are still susceptible to these diseases. In addition, countries are required to conduct high-quality surveillance of measles and rubella as stipulated in the WHO measles and rubella elimination plan.

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ADVANCES IN DIAGNOSTICS

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Respiratory tract infections are the most common diseases of infants and young children. They are mainly due to viruses, of which influenza viruses (IVs) and respiratory syncytial virus (RSV) are the most important. Prompt identification of these viruses in the respiratory secretions of infected children is essential to plan adequate procedures to limit their spread, initiate antiviral therapy in subjects at risk of complications, and avoid unnecessary drug prescriptions. Among the methods that have been developed to diagnose IV and RSV infections, serology cannot be used for a prompt diagnosis because it requires two blood samples. Furthermore, cell cultures are complicated, expensive and time-consuming, and molecular assays have to be performed in particularly well-equipped laboratories and cannot be used outside hospital. Antigen-based assays are inexpensive, easy to perform, and the result is available in a very short time even in an ambulatory setting or (at least in some cases) at patient's home. For all these reasons, they are widely used in clinical practice. These rapid tests are useful in improving the diagnosis of common and possibly severe diseases, such as influenza and bronchiolitis. Their sensitivity and specificity mean that they are most reliable when the prevalence of infection is high, which suggests that their routine use should be limited to the peak periods of viral circulation. As the most recently marketed tests are similarly effective in identifying the viruses, pediatricians should choose those that are less expensive, less time-consuming, and easier to perform and interpret.

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A RANDOMISED CONTROLLED STUDY TO EVALUATE INDUCTION OF IMMUNE MEMORY FOLLOWING INFANT VACCINATION WITH CONJUGATE SEROGROUP C NEISSERIA MENINGITIDIS VACCINES

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Aim: We investigated serogroup C meningococcal (MenC)-specific memory B-cell responses following different MenC conjugate vaccine schedules in infancy.

Methods: Memory B-cells were measured by ELISpot on a subset of participants from a multicentre randomised control trial. Infants aged 2 months were randomised (10:10:7:4 ratio) to receive 1 or 2 doses of MenC-CRM at 3 or 3+4 months, 1 dose of MenC-TT at 3 months, or no primary MenC doses. All children received a Haemophilus influenzae type b (Hib)-MenC booster at 12 months. DTaP-IPV-Hib, pneumococcal conjugate and MMR vaccines were administered routinely. Blood was drawn at 5, 12, 12 months+6 days and 13 months.

Results: Results from at least one time-point were available for 110, 103, 76 and 44 children from each group respectively. Following primary immunisations, and prior to the 12-month booster, primed children had greater numbers of MenC memory B-cells than un-primed children ($p < 0.0001$-0.015), however there were no significant differences between 1- or 2-dose primed children. One month following the Hib-MenC booster, children primed with 1 dose MenC-TT had more memory B-cells than children primed with either 1-dose ($p=0.0004$) or 2-dose ($p < 0.0001$) MenC-CRM. Post-booster, there were no differences between children who had received either 1 or 2 doses of MenC-CRM in infancy and un-primed children.

Conclusions: 1-dose MenC conjugate vaccine priming is as efficient as the current 2-dose primary schedule in eliciting a memory B-cell response. MenC-TT priming induces more memory B-cells than MenC-CRM, which may explain improved persistence of bactericidal antibody documented with this vaccine.

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A SYSTEMATIC REVIEW OF FEVER AND FEBRILE CONVULSION AFTER INACTIVATED TRIVALENT INFLUENZA VACCINE (TIV) IN CHILDREN

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Background and aims: Influenza is a common illness encountered by children, which can rarely cause disease and death. An unexpected spike in fever and febrile convulsions amongst Australian children < 5 years of age immunised with 2010 inactivated TIV, later identified as due to CSL branded vaccine, has led to ongoing public safety concerns regarding TIV in children. Our research was to clarify fever and febrile convulsion in children after TIV.

Methods: We conducted a systematic review, covering 2005 to April 2012, of clinical trials that reported safety data of inactivated TIV in healthy children. Our primary endpoints were rates of fever, febrile convulsion, and serious adverse events (SAEs). Meta-analysis was performed for rates of fever.

Results: From 20 RCTs meeting selection criteria (17451 vaccinated children), rates of fever ≥38C with non-adjuvanted vaccine were higher after first doses (8.4%) than second doses (5.5%) of vaccine. Analysis comparing vaccines by manufacturer showed fever rates ranging from 4.0-7.0% (non CSL products); separate comparison with CSL products used in 2 non-randomised studies revealed a fever rate of 19.1%. Adjuvanted vaccines elicited more fever than non-adjuvanted vaccines. Ten febrile convulsions were documented in 3 non-adjuvanted vaccine studies involving 9268 children. 15 vaccination-related SAEs were documented in 16 studies involving 15721 vaccinated children.

Conclusions: Most studies show an acceptable fever rate for TIV. Febrile convulsions and SAEs are uncommon. Published studies utilising CSL vaccine in children appear to have shown higher relative fever rates than other products.

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INFLUENCE OF VACCINATION AGAINST INFLUENZA A (H1N1) DURING PREGNANCY ON PREGNANCY OUTCOMES IN THE NETHERLANDS; A CROSS SECTIONAL LINKAGE STUDY

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Background and aims: In 2009 an Influenza-A(H1N1) pandemic occurred. Dutch pregnant women in their second and third trimester were eligible for vaccination. The Dutch CDC aimed to assess the possible influence of vaccination (Focetria®) on pregnancy outcomes.

Methods: Pregnant women, willing to participate in a follow-up study on safety of H1N1-vaccination (n=2672), filled in questionnaires about coverage and safety, and gave permission to link questionnaire data with data of the Netherlands Perinatal Registry (PRN).

Multivariate logistic regression analysis was used to assess the association between H1N1-vaccination and

1. Small-for-date,

2. Preterm delivery,

3. Need for assisted delivery and

4. A composite outcome, i.e. having at least one of the following characteristics: low apgar-score, admission to NICU, neonatal reanimation or perinatal death.

Potential confounding variables(maternal age; country of birth; education; self-reported use of alcohol, drugs or cigarettes during pregnancy; parity; underlying medical reasons for annual influenza vaccination; Influenza A(H1N1)-infection; life philosophy) were included in the model.

Results: 2,034 Women gave permission to use questionnaire data, of which 66.7% (n=1,357) were vaccinated and 33.0% (n=669) not. Linkage with PRN-data was possible for 1,736 women.

We found no association between H1N1-vaccination and small-for-date (OR 1.19; 95%CI 0.70-2.02) adjusted for all possible confounders. The same holds for preterm delivery (OR 1.02; 95%CI 0.61-1.68), need for assisted delivery (OR 1.10; 95%CI 0.85-1.42) and the composite outcome (OR 1.16; 95%CI 0.61-2.20).

Conclusions: H1N1-vaccination during the second or third trimester of pregnancy was not associated with an increased risk of adverse pregnancy outcomes in the Netherlands.

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COHORT STUDY FOR 30 YEARS: PERSISTENCE OF MEASLES, MUMPS AND RUBELLA ANTIBODIES INDUCED BY 2-DOSE MMR VACCINATION

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Background and aims: A follow-up of a persistence of MMR vaccine induced measles, mumps and rubella antibodies, a cohort study, was started simultaneously with the two-dose nation-wide MMR vaccinations in 1982, in Finland. Since that until 2012, the persistence of MMR vaccine induced antibody levels has been studied in serum samples collected from that cohort.

Methods: In 2012, 30 years after the first MMR vaccination serum samples were collected from 162 cohort members. IgG antibody levels were measured by commercial EIA IgG antibody kits. These antibody levels were compared with previous results and seropositivity for measles, mumps and rubella was calculated.

Results: Geometric mean antibody levels were 808 mIU/ml for measles, titer of 1:828 for mumps and 28 IU/ml for rubella. The antibody levels declined during the follow-up from 1 to 30 years by 64%, 80% and 66%, and from 25 to 30 years 9.7%, 14.1% and 9.7% for measles, mumps and rubella, respectively. In 2012, out of 162 vaccinees 14 (8.6 %) had measles antibody levels < 120 mIU/ml and 34 (21 %) had rubella antibody levels < 15 IU/ml, below the suggested protective levels. Seropositivity of the 30-year samples was 89%, 81% and 100% for measles, mumps and rubella, respectively.

Conclusions: The results show a remarkable decline of measles, mumps and rubella antibody levels during 30 years after MMR vaccinations. Although, the rate of decay has been slow during the last years a number of vaccinated individuals without a protective antibody levels will increase in future.

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VACCINATIONS IN IMMIGRANT CHILDREN

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During the past years Europe was confronted with increasing migration to and within the european countries. Immigrant children come from diverse regions of the world and bring with them varying histories of immunizations received eventually in their countries of origin. In a remarkable number of cases no vaccination is documented. In addition the healthcare status is often impaired (HIV, Tbc, etc.). Most of the non-immunized belong to hard-to-reach groups with lack access to vaccines and balanced information about the importance of immunization. Immunization of migrants is a high priority issue for the EU (i. e. PROMOVAX project) health program. Reaching immigrant children plays an important role in achieving measles and congenital rubella infection. In addition, vaccinations could serve as a vehicle to provide primary care, other preventative and screeining services, as well as education to migrants. On the other hand, different recommendations, institutions and organizations are existing in Europe which are ivolved in imunization programs. On a national level it is important to know the vaccination calendars and ways to evaluate migrants access to immunization. The topic vaccinations in immugrant children will be discussed by presenting different (local) projects.

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PARENT "COCOON" IMMUNIZATION TO PREVENT PERTUSSIS-RELATED HOSPITALIZATION IN INFANTS: THE CASE OF PIEMONTE IN ITALY

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Background and aims: Parental ("cocoon") immunization has been proposed in some countries (i.e. United States, France) as a measure to protect newborns from serious pertussis outcomes. We assessed the number needed to vaccinate (NNV) to prevent hospital admissions in infants (< 12 months) and the potential cost-effectiveness of this strategy in Piemonte.

Methods: The epidemiology of pertussis in Piemonte was described by using statutory notifications (from 1995 to 2010) and hospitalization data (from 2000 to 2010). The parent-attributable infant risk and vaccine efficacy (VE) were estimated from the published literature. The hospitalization cost for pertussis was calculated on the basis of Italian DRG (Diagnosis Related Group).

Results: The incidence of pertussis in Piemonte is now at the lowest level ever reached (0.85 per 100,000 in 2010). Pertussis is still endemic in infants (54 per 100,000 between 2005 and 2010) and a shift of the age distribution of cases towards older children (10-14) has become apparent in recent years. The NNV for parental immunization was at least 5,000 to prevent one infant hospitalization in the latest epidemic cycle (2005-2010) at the cost of >€100,000. The "cocoon" program leads to net costs instead of net saving from a National Health Service (NHS) perspective (ROI< 1).

Conclusion: The parental "cocoon" program is poorly efficient and very resource intensive in preventing pertussis in Italy, where the incidence rate is too low and reliable data on parent-attributable infant risk are unavailable.

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PERTUSSIS AT A TERTIARY PAEDIATRIC HOSPITAL IN AUSTRALIA: A COMPARISON OF EPIDEMICS A DECADE APART (1997-1999 AND 2007-2012)

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Background and aims: Australia has experienced a prolonged pertussis epidemic since 2007. We compared the epidemiology and severity of pertussis hospitalisations at a tertiary paediatric hospital during a period of whole cell pertussis vaccine use (1997-1999) with a period of acellular vaccine use, pertussis genotype changes and widespread access to PCR for diagnosis (2007-2012).

Methods: Medical and vaccination records of pertussis cases with an ICD discharge code and/or a laboratory confirmed diagnosis of pertussis presenting between from 1997-1999 and 2007-2012 were reviewed.

Results: Comparing 2007-12 to 1997-99: average annual hospitalisations increased from 35 to 49 cases; more were infants < 2 months (35% vs 26%); more required intensive care (18% vs 13%); nearly all cases were laboratory confirmed (92% vs 49%), with culture positivity proportions similar (42% vs 35%). Despite the increase in PICU admissions (2007-2012) there were no deaths compared to one (1997-1999). PICU cases were significantly younger than hospitalised cases not requiring PICU admission (1.6 vs 3.3 months, $p< 0.05$) and most were unimmunised. Indigenous Australians were overrepresented in PICU admissions (15%).

Conclusion: Despite wide availability of PCR and high DTPa vaccine coverage (2007-2012) infants < 6 months remain the highest risk for hospitalisation and most are too young to be protected by current vaccine schedules. Timely immunization, particularly the first 2 doses, in infancy is essential and highlights a potential role for maternal immunisation for even earlier protection.

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THE BUDGET IMPACT OF PALIVIZUMAB PROPHYLAXIS COMPARED TO OTHER CHILDHOOD PREVENTIVE HEALTH PROGRAMS IN FINLAND

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Background and aims: Respiratory syncytial virus (RSV) is a leading cause of upper and lower respiratory tract infection in children and leads to substantial childhood morbidity and mortality. Palivizumab is shown to significantly reduce hospitalization rates for RSV infection in high-risk populations. However, the costs of implementing this childhood prophylaxis program are not well defined. This study compares the short-term budget impact of a prophylaxis against severe RSV infection with three currently-implemented pediatric immunization programs in Finland.

Methods: Models were developed to estimate one-year budget impact of childhood programs targeted at preventing severe RSV disease, pneumococcal disease, Haemophilus influenzae serogroup b (Hib) associated diseases, and pertussis-associated diseases, from the national healthcare perspective. Model inputs were derived from clinical trials, published literature, Finnish costs, and population demographics. Outputs included total disease costs and cost offsets.

Results: Total disease costs were highest for RSV disease in high risk infants (€889,618), followed by pneumococcal disease (€781,634), Hib-associated diseases (€663,367), and pertussis-associated diseases (€100,900). Under current Finnish guidelines and uptake rates, estimated cost offsets were €62,709 for RSV disease, €96,552 for pneumococcal disease, €660,262 for Hib-associated diseases, and €84,655 for pertussis-associated diseases. RSV prophylaxis costs were €1,600,771 compared with vaccine costs of €15,459,478 (pneumococcal), €8,735,190 (Hib), and €8,735,190 (pertussis). In the expanded scenario, assuming 100% uptake of RSV prophylaxis for all currently eligible children, cost offsets and prophylaxis costs increased to €246,845 and €7,696,638, respectively.

Conclusions: The national one-year budget impact for RSV prophylaxis in high risk infants is positioned well within the context of other childhood preventive health programs.

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MULTIPLE STREPTOCOCCUS PNEUMONIAE (SP) SEROTYPES (ST) ARE FOUND IN AURAL DISCHARGE FROM CHILDREN WITH ACUTE OTITIS MEDIA WITH SPONTANEOUS OTORRHOEA (AOMSO)

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Background and aims: The co-existence of more than one bacterial species in the middle ear in AOM has been described previously but not multiple pneumococcal serotypes.

Methods: We prospectively studied 114 children with AOMSO (< =14 days duration) presenting to the emergency service at Coimbra Children's Hospital, Portugal during winter 2010-11. Demographic and clinical data were recorded and nasal and aural discharge swabs stored at -80°C in STGG broth until batched analysis by semi-quantitative culture. Sp positive samples were serotyped by microarray.

Results: Of 61 children with positive bacterial cultures from aural discharge, 28 (mean age 38M, range 5-125) isolated Sp (6 ear only, 22 both ear & nose, STs: 3, 6C, 7F, 9V-like, 10A, 10C-like, 11D, 14, 15B, 16F, 19A, 19F, 23A, 23B, 24F, 33F, 36-like, NT). In 11, >1 Sp-ST was identified in the ear (9-2 STs, 1-3, 1-4). In 22/28 who had Sp in both sites, individual STs could be found in one, the other and 21 had at least 1ST in both. Multiple aural STs were found both in children with and without a history of recurrent AOM or previous ear surgery and single-ST and >1 ST cases had the same mean age (35-36M). 9/11 multi-ST cases also had other bacterial species (M. catarrhalis=5, H. influenzae=4, S. aureus=2, S. pyogenes=1) isolated from the ear. This occurred in only 4/17 single-ST aural cases ($Chi^2 = 9.122$, $p = 0.003$).

Conclusions: In Sp AOMSO several ST frequently infect the ear, often in association with other bacterial species.

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TRENDS IN CANDIDEMIA IN U.S. CHILDREN'S HOSPITALS, 2003-2011

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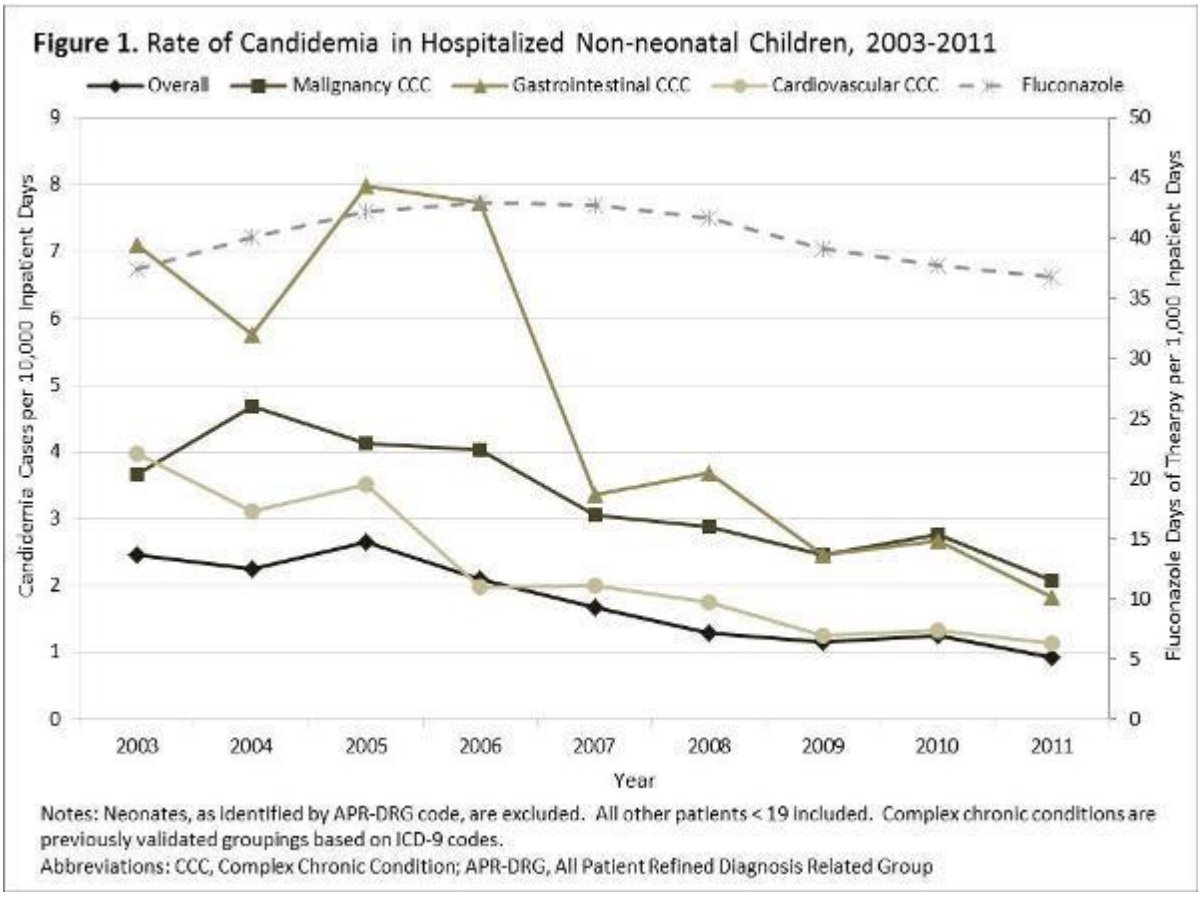
Background and aims: Recent studies suggest a decrease in the incidence of candidemia in neonates and it has been hypothesized that increased antifungal (e.g., fluconazole) prophylaxis might account for this observation. In other high-risk pediatric patient populations, data are limited on candidemia incidence. We aimed to determine the incidence of candidemia in hospitalized children and explore trends in antifungal use from 2003 to 2011.

Methods: The Pediatric Health Information System, a database of 43 U.S. children's hospitals, was used to determine rates of candidemia (using the ICD-9 code 112.5 disseminated/systemic candidiasis) and antifungal use between 2003 and 2011. Neonates were identified using APR-DRG codes. Non-neonatal patients with chronic health conditions were identified using validated groupings of ICD-9 diagnosis codes.

Results: Candidemia rates declined 62% in non-neonatal hospitalized children (figure 1) and 89% in hospitalized neonates (figure 2). These trends were consistent across subgroups of neonatal (by birth weight) and non-neonatal (by chronic condition) patients. Fluconazole use increased from 2003 to 2007 and decreased from 2007 to 2011 for both neonatal and non-neonatal populations.

Conclusions: Rates of candidemia have decreased across multiple populations of hospitalized children. The initial increase in fluconazole use might have contributed to the initial decrease in candidemia. However, the continued decline in candidemia, especially across populations for which fluconazole prophylaxis is uncommon, suggest that other factors, such as infection control interventions and antibiotic stewardship, may be responsible.



[Figure 1]

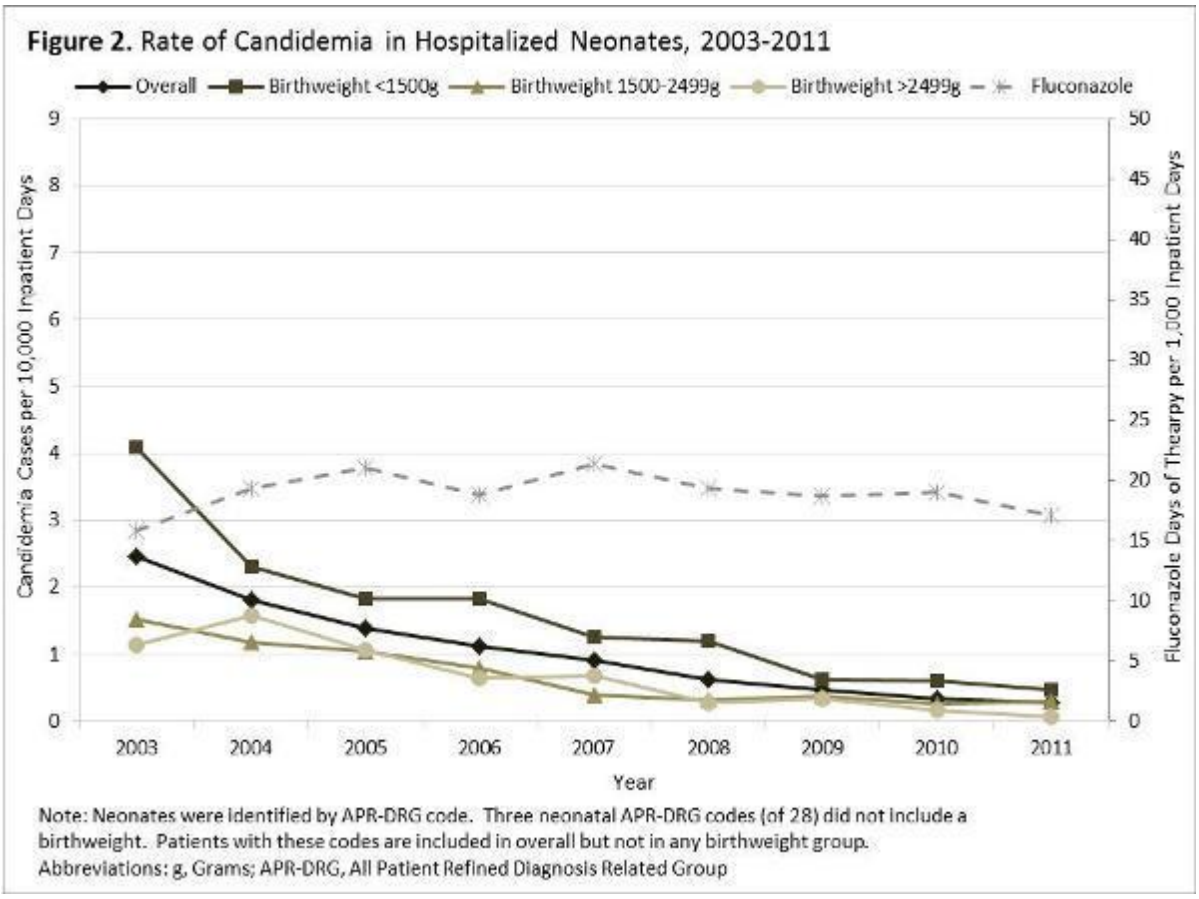


Figure 2. Rate of Candidemia in Hospitalized Neonates, 2003-2011
Overall
Birthweight <1500g
Birthweight 1500-2499g
Birthweight >2499g
Fluconazole
Candidemia Cases per 10,000 Inpatient Days
Fluconazole Days of Thearpy per 1,000 Inpatient Days
0
1
2
3
4
5
6
7
8
9
0
5
10
15
20
25
30
35
40
45
50
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year
Note: Neonates were identified by APR-DRG code. Three neonatal APR-DRG codes (of 28) did not include a birthweight. Patients with these codes are included in overall but not in any birthweight group.
Abbreviations: g, Grams; APR-DRG, All Patient Refined Diagnosis Related Group

[Figure 2]

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THE ROLE OF SERUM GALACTOMANNAN IN THE EARLY DIAGNOSIS OF INVASIVE FUNGAL INFECTIONS IN FEBRILE NEUTROPENIC PATIENTS WITH HEMATOLOGICAL MALIGNANCY

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Background and aims: Early diagnosis and treatment of invasive fungal infections(IFI) that are causes of high morbidity and mortality rate is very important. In this study, we aimed to investigate the role of serum galactomannnan (GM) EIA test in the early diagnosis of IFI.

Methods: Seventy-five febrile neutropenia episodes of 55 pediatric patients (1-17 years old) with hematologic malignancy who were hospitalized because of febrile neutropenia between October 2011 and October 2012 at Hacettepe University Children´s Hospital were observed. On the first, third, fifth, seventh day of the episodes, and twice a week during the neutropenic period, a total of 417 serum samples were tested with Platelia® Aspergillus galactomannnan EIA.

Results: Among 27 IFI episodes, 2 (%7.4) were proven, 12 (%44.4) probable and 13(%48.1) were possible IFI. When at least 2 GM index (GMI) of ≥0.5 were considered positive, the sensitivity, specifity, positive predictive value, negative predictive value and false positivity of GM test were % 55.6, % 97.9, % 93.7, % 79 and %3.0, respectively. Age, duration of neutropenia, fever and the last chemoteraphy agents used($p < 0.05$) were risk factors for GM positivity. The highest overall GM positivity ratio(%32.7) and the highest GMI values of episodes with positive thorax BT findings was on the first day(%75). Among the episodes with prolonged fever and IFI, the highest GMI positivity was on the fifth day.

Conclusion: These findings suggest that making GM evaluation frequently at the early period of the febrile neutropenic children with hematologic malignancy will be useful for earlier diagnosis of IFI.

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DEVELOPMENT AND VALIDATION OF CANDIDA PEDIATRIC RISK SCORE IN SPAIN PEDIATRIC POPULATION. THE ERICAP STUDY

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Objective: Invasive candidiasis (IC) has elevated morbidity-mortality, especially due to the late diagnosis. The aim was to develop and validate a "Candida Pediatric Risk score" (CPRS), for discriminating IC in critically ill patients.

Patients and method: Prospective, cohort, observational study. Thirty-six Pediatric Intensive Care Units (PICU) of Spain included. Statistically estimated number of patients was 858. Logistic multivariate regression was used to evaluate IC risk factors. To define the score, a punctuation of 2 was given to the variables with odds ratio (OR) > 3.5; 3 for a OR > 3.5 and < 5; and 4 for OR > 5. Maximum score punctuation was 16 points.

Results: 1157 patients were recruited. Mean age was 3.4 years (55.7% under 2 years). 45 patients (4,2%; IC95%: 3,0-5,4) had IC, with incidence rate of 1,1 cases 1.000 patients/year. The statistically significant variables for IC included in the score were: PRISM II > 6 points (OR: 3.2), previous fever (OR: 4.1), Candida colonization (OR: 4.1), extra renal depuration (OR: 3.7), length of stay > 15 days (OR: 2.9) and abdominal surgery (OR: 8.8). IC incidence was higher as the score punctuation increased. When the score was higher than 4, the sensibility and specificity to predict IC was 77 % and 76%, (PPV 12.6%, NPV 98.7%) respectively. For score values above 4, the score model has the best AUC: 0.83.

Conclusions: The CPRS may be helpful to discriminate IC at PICU. Antifungical treatment would be indicated if the score punctuation was higher than 4 points.

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EPIDEMIOLOGIC TRENDS OF CANDIDEMIA IN A TERTIATY- CARE INSTITUTION OVER A 12-YEAR PERIOD

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Purpose: To record the changes in the epidemiology of candidemia in the pediatric population of a tertiary hospital over a 12-year period.

Methods: All episodes of candiemia in children (excluding neonates) were identified in the microbiology laboratory database, during the period 2001-2012. Candida species and department origin (PICU, general pediatric wards, pediatric surgery and pediatric oncology wards) were recorded.

Results: Between January 2001 and December 2012, 105,558 children were admitted in Ippokration Hospital of Thessaloniki and 41 episodes of candidemia were recorded, accounting to a frequency of 0.38 episodes/1000 admissions. PICU patients comprised 46% (19/41) of the total episodes, oncology patients 12.1% (5/41) while the rest belonged to pediatric and surgical wards.

Althought there was no singnificant increase in the number of pediatric admissions, the mean number of candidemia episodes increased from 1.8 to 5 / year during the period 2001-2006 and 2007-2012 respectively. Candida albicans spp was isolated in 12/41 episodes and an increasing frequency towards non-albicans spp was noted over time. Non-albicans candidemia increased from 43% to 64% during the period 2001-2006 to 2007-2012 respectively. Mortality decreased from 72% to 46% (p=0.28). There was a decreasing frequency and no episode of candidemia during the last 3 years in pediatric oncolgy patients probably due to implementation of prophylactic protocols.

Conclusions: The rate of candidemia continues to increase in children and almost half of the episodes occur in PICU population, althought there is a trend towards improved mortality. Non- albicans species occur with increasing frequency.

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ADJUNCTIVE AND COMPLEMENTARY THERAPIES IN RESPIRATORY INFECTIONS

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Upper respiratory tract infections (URTI) are very common in the first years of life. Despite the fact that they have no major defect in immune response, some children seem to be particularly prone to such diseases and experience significantly more recurrent episodes than their peers. On average, a healthy three-year-old child suffers from 6-10 colds per year, each lasting 7 to 9 days.

URTI are usually mild, viral, and self-limiting; however, the symptoms can have a significant impact on child and family life. Symptoms often require medical attention and almost 40% of visits to paediatricians by children younger than 5 years are because of URTIs symptoms. To alleviate these symptoms, children are frequently given drugs such as decongestants, antihistamines and cough suppressants, even if there is little, if any, evidence that these medications are efficacious in children younger than 12 years.

The lack of efficacy of conventional medications for URTI is the possible cause for the wide use of alternative forms of treatments.

Complementary and alternative medicine (CAM) has been defined in the Cochrane Collaboration as "a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historic period". The use of CAM in pediatrics has grown dramatically in the Western world over the last few years. Approximately 20-40% of healthy children seen in outpatient clinics and more than 50% of children with chronic, recurrent or incurable conditions use CAM, almost always in conjunction with mainstream medicine.

Several studies have been published on the efficacy and safety of CAM for the prevention and treatment of URTI in children. In summary:

(a) Echinacea did not reduce the duration and severity of URTI;

(b) a combination of echinacea, propolis, and ascorbic acid decreased the number of URTI episodes, the duration of symptoms, and the number of days of illness,

(c) Echinacea was associated with a higher frequency of rash compared with placebo,

(d) homeopathy showed inconclusive results for the treatment of earache and acute otitis media, and

(e) in our experience, a preparation containing an extract of propolis had a significant beneficial effect in preventing new episodes of AOM in children with a recent history of recurrent AOM.

When considering CAM therapies, the physician has to face not only the clinically perspective but also the legal one. In the United States, as in many European countries, herbal products are not regulated by law as medicines and are considered dietary supplements. Thus, they do not necessarily undergo quality-control analysis to document the amount and purity of active ingredients and to support their claims of efficacy and safety. The safety of these products may thus be of concern: a survey of parents in a paediatric emergency department found that 77% of parents who gave herbal medicines to their children were unaware of any potential adverse effects or drug interactions and considered the products to be safe.

Most families use CAM services without spontaneously reporting the fact to their clinicians but, as paediatricians are responsible for advising families about safe, effective and age-appropriate health services and therapies (including CAM), this means that they need to include questions regarding the use of CAM when they examine their patients, and they also need to keep themselves informed about popular complementary therapies and evidence-based findings concerning them.

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CORRELATES OF PROTECTION AND THE ROLE OF CELL MEDIATED IMMUNITY

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Protective immunity against microbial pathogens after vaccination is best evaluated using well-designed studies which directly assess vaccine efficacy in populations containing susceptible individuals. In such studies a sample size is selected to provide sufficient cases to allow assessment of relevant endpoints such as disease, hospitalization or death. However, in the case of rare diseases, the sample size required is large, and thus the logistic and financial risk for the vaccine developer is increased and may be unacceptable. Where a correlate of protection is known, such as an antibody level above which there is protection, a relatively small study with immunological endpoints can provide some confidence for the vaccine developer to move to field efficacy trials, or may be sufficient to convince a regulator that the vaccine will be effective, without the need for efficacy data (e.g. meningococcal vaccines). Most of the accepted correlates of protection are measured as an absolute antibody concentration (e.g, 0.15mcg/ml for Haemophilus influenzae type b) or a serum dilution in a functional assay (e.g. the serum bactericidal assay for meningococcal vaccines or an agglutination or neutralization assay for viruses such as influenza). While antibody is clearly essential for preventing primary infection (cf antibody deficient individuals), cell-mediated immunity is critical for limiting infection by pathogens, especially viruses (e.g. fatal varicella in individuals with T cell deficiency correlate of protection for zoster vaccine). Much less is known about the relationship between T cell responses and protection against primary infection by bacteria and viruses, though development of new vaccines for several important diseases (e.g. TB, malaria and HIV) has focused on the induction of cell-mediated immunity.

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FUTURE VACCINES

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Traditional vaccines can only be really effective when the antigenic diversity or variability of the micro-organisms in the same bacterial species or viral family is no more than marginally different, and/or protection is mainly dependent from antibody-mediated immunity. This is the case of polio, tetanus, diphtheria, measles, mumps and rubella vaccines, which maintain a high degree of immunogenicity and efficacy, and confer significant protection for a long period of time. However, when the pathogens in the same group are antigenically diverse or variable, and/or protection is mainly derived from T-cell dependent immunity, traditionally prepared vaccines have often proven to be inadequate, as in the case of influenza and pneumococcal vaccines. In cases such as the meningococcal B vaccine, it is not possible to produce a protective vaccine by means of traditional methods because the characteristics of the antigen used for the formulation of vaccines against all the serogroups of the same bacterial species are often inadequate. In order to overcome these problems, one solution is to identify the antigens common to all of the strains in a species or family that are significantly capable of eliciting inactivating antibodies. To obtain new prophylactic measures, various and sometimes highly innovative approaches including large-scale high-throughput genomic, transcriptomic and proteomic analyses, have been experimented. Although none of the new vaccines prepared with these methods has yet been licensed for human use, some have been widely studied in experimental animals and humans, and seem to increase the possibility of preventing previously uncovered infectious diseases.

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ARE IMMUNOMODULATORS / IMMUNOSTIMULANTS EFFECTIVE IN CHILDEN?

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Aims: Respiratory tract infections (RTIs) constitute a major healthcare burden in children throughout the world. They tend to be recurrent, often causing multiple episodes of illness within a single year. Immature or deficient immune systems, the presence of genetic and environmental factors, and exposure to pathogens make young children highly susceptible to RTIs. These are commonly treated with antibiotics, despite the fact that the majority is caused by viruses. Even more, overuse and misuse of antibiotics are contributing to the major healthcare problem of increasing antibiotic resistance. Priority must be given to preventive measures including parent education, active immunization and non-specific immunostimulation. OM-85 is the most studied immunostimulant and has the longest post-marketing experience with regards to efficacy and safety.

Methods: Meta-analysis of recent placebo-controlled trials of OM-85 in children with recurrent RTIs.

Results: Following treatment, there was a significant decrease in the percentage of children with recurrent RTIs, as defined as a least three such episodes in six months. There is an association between OM-85 efficacy and the number of RTIs in the year prior to treatment indicating that patients with the highest frequency of RTIs benefit the most from treatment. The safety profile of OM-85 was found to be good.

Conclusions: Preventive measures represent the most wanted approach for the management of pediatric recurrent RTIs. There is a clear role of immunostimulants for this purpose; currently OM-85 being the most studied such compound.

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DEBATE ON PROBIOTICS

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According to the worldwide accepted FAO/WHO definition, probiotics are “live microorganism that, when administered in an adequate amount, confer a health benefit on the host”. The concept of “health benefit” is the key issue when referring to probiotics and the possibility to gain advantages in using them in clinical practice is a current matter of debate.

Possible benefits in preventing and treating infectious diseases in children have been extensively studied with some positive results. There is in fact some evidences from randomized control trials (RCT) of a modest benefit of giving probiotics in preventing acute gastrointestinal tract infections in healthy infants and children. Supplementation with probiotics has been associated with a reduced incidence of diarrhea as well as with a shorter duration of the episodes. Specifically, a meta-analysis on prevention of rotavirus gastroenteritis showed that supplementation of 7 children with Lactobacillus GG may prevent one case of rotavirus gastroenteritis. Other RCTs provided good data on the therapeutic benefit of probiotics in children with acute infectious diarrhea: supplementation with LGG early in the course of acute infectious diarrhea may reduce the duration of the episode by 1 day.

Data on probiotics for prevention and treatment of respiratory infections are heterogeneous and vary significantly as regard quality: even if some beneficial effects have been suggested, no definite evidence-based recommendation may be done.

Despite some good evidences, some questions still need to be answered: the optimal duration of probiotic administration, the preferred microbial dose and the most adequate species.

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ACYL-HOMOSERINE LACTONE DEGRADING ACTIVITY AS AN EFFICIENT MECHANISM IN INCREASING RESISTANCE AGAINST AHL-BASED ANTIBIOTIC PRODUCERS

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Many of Proteobacteria use Acyl homoserine lactone (AHLs) mediated quorum sensing (QS) to regulate degrading antimicrobial production. Many of soil bacteria have the ability of interrupting QS system by degrading AHLs. Although the role of this ability in biology of these bacteria is still unclear. In this survey it was demonstrated that such ability can improve the fitness of bacterial species in competition with QS regulated antimicrobial producers like Pseudomonas aeruginosa. Bacillus cereus UT26 wild type strain produces AHL lactonases encoded by aiiA to degrade AHLs and loses its AHL degrading ability by creating a site directed mutation in aiiA, using Standard Overlap Extension PCR. The results showed that the growth yield of wt strain in laboratory co-cultures with P. aeruginosa was about 1000 fold more than aiiA mutant strain. The growth yield of mutant could be restored by inhibiting AHL production in P. aeruginosa or by providing a copy of aiiA on a plasmid (pAD123). These results suggest that a possible role for AHL degrading activity could be increment of bacterial fitness in competition with AHL utilizing antibiotic producers.

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PAEDIATRIC ANTIMICROBIAL MANAGEMENT STRATEGIES IN EUROPEAN HOSPITALS WITHOUT A FORMAL ANTIMICROBIAL STEWARDSHIP PROGRAMME: BUILDING ON WHAT IS AVAILABLE

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Background and aims: Paediatric antimicrobial stewardship programmes (PASPs) aim to optimise antimicrobial prescribing. We aimed to establish whether critical elements required for their successful implementation are already in place in European hospitals currently without structured PASPs.

Methods: A project on PASPs was run through Young ESPID. An online anonymous survey was circulated from 8/05/2012 to 01/07/2012, among attendees of the 30th Annual ESPID meeting and subsequently to the Young ESPID network and through ESPID's newsletter. The answers from participants working in hospitals without a PASP were selected and analysed descriptively.

Results: A total of 76/149 answers, from 22 European countries, were analysed. Of these, 54% had previously heard about PASP. 66% believed their hospital had the necessary infrastructure for its implementation. Only 54% indicated that a PID team existed: 51% of these reported having PID ward rounds and 66% regular meetings with microbiology. Availability of information on resistance patterns was reported by 66% respondents. 42% reported the use of electronic prescribing in their hospital. Relevant activities included restriction of the use of certain antimicrobials (45%), antimicrobial order forms (25%), automatic review dates for antimicrobial prescriptions (11%) and antimicrobial cycling (3%). Only 20% indicated regular education on antimicrobial use, but with hospital and national guidelines available in 87% and 78% of cases, respectively.

Conclusions: Many hospitals without a formal PASP already use a wide range of strategies to improve antimicrobial prescribing. Given the different resource and funding availability amongst European countries, these activities could be built on for future implementation of PASPs.

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SUCCESS OF A PARENT'S THERAPEUTIC EDUCATION ABOUT ANTIBIOTIC USE IN A PEDIATRIC EMERGENCY DEPARTMENT: A RANDOMIZED CONTROLLED STUDY

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Background and aims: To evaluate a therapeutic educational intervention performed in a pediatric emergency department designed to improve parent's knowledge and behaviors about judicious use of antibiotics.

Methods: Randomized controlled trial in a Pediatric emergency department of a tertiary care children´s teaching hospital.

Participants**:** Children aged between 1 month and 6 years, discharged with an oral antibiotic prescription for 5 to 10 days for an acute respiratory or urinary tract infection.

Intervention**:** Children were randomized to receive either educational intervention regarding judicious use of antibiotics (intervention group) or fever treatments and care (control group). A pharmacist trained in therapeutic education delivered the intervention which consisted in a 30 minutes face to face session with parents and children. Intervention includes the four educational usual stages: educational diagnosis, educational contract, education and evaluation.

Outcome Measure: Parents' satisfaction concerning the information about antibiotics received at the hospital assessed in a phone survey at D14.

Results: Three hundred children were randomized: 150 per arm. A total of 259 patients were evaluated at D14. Satisfaction about antibiotics information received at hospital was higher in the intervention group (96.9% versus 83.0%; p=0.002). Knowledge about judicious use of antibiotics was better in intervention group with 103/129 (79.8%) caregivers who answered correctly to at least 5 knowledge questions compared to 84/130 (64.6%) in the control group (p=0.006).

Conclusion: Education intervention showed promising results for educating parents about appropriate use of antibiotics raising the question of the presence of a clinical pharmacist working full time in pediatric emergency departments.

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ANTIMICROBIAL STEWARDSHIP PROGRAM WITH A COMPUTER-BASED PREAUTHORIZATION AT CHILDREN'S HOSPITAL IN JAPAN

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Background : The importance of Antimicrobial Stewardship Program (ASP) cannot be emphasized more as multi-drug resistant organisms were concerned globally. We implemented a computer-based preauthorization of antibiotic prescriptions. Our aim of study is to evaluate the effectiveness of the ASP on broad-spectrum antibiotics.

Methods: We retrospectively reviewed medical records on antibiotic prescriptions between March 2010 and December 2012. We compared DOTs (Days of Treatment) per 1000 patient-days and lengths of hospital stay in 3 periods; the first period without ASP between March 2010 to September 2010, the second period with passive consultation based ASP between October 2010 and September 2011 and the third period ASP with preauthorization that required approval of Infectious Diseases physician between October 2011 and December 2012.

Results: DOTs in the three periods was 7.4, 3.5 and 2.4 for Carbapenems, 13.4, 13.4 and 9.1 for Cefepime, and 9.1, 6.0 and 3.6 for Piperacillin/Tazobactam, respectively. The all of antibiotics were decreased significantly from the first period to the third period. The average days of hospital stay in the three periods were 17.8, 21.2 and 20.2, respectively. There were no statistically differences among the three periods.

Conclusion: ASP with preauthorization was an effective intervention for reducing Cefepime and Piperacillin/Tazobactam. A passive consultation based ASP reduced Carbapenems prescription. ASP successfully reduced prescriptions of broad-spectrum antibiotics without causing the prolongation of hospital stay.

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RESISTANCE DECREASE AND SEROTYPE MODIFICATIONS OF PNEUMOCOCCUS ISOLATED DURING ACUTE OTITIS MEDIA IN CHILDREN; 2001-2011 SURVEY OF THE FRENCH NETWORK

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Background and aims: In France, a national campaign to improve antibiotic use was launched in 2002. In 2003, and 2010 respectively were introduced the 7-valent pneumococcal conjugate vaccine (PCV7) and PCV13 for children < 2 years. To evaluate trends in antibiotic resistance and changes in circulating serotypes of Streptococcus pneumoniae (Spn) isolated in middle ear fluid in children (< 16 years) during acute otits media (AOM) over a 10 years period (2001-2011), data from the French Pneumococcus Network, a national survey program, were analysed.

Methods: During this period, 6,683 Spn isolated from middle ear fluid in children were collected and studied for their resistance to penicillin G (PEN), amoxicillin (AMX), cefotaxime (CTX). Serotypes were determined on a systematic sample of 1,569 of these strains.

Results:

Year		2001	2003	2005	2007	2009	2011
N° of strains		*1695*	*1378*	*1159*	*974*	*922*	*555*
PEN (% I+R)		77	70	64	60	63	57
AMX (% I+R)		43	42	35	29	37	30
CTX (% I+R)		29	27	22	16	21	13
Serotype distribution (%)							
N° of strains		*341*	*367*	*200*	*308*	*201*	*152*
	14	19	16	11	2	1	1
	18C	1	1	2	1	0	1
PCV7	19F	16	21	17	11	4	10
	23F	11	7	8	2	0	1
	4	1	1	1	1	0	0
	6B	11	8	3	2	0	0
	9V	5	3	2	0	0	0
	1	1	2	3	2	3	1
	19A	20	19	23	35	51	38
PCV13	3	5	12	8	17	9	9
	5	0	0	0	0	0	1
	6A	2	2	3	2	1	0
	7F	1	1	0	4	5	1
	12F	0	0	0	0	1	2
	15A	0	1	1	2	3	7
Non-vaccine	23A	1	0	2	1	0	4
	others	8	8	18	19	19	25

[Table]

Conclusions: A dramatic decrease was observed over the 2001-2011 period in France in antibiotic resistance of Spn isolated from AOM. This phenomenon coincided with a general reduction in antibiotic consumption in France and with the introduction of the PCV7 then the PCV13 conjugate vaccines ($p< 0.01$). A reduction in the rates of PCV7 serotypes was observed (2001: 63.0% vs 2011: 13.2%) ($p< 0.01$). In the pre-PCV7 period, most PNSP isolates belonged to serotypes included in PCV7 (2001: 77%, 2011: 18%). In 2011 PCV13 covered 62% of the serotypes involved in AOM and among them, 75% of the PNSP. Continued surveillance is essential to track modifications in circulating serotypes since the introduction of the PCV13 vaccine.

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ANTIBIOTIC MANAGEMENT OF BACTERIAL MENINGITIS IN BABIES < 90 DAYS OF AGE: A UK AND REPUBLIC OF IRELAND PROSPECTIVE STUDY

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Background and aims: Bacterial meningitis requires early and appropriate empirical antibiotic therapy. An audit conducted 6 years ago in the UK showed that policies varied between neonatal units. This study aimed to define the current antibiotic management of bacterial meningitis in babies < 90 days of age.

Methods: Bacterial meningitis cases were identified through a comprehensive prospective surveillance system between July 2010 - July 2011. Treating clinicians completed a standardised proforma.

Results: There were 37 different empiric antibiotic combinations used in 329 cases. The most common were amoxicillin plus 3rd generation cephalosporin (26%); cephalosporin alone (20%); benzyl penicillin plus gentamicin (19%); and benzyl penicillin plus cephalosporin plus gentamicin (6%). Overall, a 3rd generation cephalosporin was included in 68% and an aminopenicillin was included in 64% of empiric combinations. The median (IQR) duration of antibiotic treatment was 14 (14-21) days for all surviving cases. The duration in days (IQR) varied between bacteria: Neisseria meningitidis 8 (7-14), Group B Streptococcus 14 (14-21), Streptococcus pneumoniae 14 (14-18), Escherichia coli and Listeria monocytogenes 21 (21-21) and culture negative cases 14 (10-14).

Conclusion: There is significant variation in the empiric antibiotic policies for treating babies with bacterial meningitis in the UK and ROI. Harmonization of empirical antibiotic policies should be considered.

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A POINT PREVALENCE SURVEY (PPS) OF NEONATAL AND PAEDIATRIC ANTIMYCOTIC USE IN EUROPE

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Background: There is limited evidence-based guidance for empiric antifungal therapy despite significant morbidity and mortality of invasive fungal infections. We describe patterns of antimycotic use in European hospitals participating in the PPS of the Antimicrobial Resistance and Prescribing in European Children (ARPEC) project.

Methods: Data collection was completed in 169 hospitals across Europe during November 2012 using the validated and standardised ARPEC-PPS method for data collection, entry and reporting.

Results: Antifungal prescriptions comprised 85 (5.7%) of 1494 and 347 (6.3%) of 5479 neonatal and paediatric systemic antimicrobial prescriptions, respectively.

Overall, 49 (58%) neonatal antifungal prescription occurred in (ELBW) (< 1000g) neonates with 89% of these administered parenterally. Fluconazole 57 (67%) and amphotericin B 19 (22%) accounted for 89% of all neonatal antifungal prescriptions with 55% of all neonatal prescriptions reported as prophylaxis.

Paediatric patients had a median age of 5 years (IQR 1.7,11), 230/331 (70%) children on antifungals had an underlying haemato-oncology diagnosis. Most frequently recorded antifungals in paediatrics were fluconazole in 123 (36%), amphotericin in 97 (28%), and voriconazole in 43 (12%) children, with 50% of all paediatric prescriptions due to prophylaxis. For Fluconazole once daily dosing was most frequently used, with a median of 5.5 mg/kg (IQR 3,7) for 50 children receiving treatment and 5mg/kg (IQR 3.9,6.4) for 69 children on prophylaxis.

Conclusion: Antifungals were mainly used in ELBW neonates and in children with haemato-oncology underlying diseases. Predominantly older generation antifungals were prescribed in both settings. The dosing used for treatment identifies future options for improving targeted therapy.

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A SURVEY FOR ASSESSING THE AVAILABILITY OF ANTIBIOTIC PRESCRIBING GUIDELINES IN PAEDIATRIC HOSPITALS IN EUROPE

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Background and aims: Antibiotic practice guidelines have been extensively used in different health care settings with variable success. The aim of this study is to explore the availability of antibiotic prescribing guidance for common infections in European paediatric hospitals.

Methods: This survey was in the context of the broader Antibiotic Resistance and Prescribing in European Children study (ARPEC). A web-based preformed questionnaire disseminated twice (September 2011 and November 2012) to ARPEC participants. We explored the availability, source of guidelines and recommended treatment (drug and duration) for frequently encountered paediatric infections: respiratory, skin and soft tissue, bone, urinary tract and sepsis.

Results: Seventy three (73) hospitals from 18 European countries responded in the survey and 65 (89%) confirmed the use of guidelines for specific infections. Half (50%) of these hospitals report the use of local guidelines, 32% use national guidelines and 10% regional. Only 16/65 hospitals (24%) stated that guidelines were made available by a public organization (paediatric or infectious diseases society). Complete guidelines for the infections listed in the questionnaire reported by 17/65 hospitals (26%). Guidelines most commonly available were those for pneumonia (77%) followed by urinary tract infections (71%), neonatal sepsis (66%) and upper respiratory tract infections (64%).

Conclusions: The majority of European hospitals participating in the survey use local guidelines for antibiotic use. Source of guidelines varies between hospitals and type of infection. Reducing antibiotic use is a key priority in Europe and adoption of evidence based guidelines can play a leading role.

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LISTERIA MONOCYTOGENES (LM) MENINGITIS IN CHILDREN IN FRANCE IN THE LAST TEN YEARS

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Background and aims: To analyze epidemiological and clinical characteristics of Lm meningitis in children from 0 to 18 years old.

Methods: Diagnosis of meningitis due to Lm was based on the combination of a febrile meningeal syndrome with positive culture of cerebrospinal fluid (CSF) and/or positive antigen in CSF and/or a positive blood culture associated with pleocytosis (> 10 cells/ml).

Data were collected since 2001 to 2011 from the French Network of Surveillance of Bacterial Meningitis in childhood.

Results: 30 cases recorded in 10 years (sex ratio: 0,93). Mean age was 24 to 26 months old (median : 28,32 months). 14 patients were younger than 1 month old. The CSF direct examination was negative in 13 cases, but the culture of CSF was positive for 28 patients and blood culture was positive for the 2 others. The Lm serovar was 4b in 12 patients. Three patients presented an acquired or congenital immunodeficiency. All patients were treated with amoxicillin for a median of 21 days, associated to an aminoside for 29. Four of 30 patients died between 2 and 12 days after their admission: 4 newborns including two premature of 25 and 29 weeks of gestational age.

Conclusion: Meningitis due to Lm is a rare disease including in neonatal period. Newborns are specifically at risk, particularly the premature. Their number is stable since 2001 in France. The diagnosis remains difficult because direct examination is not always contributory. Since 2009, PCR diagnosis is introduced in the diagnostic's definition.

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SOURCES OF PERTUSSIS INFECTION IN YOUNG BABIES FROM SÃO PAULO STATE, BRAZIL

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Background and aims: The number of pertussis cases is growing substantially in São Paulo state, and the aims of this study are: to identify the sources of B. pertussis among contacts of babies (< 7 months) with pertussis confirmed by RT-PCR and/or culture, to compare the sensitivity of lab tests and to analyze the positive cases according to presence of symptoms and antecedents of vaccination.

Methods: Prospective study, including 1-5 contacts (median=4) of 97 babies with confirmed pertussis from Nov/2011 until May/2012. A nasopharyngeal sample for culture and RT-PCR (ptxS1 and IS481) was collected, and tests were performed in Institute Adolfo Lutz, the Brazilian national reference center for pertussis diagnosis.

Results: 351 contacts were included and 8% had positive lab tests for pertussis (23 PCR+; 12 culture +; 7 PCR and culture +). 22% of familiar clusters had at least one contact with confirmed pertussis confirmed by bacteriology. Among the contacts the positivity was higher for parents (12%; CI 6.0-23.0) than for other family members (5.6 3.0-9.5). Positivity was not affected by the cough presence and vaccine status. The positivity was higher when the samples were collected < 14 days after the initial symptoms in index-cases (17.2% vs. 4.0%).

Conclusions: Parents and other family members can transmit pertussis even with asymptomatic infection. The introduction of serology probably would detect higher number of pertussis in family contacts, because the positivity of culture and RT-PCR is reduced 2-3 weeks after initial symptoms.

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FREQUENCY OF VISITS FOR OTITIS MEDIA IN QUEBEC: FACE-TO-NAPE COMPARISON OF CHILDREN EXPOSED TO PCV-7 OR PHID-CV

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Background: In the province of Quebec, Canada, the 10-valent Haemophilus influenzae protein D pneumococcal conjugate vaccine (PHiD-CV) was introduced in 2009, replacing the 7-valent CRM197 vaccine (PCV-7) in a 2+1 doses schedule. There is no published study comparing the effectiveness of these two vaccines to prevent otitis media (OM).

Methods: The monthly frequency of physicians claims for OM in children aged < 2 years and born in 2007-2010 was obtained from the provincial health insurance board. Exposure to PCV-7 or PHiD-CV for the primary immunization series and booster dose was measured in the Quebec City Immunization Registry in each of the 48 monthly birth cohorts. Cumulative OM visits frequencies (COMVF) were compared.

Results: A total 510,271 OM visits were recorded among 349,645 children representing 8,017,083 person-months of observation. COMVF was 1.54 in children born in June-October 2007 and exposed to PCV-7 + PCV-7, and was 1.57 in children born in June-October 2009 and exposed to PHiD-CV + PHiD-CV (relative rate difference = 1.86%; p=0.0014). COMVF was 1.55 in children born in August 2007-January 2008 and exposed to PCV-7 + PCV-7, and was 1.46 in children born in August 2008-January 2009 and exposed to PCV-7 + PHiD-CV (relative rate difference = 5.75%; p< 0.0001).

Conclusion: There was no clinically important difference between the two vaccines used in a 2+1 schedule. In this context, vaccine effectiveness against invasive diseases and purchase cost become important issues in decision-making.

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EPIDEMIOLOGY OF PERTUSSIS IN A TERTIARY PEDIATRIC HOSPITAL IN ATHENS, 2010-2012

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Background and aims: Pertussis is a fairly common often unrecognized endemic infection worldwide. Aim was to describe the epidemiology of pertussis cases hospitalized in a major tertiary hospital in Athens.

Methods: Records of pertussis cases were reviewed retrospectively in children hospitalized to the Infectious Diseases Unit of Aghia Sophia Children's Hospital in the period 2010-2012. The diagnosis of all cases was confirmed by Multiplex Real Time PCR (Light Cycler 2.0 Roche) Insertion Sequence 481 and 1001.

Results: Totally, 123 cases (52, 31 and 40 in each year respectively) were reviewed of which 7 (5.7%) had confirmed parapertussis. Girls were more affected with a male-to-female ratio of 0.84:1. Mean age was 5.6±13.3 months with 89.7% ≤6 m.o. (42.2% ≤2 m.o.). A substantial 61.2% belonged to special subpopulation groups (37.9% were Greek Roma and 23.3% were immigrants). The vaccination status was known in 112/116 (96.6%) cases. Of these 101 (90.1%) were unvaccinated, 6 (5.4%) were vaccinated with 1 dose, 4 (3.6%) with 2 doses and 1 (0.9%) with 4 doses. The outcome was favourable in all patients; no death was recorded.

Conclusions: Despite the existence of DTaP vaccines in the National Immunization Programme cases of pertussis still occur. The majority of them concern young infants who are either unvaccinated or too young for vaccination while the incidence is higher in subpopulation groups as the Roma minority. This highlights the need of increased awareness of circulation of the bacteria in adults and strengthening systematic access and vaccination of sensitive susceptible population groups.

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PREDICTORS OF PERTUSSIS SEVERITY IN HOSPITALISED INFANTS AGED LESS THAN SIX MONTHS

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Aims: Determine predictors of pertussis severity in hospitalized infants (< 6months).

Methods: A multicenter analytic study included 383 hospitalized infants (< 6months) with laboratory-confirmed pertussis in Portugal between 2007 and 2012. Patients were divided in three groups according to disease severity: mild, moderate (apnoea, ALTE and/or hypoxemia) and severe (refractory hypoxemia, pneumonia, pulmonary hypertension, seizures and/or cardiogenic shock).

Results: The median age was two months (51.4% female; 61.7% non-vaccinated). There were 252 (66.3%) mild, 88 (23.2%) moderate and 40 (10.5%) severe infections. Of the later, nine patients had pulmonary hypertension, six developed sequelae and six died.

Young age (< 3 months), respiratory distress, crackles and pulmonary consolidation/atelectasis were associated with moderate/severe pertussis ($p< 0.05$). Prematurity only predicted severe disease ($p< 0.05$).

White blood cell count (WBC) on admission was significantly higher in moderate/severe compared to mild pertussis (median: 25050/µl vs. 13970/µl; $p< 0.001$). WBC on admission above 17000/µl was strongly associated with the occurrence of complications (age-adjusted OR=10.74; 95%CI: 5.99-19.27; sensitivity:76.0%; specificity:70.8%, positive likelihood ratio: 2.61).

Considering complicated pertussis, WBC peak was significantly higher in severe compared to moderate pertussis (median: 49290/µl vs. 26495/µl; $p< 0.001$). WBC peak above 50000/µl was a predictor of severe complications (age-adjusted OR=7.81; 95%CI: 3.05-19.97; sensitivity:50.0%; specificity:87.6%; positive likelihood ratio: 4.05).

Conclusions: WBC on admission is a good predictor of complicated pertussis. WBC peak predicts severe complications. Early and periodic WBC measurements identify pertussis patients at risk of complicated outcome and may allow prompt intervention, like exchange transfusion in those with hyperleukocytosis.

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MEMORY B CELLS AGAINST STREPTOCOCCUS PNEUMONIAE ARE LOST AFTER SPLENECTOMY

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Background and aims: IgM memory B-cells are indispensable for the T-independent response to polysaccharides, thus being the major players in the defense against pneumococcus, and need the spleen for their generation and survival. Switched memory B cells are generated in all lymphoid tissues by the T-dependent germinal center reaction.

Splenectomized patients have increased susceptibility to bacterial infections by S.pneumoniae.

The aim of our research is to study specific memory for pneumococcus in splenectomized individuals compared to healthy donors (HD).

Methods: In 21 asplenic and 19 healthy children and in 60 asplenic and 45 healthy adults we studied the frequency of peripheral blood B cells, IgM and switched memory B cells by flow-cytometry, and the number of antigen-specific memory B cells by ELIspot.

Results: We observed a significant reduction in splenectomized individuals compared to HD in frequency of circulating memory B cells (median 31 vs 13%, $p< 0.001$) and in number of pneumococcus polysaccharide (PnPS)-specific memory B cells, both of IgM (median 260 vs $80/10^6$, $p< 0.001$) and IgG isotype (median 40 vs $10/10^6$, $p< 0.001$). The number of PnPS-specific IgG memory cells were close to normality in splenectomized children vaccinated with pneumococcus conjugated vaccine (PCV) after splenectomy.

Conclusions: The loss of memory B cells (in particular IgM memory B cells) with splenectomy compromises the response to pneumococcal polysaccharides, impairing both the defense from the natural infection and the response to pneumococcal polysaccharide vaccine (PPV). Our results show that use of PPV in splenectomized individuals may not be biologically plausible.

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EFFICACY OF 13-VALENT VERSUS 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13, PCV7) IN PREVENTING NASOPHARYNGEAL COLONIZATION OF ANTIBIOTIC-RESISTANT S. PNEUMONIAE (ARSP)

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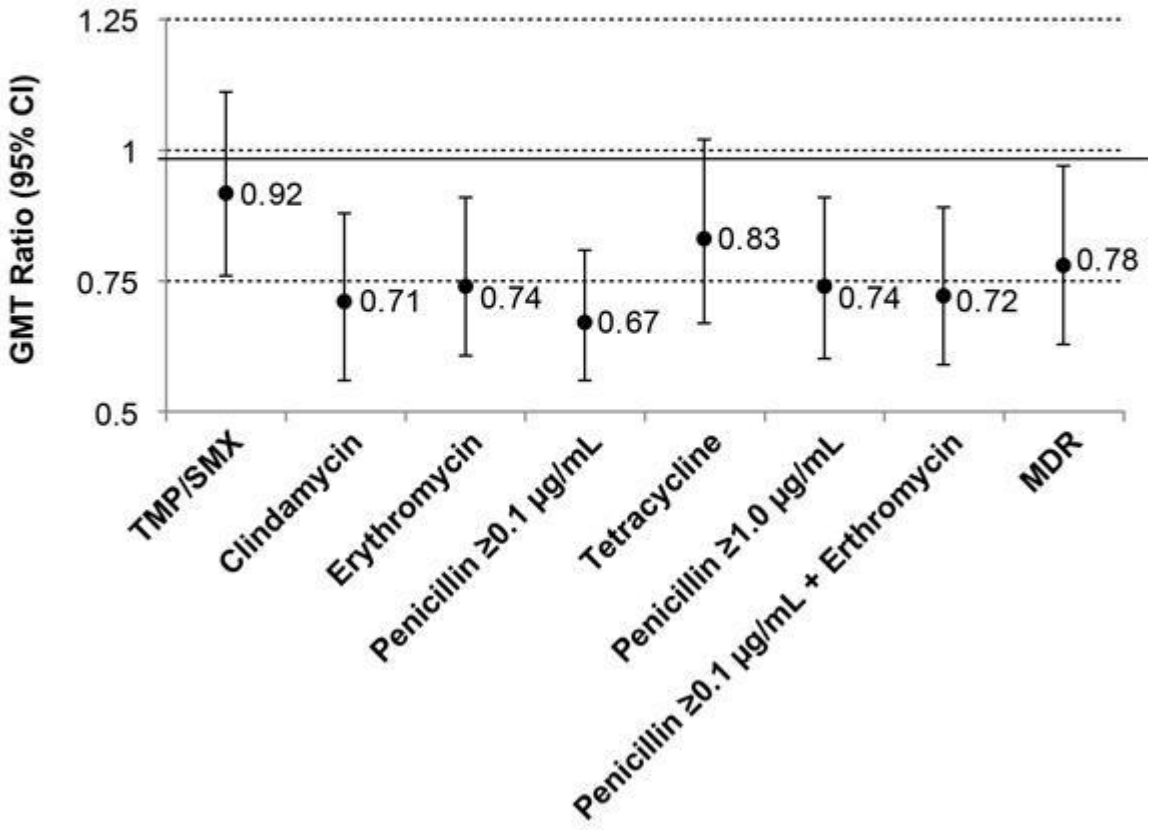
Background and aims: ARSP continues to present an important challenge to antibiotic treatment of pediatric respiratory infections even after implementation of PCV7. In this double-blind, randomized study, the potential additional impact of PCV13 over PCV7 on reduction of ARSP carriage was compared.

Methods: Healthy infants were randomly assigned to receive PCV13 (n=932) or PCV7 (n=934) at ages 2, 4, 6, or 12 months. Eight nasopharyngeal swabs were collected between ages 2-24 months. Age-specific and cumulative acquisition and prevalence rates within ages 7-24 months were calculated and compared between the 2 arms (OR; 95% CI). Antibiogram was defined by E-test (penicillin) and by disc diffusion (all other antimicrobial drugs).

Results: In general, acquisition of penicillin-, macrolide-, and clindamycin-nonsusceptible pneumococcus, as well as dual penicillin+erythromycin-nonsusceptible and multidrug-resistant (MDR, ≥3 categories) pneumococcus, was significantly lower in the PCV13 than the PCV7 group **(Figure 1)**.

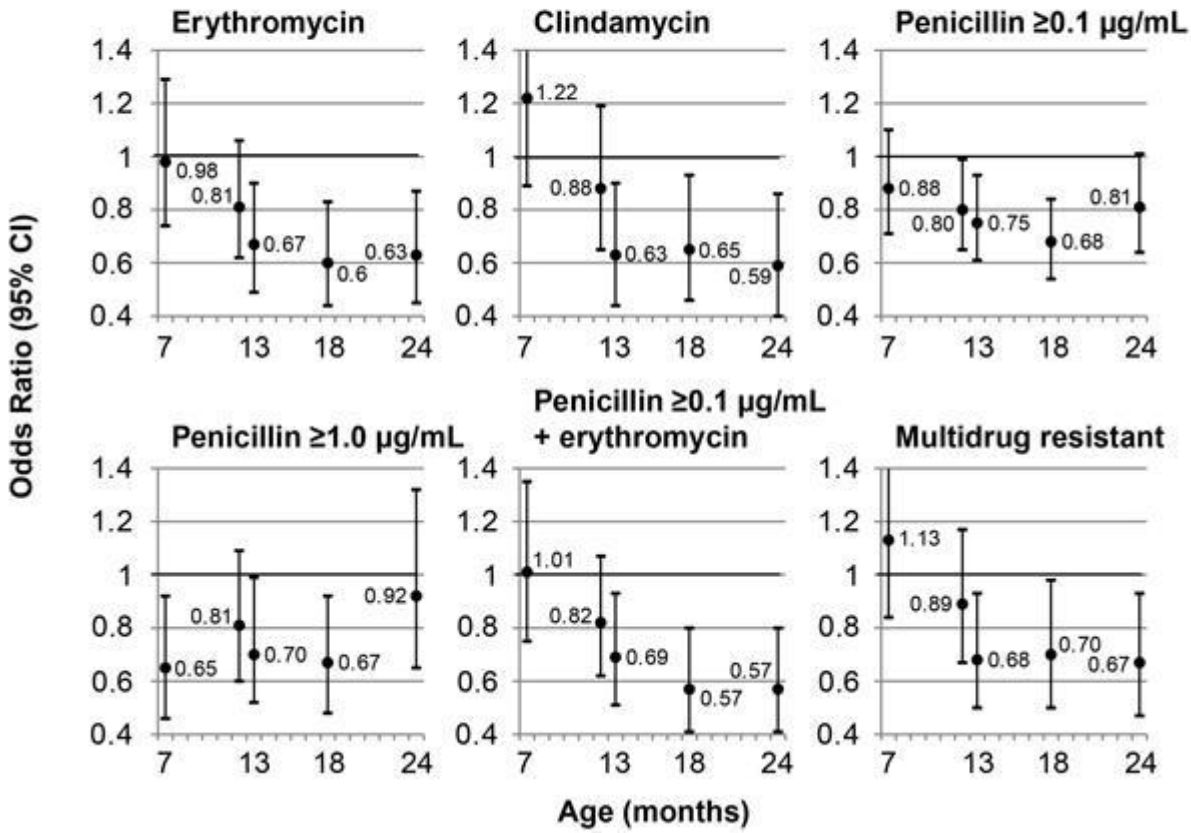
Figure 1: Odds Ratios for *Cumulative New Nasopharyngeal Acquisition* of Antibiotic-nonsusceptible *S. pneumoniae* from Age 7m through Age 24m: PCV13 vs PCV7



[Figure 1]

The cumulative prevalence figures were similar to those of acquisition. Furthermore, the differences in carriage were generally more pronounced at ages 13-24 months than after primary series (7 and 12 months) **(Figure 2)**.

Figure 2: Odds Ratios for *Age-specific Prevalence* of Antibiotic-nonsusceptible *S. pneumoniae* Carriage from Age 7m through Age 24m: PCV13 vs PCV7



[Figure 2]

Conclusions: PCV13 has a significant added benefit in reducing carriage of ARSP over PCV7. Because carriage determines transmission, these results suggest additional protection against antibiotic-resistant pneumococcal diseases beyond that provided by PCV7 in all ages.

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COMPARISON OF POSTERIOR PHARYNGEAL WALL AND NASOPHARYNGEAL SWABBING AS MEANS OF DETECTING THE CARRIAGE OF NEISSERIA MENINGITIDIS IN ADOLESCENTS

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Background and aim: It has not been definitely established which pharyngeal site allows the most precise evaluation for meningococcal carriers. The aim of this study was to evaluate the effectiveness of posterior pharyngeal and nasopharyngeal swabs in identifying and quantifying meningococcal carriage.

Methods: Two swab samples were obtained from 564 healthy adolescents aged 15-19 years, the first taken from the posterior pharyngeal wall through the mouth and the second through the nose. Bacterial genomic DNA was extracted and screened for Neisseria meningitidis by means of two separate singleplex real-time polymerase chain reactions (PCRs). Subsequently, N. meningitides-positive samples underwent a further singleplex real-time PCR in order to determine the N. meningitidis serogroup, and the DNA bacterial load.

Results: Thirty-seven subjects (6.6%) were found to be carriers of N. meningitidis. The most frequently carried serogroup was serogroup B (15 cases, 40.5%); serogroups A, Y, X, W135 and Z were found in respectively two (5.4%), five (13.5%), four (10.8%), three (8.1%) and one subject (2.7%); the serogroup was not identified in seven cases. The detection of carrier status was significantly more frequent using posterior pharyngeal swabs (5.3% vs 2.1%; $p=0.004$), which also contained a significantly larger number of N. meningitidis genomic copies (4.91 ± 1.39 vs 2.50 ± 0.8 log10 genomic copies/mL; $p< 0.001$).

Conclusion: Posterior pharyngeal swabs seem to be better than nasopharyngeal swabs for detecting N. meningitidis carriage in large-scale epidemiological studies because they identify a significantly larger number of pathogen carriers and recover a significantly larger amount of bacterial DNA.

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IMMUNE EVASION BY MORAXELLA CATARRHALIS IS MEDIATED THROUGH BINDING OF HUMAN COMPLEMENT FACTOR H

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Background and aims: Moraxella catarrhalis (M. catarrhalis) is the third most common pathogen causing acute otitis media in children. Escape of complement-mediated killing is an essential evasion strategy for M. catarrhalis. The pathogen attracts C4b binding protein (C4BP) via the family of ubiquitous surface proteins A (UspA). In addition to C4BP, UspAs bind C3 and vitronectin and thus efficiently inhibit the complement cascade. Moraxella-dependent complement resistance is, however, not only limited to the UspAs. The present study aimed to investigate the interaction of the human complement factor H with M. catarrhalis.

Methods: The factor H-binding outer membrane protein in M. catarrhalis was identified by 2-dimensional SDS-PAGE, immunoblots and MALDI-TOF-MS. Isogenic mutants as well as complemented mutants were constructed and functional assays including serum resistance were performed.

Results: We identified an outer membrane protein of M. catarrhalis which binds to complement factor H. The susceptibility to the bactericidal effect of normal human serum was increased in the isogenic mutant lacking the factor H-binding protein. The serum resistant phenotype was restored by complementation of the isogenic mutant.

Conclusion: Binding of human complement factor H is an important immune evasion strategy of M. catarrhalis. We identified the factor H-binding protein in M. catarrhalis, and show that it is directly involved in complement resistance. Future studies will reveal whether this novel factor H-binding protein may be a potential vaccine candidate.

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NASOPHARYNGEAL CARRIAGE OF S.PNEUMONIAE SEROTYPES IN 0-6 YEARS OLD CHILDREN WITH RESPIRATORY DISEASE IN LITHUANIA. FIRST RESULTS

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Distribution of nasopharyngeal carriage of S.pneumoniae (SP) serotypes among children with acute respiratory diseases (ARD) in children in Lithuania is not known.

Objectives. To assess the distribution of SP serotypes among children aged below 6 years with ARD and estimate susceptibility of SP to antibiotic.

Methods. Nasopharyngeal swabs were taken from children with ARD at 7 outpatient centres (OC) in different cities of Lithuania and at the Emergency department of Vilnius University Children's Hospital (ED ChH). Children who received antibiotics one month period prior the study and who were vaccinated with pneumococcal vaccines were not enrolled. Nasopharyngeal swabs collected in remote centres were transported to Children's Hospital microbiology laboratory using isothermal containers within 48 hours.

Results. In total 590 samples for SP nasopharyngeal carriage were examined. Out of them 204 samples were taken at the ED ChH and 386 samples at outpatients centers. There were 252 positive samples (43%): respectively 101 (50%) from ED ChH and 151 (39%) from (OC).

Serotyping was performed. Serotypes 3, 6A, 6B, 14, 15, 18 19F, 23F dominated in both groups and rep-resented 80.5% of all isolated SP.

Conclusions.SP is wildly prevalent. Data of ChH represent the distribution of SP in all Lithuania. Most of dominated serotypes are included in new conjugated pneumococcal vaccines

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PBLB OF STREPTOCOCCUS PNEUMONIAE INFLUENCES PNEUMOCOCCAL COLONIZATION AND PNEUMONIA

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Background: Pneumococcal serotype 14 sequence type (ST) 46 had been the most prevalent clone causing pneumonia in children in Taiwan.

Methods: A microarray was constructed using the genomic DNA of a clinical strain (NTUH-P15) of serotype 14 ST46. Using DNA hybridization, genomic variations in NTUH-P15 were compared to those of 3 control strains.

Results: Microarray analysis identified 7 genomic regions that had at least 10-fold increases in DNA levels in the NTUH-P15 strain compared to the control strains. One of these regions encoded PblB, a phage-encoded virulence factor implicated (in Streptococcus mitis) in infective endocarditis. Among 77 pneumonic strains, the prevalence of pblB was significantly higher in strains of the ST46 (the largest clone) and ST76 (the second largest clone) compared to other genotypes (25/25, 100% vs 16/52, 30.8%, P< 0.001). The isogenic mutant ∆pblB decreased adherence to lung epithelial cell compared to the wild-type NTUH-P15 strain (P=0.02). Complementation with PblB restored the adherence. In murine model of colonization and pneumonia, the pblB mutant was outcompeted by the wild type strain (P=0.003 in colonization; P=0.001 in pneumonia). Competition capability in colonization or lung infection could be restored by reintroducing pblB gene into the pblB mutant.

Conclusions: The pblB gene promotes colonization of S. pneumoniae, thereby providing a competitive advantage for the pathogen to successfully transmit and gain access to cause pneumonia.

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EXPANSION AND EVOLUTION OF STREPTOCOCCUS PNEUMONIAE SEROTYPE 19A ST320 CLONE: WITH COMPARISON TO ITS ANCESTRAL TAIWAN ^{19F}-14(ST236) CLONE

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Background: Streptococcus pneumoniae serotype 19A ST320 clone, derived from an international Taiwan ^{19F}-14(ST236) clone, emerge to be prevalent in many countries.

Methods: Dynamics of invasive pneumococcal disease (IPD) were determined using Taiwan national notifiable disease surveillance database. The virulence of 19AST320 and Taiwan ^{19F}-14(ST236) were assessed in mice. By constructing an isogenic serotype 19F variant of the 19AST320 strain (19FST320), we analyzed the role of capsular type and genetic background on the difference in virulence between 19AST320 and Taiwan ^{19F}-14(ST236).

Results: Between 2008 and 2011, IPD due to serotype 19A increased from 2.1 to 10.2 cases per 100,000 population ($p < 0.001$); overall IPD also significantly increased ($p=0.01$). Most serotype 19A isolates belonged to ST320. Using competition experiments in a murine model of colonization, we demonstrated that 19AST320 outcompeted Taiwan ^{19F}-14(ST236) (competitive index (CI) of 20.3; $p= 0.001$). 19FST320 was two-fold less competitive than the 19AST320 parent (CI of 0.47; $p=0.04$), but remained 14-fold more competitive than Taiwan ^{19F}-14(ST236) (CI of 14.7; $P< 0.001$).

Conclusions: Genetic evolution of pneumococcal clones from Taiwan ^{19F}-14(ST236) to 19AST320 has made this pneumococcus better able to colonize of the nasopharynx. This evolution reflects not only a switch in capsular serotype but also change in other loci.

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POLYMORPHISMS IN CD209 AND CD209L GENES ARE ASSOCIATED WITH SUSCEPTIBILITY TO TUBERCULOSIS INFECTION IN A NORTHEASTERN BRAZILIAN POPULATION

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Background: Tuberculosis (TB), due to Mycobacterium tuberculosis infection, is major cause of morbidity and mortality worldwide. So far, many candidate genes have been investigated for their possible association with TB. Dendritic cell-specific intercellular adhesion molecule 3 grabbing non-integrin (DC-SIGN) and Liver/lymph node-specific intercellular adhesion molecule-grabbing non-integrin (L-SIGN), encoded by CD209 and CD209L genes respectively, are known for binding to M. tuberculosis on human dendritic cells and macrophages.

Methods: We analyzed CD209 and CD209L polymorphisms looking for association with TB in a Northeastern Brazilian population from the state of Pernambuco. We screened 4 single nucleotide polymorphisms (SNPs) in the promoter region of CD209, namely -939G>A (rs735240), -871A>G (rs735239), -336A>G (rs4804803) and -139G>A (rs2287886) and exon 4 tandem repeat polymorphisms in both CD209L and CD209.

Results: The -139G>A and -939G>A SNPs were associated with susceptibility to TB, particularly in subjects with pulmonary (-139A) and extra-pulmonary (-939A) forms. The -871A>G and -336A>G SNPs were associated with protection to TB, in pulmonary (-871G, -871G/A, -336G and -336G/A) and extra-pulmonary (-871G and -871G/A) forms. Moreover we found a strong trend of association between GGAG haplotype and protection to TB infection. Tandem repeat polymorphism in CD209L exon 4 was associated with protection (5 allele and 6/5 genotype) and susceptibility (9 allele) to TB infection.

Conclusions: This study provides evidence of an association between CD209 and CD209L polymorphisms and TB development in a Northeastern Brazilian population, suggesting that polymorphisms in these genes may influence the protection and susceptibility to infection caused by M. tuberculosis.

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INTERACTION OF MUCINS, PATHOGENS AND HUMAN MILK OLIGOSACCHARIDES

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Background: Infants benefit from diverse health-promoting aspects of human breast milk, including protection against pathogens by human milk oligosaccharides (HMO). HMO act as soluble glycosylated receptor analogous, which irreversibly bind pathogens. In the host, a mucus layer coating the gastrointestinal tract serves as first line of defence. Pathogens bind to mucus, which consists of various types of mucins. Thereby, some pathogens are trapped in the mucus layer and removed from the gut, while others use this mechanism to protect themselves from host cellular immune response. As mucins and HMO provide similar glycosylated pathogen binding sites, we investigated if pathogen-mucin binding could be influenced by HMO.

Methods: 96 well plates were coated with mucins from porcine stomach, bovine buccal mucins, bovine serum albumin (BSA) and buffer solution (PBS). Pre-coated plates were co-incubated with pathogens (either Salmonella enterica serovar fyris (S. fyris), enteropathogenic Escherichia coli (EPEC) or Pseudomonas aeruginosa (P. aeruginosa)) and human milk oligosaccharides (either 2'-fucosyllactose (2'-FL) or 3-fucosyllactose (3-FL)). Lactose served as negative control and mannose as positive control for type-1 fimbria-mediated binding. Pathogen binding was measured by Alamar blue proliferation assay.

Results: 3-FL inhibited interaction of S. fyris and mucins in a dose-dependent manner, whereas 2'-FL did not show any significant effect. EPEC- and P. aeruginosa-binding were altered by addition of 2'-FL as well as by 3-FL.

Conclusions: HMO might serve as a preventative tool to counteract pathogen-host interaction. Further studies are needed to investigate more complex HMO and subsequent effects on host cells.

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POLYMORPHISM OF ANGIOTENSIN-CONVERTING ENZYME INSERTION/ DELETION GENE IN CHILDREN WITH GASTRITIS ASSOCIATED WITH HELICOBACTER PYLORI INFECTION

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Some cases of gastritis associated with Helicobacter pylori infection do not heal despite the correct application of treatment regimens due to the virulence of microorganisms in association with hosts` genetic predisposition.

The aim of our study was to evaluate genetic factors related to ACE gene in children with H. pylori gastritis - whether this patients differ from children without digestive pathology regarding ACE genotype distribution, and whether the ACE genotypes affect the evolution under treatment and response antibiotic schemes.

Materials and methods: The study included two comparable age and sex groups of children: 49 patients with gastritis associated with H. pylori infection (diagnosis was established by corroborating clinical findings with mucosal appearance at esogastroduodenoscopy, rapid urease-test and histological examinations of biopsies) and 90 children admitted for non-digestive pathology (with negative tests for H. pylori detection). All children were genotyped for I/D gene ACE polymorphism using the polymerase chain reaction with specific primers.

Results: The distribution of ACE DD (deletion gene), ID (insertion/deletion gene), and II (insertion gene) genotypes in gastritis group were 38.77%, 42.85%, 18.36%, while for the control group were 45.55%; 38.88% and 15.55% respectively.

The ACE genotype differ between study groups, with statisticaly significant differences ($p < 0.0001$) for allelic and genotype frequencies between children with H. pylori gastritis and controls.

Conclusions: ACE polymorphism may be a factor for Helicobacter pylori infection and may contribute to the terapeutical aproach; further studies are warranted to investigate the relation between ACE polymorphism, H. pylori infection and response to terapy.

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INFLUENCE OF INNATE IMMUNITARY RESPONSE ON SEVERE INVASIVE PNEUMOCOCCAL DISEASE: GENETIC POLYMORPHISMS IN TOLL-LIKE RECEPTORS PATHWAY

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Background and aims: Invasive pneumococcal disease (IDP) has an elevated morbility and mortality rate. Severity is conditioned by pneumococcus itself and host factors as Toll-like receptors (TLR). TLR genetic alterations recently discovered lead to higher susceptibility to infections. Development of severe IPD may be conditioned by genetic polymorphysms (SNP) in critical regions of TLR-mediated intracellular signaling pathway, and these may influence evolution and prognosis.

Aims: To define SNP prevalence in IRAK1, IRAK4, IRAKM and MyD88 genes in patients with severe IPD. To compare that prevalence with a control group. To compare patients evolution regarding SNP detected.

Methods: Case-control prospective observational study. Cases: 60 patients with IPD and systemic inflammatory response syndrome Controls: 120 healthy blood donors. Exclusion criteria: known immunodeficiency. Variables: SNP genotype and allele freqüencies, demographic data, medical history and evolutive data of severe IPD (clinical, analytical and microbiological).

Results: In case-control study, we have found association between presence of severe IPD and IRAK4 rs4251513 (p=0.0123), rs1461567 (p=0.0446) and rs1151168 (p=0.0088); and MyD88 rs6853 (p=0.0457).

In cases group, we have found association between severity data and SNP:

-Leukocytosis >15000/mmc and IRAK1 rs1059701 (p=0.0487) and rs1059702 (p=0.0025); and MyD88 rs6853 and rs7744 (p=0.0487).

-C-reactive protein >250mg/l and IRAK4 rs1141168 (p=0.0001) and rs4251513 (p=0.0000); and MyD88 rs6853 (p=0.0432).

-Presence of sequelae and IRAK4 rs4251513 (p=0.0000).

Conclusions: We conclude that genetic variability in IRAK4 and MyD88 genes is associated with an increased risk of developing severe IPD in comparison with general population, higher levels of inflammatory markers and poorer outcome.

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SERUM INTERLEUKIN-21 (SIL21) IN PERINATALLY ACQUIRED HIV-1 INFECTION (PAHIV) AND THE SEROLOGICAL RESPONSE TO 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13)

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Background: Interleukin-21 (IL21) is a key cytokine involved in T cell-dependent antibody responses. Studies in HIV-1 infected (HIV+) adults demonstrate reduced sIL21, only partially restored by antiretroviral therapy. An increase in sIL21 1-month post H1N1/09 flu vaccine was associated with more robust antibody responses. We hypothesised that decreased sIL21 might be observed in children with paHIV which might influence responses to PCV13.

Aim: To measure sIL21 in children with paHIV and to investigate any association with serological response to PCV13 vaccination.

Methods: sIL21 was measured in 43 HIV+ children, 28 healthy children and 26 healthy young adults using the Mesoscale Discovery platform. Young adult and HIV+ cohorts received 1 dose of PCV13. sIL21 measurement was repeated 1 month post-immunisation. ELISA was used to measure pneumococcal serotype specific IgG at the same time-points.

Results: sIL21 significantly positively correlated with CD4 count for the HIV+ group but not healthy controls. There was no significant difference in sIL21 between the 3 groups. There was no significant change in sIL21 concentration 1-month post-immunisation in either vaccinated group and no difference between groups. Robust IgG responses were observed for most serotypes, however there was no significant association between sIL21 and antibody concentration.

Conclusions: Unlike in HIV+ adults, HAART treated children have equivalent sIL21 to healthy controls. A lack of association between sIL21 and response to PCV13 suggests differences in mechanism of action of conjugate vs. flu vaccines. IL21 may not be playing such an important role in conjugate vaccine responses in this patient group.

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PREVALENCE OF MALARIA AMONG CLINICALLY MALARIA SUSPECTED ACUTE FEBRILE PATIENTS IN ZEWAY HEALTH CENTER, ETHIOPIA

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Misdiagnosis and mistreatment of malaria is common in developing countries. The prevalence of malaria and non- malarial fever causing diseases were assessed in 281 malaria suspected patients attended Zeway health center. Each participant was subjected for clinical and laboratory examination of malaria, relapsing fever, typhoid, typhus and brucellosis. Data entry and analysis was done using Epi-info version 3.1software. Malaria was accountable for only 17 % clinical malaria and the remaining causative agents were associated with typhoid fever (18.5%), typhus (17.8%), brucellosis (1%), relapsing fever (2%) and unidentified fever causes (44%). Coinfections were found in 7% of cases, of which 2% were treated as mono-infection. About 1.4 % non-malarial patients received antimalarial treatment. Sensitivity (Se) and specificity (Sp) of Carestart Pf/pan RDT compared to microscopy were100% and 91% respectively and positive and negative predictive values (PPVs & NPVs) were 94% and 100% respectively. HumaTex febrile antigens card agglutination were compared to titration >4 fold results and recorded as typhoid Se 100%, Sp 75%, PPV 48% and NPV 100%; typhus tests Se 100%, Sp 82%, PPV 54% and NPV 100% and, brucellosis Se 100%, Sp 98%, PPV 33% and NPV 100%. Positive predictive values of malaria symptoms were very low (fever 17%, sweating 30%, headache18%, general body ache 22% and loss of appetite 21%) compared to microscopy results. The study finding revealed high proportion of non-malarial illness clinically categorized as malaria cases. Relaying on parasite based diagnosis is important to identify malaria cases and prescribe treatments.

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DIHYDROARTEMISININ-PIPERAQUINE VS. ARTEMETHER-LUMEFANTRINE FOR FIRST-LINE TREATMENT OF UNCOMPLICATED P. FALCIPARUM MALARIA IN AFRICAN CHILDREN: A COST-EFFECTIVENESS ANALYSIS

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Background and aims: Recent randomized multi-center trials show that dihydroartemisinin-piperaquine (DHAPQ) is as efficacious as artemether-lumefantrine (AL) in treating uncomplicated P. falciparum malaria in African children. The trial results also indicate that DHAPQ has a longer post-treatment prophylactic effect compared to AL, reducing the risk of re-infection. In view of these findings, we compared the health outcomes and costs of treating children with uncomplicated malaria with DHAPQ or AL.

Methods: We developed a Markov model to simulate the incidence of malaria, costs of treatment, survival, and disability adjusted life years (DALYs) for a cohort receiving DHAPQ or AL over one-year period. The model included assumptions about malaria-related clinical events, malaria mortality, and costs of drugs. Probabilistic sensitivity analysis was used to account for uncertainty in key model parameters.

Results: The preliminary results showed that the cumulative number of malaria cases over one-year period were 2.24 (95%CI: 2--2.49) and 2.54 (95%CI: 2.27--2.82) per child when treated with DHAPQ or AL, respectively. Based on recently published treatment costs, DHAPQ dominated AL with greater than 99% confidence with both an increase in DALYs averted per child (0.44, 95%CI 0.01—0.11) and a reduction in costs per child (2.43, 95%CI 0.34--5.52). Based on a cost per treatment of I$0.69 for AL, DHAPQ was the dominant strategy for any cost per treatment below I$1.65.

All values per initially treated child over a one year period	Standard scenario	Scenario with declining infection rates	Scenario with decreasing post-treatment prophylactic effect
DHAPQ treatment	**Median (95% CI)**	**Median (95% CI)**	**Median (95% CI)**
Cases of uncomplicated malaria	2.48 (2.39 - 2.58)	1.74 (1.64 - 1.83)	1.79 (1.69 - 1.89)
Cases of severe malaria	0.04 (0.02 - 0.07)	0.03 (0.01 - 0.05)	0.03 (0.01 - 0.05)
Deaths	0.03 (0.01 - 0.05)	0.02 (0.01- 0.03)	0.02 (0.01 - 0.04)
DALYs	0.70 (0.31 - 1.30)	0.49 (0.20 - 0.94)	0.50 (0.21 - 0.97)
Total treatment cost n US$	4.29 (3.44 - 5.15)	3.37 (2.70 - 4.06)	3.44 (2.76 - 4.14)
AL treatment	**Median (95% CI)**	**Median (95% CI)**	**Median (95% CI)**
Cases of uncomplicated malaria	2.93 (2.81-3.04)	2.12 (2.00 - 2.23)	1.96 (1.85 - 2.08)
Cases of severe malaria	0.05 (0.02 - 0.08)	0.03 (0.02 - 0.06)	0.03 (0.02 - 0.06)
Deaths	0.03 (0.01 - 0.06)	0.02 (0.01 - 0.04)	0.02 (0.01 - 0.04)
DALYs	0.82 (0.38 - 1.51)	0.60 (0.26 - 1.12)	0.55 (0.23 - 1.05)
Total treatment cost in US$	4.84 (3.88 - 5.81)	3.84 (3.08 - 4.63)	3.65 (2.92 - 4.40)
DHAPQ vs. AL	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Incremental cost	-0.55 (-0.42 - -0.69)	-0.47 (-0.35 - -0.61)	-0.21 (-0.12 - -0.32)
saving DHAPQ cost to AL cost	11% (9% - 14%)	10% (7% - 13%)	4% (2% - 7%)
Incremental DALY	-0.13 (0.03 - -0.32)	-0.11 (0.03 - -0.29)	-0.05 (0.10 - -0.22)
saving DHAPQ DALY to AL DALY	16% (-3% - 39%)	14% (-4% - 36%)	6% (-13% - 27%)

[Results table]

Conclusion: Changing the first-line therapy of uncomplicated P. falciparum malaria from AL to DHAPQ is both cost-saving and life-saving in high endemic settings.

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PHARMACOKINETICS OF PAEDIATRIC LOPINVAIR/RITONAVIR TABLETS IN CHILDREN WHEN DOSED TWICE DAILY ACCORDING TO FDA WEIGHT BANDS

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Background and aims: Paediatric lopinavir/ritonavir (LPV/RTV 100/25mg) tablets are approved by the FDA and EMA. Dosing is based on body weightbands or body surface area under FDA approval, and body surface area by the EMA. This can lead to different numbers of tablets recommended, and is undesirable from a global perspective. Also, FDA recommended weightband dosing has not formally been studied in the target population. We evaluated the pharmacokinetics (PK) of LPV/RTV, administered twice daily using paediatric tablets.

Methods: This PK study is part of the PENTA18 trial (KONCERT), in which children, with fully suppressed HIV viral load, are randomized to receive LPV/RTV twice or once daily, according to FDA weightbands. PK assessment was planned to be conducted on the first 16 children enrolled in each weightband [15-25kg (lower); ≥25-35kg (middle), >35kg (highest)], before randomization while children took the tablets twice daily. Rich sampling was performed after observed intake. PK parameters were calculated by non-compartmental analysis.

Results: Geometric mean (95% CI) AUC_{0-12} for LPV for the lower (n=17), middle (n=16) and highest (n=20) weightband were 104.1 (84.9-127.5), 116.9 (100.6-135.8) and 101.9 (89.1-116.6) hr*mg/L, respectively. LPV C_{last} values were 4.2 (3.1-5.8), 5.1 (3.5-7.4) and 5.4 (4.2-7.0) mg/L, respectively. There were no significant differences in PK parameters between the weightbands (ANOVA, p>0.17).

Conclusions: Lopinavir PK was not significantly different between the weightbands. Exposure to LPV was higher than observed in children receiving the LPV/RTV solution as described in the label information. Weightband based dosing provides adequate exposure when using the paediatric tablets.

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THE ROUTE OF TRANSMISSION IS ASSOCIATED WITH THE PREVALENCE OF X4 TROPIC VARIANTS

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Background: The factors associated from R5-to-X4 switch remain unclear. We evaluate the influence of the transmission route in the prevalence of X4-variants.

Methods: Co-receptor usage was determined in 170 HIV-1-infected patients.

Results: 50.6% patients were infected through vertical transmission (VT), 28.8% through sexual contacts and 20.6% parenterally. 73.5% had plasma HIV-1 RNA>50copies/mL being the median lower in VT subjects (3.4log) than subjects infected through sexual contacts or blood transmission (IDU) (4.4 and 4.3log, respectively; P< 0.05). Median CD4-count was 226cells/µL in IDU, significantly lower than in VT and sexual contacts patients (672 and 383cells/µL, respectively). 52.9% patients harbored DM/X4-viruses: 80.2%-VT, 16.3%-sexual and 37.1%-IDU. An increase in the rate of X4-variants was observed according to the diagnosed-years (< 1 year: 11.8%; >15≤20 years: 72.7%; P< 0.001). VT patients with>5 years of HIV-diagnose presented a high prevalence of X4-viruses compared to sexual or IDU patients (80% vs 33.3% vs 33.3%, respectively; P>0.05) reaching the highest prevalence of X4-viruses when infected >15years (86.8% vs 23.1% vs 42.9%; P< 0.001). A significant correlation was observed between X4-tropism and gender, years of diagnosed infection, nadir, age, CD4-count and HIV-1 RNA. Patients infected through sexual contacts or IDU were 15.6 (95%CI 1.66;147) and 8.46 (95%CI 0.77;92.3) times more likely to have R5 variants than patients infected through VT (P=0.016 and P=0.08, respectively) independently of the gender, age, years of diagnostic, nadir and CD4-count and treatment while was dependent of the HIV-1 RNA (P=0.004).

Conclusions: The route of transmission is associated with the prevalence of X4-variants.

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SPECTRUM AND MORBIDITY PATTERN OF SEVERE PLASMODIUM VIVAX MALARIA IN CHILDREN: AN INDIAN PERSPECTIVE

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Background and aims: Recent observations from different parts of world have confirmed the existence of severe Plasmodium vivax malaria. This clinico-epidemiological study describes the occurrence and spectrum of severe P.vivax malaria in children in Indian perspective.

Methods: This prospective study was conducted on 1268 admitted children of malaria from January 2010 to November 2012. The species diagnosis was done by peripheral blood smear and rapid diagnostic test. Polymerase chain reaction confirmation on 100% of severe P.vivax malaria revealed 98.55% accuracy. Severe malaria was defined strictly on WHO criteria (2000). The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently.

Results: In this cohort study, the proportion of P.falciparum, P.vivax and mixed malaria was 48.89%, 42.57% and 8.52% respectively. Severe malaria was present in 50.47% children, with the highest relative risk among P.vivax monoinfection (62.96%) compared to P.falciparum monoinfection (40%; RR=1.574[95% CI 1.414-1.767], p< 0.0001) and mixed infections (38.89%; RR=1.619[95% CI 1.276-2.213]). Severe anemia (81.18%) was the major severe manifestation of severe P.vivax malaria followed by thrombocytopenia (70.59%), hepatic dysfuction (32.94%), cerebral malaria (16.47%), renal dysfunction (15.29%), abnormal bleeding (11.18%), and acute respiratory distress syndrome (ARDS) (7.65%). Multiorgan dusfunction was seen in 47.65% children. The proportion of all these severe manifestations were highly significantly in < 5 years age children (p< 0.001). The case fatality rate of severe P.vivax malaria was 2.9% in comparision to 3.5% of severe P.falciparum malaria (p=1.0).

Conclusions: This study reaffirms the evidence of potential of P.vivax monoinfection to cause severe malaria in children.

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RELATIONSHIP BETWEEN LOW BONE DENSITY AND ACTIVATION AND PREMATURE SENESCENCE OF THE IMMUNE SYSTEM IN HIV-INFECTED CHILDREN AND ADOLESCENTS

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Background and aims: Low bone mass has been reported among HIV-infected children and adolescents. The aim of this study is to investigate whether bone metabolism disorders are related to activation and premature senescence of the immune-system induced by HIV infection.

Methods: A cross-sectional study was performed**.** Dual-energy X-ray absorptiometry (DXA) measured bone mineral density (BMD) in a group of 31 vertically HIV-infected children and adolescents. Low BMD was defined as BMD Z-score < -1 and osteopenia as BMD Z-score ≤ -2. T cell immune activation (CD38+HLADR+) and senescence (CD28-CD57+) were analyzed by flow cytometry.

Results: Median age was 16 years (IQR 13.3-18.5), 68% caucasian and 71% female. All of them were on ART, but only 77.4% virologically suppressed. Median CD4-T cell count was 540 (IQR 160-1012). Median Z-score BMD was -0.7 (IQR: -1.8-0.5). 10 subjects (32.5%) met the criteria for low BMD and 4 (13%) for osteopenia. 50% had vitamin level < 20ng/mL. No association could be found between low BMD and immune activation and senescence.

Low BMD was significantly associated with older age, lower body mass index Z-score, cumulated protease inhibitor exposure, cumulated antiretroviral therapy exposure, time of severe immunosuppression, CD4 nadir and time of detectable viral loads. 35.5% has been exposed to tenofovir, but no association was found with BMD.

Conclusions: High prevalence of hypovitaminosis D and low BMD was observed in this cohort of HIV-infected children and adolescents. Severe immune suppression, detectable viral loads and PI exposure during growth might be determinant factors for osteopenia.

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SEVERE MALARIA AND BACTERIAL INFECTION IN CHILDREN IN BURKINA FASO: PROPORTIONS, ADMISSION DIAGNOSIS AND ACCURACY OF MALARIA RAPID DIAGNOSTIC TESTS

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Background and aims: Severe malaria (SM) and invasive bacterial infection (IBI) are major killing diseases in African children and clinically indistinguishable. Resources are often limited and malaria rapid diagnostic tests (RDTs) the only tool for diagnostic work-up of severe febrile illness.

Methods: We prospectively included children admitted with severe febrile illness at the hospital and health center in Nanoro, Burkina Faso. We looked at the frequencies of SM and IBI, the accuracy of admission diagnosis and RDTs for malaria diagnosis with expert microscopy (EM) as the reference standard.

Results: From July-December 2012, 503 children were included and 26 died (5.2%). In total, there were 348 children with SM and 38 with IBI. Proportions changed after the rainy season (June-October, Figure). In 94.4% the admission diagnosis was SM (PPV 71.2%, NPV 64.3%). RDT had a sensitivity, specificity, PPV and NPV of 98.6%, 38.1%, 78.1% and 92.2% respectively. The main pathogens isolated were non-typhoid Salmonella (NTS) (39.5%), Salmonella Typhi (21.1%) and Streptococcus pneumoniae (13.2%). NTS was only observed after the rainy season and associated with past malaria infection ($p < 0.0001$, RDT positive and EM negative). Among IBI, EM and RDT were positive in 21.1% and 68.4% respectively. WBC count was normal in 47.4% of IBI.

Conclusion: Severe malaria is clinically overdiagnosed and IBI neglected. RDTs improve malaria diagnosis but IBI will be overlooked. WBC count is not useful to guide antibiotic treatment. Improved diagnosis for IBI in resource poor settings are needed.

Figure 1. Severe malaria and Bacteremia cases by month

Month	Inclusions (number)	Severe malaria (%)	Bacteremia (%)	NTS among bacteremia (%)
July	54	74.1	7.4	0
August	132	84.1	1.5	0
September	146	74.0	5.5	0
October	82	68.3	4.9	25.0
November	60	40.0	21.7	92.3
December	29	31.0	24.1	57.1
Total	504	69.2	7.5	39.5

[Severe malaria and Bacteremia cases by month]

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DYSFUNCTION OF HDL PARTICLES IN HIV-INFECTED CHILDREN AND ADOLESCENTS

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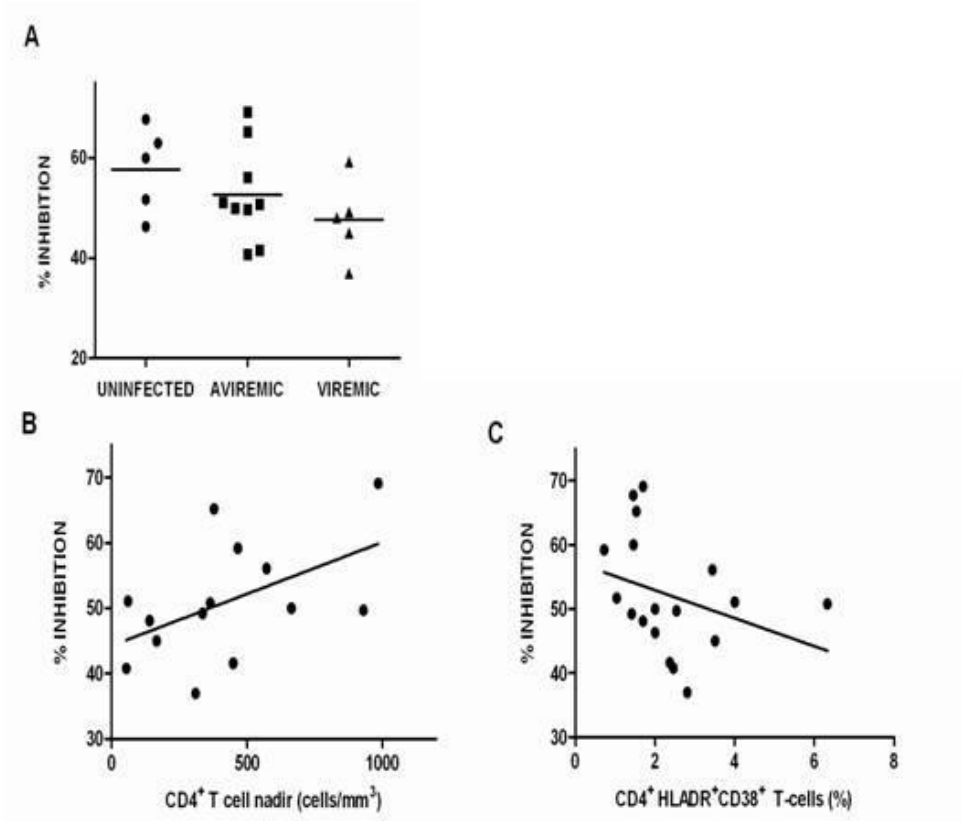
Background: We hypothesized that pro-atherogenic mechanisms related to immune activation during HIV-infection may impair HDL functionality, increasing cardiovascular risk in HIV-infected subjects.

Methods: Plasma was obtained from healthy controls and vertically HIV-infected children on ART. HDL were isolated and tested in vitro for its ability to inhibit the chemotaxis of monocytes, assessed by Transwell® cell culture chambers, in the presence of monocyte chemoattractant protein (MCP-1). T-cell activation (HLADR+CD38) was measured by flow-cytometry.

Results: We included 14 HIV-infected subjects and 5 healthy controls; 13 (65%) were female, and the mean age was 16.3±2.2 years. All patients were on ART (7 in a LPV/r containing regimen, 3 ATZ/r and 2 EFV), but only 9 had achieved virological suppression. Median CD4 cell count was 841 cells [498-1126], CD4% 31[25.7-38.1] and CD4 nadir 371 cells [160-595]. HIV-infected subjects showed a slightly worse lipid profile, although the differences were not statistically significant. HDL anti-inflammatory function was decreased in HIV-infected subjects (p=0.494), and especially on those with detectable viral load, as shown in the graph A (all p >0.05). No association to ART regimen was found, but there was a significative correlation between inhibition and CD4 nadir (Spearman Rho= 0.547, p=0.043, graph B) and immune activation (Spearman Rho= -0.407, p=0.083, graph C).



[Graphs A, B, C]

Conclusions: Our observations suggest that the anti-inflammatory properties of HDL particles are defective in HIV-infected children. New strategies to increase HDL functionality rather than HDL levels might be of interest in HIV infection.

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SAFETY AND EFFICACY OF TREATMENT SIMPLIFICATION IN HIV-INFECTED CHILDREN AND ADOLESCENTS

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Background: Achieving and maintaining good adherence to ART is a challenge for clinicians treating HIV-infected children and adolescents. Simplification strategies may improve adherence and decrease medication's adverse effects.

Methods: Data from subjects who underwent ART simplification between 2001-2012 were analyzed, considering simplification every switch in ART in virally suppressed patients that reduces pill burden, dosing frequency or enhances tolerability.

Results: We evaluated 122 episodes corresponding to 81 patients (55.5% females). Medium age at the moment of ART switch was 14±3.9 years, median CD4 cell count 813/mm³ (IQR: 627-1060). Pill burden was reduced in 90% of simplifications, 35% decreased dosing frequency to QD and 65% enhanced tolerability. Fixed-dose combinations were used in 54% of simplifications; mostly EFV/FTC/TDF (43%). Medium follow-up time was 20 months (11-31), with loss of virologic suppression only in 5.7% of cases. Percentages of CD4 T cells significantly increased at months 12, 24 and 36 of follow-up (all $p < 0.05$). When considering the group of adolescents over 12 years that underwent simplification resulting in reducing pill burden or dosing frequency, compared to children below 12, not only CD4 percentage but also absolute number increased. In those cases in which simplification aimed to reduce metabolic toxicity, total cholesterol, triglycerides and low-density lipoprotein levels decreased along the study period (all $p < 0.05$).

Conclusions: Most subjects maintained virological suppression and CD4 T cells increased, suggesting an improvement in adherence. Simplification strategies are to be considered to reduce toxicity and improve adherence and quality of life of HIV-infected children on suppressive ART.

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VENTRICULAR FUNCTION AND CARDIOVASCULAR RISK IN HIV-INFECTED CHILDREN AND ADOLESCENTS:THE CAROVIH STUDY

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Background: HIV-infected adults show premature atherosclerosis and ventricular dysfunction. We evaluated cardiovascular risk and ventricular function through carotid intima-media thickness (IMT) and Speckle Tracking Echocardiography (STE) in HIV-infected children and adolescents.

Methods: Inflammatory and cardiovascular biomarkers were determined in a cohort of vertically HIV-infected children and adolescents and age-and-sex matched controls. A complete echocardiographic study was performed, including IMT, shortening and ejection fraction (SF, EF), tissue Doppler and STE.

Results: 150 HIV-infected subjects and 150 controls were included. Mean age was 14.8±4.9 years, 62% were female. Most HIV patients had undetectable viral load (76.4%), were vertically HIV-infected (96.7%) and all but 2 patients were on ART. HIV-infected subjects showed thicker IMT compared to uninfected controls (0.434mm ± 0.025 vs 0.424 ± 0.018, respectively), and lower systolic function (p< 0,001), although values were within normal ranges. Ventricular torsion was greater in this group: 6,06° (SD 2,25) vs 5,49° (SD 1,97) (p=0,09), according to a premature senescence of the myocardium. Among cardiac biomarkers, only tPA and VCAM were higher in HIV+ subjects compared to controls (all p< 0.05), and there was a non-significant trend to higher hsCRP.

Conclusions: Our findings suggest that cardiovascular risk is increased in vertically HIV-infected children and adolescents, despite ART. Thus, cardiovascular risk should be carefully monitored since childhood, and preventive measures are to be implemented in vertically HIV-infected patients.

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SWITCH TO SECOND-LINE ANTIRETROVIRAL THERAPY AND EVIDENCE OF RE-SUPPRESSION WITHOUT TREATMENT CHANGE AFTER VIROLOGICAL FAILURE IN CHILDREN IN THE UK/IRELAND

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Background: There are limited data on switch to second-line antiretroviral treatment (ART) in children. We describe switch to second-line following virological failure (VF) among children in the Collaborative HIV Paeditric Study (CHIPS).

Methods: Initial VF was defined as either rebound (2 consecutive viral load (VL) >400 c/ml within 12 months) after suppression or VL >400 c/ml after 12 months on ART without suppression. Switch to second-line was defined as changing ≥3 drugs, or ≥2 drugs for treatment failure. Factors associated with time to switch following VF were assessed using Cox regression.

Results: 202 children experienced VF: 31 (15%) started ART with 3-drug boosted PI, 120 (59%) 3-drug NNRTI-, 30 (15%) 4-drug NNRTI- and 21 (10%) 3-drug abacavir-based regimens. Median age at VF was 9.2 (IQR 3.7-12.8) years, median CD4 count 560 (335-1,075) cells/mm^3 and median follow up was 4.3 (2.4-6.8) years after VF. 169 (84%) with VF had previously suppressed, VF occurred at median 18.5(9.7-36.8) months after ART initiation. Of these 169 children, 89 (53%) subsequently re-suppressed without switching. 33 (16%) had initial failure without suppression, with 17 (52%) subsequently suppressing before switching. 71 (35% of 202) switched to second-line at median 4.9 (1.7-15.4) months after VF. In multivariable analyses, only lower VL at VF and boosted PI-based regimens were associated with slower switching following VF.

Conclusions: Over half of children with VF re-suppressed without switching. Switching to second-line following VF was faster in children on NNRTI-based ART likely due to lower resistance threshold.

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DEVELOPMENT AND IMPLEMENTATION OF A PAEDIATRIC LAMIVUDINE, ABACAVIR AND NEVIRAPINE INDIVIDUALIZED DOSE COMBINATION SUSPENSION

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Background: The liquid formulations of Lamivudine, Abacavir and Nevirapine are standard first line regimen in HIV-positive infants, but need to be dosed and administered separately. As dosing of Nevirapine is based on body surface area, but Lamivudine and Abacavir are calculated per body weight, fixed dose combinations (FDCs) can't allow precise dosing. In fact FDCs in tablet form deliver somewhere between 50 and 200% of the target dose for individual patients.

Objective: To develop a triple combined antiretroviral suspension with variable amounts of the three ARVs, test it for stability and compatibility and - if suitable - adopt it as first line therapy in a pilot study.

Methodology: Analytical methods were developed, validated and stability and compatibility was studied under controlled conditions at 30°C/75%RH.

Given the positive results, ten HIV-positive infants were identified and received the individualized dose combination suspension twice daily for six months.

Results: Starting from cheap adult generic tablets of the three ARV's and taking into account different weight/surface area ratios a method was developed that allows easy compounding of a fixed volume, individualizable, liquid triple ARV combination which is stable for at least 42 days even in tropical climate without refrigeration.

During the first six months of treatment no clinical or laboratory differences as compared to standard treatment were detected, while compliance was optimal.

Conclusion: The results may allow centers to compound a cheap liquid formulation, delivering 100% of the target dose for each individual child with a bodyweight between 3 - 15 Kg.

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PERINATALLY INFECTED HIV POSITIVE YOUNG ADULTS HAVE LOW LEVELS OF CARDIOPROTECTIVE NATURAL ANTIBODIES TO PHOSPHORYLCHOLINE, AN EPITOPE OF OXIDISED LDL

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Background: We measured levels of natural antibodies (NA) against phosphorylcholine (PC) to assess aetiology of cardiovascular risk in young adults perinatally infected with HIV. NA are part of the innate immune system, active in clearing up cellular debris. These polyreactive antibodies, found in the absence of exogenous antigenic stimulation, recognise oxidised cellular debris. Oxidised LDL(ox-LDL) is a potent driver of atherosclerosis. NA play an active cardioprotective role in clearing ox-LDL.

Methods: Perinatally infected HIV positive 18 to 24 years olds were recruited from the transition clinic and race, smoking, sex matched negative controls from the genitourinary service, Imperial College NHS Trust, London, UK. Serum NA levels of IgM/IgG anti-PC were determined by ELISA validated to less than 5% variability, assays were performed in triplicate. Differences assessed by ANOVA (SPSS v19).

Results:

Results	HIV Positive	Controls	Significance
N	20	16	
Age mean(SD)	20.7(1.7)	21.9(1.7)	
Male N(%)	5(25)	4(25)	
Smoker N(%)	4(20)	4(25)	
Black Race N(%)	18(90)	15(93.8)	
Total Cholesterol mmol/L mean(SD)	4.07(0.70)	3.7(0.64)	Not significant
IgM anti-PC OD mean(SD)	0.91(0.31)	1.22(0.29)	P=0.004
IgG anti-PC OD mean(SD)	0.73(0.27)	0.97(0.30)	P=0.016

[Table 1]

N=Number, SD=standard deviation, OD=Optical density

Conclusions: HIV positive, young adults have lower levels of NA to phosphorylcholine. Low levels of cardioprotective NA may represent a cardiovascular risk factor.

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PREVALENCE OF HIV MOTHER TO CHILD TRANSMISSION IN A TERTIARY HOSPITAL: RETROSPECTIVE ANALYSIS OF 13 YEARS

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Background and aims: Implementation of recommendations regarding HIV screening, treatment of pregnant women and prophylaxis for perinatal transmission have resulted in a reduction of perinatal HIV mother to child transmission (MTCT) to less than 2% in USA and Europe. The objective of the study was to describe our experience in the management of MTCT during the last thirteen years.

Methods: Retrospective case series of HIV infected mothers who delivered at a tertiary center in Seville, Spain from January 2000 to December 2012. Information on HIV status and retroviral therapy during pregnancy as well as obstetric and newborn data were collected.

Results: Of the 99171 mothers reviewed 101 pregnacies of 78 HIV-positive women (HIV sero-prevalence rate 10,2/10000 pregnancies) were recorded. HIV transmission rate was 1,98/1000 newborn. All infants received exclusive formula feed. Two children was infected, one of them due to an uncontrolled pregnancy, the second case despite compliance with published recommendations. Data are shown in Table 1 and 2.

HIV CDC stage	Coinfection	ART therapy initiation	Idetectable viral load
A 67 (66,3 %)			Pregestacional 29/101
B 21 (20,8 %)	HBV 19 (18,8 %)	Pregestacional 35/101	< 12 week 5/101
C 9 (8,9 %)	HCV 3 (2,9 %)	< 12 week 14/101	13-24 week 11/101
UK 4 (3,9 %)	HBV/HCV 1 (0,9 %)	13-24 week 30/101	> 24 week 29/101
		> 24 week 4/101	Perinatal detectable viral load 20/101
		No ART 13/101	UK 13/101

NK: not known; HBV: hepatitis B virus, HCV: hepatitis C virus, ART: anti-retroviral therapy

[Table 1]

Table 1: HIV status and retroviral therapy during pregnancy

Intrapartum AZT	Membranes rupture	Delivery mode	Weeks' gestacion at birth	Birth weight
Yes 94/101 No 4/101 UK 3/101	0 h 15/101 < 6 h 64/101 6-24 h 10/101 >24 h 4/101 UK 9/101	Vaginal 52/101 Forceps/ 11/101 vacuum Scheduled 12/101 cesarean Urgent 26/101 cesarean	Term (37-42 w) 83/101 Moderate preterm 11/101 (32-37 w) Very preterm 3/101 (28-32 w) Extremely preterm 1/101 (<28 w) Posterm (>42 w) 3/101	>4000gr 3/101 2500-4000gr 80/101 1500-2500gr 12/101 500-1500gr 3/101

[Table 2]

Table 2: Obstetric and neonatal data

Conclusions: Prevalence of HIV MTCT was low using effective interventions although

- Delayed viral supression near delivery was observed in up to 20% of HIV infected mothers despite appropiate initiation ART.
- A high rate of urgent cesarean sections (>25%) was performed.
- No different of the rate of neonates with intrauterine growth retardation between healthy and HIV pregnancies was reported.

Optimization of access to healthcare system remains being a key issue in order to further minimize the risk of HIV MTCT.

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POOR GROWTH IN HIV-INFECTED CHILDREN IS ASSOCIATED WITH CHANGES IN IGF SYSTEM AND PERMANENT CHRONIC INFLAMMATORY PROCESS

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Background: HIV-infected children usually show impaired growth. Reports on GH-IGF-IGFBPs system in these children are scarce.

Aim: To analyse serum concentration of the components of IGF-IGFBPs system in these children and compare them to growth parameters and to cytokines levels.

Methods: 37 prepubertal HIV-infected children, aged 8.2±1.7 years, were evaluated every 6 months during one year when anthropometric data and blood samples were collected for IGFs, IGFBPs, cytokines and viral load (VL) determinations. Thirty healthy prepurbetal children were studied as controls. IGF-I, IGF-II, IGFBP-3 and IGFBP-1 were determined by ELISA, IGFBP-2 and IGFBP-4 by Western-ligand blotting(WLB) and IL-6 and tumoral TNFa by Luminex®. We defined VL< 5.000 and VL>5.000 copies/mL as good(GC) and poor(PC) disease control.

Results: BMI in HIV-infected children was similar to controls. Height was lower in HIV-children than in controls ($p< 0.001$). Serum IGF-I, IGF-II and IGFBP-3 were similar in PC and in GC but lower than in controls. IGFBP-1 and IGFBP-4 levels were similar among PC, GC and controls. IGFBP-2 levels were higher in PC than in GC. IL-6 and TNFa concentrations were similar in PC and in GC but higher than in controls. No correlation was observed between IL-6 or TNFa and IGF-I, IGF-II or IGFBP-3. IGFBP-1 levels were lower (< 58ng/ml) in samples with higher TNFa ($P=0.0006$) or IL-6 ($P=0.05$).

Conclusion: HIV-children present poor growth comparatively to healthy children. It may be explained by changes in IGF-IGFBPs system that reduces IGF bioavailability/activity. The permanent and chronic inflammatory process may contribute to IGF-IGFBPs alterations.

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INDIRECT EFFECTIVENESS OF TEN-VALENT PNEUMOCOCCAL HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE (PHID-CV10) AGAINST NASOPHARYNGEAL CARRIAGE: FINIP INDIRECT CARRIAGE STUDY

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Background: FinIP trial was designed to evaluate effectiveness of PHiD-CV10 (GlaxoSmithKline) against diseases associated with S.pneumoniae and H.influenzae. We conducted a satellite study in siblings of the FinIP-vaccinated children to evaluate indirect effectiveness against nasopharyngeal carriage.

Methods: FinIP was a cluster-randomised, double-blind trial, where 29126 children < 7 months were recruited from February'09 to August'10. Children received PHiD-CV10 in 2/3, and control vaccine in 1/3 of 72 clusters according to 3+1 or 2+1 schedules. For our indirect carriage study, we obtained a nasopharyngeal sample from unvaccinated 3 to 7-year-old siblings of FinIP participants during April'11-November'11. Generalized linear mixed model was used to estimate indirect effectiveness against nasopharyngeal carriage due to S.pneumoniae (Pnc), H.influenzae, M.catarrhalis and S.aureus.

Results: 1445 samples were obtained in 72 clusters. Table reports indirect effectiveness of PHiD-CV10 against carriage (1-odds ratios) in older siblings of FinIP-vaccinated children.

Pathogen	N positives			Carriage percentage			Effectiveness (%) of PHiD-CV
	Control (N=518)	PHiD-CV 2+1 (N=482)	PHiD-CV 3+1 (N=445)	Control (N=518)	PHiD-CV 2+1 (N=482)	PHiD-CV 3+1 (N=445)	Estimate (95%CI)
Overall Pnc	197	155	174	38.0	32.2	39.1	10 (-12,28)
Vaccine-type Pnc	100	69	65	19.3	14.3	14.6	29 (6,47)
H.influenzae	71	63	54	13.7	13.1	12.2	9 (-25,34)
S.aureus	112	124	104	21.7	25.7	23.4	-17 (-52,9)
M.catarrhalis	175	158	160	33.8	32.8	36.0	-5 (-40,21)

[Indirect effectiveness against carriage]

Conclusions: Indirect effectiveness against vaccine-type pneumococcal carriage was demonstrated, and was consistent under both 3+1 and 2+1 schedules. This is the first study to provide evidence for indirect impact of PHiD-CV10, suggesting indirect protection also against vaccine-type S.pneumoniae disease.

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SUSPENSION OF THE BCG-VACCINATION-PROGRAMME IN ROMANIA, AND RESUMPTION FOLLOWING THE SAFETY ASSESSMENT BY A JOINT WHO EURO-ECDC MISSION

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Background: In 2011, Romania switched to a different BCG-vaccine for neonates, after a period of supply-problems and several BCG-vaccines. From January 2012, the signal of increased AEFI-reports prompted a series of actions, including written recommendations on administration and dosage, distribution of guidelines for BCG-AEFI-reporting and a national case-management-plan for clinicians and vaccine administrators. Increasing media attention led to a temporary suspension of the programme on 20 November 2012. Simultaneously, the Minister of Health (MoH) requested a joint WHO EURO-ECDC expert safety-assessment of the BCG-vaccination-programme.

Methods: The expert-mission arrived in Romania on 26 November 2012. Meetings with responsible stakeholders were organized, relevant documents studied and AEFI-reports analysed. Assessment results and recommendations were reported to the MoH. Conclusions were shared with national media at a Press-Conference on 30 November 2012. The vaccine under study was BCG-SSI from Denmark (batch 110021A).

Results: 154 AEFI-reports (60% male) reflected the batch used from June 2011 until July 2012 (136,056 vaccinees). The majority (n=145) concerned enlarged regional lymph-nodes/adenitis, with in 41 cases abscess/suppuration/fistula, spontaneously or after treatment. No severe adverse reactions such as osteomyelitis were detected. Hospitalisation rate appeared high (63%) with a median of 13 days admission. Treatment was diverse, with 70% getting tuberculostatics (64%) in some sort of regimen and/or surgery (21%). Analyses unveiled no clustering of cases and no indication of systematic administration errors.

Conclusion: The BCG-vaccination-programme was resumed, as announced at the Press-Conference. Recommendations on strengthening the safety surveillance, enforcement of standardised treatment guidelines and a communication plan are being addressed.

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POLYSACCHARIDE-SPECIFIC MEMORY B CELL RESPONSES AND CARRIER PROTEIN-SPECIFIC CD4+ T CELL RESPONSES FOLLOWING HIBMENCY-TT GLYCO-CONJUGATE VACCINATION IN HUMAN INFANTS

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Background and aims: Glyco-conjugate vaccines have led to significant reductions in the prevalence of disease caused by polysaccharide-encapsulated bacteria, including Haemophilus influenzae b (Hib) and Neisseria meningitidis (e.g. MenC and MenY). These vaccines induce T-dependent antibody responses in infants who are most susceptible to these infections. Little is known of the contribution of the quantity or quality of carrier protein-specific CD4+ and polysaccharide-specific memory B cell responses in maintenance of polysaccharide-specific antibody following glyco-conjugate vaccine priming.

Methods: PBMCs were collected from a cohort of 44 human infants who received HibMenCY-TT vaccine in a 2-4-6 month priming schedule and following a 12 month boost. We identified TT-specific CD4+ T cells through up-regulation of CD154 expression via flow cytometry following stimulation, MenC and MenY -specific memory B cells via ELISpot, and IgG titres via ELISA.

Results: MenC- and MenY- specific memory B cell numbers after priming did not correlate with IgG titre pre-boosting but induction of MenC-specific memory B cells post-priming was significantly ($p=0.003$) correlated with the magnitude of IgG response post-boosting. Analysis of the CD4+ T cell response showed that the number and quality (defined by TNFα, IL-2 and IFNγ expression) of TT specific CD4+ T cells following HibMenCY-TT priming did not correlate with polysaccharide-specific IgG at any time point.

Conclusions: MenC- and MenY-specific memory B cells induced at priming are influential in secondary antigen-specific IgG responses, and only a threshold level of CD4+ T cell help is required in priming for a secondary B cell response following glyco-conjugate vaccination.

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THE NEONATAL EXPOSURE TO THIMEROSAL CONTAINING VACCINES HAS NO INFLUENCE ON CHILDREN'S COGNITIVE DEVELOPMENT

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Background and aims: The controversial topic of the early human exposure to mercury is ethylmercury, which is present in the thimerosal-containing vaccines (TCV). The objective of this analysis was to determine the relationship between the neonatal exposure to TCV and cognitive development of children during the first 7 years of life.

Methods: The cohort recruited prenatally in Krakow, Poland, included 310 children vaccinated in neonatal period against hepatitis-B using formula with or without thimerosal. The children development was assessed using the Fagan test (6th month of life), the Bayley Scales of Infant Development BSID-II (12th,24th,36th month), Raven test (5th year) and Wechsler Intelligence Scale (6th and 7th year). Results were determined by multivariable linear and logistic regression, adjusted to potential confounders.

Results: Children exposed and not exposed to TCV in neonatal period had similar outcomes of cognitive developmental tests, only the Fagan and BSID-II in 36th month results were significantly higher for exposed to TCV. After standardization to gender, maternal education, mercury level in cord blood, thimerosal exposure in period from 2nd to 6th month of life and breastfeeding up to 6 months only the difference in BSID-II remained significant β =4.17(95%CI:0.85-7.51). The results of all other tests did not showed significant differences.

Conclusions: Our study demonstrated that TCV administration in neonatal period had no harmful influence on children's cognitive development.

All studied children were a sample from cohort study on the susceptibility of fetus and child to environmental factors followed in Krakow with Columbia University in New York

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DIMINISHED VARICELLA-ZOSTER-VIRUS (VZV)-SPECIFIC IMMUNITY IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: In solid organ transplant (SOT) recipients, varicella-zoster-virus (VZV) infection is associated with significant morbidity and mortality. The study was aimed to measure immunity against VZV not only by IgG-anti-VZV antibody concentrations (“quantity” of antibodies), but also by investigating the antibody binding strength (avidity, “quality” of antibodies) and the VZV-specific cellular response in SOT patients.

Methods: The IgG-anti-VZV relative avidity index (RAI) and the frequency of VZV-specific peripheral blood mononuclear cells (PBMCs) were assessed in 19 liver transplant (LTx) and 23 kidney (KTx) recipients including children and adults compared to 48 healthy controls (HC) after VZV vaccination (vacc) or wild-type infection (wt) using an adapted ELISA and IFN-gamma ELISPOT.

Results: Despite equally distributed IgG-anti-VZV concentrations between the groups, LTx(wt) (mean RAI 63.6%), LTx(vacc) (69.1%), KTx(wt) (66.8%) and KTx(vacc) (84.2%) showed lower avidities compared to HC(wt) (87.3%) and HC(vacc) (93.5%). Only 69.0% of SOT patients showed RAI>60% (high avidity), but 100% of HC. HC(vacc) (314 spot forming units SFU/500,000 PBMCs) demonstrated significantly higher VZV-specific cellular responses compared to KTx(vacc) (79 SFU) and LTx(vacc) (83 SFU).

Conclusions: Impaired antibody avidities and cellular reactivity to VZV have to be considered in SOT patients receiving immunosuppressive treatments when assessing VZV-specific immunity. IgG-anti-VZV avidity and VZV-specific cellular responses may serve as additional markers to evaluate immunity against VZV in immunocompromised SOT patients. However, so far, the role of wild-type exposures and endogenous VZV re-activation on long-term immunity in SOT patients has to be investigated before establishing recommendations for vaccinations and laboratory tests.

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ANTIBODY PERSISTENCE ONE YEAR AFTER VACCINATION WITH FOUR DOSES OF THE INVESTIGATIONAL MENINGOCOCCAL SEROGROUP B VACCINE, 4CMENB

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Background: Four doses of the investigational, multicomponent serogroup B meningococcal vaccine, 4CMenB, were well tolerated and immunogenic in infants when administered with routine vaccines at 2, 4, 6 and 12/13 months. We assessed antibody persistence 1 year after the last immunisation, in comparison with vaccine-naive two year-olds.

Methods: In this extension study we enrolled 421 two year-old children, 305 previously vaccinated with four doses of 4CMenB at 2, 4, 6 and 12/13 months of age, and 116 vaccine-naive controls. Serum bactericidal activity with human complement (hSBA) was assessed against serogroup B strains representative for individual vaccine antigens - factor H binding protein (fHbp), Neisserial adhesin A (NadA), Neisseria heparin binding antigen (NHBA) and New Zealand strain outer membrane vesicles (NZOMV).

Results: One month after their 4th dose, 94−100% of vaccinated children had protective hSBA levels (titre ≥ 5) against the four antigens. One year later antibody titres had waned, but 62% (95% CI: 56−67) still had titres ≥ 5 against fHbp, 97% (95−99) against NadA, 36% (31−42) against NHBA and 17% (13−22) against NZOMV. The equivalent proportions in the age-matched, vaccine-naive subjects were 3% (1−8), 1% (0.02−5), 26% (18−35) and 0% (0−3), respectively. GMT ratios between the vaccinated and naive groups were 5.7 (4.4−7.3), 74 (58−95), 1.5 (1.1−2.0) and 1.8 (1.4−2.2), respectively.

Conclusions: The hSBA antibodies induced by a four dose vaccination series of 4CMenB in infants waned over the 12 months following the last dose, but levels remained higher than those in non-vaccinated children, particularly for fHbp and NadA.

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VALUE OF PCR IN THE DIAGNOSIS OF GROUP B STREPTOCOCCUS (SGB) NEONATAL INFECTION

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Background and aims: Identification of GBS can be difficult after antibiotics exposure or with inadequate culture. A GBS PCR was developed in our hospital and used on blood and/or CSF of the newborns. Our study aims to determine its added value to diagnose GBS neonatal infection.

Methods: Retrospective study of infants less than 3 months old admitted in our hospital from 01/01/2006 to 31/12/2009. All patients in whom PCR was requested or with GBS demonstrated by culture were selected. Clinical and biological data of infants with a positive result in a normally sterile site were analyzed. GBS infections were confirmed or refuted, and sorted as early or late. Sensitivity and specificity of the PCR were calculated.

Results: 2668 GBS PCR were performed (95% on blood and 5% on CSF). Twelve patients met criteria for GBS infection: 10 early and 2 late. Cultures were positive in only 5 of them. Incidences of early and late GBS infection were 1.05 ‰ and 0.2 ‰ of live births. On blood, PCR's sensitivity was 50%, specificity 99.9% and negative predictive value 99.8%. On CSF, sensitivity and specificity were 100%.

Conclusions: To diagnose meningitis, PCR GBS seems to be a valuable tool. Given its price and lack of sensibility on blood, its use is not justified in the asymptomatic child evaluated for risk factors. In addition to rapid identification of GBS, PCR results would allow an adaptation of the spectrum, dosage and duration of antibiotic therapy when the culture is negative in infected newborn.

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RESURGENCE OF SEROTYPE(ST) 19F CARRIAGE IN PRE-SCHOOL CHILDREN IN PORTUGAL IN THE CONTEXT OF CONTINUING MODERATE CONJUGATE PNEUMOCOCCAL(SP) VACCINE UPTAKE

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Background and aims: We have previously reported progressive diminution of Sp conjugate vaccine STs and overall Sp carriage rates in children attending daycare in Coimbra, Portugal but persistence of ST19F until early 2009. Vaccination coverage in infants, entirely through private market sales, peaked at around 80% in 2007 & has since fallen to 65% or less. In 2009-10 some children received PCV10.

Methods: In February-March 2010 we again swabbed the nasopharynges of children, 6M-6Y, attending 6 nurseries in Coimbra, Portugal. Sp isolates were serotyped by multiplex microarray.

Results: Swabs were obtained from 586 children, 326 (56%) male. Mean age was 41.5M (range 6.3 - 74.5). 507 (86.5%) had received at least one dose of PCV7/10. Sp carriage rate was 57.6% with 18.9% of all the children carrying >1 ST, 11.2% PCV10 vaccine types (VTs) and 8.7% ST 19F which was more commonly detected than any other ST although less commonly than non-typables (13.3%).

Conclusions: ST19F (covered by PCV7,10&13) is emerging as the most commonly carried encapsulated type of Sp in this series of ecological studies which has been running since 2007, with rates rising from 3.6% in 2008 to 8.7% in 2010. 19 cases of invasive disease due to 19F were reported to the Portuguese national surveillance scheme between 2007 and 2012. Moderate overall (65-80%) PCV coverage through non-universal delivery in a 2/3+1 schedule is not sufficient to control ST19F circulation in daycare and occurrence of invasive disease, despite somewhat higher vaccine uptake among nursery attendees.

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DEBATE ON THERAPY OF COMMUNITY-ACQUIRED PNEUMONIA

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Community-acquired pneumonia (CAP) is one of the most important causes of childhood mortality in developing countries and, despite the availability of effective preventive and therapeutic measures, remains a significant cause of morbidity and hospitalisation in the industrialised world. Some attempts to prepare specific official guidelines have been made in order to rationalise the approach to pediatric CAP, and a detailed analysis of these highlights the fact that the suggested solutions are rarely based on high-quality evidence. It is possible to prepare recommendations for most of the problems that emerge in patients with severe pediatric CAP, who are identified on the basis of clinical findings and can be rapidly admitted to hospital where they can undergo all of the necessary laboratory and instrumental evaluations. However, identifying the etiology is not easy in many of these cases because the currently used microbiological and radiological methods are frequently unable to provide precise information, and so combined therapy with different antibiotics is frequently prescribed. This explains why the recommended approach to mild or moderate cases is always based on mainly moderate or poor quality evidence. This can lead to an exaggerated number of diagnoses and hospital admissions, and increase the unnecessary use of antibiotics, which can have significant medical and socioeconomic consequences. There is an urgent need for further studies aimed at defining first- and second-line antibiotic therapy for mild and moderate CAP. In the absence of new data, it is necessary to be aware that a substantial number of patients will not be optimally treated.

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DEBATE ON THERAPY OF COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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In contrast to the developing world where pneumonia is diagnosed base on WHO clinical criteria, in developed countries it includes temperature, white blood cells count, chest radiographs and detection of bacterial and viral etiologies. The lack of uniformity in CAP definition has been a crucial hurdle to studying appropriated antibiotic treatment resulting in heterogeneous recommendations.

The most commonly recommended antibiotic for CAP is amoxicillin. Since most developed countries are routinely using Haemophilus influenzae type b vaccines there is no need most of the times to use a β-lactamase stable drug. Although many countries are using the new pneumococcal conjugated vaccines, it is still recommended in some countries due to a high rate of penicillin non-susceptible S. pneumoniae to use high-dose amoxicillin.

Studies from the developing world, using the WHO clinical criteria, suggested that in children even a 3-day treatment course is appropriate. Moreover, no significant differences were found between a 3-day amoxicillin and placebo treatment, suggesting that the WHO clinical criteria may not appropriately identify children with true bacterial pneumonia necessitating antibiotic treatment. Thus, extrapolating from studies conducted in the developing world to developed populations may be inappropriate.

In school-aged children, macrolide therapy is sometimes added to b-lactam therapy to cover atypical pathogens such as Mycoplasma pneumoniae.

Viral and bacterial co-infection can be detected in many CAP cases predominantly in the first years of life. Thus anti-viral treatment and prevention modalities such as for Influenza (i.e. Oseltamivir and vaccine) or for RSV (RSV-Ig) should be used.

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NONTYPHOIDAL SALMONELLA INFECTIONS IN CHILDREN WITH ACUTE GASTROENTERITIS: PREVALENCE, SEROTYPES AND ANTIMICROBIAL RESISTANCE IN SHANGHAI, CHINA

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Background and aims: Nontyphoidal Salmonella (NTS) infection is a leading cause of foodborne gastroenteritis. Information about Nontyphoidal salmonella (NTS) infection in children is limited in mainland China. The objective of this study was to investigate the prevalence, serotypes and resistance patterns of NTS infection in children in Shanghai.

Methods: All cases with a clinical diagnosis of bacterial gastroenteritis were enrolled from the enteric clinic of a tertiary pediatric hospital between July 2010 and December 2011. Salmonella isolation, serotyping and antimicrobial susceptibility testing were conducted by the microbiological laboratory.

Results: NTS isolates were recovered from 316 (17.2%) of 1833 cases. NTS infection was prevalent year-round with a seasonal peak during summer and autumn. The median age of children with NTS gastroenteritis was 18 months with 92.7% of cases occurring in children < 5 years. Fever and blood-in-stool were reported in 52.5% and 42.7% of cases, respectively. S. enteritidis and S. typhimurium were the most common serotypes. Antimicrobial susceptibility showed 60.5% resistant to ≥1 clinically important antibiotics. Resistance to ciprofloxacin and the third-generation cephalosporins was detected in 5.5% and 7.1%-11.7% of isolates, respectively.

Conclusions: NTS is a major enteropathogen responsible for bacterial gastroenteritis in Chinese children. Resistance to the current first-line antibiotics is of concern. Ongoing surveillance for NTS and control measures for drug resistance is needed to control this pathogen in Shanghai.

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OUTBREAK OF SCARLET FEVER ASSOCIATED WITH EMM12 TYPE GROUP A STREPTOCOCCUS IN 2011 IN SHANGHAI, CHINA

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Background and aims: An unprecedented large outbreak of scarlet fever among children occurred in Shanghai in 2011. The objective of this study is to investigate the 2011 scarlet fever outbreak in Shanghai and molecular epidemiological markers of circulating GAS isolates, as well as to monitor current antibiotic resistance of GAS.

Methods: We analyzed the demographic and seasonal characteristics of children with scarlet fever and outcome. During the peak month of the 2011 outbreak, 45 GAS isolates recovered from 114 pediatric patients and 13 (43.3%) GAS isolates recovered from 30 asymptomatic contacts were characterized by emm typing, superantigen profiles, PFGE genotypes and MLST and antimicrobial susceptibility.

Results: 1282 culture-proven scarlet fever cases were reported from our Hospital between Janurary and August 2011. Boys outnumbered girls (65.1% versus 34.9%). Preschool and primary school children accounted for 96% of cases. No severe outcome was found. The 2011 outbreak of scarlet fever started in April and peaked in May and June. emm1, emm12 and emm75 were identified among 58 GAS isolates and 53 (91.4%) isolates belonged to emm12, st36. Ten PFGE genotypes were identified among emm12 GAS isolates, 43 (81.1%) shared SPYS16.001 genotype and the remaining seven genotypes detected were related to SPYS16.001 closely or possibly. No speA and speM were detected in 58 isolates. All emm12 GAS isolates were resistant to azithromycin and clindamycin.

Conclusions: emm12 GAS strain caused the 2011 large outbreak of scarlet fever in Shanghai. The antibiotic resistance to macrolides and clindamycin in GAS was serious currently in Shanghai.

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TOXIN PROFILES OF STAPHYLOCOCCUS AUREUS FROM CLINICAL ISOLATES IN CHILDREN IN JAPAN

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Background and aims: Staphylococcus aureus is a common pathogen for children both in community and hospital settings. The toxins are known for virulent factors, but little is known regarding to the prevalence in Japan. Our aim of study is to identify toxins profile from clinical strains of children.

Method: We evaluated toxins in S. aureus isolates at Tokyo Metropolitan Children´s Medical Center from March 2010 to August 2012. We investigated the strains with toxin assays for Staphylococcal Enterotoxins (SEs), Toxic Shock Syndrome Toxin-1 (TSST-1), Exfoliative Toxins (ETs) and Panton-Valentine Leukocidin (PVL).

Results: We identified 68 S. aureus isolates; 30 MSSA (44.1%) and 38 MRSA (55.9%). The specimens obtained from blood, skin, joint fluids, lympho nodes and sputum were 37, 26, 2, 2 and 1, respectively. Thirty two (47.1%) isolates with diverse infections were positive for SE. Seventeen (25%) isolates were positive for TSST-1; 3 strains caused Neonatal TSS-like exanthematous disease (NTED). Among those, 15 (88.2%) isolates were MRSA. Six (8.8%) isolates with Staphylococcal Skin Scalded Syndrome were positive for ETs. Among those, 5 (83.3%) were MRSA. Eight (11.8%) isolates were positive for PVL and all of them were MRSA with skin and soft tissue infections.

Conclusions: MRSA were predominantly identified in the strains with TSST-1, ETs and PVL. Among MRSA strains, 21% were positive for PVL. This is the first report of PVL prevalence in Japanese children. Although SEs and TSST-1 were not associated with specific infection, ETs and PVL were found more in skin and soft tissue infections.

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SEROPREVALENCE OF IGG ANTIBODIES TO PERTUSSIS TOXIN IN CHILDREN AND ADOLESCENTS IN ESTONIA

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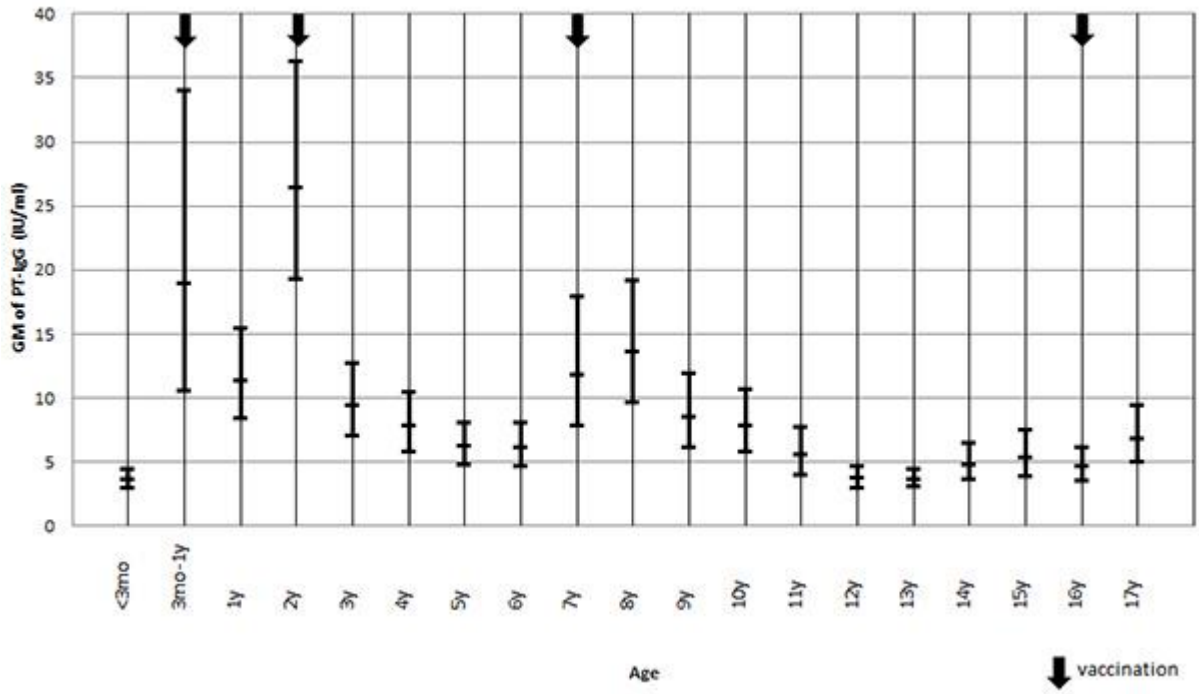
Background and aims: Estonia is characterised with 6 doses of acellular pertussis vaccine in immunisation programme and high immunisation rate (in 2011 at age of 2 years 93.3% and of 6-7 years 87.6%).We aimed to measure the concentration of IgG antibodies to pertussis toxin (anti-PT IgG) in children below 17 years in Estonia in 2012.

Methods: The leftover sera of 1053 children and adolescents (equally distributed across age groups) without known diagnosis of pertussis were collected by the laboratory of the Children´s Clinic of Tartu University Hospital. Anti-PT IgG concentration was measured by ELISA (Euroimmune). The antibody titres ≥125IU/ml were considered suggestive to pertussis in last 6 mo and those ≥62.5IU/ml in a last year.

Results: The highest, but rapidly declining GM of anti-PT IgG was observed at age when immunisations are given (Figure 1).

Figure 1: Age-specific distribution of anti-PT IgG GM and 95% CI



[Figure 1: Age-specific distribution of anti-PT IgG]

By excluding these age groups (< 3y, 7-8y and 15-17y) we observed that 1% (95% CI 0.4-2.3) of 3 to 6y and 9 to 14y old children had anti-PT IgG titres ≥125IU/ml and 2.1% (95% CI 0.7-4.8) and 3.6% (95% CI 1.9-6.2), respectively ≥62.5IU/ml. About half of sera in all age groups had antibody levels below 5IU/ml.

Conclusions: Despite 6 doses of acellular vaccine and high immunisation rates pertussis is still circulating in significant numbers in Estonia suggesting for the need of more efficacious vaccines than those currently available.

Acknowledgements: This study was founded by grant from the Estonian Science Foundation (9259).

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EPIDURAL ABSCESS CAUSED BY SCEDOSPORIUM APIOSPERMUM IN AN APPARENTLY IMMUNOCOMPETENT CHILD

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We report the case of a 7-year old boy without any known risk factors who presented with low grade fever, severe headache, back pain and stiffness 5 months after hurting his back on a tree stump. At the time of injury a superficial external wound in the lumbar area was stitched. Back pain and rachis stiffness appeared the week following the trauma. Both disappeared. The symptoms insidiously reoccurred. Five months post-trauma, the symptoms worsened with a lethargic state. An urgent spine MRI revealed an epidural abscess at L2-L3 level. He was managed with intravenous therapy including Ceftriaxone, Vancomycine and Metronidazole and referred to our centre for further management. Surgical debridement was performed with extraction of three pieces of wood in the muscular and epidural area at L2 level responsible for compression of the dural sac, drainage of the muscular mass abscess regarding to L3-L4, and debridement of the necrotic tissues. Scedosporium apiospermum grew on several specimens. Voriconazole was initiated and dosages were adapted according to serum level. The patient developed chronic meningitis and hydrocephalus requiring ventriculoperitoneal shunt. Immunologic study including complete phagocytic function was normal. After one year of antifungual treatment, despite a Voriconazole-induced photosensitivity, he is now asymptomatic and the control MRI shows reduction of meningeal enhancement. We decided to empirically stop the therapy and to follow clinically.

Central nerve system scedosporiosis remains rare and difficult to treat. To your knowledge this is the first case of a child described in the medical literature with such presentation.

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TRENDS IN THE EPIDEMIOLOGY OF BLOODSTREAM INFECTIONS AT A MAJOR EUROPEAN PEDIATRIC CANCER CENTER

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Background: Little data exist on the current epidemiology of bloodstream infections (BSI) in pediatric patients with cancer and/or hematopoietic stem cell transplantation (HSCT).

Methods: In a single-center, retrospective study, we analyzed all BSI in children and adolescents with cancer and/or allogeneic HSCT and compared the time periods 2000-2004 and 2006-2010. All pts. received MRSA-Screening, twice weekly TMP/SMX and non-absorbable polyenes. Quinolone prophylaxis was restricted to allo-HSCT pts., and systemic antifungal prophylaxis to pts. with AML, recurrent leukemia, and allo-HSCT.

Results: 446 BSI were observed in 289 pts. (55% male; median 8 yrs; 59.2% hem. malignancies, 35.6% solid tumors, 5.6% other; 24.9% s/p allo-HSCT; 23.6% recurrent cancer; 96.7% with indwelling permanent catheter). There was a significant increase in BSI over time from 32 to 46.7 /1000 discharges and from 5.6 to 8.4 /1000 inpatient days, respectively ($p< 0.001$) with a predominance of Gram-positive organisms (75.8%; Gram-negative, 22.3%; Candida spp., 1.9%; no trends). Coagulase-neg. staphylococci were most frequent (41.5%), followed by viridans streptococci (8.1%), Pseudomonas spp., E.coli (6.7% each). While MRSA and glycopeptide-resistant enterococci were not observed, ESBL producers and multiresistant E.coli and P.aeruginosa emerged in the second period (from 0% to 3.9, 1.4 and 1.4%, respectively ($p< 0.001$)). 31.5% of catheters were removed, and 5.5% of episodes resulted in ICU transfer. The 30-day overall mortality rate was 6% without trend.

Conclusions: This analysis documents a significant increase in the incidence of BSI and the emergence of resistant Gram-negative organisms in pediatric cancer/HSCT pts. receiving care at a major European treatment center.

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FREQUENCY OF DETECTION OF CLOSTRIDIUM DIFFICILE IN FECAL SAMPLES FROM CHILDREN WITH COMMUNITY-ACQUIRED DIARRHOEA IN NORTH-EASTERN PART OF POLAND

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Background and aims: C. difficile is emerging as a possible pathogen for community-acquired diarrhoea in children.

Methods: Prospective study was conducted in 491 children with community-acquired diarrhoea and in 137 patients without diarrhoea. Exclusion criterion was hospitalisation during 12 weeks prior to diagnosis.

Results: C.difficile was significantly more common in stool of children with diarrhoea (166/491; 33.8%) that without diarrhoea (33/137; 24.1%) (p=0.0306). Significant differences in C. difficile occurence were found in children divided according to age groups (in 1-2 y.o. 41/116 [35.5%] children with diarrhoea and 4/31 [12.9%] children without diarrhoea; p=0.0160; in 2-3 y.o. 22/57 [38.6%] children with diarrhoea and 4/26 [15.4%] children without diarrhoea; p=0.0345). Analysis of other age groups did not show significant differences in C. difficile occurence (p>0.05). C. difficile was found with similar frequency in children with diarrhoea who were and were not previously treated with antibiotics (106/298; 35.6% and 60/193; 31.1%; p=0.3051). Gender, place of residence and previous nursery/kindergartens/school attendance vs. staying only at home did not influence C. difficile infection. In 66/166 (39.8%) C. difficile was concomitant to other enterpathogens (in 26 cases other bacteria were found- Salmonella, EPEC, Klebsiella, S.aureus; in 33 patients viruses were present- Rotavirus, Adenovirus; and in 7 children both viruses and other bacterias were noted). In 100/166 (60.2%) Clostridium difficile associated diarrhoea diagnosis was made.

Conclusions: C.difficile could be important etiological agent of community-acquired diarrhoea in children and therefore routine screening for this pathogen should be conducted, despite previous antibiotics exposure or lack thereof.

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OVERLAPING SEASONALITY OF PARANEUMONIC EMPYEMA AND BACTEREMIA DUE TO PNEUMOCOCCUS IN SOUTHERN CALIFORNIA CHILDREN: DOES INFLUENZA MATTER?

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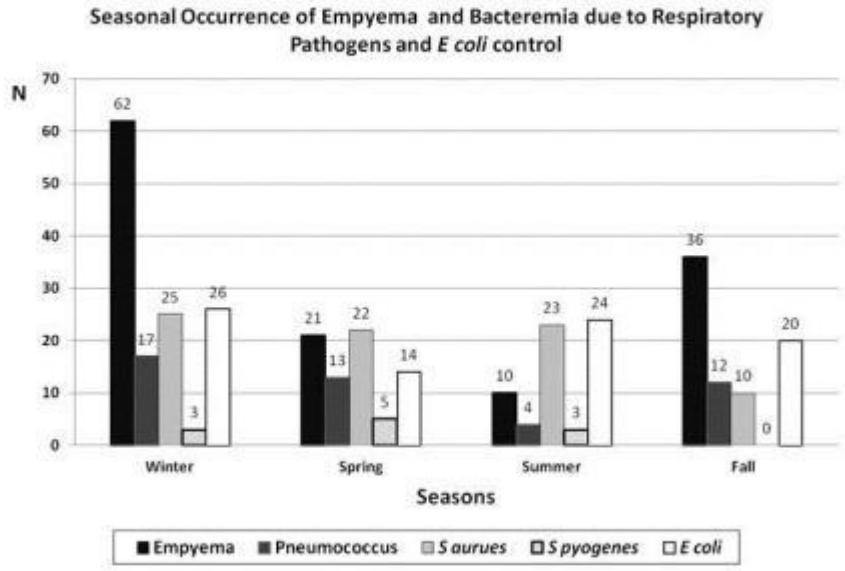
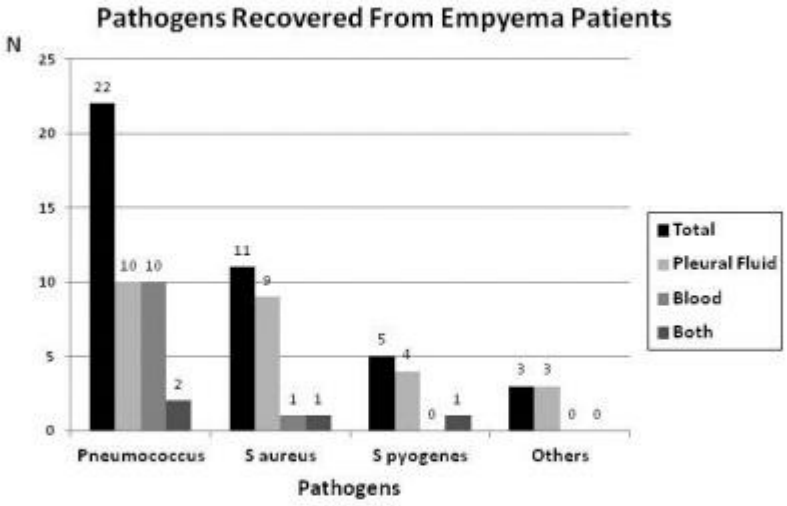
Background and aims: Parapneumonic empyema is common in children. Recent reports indicate increasing rates in contrast to decreasing rates of pneumonia. Although cultures are often negative pneumococcus and S aureus are common etiologies. Viral respiratory infections, particularly influenza, have been implicated preceding bacterial pneumonia. We hypothesized that the seasonality of empyema overlaps with pneumococcal bacteremia and both would be more prevalent during influenza season supporting etiologic role of pneumococcus and add information on treatment and prevention of empyema in children.

Methods: Retrospective chart review of patients discharged from our institution (July, 2005-December, 2012) with diagnosis of empyema, as well as those with bacteremia due to pneumococcus, S aureus and S pyogenes was performed using E coli bacteremia as control.

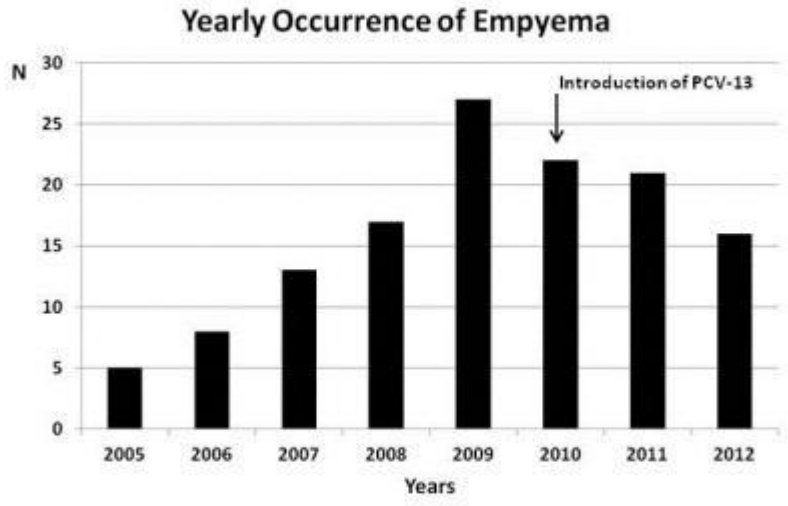
Results: Yearly cases of empyema increased until 2009. (Fig 1) Empyema (10/129) and pneumococcal bacteremia (4/46) decreased significantly during summer. (Fig 2) Blood and/or pleural fluid cultures were positive in 41 (31.8%) empyema patients, pneumococcus was most frequent (Fig 3); 19A(6 and 12) and 3(6 and 7) were most common serotypes from empyema and bacteremia respectively; 10/11 (empyema) and 17/70 (bacteremia) S aureus were MRSA.



[Fig 1]


Pathogens Recovered From Empyema Patients
N
25
20
15
10
5
0
22
10 10
2
11
9
1 1
5
4
0
1
3 3
0 0
Pneumococcus
S aureus
S pyogenes
Others
Pathogens
Total
Pleural Fluid
Blood
Both

[Fig 2]



[Fig 3]

Conclusions: Yearly cases of empyema increased during study until 2009. Seasonal occurrence of pneumococcal bacteremia closely overlaps with empyema supporting etiologic role. S aureus and S pyogenes were not seasonal. Influenza had no impact on empyema or pneumococcal bacteremia.

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ANTIBODY RESPONSE TO STREPTOCOCCUS PNEUMONIAE, HAEMOPHILUS INFLUENZAE AND MORAXELLA CATARRHALIS PROTEINS AMONG CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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Background and aims: We aimed to investigate antibody responses to bacterial antigens in children with non-severe CAP and explore their use for etiologic diagnosis.

Methods: Acute and convalescent serum samples were collected from 733 children aged 2-59months with non-severe CAP. A fluorescent multiplexed microsphere immunoassay(FMIA) quantified IgG antibodies against 8 Streptococcus pneumoniae proteins: PcpA and PhtD(supplied by Sanofi-Pasteur), Ply, CbpA, PspA1,and PspA2(supplied by St.Judes Children's Research Hospital, Memphis,TN and University of Alabama, Birmingham,AL), SP1732-3,and SP2216-1; 3 Haemophilus influenzae proteins(NTHi-Protein-D, NTHi-0371-1,and NTHi-0830); and 5 Moraxella catarrhalis proteins(MC-Omp-CD, MC-RH4-2506, MC-RH4-1701, MC-RH4-3729-1,and MC-RH4-4730). Increase in antibody level was used for etiologic diagnosis. Continuous variables were analyzed using Mann Whitney test and categorical using Chi-square test.

Results: The rates of immune responses are depicted in table1. H. influenzae infection was more often among patients with paired samples collected 21-28 days apart(14.8%[n=31]vs.8%[n=42],p=0.005; and 10%[n=21]vs.4.4%[n=23],p=0.004) compared to patients with different time intervals by using≥1.5-fold and≥2-fold increase, respectively. By considering≥2-fold increase, children with infection by each bacterium were younger(median[25th-75thpercentile] months) than those without the infection by: S. pneumoniae:23.8[13.5-33.9]vs.26.1[14.1-41.6],p=0.02; H. influenzae:15[10-33.9]vs.26.2[14.3-40.4],p=0.003; M. catarrhalis 16.2[10.9-30.4]vs.25.8[14.1-40.2],p=0.04).

Conclusions: The frequency of immune responses varied widely by using different cut-offs of antibody level increases. Interval between paired serum samples and age also influenced the diagnosis of these bacterial infections.

Acknowledgements: We thank Intercell for supplying:SP1732-3,SP2216-1,NTHi-Protein-D,NTHi-0371-1,NTHi-0830,MC-Omp-CD,MC-RH4-2506,MC-RH4-1701,MC-RH4-3729-1,and MC-RH4-4730.

IgG increase	S. pneumoniae	H. influenzae	M. catarrhalis	Total recovery rate
≥1.5-fold	203 (27.7%)	73 (10%)	33 (4.5%)	256 (34.9%)
≥2-fold	111 (15.1%)	44 (6%)	20 (2.7%)	153 (20.9%)
≥4-fold	33 (4.5%)	10 (1.4%)	2 (0.3%)	42 (5.7%)

[Table1. Antibody responses using distinct cut-offs]

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THE HUMAN BOCAVIRUS IS ASSOCIATED WITH LUNG- AND COLORECTAL CANCERS AND PERSISTS IN SOLID TUMOURS

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The human bocavirus (HBoV) is the second human pathogenic parvovirus. It causes respiratory infections and gastroenteritis. Some autonomous animal parvoviruses and also some human non-autonomous parvoviruses are known to persist and even integrate into the host genome resulting in transformation of the infected cells and eventually contribute to the multi-step development of cancer. Surprisingly, also HBoV persists in a so far unknown percentage of patients without causing clinical symptoms beyond those of the primary infection.In total, 11 of 60 (18.3%) lung and 9 of 44 (20.1%) colo-rectal tumors were tested positive for HBoV DNA, confirmed by sequencing and/or Southern-blotting. HBoV DNA thereby is present in the nuclei of infected cells, either in single or multiple copies, and appears also to form filaments. The data show that HBoV is present in lung and colorectal cancers. This gives rise to the hypothesis that the virus plays an active role in cancer by interactions with the host genome, or contributes to cancer development indirectly by inducing a persisting inflammation, as other DNA viruses like the human hepatitis B virus do. The occurrence of HBoV-DNA-filaments could confirm the postulated sigma- or rolling- hairpin replication mechanism. Moreover it must be concluded that it should be our foremost challenge to avoid human bocavirus infections to convert to a persistent form. This has to be done in childhood, when the majority of HBoV infections occur, e.g by development of novel vaccines.

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CLINICAL CHARACTERISTICS OF CHILDREN WITH VIRAL SINGLE- AND CO-INFECTIONS AND A PETECHIAL RASH

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Background: Children with petechial rash are more likely to undergo invasive diagnostics, to be treated with antibiotics for potential bacterial infection and be hospitalized. However, viruses have also been associated with petechial rash. Nonetheless, a systematic analysis of viral infections with modern available techniques as quantitative real time polymerase chain reaction (q-PCR) in the context of petechial rash is lacking. The purpose of this study was to prospectively uncover viral pathogens that may promote the emergence of petechiae in children and analyse the correlation with the clinical characteristics and course.

Methods: We conducted a prospective study in children (0 to 18 years) presenting with petechiae and suspected infection at the emergency department between November 2009 and March 2012. In nasopharyngeal aspirates the following viruses were analysed by q-PCR: Cytomegalovirus, Epstein-Barr virus, parvovirus B19, Influenza A and B, parainfluenza viruses, human respiratory syncytial virus A and B, human metapneumovirus, rhinovirus, enterovirus, adenovirus, human coronavirus OC43, 229E, NL63 and human bocavirus.

Results: A viral pathogen was identified in 67% of the analysed 58 cases with petechial rash. Virus positive patients showed a significant higher incidence of lower respiratory tract infections. Forty-one percent were viral co-infections, which were significantly younger than virus negative patients, had a higher leukocyte count and were longer hospitalized.

Conclusions: A petechial rash is frequently caused by viral single- and co-infections and can rapidly be identified via q-PCR. The specific role of viral pathogens in children with a petechial rash has further to be clarified in future studies.

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SURAMIN INHIBITS ENTEROVIRUS 71 REPLICATION IN VIVO BY BLOCKING VIRUS ENTRY INTO TARGET CELLS THROUGH BINDING OF THE NAPHTHALENE TRISULFONIC ACID GROUP TO THE VIRAL CAPSID

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Background: Enterovirus 71 (EV71) is the causative of Hand Foot and Mouth Disease, which caused diseases in millions of children. There is no approved anti-viral nor vaccine. The aim of our study is to identify therapeutics to treat and prevent severe EV71 infections.

Methods: A clinically approved drug collection was screened in a quantitative RT-PCR based platform. Potency of hits was evaluated by plaque assay. Time of addition (T.O.A.) test was used to identify the target steps in viral life cycle. The binding between Suramin and EV71 viral particle was evaluated by STD-NMR. In vivo efficacy was tested in EV71 infected 10-day-old ICR mice and adult rhesus monkeys.

Results: IC_{50} and IC_{90} of suramin in rhabdomyosarcoma cells are 0.08 µM and 0.49 µM, and CC_{50}>1mM. Treatment with Suramin at 50 mg/kg/day in EV71 infected 10-day-old mice reduced the mortality for 30% and in monkey peak viral load was reduced. Suramin blocks the virus-cell attachment in T.O.A.. Inhibition by a set of poly-sulfonated and poly-sulfated compounds indicates that sulfur groups are involved in the mechanism of action. STD-NMR analysis confirmed the binding between Suramin and EV71 particle on sulfonate groups.

Conclusions: We identified suramin as EV71 entry inhibitor both in vitro and in vivo, which sulfonated groups bind to EV71 particle and compete with cellular receptors or attachment factors. Suramin is an approved pediatric drug with a long history of clinical using, and represents a promising candidate for therapy and prevention of severe EV71 infections and HFMD.

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A 3 YEAR RETROSPECTIVE REVIEW OF VIRAL RESPIRATORY ISOLATES IN PAEDIATRICS INTENSIVE CARE ADMISSIONS

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Introduction: During the H1N1 2009 Pandemic season, all children ventilated on Paediatrics Intensive Care (PICU) for respiratory failure had respiratory samples taken for virology screen.H1N1 (2009) was declared eradicated both national and internationally in August 2010.We reviewed results of samples taken during and beyond this period and compared the respiratory isolates.

Methods: All Nasopharyngeal Aspirates, Non -direct bronchoalveolar lavage or tracheal secretions from admissions in the months of September to April of 2009/2010, 2010/2011and 2011/2012 was reviewed. The months of May to August of each year were regarded as 'offpeak' and so left out of the study. PICU admissions, discharges and death notifications records werecorrelated with virology reports.

Results: Samples were processed from 287 PICU patients/episodes. 192(67.1%) of the children were ages 0-2 years.(154)53.8% of the patients were male. One or more Respiratory viruses was isolated in 159 samples(55%). RSV accounted for 77(48.4%) of the positive samples, Rhinovirus 45(28.6%), Para-influenza Virus Type1-4, 14(8.8%), Adenovirus 9(5.7%), Pandemic H1N1 (2009) 8(5.1%) and HumanMetapneumovirus 2(1.3%) . Coinfection was found in 12 (7.5%) of the positive samples. There were ten(3.4%) mortalities from the study population. A serious co-morbidity was present in all10(100%) mortalities. A respiratory virus was isolated in 7/10 (75.%) of the deaths. No positive swabs for H1N1 (2009) was found afterJanuary 2011.

Conclusion: With the Pandemic H1N1 (2009) truly over, resources needs to be devoted to common viruses with greater burden of disease.

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PERSISTENT OUTBREAKS OF HAND, FOOT, AND MOUTH DISEASE CAUSED BY EV71 IN SHANGHAI SINCE 2007

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Background and aims: Since 2008 Hand-foot-mouth disease (HFMD) has become a major infectious disease in China. Understanding of the local epidemiology of HFMD is helpful to formulate the strategy of preventing the outbreak of HFMD.

Methods: This study analyzed the demographic data, seasonal pattern, pathogen of HFMD in children in Shanghai between 2007 and 2011.

Results: A total of 39807 outpatients were diagnosed as HFMD, 1169 (2.9%) were confirmed to have neurological complications and 15 (0.04%) developed pulmonary edema/hemorrhage and 12 (0.03%) died. HFMD peaked from April to July in Shanghai. Since 2008, the major population affected has shifted from local preschool-attending children to migrant and home-care younger children. Between 2009 and 2011, 3254 stool samples taken from inpatients were tested for EV-A71 and Cox-A16, which were detected in 1906 (58.57%) and 407 (12.51%) samples, respectively. Besides, EV-A71 and Cox-A16 were detected in 871 (88.97%) and 15 (1.53%) of 979 specimens from severe cases, and in 1035 (45.49%) and 392 (17.23%) of 2275 specimens from uncomplicated cases. All 16 cases with pulmonary edema or hemorrhage were attributable to EV-A71 infection.

Conclusion: HFMD is a top health priority problem in Shanghai. Home-care, migrant young children are the predominantly susceptible population. The dominant circulation of EV71 is associated with the outbreak of HFMD and the occurrence of severe and fatal cases.

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IDENTIFICATION AND CHARACTERIZATION OF A NON-SIALIC ACID-BASED DRUG AS AN INHIBITOR OF HPIV-3'S HEMAGGLUTININ-NEURAMINIDASE WITH ANTIVIRAL ACTIVITY IN VITRO

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Background and aims: The human parainfluenza type-3 virus (hPIV-3) is one of the principal etiological agents of acute respiratory infections (ARIs) in less than 2-years old worldwide. Although a few molecules have shown antiviral potency in vitro, they remain poorly efficient. This study aims to discover non-sialic acid-based inhibitors of hPIV-3 hemagglutinin-neuraminidase (HN) that could help better understand the mechanism of sialidases, and potentially give rise to combinatorial therapies.

Methods: A library of 1280 approved-drugs was screened by neuraminidase-inhibition assay. The hit compounds were then characterized for their ability to inhibit both functions of HN, as well as infection in vitro. Their inhibitory mechanism towards HN was then investigated by enzyme kinetics, and confirmed by competition STD-NMR experiments.

Results: The drug E02 was found to efficiently inhibit both the neuraminidase and hemagglutinin activities of HN with IC_{50}s of respectively 12.67 µM and 30 µM. In addition, the drug inhibits viral propagation at binding stage in vitro with an IC_{50} of 3 µM. The enzyme kinetics data suggest that the drug inhibits the sialidase via a non-competitive mechanism (Ki=4.9 µM), which was confirmed by competition STD-NMR experiments in presence of a competitive inhibitor of HN.

Conclusion: We successfully identified E02 as a non-competitive inhibitor of hPIV-3 HN. Together with further investigations into the localization of the drug binding site as well as combinatorial drug tests, these findings will greatly help understand how to better impair the mechanism of HN for the development of new anti-parainfluenza therapies.

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SEVERE ADENOVIRUS INFECTION IN THE PAEDIATRIC POPULATION OF SOUTH EAST SCOTLAND

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[1]Department of Medical Paediatrics, Royal Hospital for Sick Children, [2]Department of Virology, Royal Infirmary of Edinburgh, Edinburgh, UK

Background and aims: Adenovirus infection is known to have high morbidity and mortality in paediatric severely immunocompromised patients. However, there are limited reports for patients without immunocompromise. Our aim was to characterise severe adenoviral infection in the paediatric population in South East Scotland.

Methods: Patients with systemic adenoviral infection were identified from positive blood PCR results between Sep 2011 and August 2012. Further information was gathered from clinical and laboratory records.

Results: 16 patients with positive blood adenovirus (Adv) PCR were identified. The adenovirus types were Adv2 (1 case), Adv3 (13 cases), and Adv14 (2 cases). 9 (56%) were male, 7 (44%) female, with median age 16 months (range 6 months to 15yrs 5 months). Two patients had significant immunocompromise, 6 had other underlying conditions and 8 were otherwise well.

Symptoms observed at presentation were fever, respiratory symptoms, sepsis/septic shock, gastrointestinal symptoms, petechial rash, stridor, prolonged febrile convulsion and intussusception.

Mean CRP at presentation was 86, mean white cell count was 11.6, mean neutrophil count 6.9 with 58% having normal cell counts.

Of the 16 patients identified, 5 required intubation and ventilation. 1 required inotropic support. 4 patients were treated with the antiviral cidofovir according to local protocol. There were no fatalities.

Conclusion: Severe adenoviral infection is emerging as a cause of severe disease in immunocompetent children as well as significant morbidity in children with underlying conditions. It is not restricted to one adenovirus type. Inflammatory markers are often normal. Cidofovir has been used successfully in severe cases.

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CLINICAL SPECTRUM OF DENGUE FEVER AND DENGUE HEMORRHAGIC FEVER IN CHILDREN'S HOSPITAL, LAHORE DURING DENGUE EPIDEMIC OF 2011

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Aim: To find out the clinical spectrum in children suffering from dengue fever age 1 to 14 year admitted from September 2011 to November 2011 in Children Hospital and ICH Dengue ward.

Material and methods: A descriptive study. During this period, 10250 patients visited the triage area of dengue. Patients were divided into three groups on basis of their ages. Data was recorded on a pre-designed pro forma. Relevant investigations were done. Children having enteric fever, hematological and oncological problems were excluded. Informed consent was taken for all patients.

Result: 450 children were included in study. 54.44% patients were seen in group-III. (n=245) and then in group II: 32.66%. High grade fever was present in 86.66% in group II & III. Common clinical features were bone pains and myalgias (28%), pain abdomen (25.7%) and vomiting (24.8%). Systemic findings were: Hepatomegaly (49.7 %), Lymphadenopathy (33.7%), Tachypnea (22.8%), ascites (14.8%), pleural effusion (11.3%) and rapid pulse (12.6%). Signs of circulatory failure; cold clammy skin (32.8%) and low grade fever with weak pulse (27.5%). Investigations showed Low TLC (47.3%), low platelets count (47.3%) and raised hematocrit in 35.1% of patients. Anti-Dengue IgM antibodies were present in 327 cases. Out of these, 63.7% were diagnosed as Dengue fever and 8.8% were labeled as Dengue Hemorrhagic Fever on the basis of clinical criteria and investigations.

Conclusion: More cases of Dengue fever were present in children from age 10 to 14 year of age. DHF was less common in children of any age.

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THE EPIDEMIOLOGY OF VARICELLA-RELATED HOSPITALIZATIONS IN TURKEY FROM 2008 TO 2012: A NATIONWIDE SURVEY DURING THE PRE-VACCINE ERA (VARICOMP STUDY)

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Background: Although it is usually self-limiting, varicella can cause complications that are potentially serious and require hospitalization. The aim of VARICOMP study was to evaluate pediatric varicella-related hospitalizations in children before vaccine introduction.

Methods: Medical records of children requiring hospitalization due to varicella from 28 health care centers in 14 cities (representing 50% of the childhood population in Turkey) from 2008-2012, have been evaluated.

Results: 1936 children (69.2% previously healthy) were hospitalized for varicella over the 4-year period. Most cases occurred in January-March and May-July. The median age was 3 years, and boys outnumbered girls. Most cases were in children under 5 years of age, and 28.1% were < 1 year of age. Among the 1936 children, most common complication is neurological (18.6%). Secondary bacterial infections are reported in 17.8%, respiratory complications in 15.6%, hematological complications in 4.9%. 17.6% out of children have been hospitalized due to underlying disease, 9.6% due to severe varicella, 6.7% due to fever, 8.5% due to feeding difficulties. The median length of the hospital stay was 6 days and the mortality rate was 0.36%.

Conclusion: This study confirms that varicella-related hospitalizations are common, especially in previously healthy children. The incidence of this disease was higher in children < 1 year of age. Varicella vaccine was introduced to the National Immunization Program in January 2013 and we plan to evaluate vaccine effectiveness in the next 4 year period in same geographical area and to evaluate potential need for the second dose at preschool period.

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INVASIVE GROUP A STREPTOCOCCAL INFECTIONS IN CHILDRENS ADMITTED WITH VARICELLA IN MIDWESTERN REGIONAL HOSPITAL

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Introduction: Group A streptococci(GAS) are bacteria commonly found in the throat and on the skin. The vast majority of Group a Strep infections are mild illnesses, such as strep throat and impetigo. Occasionally however, these bacteria can cause much more severe and even life-threatening diseases, such as necrotizing fasciitis and Streptococcal Toxic Shock Syndrome (STSS). the risk of invasive GAS infection during the varicella zoster infection is much higher.

Aim: To audit number of childrens admitted in Mid western regional hospital with varicella infection complicated by group a streptococcal infection.

Methods: Number of childrens admitted with varicella and associated complication with group A stertococal infections in Midwestern Regional Hospital from June 2002-June2012 from HIPE search,Microbiology laboratory data search,Canvasing the paediatrics consultant about children admitted under their care. Chart review of the admissions, Date of birth, Gender, Date of admission, Date of discharge, Area infected by group A streptococcal infection.

Results: 193 children admitted with varicella during this study period. 94(48%) female and 99(52%) male median length of stay in hospital was 5.5 days ranges from 1-12 days.9 children that is 3% of the total admission with varicella had necrotizing fascitis secondary to invasive group a sterptococcal infection at various different sites of the body.

Conclusion: This study provides a minimum estimate of severe complications resulting from varicella in children in the midwetern region. Most complications, excluding the death, occur in otherwise healthy children and thus would be preventable only through a universal childhood immunisation programme in Ireland.

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WHAT IS THE NORMAL INCIDENCE OF RESPIRATORY COMPLAINTS IN CHILDREN? FIRST RESULTS OF THE CHILD-IS-ILL STUDY ('KIND-EN-ZIEKMETING')

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Background and aim: Many children with respiratory tract infections (RTI) are referred to a paediatrician because they are ill 'too often'. But what is too often? And when should investigations into potential underlying disease be undertaken? In the Child-is-ill study respiratory tract symptoms (RTS) matching possible RTI are studied in 2-18-year-old children from the Dutch general population.

Methods: In an online prospective 2-year cohort study parents are weekly asked about RTS in their child(ren) during the preceding week; if present, additional questions about complaints, doctor visits and use of antibiotics are asked. The study was advertised through social media and the internet.

Results: During 2012, parents enrolled 749 children (376 boys; 1/3< 4yrs, 1/3=4-9yrs, 1/3>9yrs; families: 640 non-smoking, 283 non-atopic); 24,033 childweeks were reported, with 'no complaints' in 84% of them. The number of weeks with 'no complaints' increased in spring and summer, and with decreasing age. Cough, stuffy nose, runny nose, throatache and headache were reported most often (1581x, 1093x, 966x, 798x, 728x); earache, hoarseness and dyspnea were reported 312x, 302x and 213x. Rather unexpectedly, ear discharge was seldom reported (74x). Often, several complaints were concomitantly reported.

Conclusion: The - preliminary - results may be 'stating the obvious'. However, it is important to collect solid evidence to support clinical experience; this will help to identify children who are 'different'. Also, these data can be used to compare with groups of children with identified underlying disease. The Child-is-ill study aims to reach 1000 inclusions (100,000 childweeks) to help solve these clinical questions.

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INCIDENCE OF RESPIRATORY SYMPTOMS IN CHILDREN WITH DOWN SYNDROME: FEASIBILITY OF A WEB-BASED PARENT-REPORTED PROSPECTIVE STUDY

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Background and aims: Respiratory tract symptoms (RTS) are common in children with Down syndrome (DS), they are often, but not always, the result of respiratory tract infection (RTI). We designed a web-based study to determine the rate of RTS in DS children in relation to common comorbidity ('KiDS-dagboekstudie').

Methods: Parents were informed about the study through social media. Upon enrollment, parents weekly receive a web-based questionnaire for two years. When the child has had symptoms in the preceding week, additional questions about the type of complaints, doctor visits and use of antibiotics are shown. Additionally, parents receive three questionnaires (t=0,1&2yrs) on the family situation, comorbidity and daily (school) activities. The results will be compared to the Child-is-ill study ('Kind-en-Ziekmeting') that is being run in an identical fashion in children that are considered to be 'normal as to being ill' by their parents.

Results: Between January-August 2012, 98 DS children were enrolled (mean age 6yrs, range 0.1-17.6; 57% boys). Table 1 shows comorbidity; Table 2 shows data on RTS. In the first 3 months, the weekly response rate was stable and remained high at 89% (range 84.7-92.9%).

Conclusion: We designed a feasible web-based study to collect prospective data on parent-reported RTS in DS children. The preliminary results show that parent-reported RTS are a considerable problem in DS children that warrants further study.

TABLE 1 ***Comorbidity in DS children***		***TABLE 2*** ***RTS in children with DS***	
Congenital heart disease	37%	History of suffering from frequent serious RTI	73%
Hypothyroid disease	15%	History of RSV infection	25%
Diabetes mellitus	0%	History of wheezing	29%
Celiac disease	2%	≥6 courses of antibiotics for RTI	52%
Hearing loss	41%	History of antibiotic prophylaxis	18%
Chronic snoring	13%	History of inhaled corticosteroids	31%

[Tables]

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LYMPHOPENIA IN CHILDREN - IS POTENTIAL SUSCEPTIBILITY TO INFECTIOUS DISEASE BEING IGNORED?

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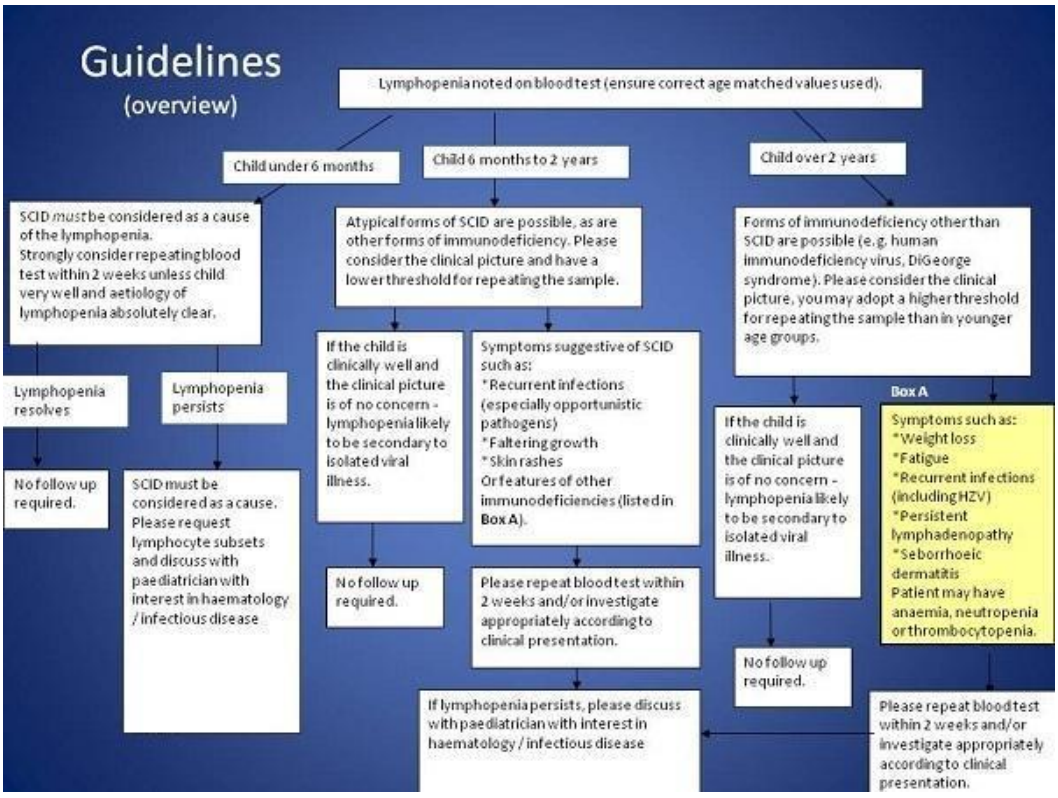
Background and aims: Paediatric lymphopenia may reflect immunodeficiency and therefore susceptibility to Infectious Disease. A systematic approach is required to manage lymphopenia. The only UK guideline is the archived primary immunodeficiency network guideline which recommends that lymphopenic infants should be followed-up and severe combined immunodeficiency (SCID) considered if lymphopenia persists. A retrospective audit was conducted at Sandwell Hospital UK to assess if paediatric lymphopenic patients were appropriately identified, investigated and referred. The standards used were best practice recommendations from immunologists.

Methods: All paediatric patients >28 days with lymphopenia were identified from laboratory records over a period of 11 months. The group was divided into those < 1 year (age group at greater risk of SCID) and ≥1 year. Data regarding diagnosis, lymphocyte counts, further investigations and referrals was analysed.

Results: 209 lymphopenic patients were identified. 26 were < 1 year; 27%(7/26) had their lymphocyte count re-checked within 2 weeks. The lymphopenia had resolved in 71% (5/7), the remaining 2 patients died shortly after the abnormal result. 183 patients were ≥1 year old. 18%(33/183) had their lymphocyte count re-checked within 2 weeks. Lymphopenia had resolved in 85%(28/33). In no cases were further investigations performed or referrals made. In 4 cases the lymphopenia was commented upon in the discharge summary, although no plan documented.

Conclusion: The best practice recommendations for lymphopenic patients were not followed. It is important to identify children who may have underlying immunodeficiency. We have drafted guidelines for managing lymphopenia.



[A Guideline to Managing Paediatric Lymphopenia]

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PROBIOTIC AND ZINK TREATMENT SHORTENED THE COURSE OF ACUTE VIRUS DIARRHEA IN INFANTS AND CHILDREN

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Aim: To evaluate the efficacy of the probiotic & zink use in shortening the duration of acute virus diarrhea in hospitalized children under 3 years old.

Methods: A single-center, randomized, controlled trial was conducted to collect 356

patients aged 3 mon. - 3 y. and hospitalized in Lviv Infection Diseases Hospital with virus gastroenteritis between October 2010 and 2012. Included were all previously healthy children with acute diarrhea and / or vomiting. Stool samples were tested for rotavirus & norovirus by enzyme immunoassay (ELISA) and stool samples were also cultured to exclude the presence of enteropathogenic bacteria. Patients were randomized to receive conventional treatment or add-on treatment of probiotic + zink to the conventional treatment.

Results: As a total, 310 children eligible for the study were evaluated (155 receive conventional treatment and 155 with add-on treatment of the probiotics + zink to the conventional treatmen given). Rotavirus antigen was detected in 61,4%, the rate of norovirus detection was 36,6% The virus-virus coinfection were found in 14,3%. The mean age of the children was 17,5±2,18 months. The mean duration of diarrhea was 3,7±0,29 days in a subgroup not received the probiotic + zink therapy and 2,4±0,33 days in a subgroup received it ($p < 0,05$). The administration of antimicrobials did not make any differences in diarrhea duration.

Conclusions: 5 days conventional treatment add-on treatment of the probiotics + zink were highly efficacious and safe in infants and in children for treating severe virus gastroenteritis.

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INVASIVE GROUP A STREPTOCOCCAL INFECTIONS IN PAEDIATRIC INTENSIVE CARE - AN AUDIT OF CLINICAL PRACTICE

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Aims: Describe the epidemiology, clinical features and management of children with invasive Group A Streptococcal infections requiring admission to the PICU.

Methods:

Patient population / Setting: Children aged 0-16 years of age requiring admission to the RHSC PICU over a 6 year period with invasive Group A streptococcal infections.

Case definitions / Inclusions: Patients undergoing therapy for invasive Group A Streptococcal (GAS) infections within the PICU. Invasive GAS infections were defined as one of three clinical syndromes: streptococcal toxic shock; necrotising fasciitis; or other invasive disease.

Data extraction: Data was extracted from the PICU Computerised Information System (CIS).

Study design and Patient identification: The study was a retrospective case note review.

Results: 24 patients were identified. 15 patients were boys. The median age was 3.1years. 2 patients died. The median PICU Length of stay was 7.1 days. 21/24 patients underwent invasive ventilation. The median duration of ventilation was 120 hours. 14/24 patients (58%) required inotropic support. 7/24 patients (29%) received iv steroids for primary blood pressure support. 3/24 patients (12%) received IvIG. 15/24 patients (62%) required surgical interventions. 5/24 patients (21%) had hospital acquired GAS infections (HAI), 19/24 (79%) were community-acquired infections (CAI).

Laboratory characteristics: All samples were reported as fully sensitive to all antibiotics tested. M-types reported were as follows: M1; M3.1; M12; M18; M89. The 2 patients who died had M-types M12 and M18.

Conclusion: GAS retains the ability to kill otherwise healthy children in resource rich settings and cause serious morbidity to others.

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RISK FOR APNEAS IN PEDIATRIC ACUTE RESPIRATORY TRACT INFECTIONS

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Background: Apneas in young children are seen in association with respiratory syncytial virus (RSV) infections. Based on these observations, it is recommended to hospitalize young children (< 3 months) with an acute respiratory tract infection (ARI) caused by RSV. However, apneas also occur in children infected with other viruses than RSV. We hypothesize that apneas are not related to the microorganism itself, but reflect pathophysiological changes related to infectious status. Within a prospective cohort-study, we analyzed frequency of apneas in previously healthy young children with symptoms of ARI. We correlated apneas with the isolated micro-organisms, clinical findings, disease severity and outcome.

Methods: In a cohort of 582 previously healthy children with ARI, real-time polymerase chain reaction (RT-PCR) was performed on nasal washing specimens for fifteen respiratory viruses and three bacteria. In a subgroup of 241 children < 3 months of age, we compared the clinical data of children with and without apneas.

Results: Nineteen of 241 (7.8%) children had a history of apnea. RT-PCR results were RSV 9/19 (47.4%), non-RSV 5/19 (26.3%) and negative PCR in 7/19 (36.8%). The disease severity score was significantly higher in the apnea group. They also required extra oxygen for a longer period.

Conclusions: Apneas in ARI are not restricted to RSV as causative pathogen. The disease severity score is a better predictor for risk of apneas in young children with ARI than a positive RSV test. Guidelines that recommend to hospitalize young children with RSV based on the risk of apnea, should be revised.

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FREQUENCIES AND CHARACTERISTICS OF BRONCHOOBSTRUCTIVE SYNDROME IN CHILDREN - THEN AND NOW

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Background and aims: Upper and lower respiratory tract obstruction is often found in children. The aim of this study was to compare the frequency and characteristics of bronchoobstructive syndrome (BOS; obstructive bronchitis - OB and subglottic laryngitis - SL) in primary pediatric care during the period from 1987. - 1989. (period I) and the period from 2007. - 2009. (period II).

Methods: During those periods the same number of children (N=1717) aged from 0 to 6 years was used to edit data: number of children with BOS, number of attacks, characteristics of BOS during attacks (frequency of acute respiratory infection symptoms - ARIS, children treated with antibiotics, frequency of pneumonia, number of hospitalized children).

Results: In period II, statistically significant higher frequency of BOS was found (9.1% versus 25.3%; P< 0.001), particularly the frequency of OB (5.6% versus 15.7%; P=0.018), as well as the higher consumption of antibiotics during OB attacks (17.6% versus 40.2%; P=0.015). The frequency of pneumonia was higher during OB attacks (4.3% versus 11.6%; P=0.937). There was no difference in the frequency of ARIS during OB attacks (80.0% versus 81.4%; P=0.787) or SL attacks (60.8% versus 45.4%; P=0.085). The children hospitalized because of BOS attacks was lower during period II (4.2% versus 3.8%; P=0.419).

Conclusion: Despite the current antibiotic treatments during OB attacks, that has not significantly decreased the percentage of hospitalizated children. ARIS are commonly found in the clinical presentation of OB; therefore considering their virus etiology the consumption of antibiotics should be more rational.

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MOLECULAR DIAGNOSIS OF STRONGYLOIDES STERCORALIS IN FECAL SAMPLES BY PCR COMPARED TO CONVENTIONAL TECHNIQUES

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Strongyloides is the most neglected of tropical diseases and is considered an extremely common cause of morbidity and mortality worldwide. Approximately, 100-200 million persons are infected worldwide in 70 countries.Conventional diagnostic techniques don´t efficiently detect the parasite. Therefore, the need for more efficient methods that improve diagnosis particularly in those at risk to develop the severe disease is warranted.

Stool samples were collected from 115 patients of all age groups living in rural areas in Ismailia governorate, Egypt. All samples were subjected to agar plate culture (APC), Harada-Mori culture, Baermann concentration, formalin ethyl acetate concentration (FEAC), and real-time PCR targeting the small subunit of the rRNA gene.

Among the total of 115 stool samples, S. stercoralis was detected by the four conventional methods. Harada-Mori detected 11 positive samples (9.6%), FEAC detected 13 (11.3%), Baermann concentration detected 16 (13.9%) and APC detected 18 (15.7%) samples. Real-time PCR assay detected S. stercoralis DNA in 23 (20%) samples. Threshold cycles (Ct-values) of S. stercoralis positive samples were found to be between 24.45 and 40.35 with a median threshold of 29.59 cycles.

Real-time PCR is a very sensitive and specific method, offering a two-fold increase in the detection rate of S. stercoralis by FEAC. It doesn´t require much time to perform, has the ability to detect dead larvae and easy to perform and interpret the data, but it still the most expensive method. On the other hand, PCR has the ability of detecting multiple pathogens simultaneously in one test using multiplex real-time PCR.

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SENSITIVITY OF TORCH SCREEN VS URINE FOR CMV IN DIAGNOSING INTRAUTERINE INFECTION IN MIDWESTERN REGION

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Introduction: The TORCH screening is a blood tests that is used to check for several different infections in a newborn. TORCH stands for **toxoplasmosis**, **rubella**, cytomegalovirus, herpes simplex, and HIV.Many infants with intrauterine growth retardation (IUGR) are screened for TORCH infections. A diagnosis of Congenital CMV can be made if the infant urine is tested with in one week after birth.The yield and costs of TORCH screen may not be justifiable.

Aim: The aim of the study was to determine the number of congenital infections detected with the current use of the TORCH screen Vs urine for CMV.

Methods: A review of all TORCH screen results and urine for CMV results were undertaken in a 10 year period from January 2002 to December 2012 by serology laboratory results with subsequent review of relevant medical charts.Canvasing the neonatologist about the babies admitted under their care.

Results: During this study period there where 54231 live births out of which 2964 babies were born below tenth centile out of that 419 with symmetrical IUGR for which TORCH screen was sent and only five are positive that is 1.1% of the total blood test and in comparison to that only 77 urine test was sent for CMV and 17 are positive that is 20% of the total test.

Conclusion: The yield and costs of TORCH screen may not be justifiable but CMV diagnosis can only be made if the virus is detected in infants urine during the first week of life.

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IMPROVEMENT OF DIAGNOSIS IN CHILDREN WITH PARASITIC INFECTIONS

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Background: Toxocariasis is a disease caused by roundworms larvae. Immunoglobulin E (IgE) and eosinophils play roles in allergy and defense against parasites.

Aims: 1.To evaluate Toxocara canis seroprevalence in our county; 2.To establish correlations between Toxocara infection from one side and IgE levels, eosinophils count and haemoglobin from other side; 3.To improve parasitic infection diagnosis.

Methods: We've analyzed every 10th patient admitted in pediatric department during 4 weeks period. Inclusion criteria: children between 1-15 years of age. Blood tests included: haemoglobin, total IgE (nephelometry), Toxocara canis IgG (ELISA), eosinophils counts. Stool samples were examined using Kato-Miura method. Data was statistically analyzed (independent T test).

Results: 47 children were included in study: 12 of them had positive IgG Toxocara canis serology, 38 of them had elevated IgE levels and 6 of them had parasitic co-infections (ascaridiasis, trichuriasis). 9 of 38 patients with elevated IgE had positive serology for Toxocara. In order to compare IgE levels of Toxocara seropositive patients with IgE of seronegative ones, we didn't observe significant difference (p value= 0.354). There wasn't statistical difference between mean haemoglobin value of seropositive patients versus seronegative ones (p value= 0.597). We noticed statistical difference between eosinophils counts and Toxocara serology: seropositive patients had significant eosinophilia as compare to seronegative patients (p value= 0,002).

Conclusions: 1. In our county every 4th child is Toxocara seropositive and every 8th child has parasitic co-infections; 2. Eosinophilia represents more specific indicatory than total IgE for Toxocariasis; 3. Kato-Miura / eosinophils are useful investigations for parasitic infections diagnosis.

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COMPARISON OF TUBERCULIN SKIN TEST AND QUANTIFERON®-TB GOLD IN-TUBE FOR THE DIAGNOSIS OF CHILDHOOD TUBERCULOSIS INFECTION

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Aim: Tuberculosis (TB) is an important worldwide ongoing health issue. Our aim in this study is to compare a century-old tuberculin skin test (TST) and QuantiFERON-TB Gold In-Tube (QFT-GIT) test.

Materials and methods: Three hundred fifty three children with the suspicion of TB infection or disease between 5 months and 17.5 years old and TST negative 92 healthy children from the same age group were recruited into the study. All children were performed TST and QFT-GIT test and their demographic, clinic and laboratory data were recorded.

Results: A positive QFT-GIT result was obtained in 85 (24%) of the 353 patients and in 2 among the control group. TST was only positive in 231 (%65) of 353 patients. TST was more positive with the increasing number of BCG scars. QFT-GIT test positivity was higher (p= 0.003) significantly in cases without scars compared with cases who have at least one scar. When all the cases were considered, agreement between the two tests were poor (=0.174) and concordance was 58%. There was a significant discordance between the two tests which arise from the high number of TDT (+)/QFT-GIT (-) results, especially in children with latent TB infection. The sensitivity and specifity of QFT-GIT test were 63% and 98% respectively. The sensitivity of TST was 79% and the specifity was 74.3%.

Conclusion: Although QFT-GIT test is highly specific, it is not sensitive enough to detect TB infection and the disease. Using TST and QFT-GIT test together may provide more efficient results.

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DISCITIS IN CHILDREN: AN EVOLUTION IN DIAGNOSTIC SUCCESS WITH THE USE OF 16S RDNA PCR

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Discitis in children is uncommon and it is difficult to secure a microbiological diagnosis. Fever and elevated inflammatory markers are uncommon. Effective treatment comprises prolonged antibiotic therapy, so establishing the causative pathogen is important.

In the past 3 years, 7 children with discitis aged under 36 months have been managed at a London tertiary children's hospital by a multi-disciplinary team including Paediatric Infectious Disease, Spinal, Interventional Radiology and Microbiology specialists .

Chronologically, the first patient had had 2 months of back and loin pain without fever, normal inflammatory markers before xray and MR imaging demonstrated T12/L1 discitis. Logistic difficulties precluded timely biopsy so antibiotics were started empirically without tissue for microbiology.

The subsequent 6 children presented with refusal to weight bear or sit; in all 6, a pre-antibiotics biopsy was secured at the time of diagnostic MRI under GA. All 6 biopsies (sites L4/5, L2/3, L2/3, L4/5, L5/S1 and L3/4 respectively) were culture-negative. Four of these samples were subsequently sent for 16S rDNA PCR, and in three of the four Kingella kingae was identified. The result for the fourth sample is currently pending. The first 5 children have made a full recovery following long course antibiotic therapy.

Kingella kingae is an increasingly recognized pathogen in discitis of young children due to increased availability of molecular diagnostics, specifically 16S rDNA PCR. An accurate microbiological diagnosis of bacterial infection leads to appropriate patient management, informs prognosis, allows use of narrow-spectrum antibiotics, determines treatment duration and may slow the spread of antibiotic resistance.

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EXPERIENCE OF A PERTUSSIS NATIONAL REFERENCE LABORATORY IN BRAZIL, IN THE ANALYSIS OF 7,553 SAMPLES USING CULTURE AND RT-PCR TESTS

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Background and aims: In Brazil, pertussis laboratory diagnosis is based on detection of B. pertussis using culture, a highly specific method, but with variable sensitivity. In 2010, the real-time PCR (RT-PCR), a more sensitive technique, was introduced. This study aims to describe the results of the culture and RT-PCR tests for pertussis diagnosis in samples analyzed in the Adolfo Lutz Institute - National Reference Laboratory for Pertussis.

Methods: 7,553 samples of nasopharyngeal secretions collected from patients with suspected pertussis (age range, eight days to 85 years) were tested from January/2010 to December/2012. The samples were cultured on charcoal agar with 10% sterile defibrinated sheep blood and cephalexin, and incubated at 35-37°C for ten days. RT-PCR was performed in the thermocycler LightCycler ®480 Software release 1.5.0 SP3 - Roche®, using specific primers and probes for the detection of the toxin gene ptxS1 and the insertion element IS481, and results were obtained within 24/48 hours.

Results: 19% of the samples (1,448) were positive on RT-PCR and/or culture tests, and the number of positive tests in the last three years were 151, 750, 547 in 2010, 2011 and 2012, respectively. 376 (5.0%) samples were positive using both growth culture and RT-PCR; 1,051 (14.0%) were only RT-PCR positive and 21 (0.3%), only culture positive. In 61 (0.8%) samples, RT-PCR results were not conclusive.

Conclusion: RT-PCR introduction has improved pertussis diagnosis in all age groups, including children < 6 months of age, but it should be performed simultaneously with growth culture to monitor strain variations.

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NEW, RAPID METHODS FOR DIAGNOSING BORDETELLA PERTUSSIS. BORDETELLA PERTUSSIS PCR ADDED TO CURRENT VIRAL PCR SCREENING OF NASOPHARYNGEAL SAMPLES

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Currently, clinical symptoms of pertussis guide testing protocols, but symptoms may be atypical, particularly in young or partially vaccinated children. Broad screening protocols by molecular methods are now possible which can include viruses, Mycoplasma and Bordetella pertussis.

Aims:

1. To determine if a broad screening strategy using molecular methods identified more cases of pertussis in children under 1 year of age than clinically suspected.

2. To describe clinical outcomes of children with pertussis.

Methods: Nasopharyngeal samples (NPS) submitted for respiratory PCR testing in a 3 month period in 2012 were tested by broad respiratory PCR.

PCR to diagnosis pertussis was performed on clinical suspicion from Jan 2012 and these cases were reviewed.

Results: 280 patients under 1 year had a NPS, 112 had pertussis PCR requested (40%). Of these 112 samples, 5 (4.4%) were B. pertussis positive by PCR. A further 21 cases (12%) were identified from testing 168 samples where pertussis had not been initially requested. Viral co-infections were observed in 18/26 pertussis cases.

23 cases were diagnosed from clinical suspicion. 19/23 were < 3 months. 16/19 (84%) were admitted and 2 required ITU admission. Both ITU cases required high levels of support including prolonged ventilation and inotropic support.

None of the 4 cases older than 3 months were admitted.

Conclusions: Pertussis will be missed if only tested for when classical symptoms are present. B.pertussis is often found with other pathogens. Screening strategies using molecular methods should target all possible pathogens including pertussis as classic features often absent.

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INVASIVE MENINGOCOCCAL DISEASE: THE USE OF POLYMERASE CHAIN REACTION TO INCREASE DIAGNOSTIC ACCURACY

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Background and aims: Invasive meningococcal disease (IMD) remains a serious public health problem. Bacteriological confirmation and serogroup determination is important for contact management, outbreak recognition and detailed epidemiological surveillance. Although culture is the gold standard, previous antibiotic therapy reduces its sensibility. The aim of this study is to assess the utility of polymerase chain reaction (PCR) to increase diagnostic accuracy of IMD.

Methods: Retrospective study of all children younger than 16 years with microbiologically (positive culture and/or PCR) confirmed IMD, admitted to our hospital between 2004-2012. PCR and culture were performed concomitantly in all cases.

Results: Seventy-five patients were included, median age was 3.1 years; 62.3% were male. Serogroup distribution was: B=86.7%; C=5.3% and Y=1.3% of cases. Almost 7% were caused by non serogroupable Neisseria meningitidis. Fifty-two percent of patients presented with sepsis, 30.7% with meningitis, and 17.3% with both of them. Forty-six patients had a positive culture and four of these had a negative PCR. Seventy-one patients had a positive PCR (29 with negative culture). Previously administered antibiotic was documented in 40 patients, 16 of these were confirmed by PCR only, but this was not significantly different from patients without previous antibiotic (p=0.11).

Conclusions: PCR was the only test providing evidence for IMD diagnosis and serogroup determination in 38.7% cases. Our study failed to show the association between previous antibiotic therapy and the usefulness of PCR, possibly due to the low number of patients included. The concomitant use of both techniques yields the best results in IMD diagnosis.

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COMPARISON OF TWO DIAGNOSTIC TECHNIQUES IN VENTILATOR ASSOCIATED PNEUMONIA IN A PEDIATRIC INTENSIVE CARE UNIT

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Background and aims: Ventilator associated pneumonia (VAP) is the second most common nosocomial infection in pediatric ıntensive care units. Multiresistant agents are an increasing problem causing VAP in hospitals worldwide. There is no optimal diagnostic test to discover the causative agent. The aim of the study is to compare two non-bronchoscopic techniques (endotracheal aspiration/ETA and mini-bronchoalveolar lavage/mini-BAL) for the diagnosis of suspected ventilator associated pneumonia (VAP) in pediatric cases.

Methods: Children mechanically ventilated in Pediatric Intensive Care Unit at Ege University Children´s Hospital were enrolled to the study. 42 patients had suspected VAP and specimens were collected with both methods, quantitative cultures were obtained and compared for pathogens.

Results: There was no spesific pathogen grown in specimen cultures of 14 patients in both techniques. On the other hand 14 patients had positive culture results in ETA specimens but their samples were negative when the aspirates were obtained via mini-BAL. There was no positive result with mini-BAL if ETA cultures were negative. And 13 patients had the same pathogens grown in their respiratory specimen cultures even they were collected with ETA or mini-BAL.

Conclusion: In comparison with ETA technique; mini-BAL seems more sensitive to avoid overdiagnosis and overtreatment of VAP in children similar to adults. Causes and correlations are discussed in the study.

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ORAL PENICILLIN PRESCRIPTIONS FOR CHILDREN IN THE UK: EVIDENCE OF WIDE DOSING VARIATION IN PRIMARY CARE

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Background and aims: The British National Formulary for Children (BNFC) recommends dosing oral penicillins according to age-bands, weight-bands, and weight-based calculations. This study evaluated how UK GP prescribing follows current age-band recommendations, which could lead to sub-therapeutic dosing because of rising childhood obesity.

Methods: Detailed oral penicillin prescriptions for 0-18 year-olds were analysed from the 2010 IMS Disease-Analyzer database, comprising computerised medical records from 125 general practices (approximately 2% of the UK population).

Results: For 2010, 388,926 patients aged 0-18 years received 65,737 prescriptions for oral penicillins in total: amoxicillin (63%), phenoxymethylpenicillin (17%) and flucloxacillin (20%).

The amoxicillin results (for example) showed:

(1) In the age-band under 1 year, no child was prescribed the recommended unit-dose (62.5mg); the majority received double the unit-dose (125mg);

(2) In the age-band of 1-5 years, 96% were prescribed the recommended unit-dose (125mg);

(3) 40% of 6-12 year-olds and 70% of 12-18 year-olds were prescribed unit-doses below the BNFC recommendations.

Otitis media prescriptions were analysed separately. The dose in mg/kg/day was calculated using average weights from the 2010 Health Survey of England, as patient weight was not available. From these data, only children under 1 year received the recommended dose (40-90mg/kg/day). For children aged 4-15 years, the prescriptions equated to 10-20mg/kg/day, approximately 33% of the recommended dose.

Conclusions: These results show extensive variation in the dosing of penicillins for children in primary care. There is an urgent need to review and simplify dosing guidelines, in relation to the weights of children today.

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DOSING OF FREQUENTLY USED ANTIBIOTICS IN EUROPEAN NICUS: POINT PREVALENCE STUDY OF EUROPEAN STUDY OF NEONATAL EXPOSURE TO EXCIPENTS (ESNEE)

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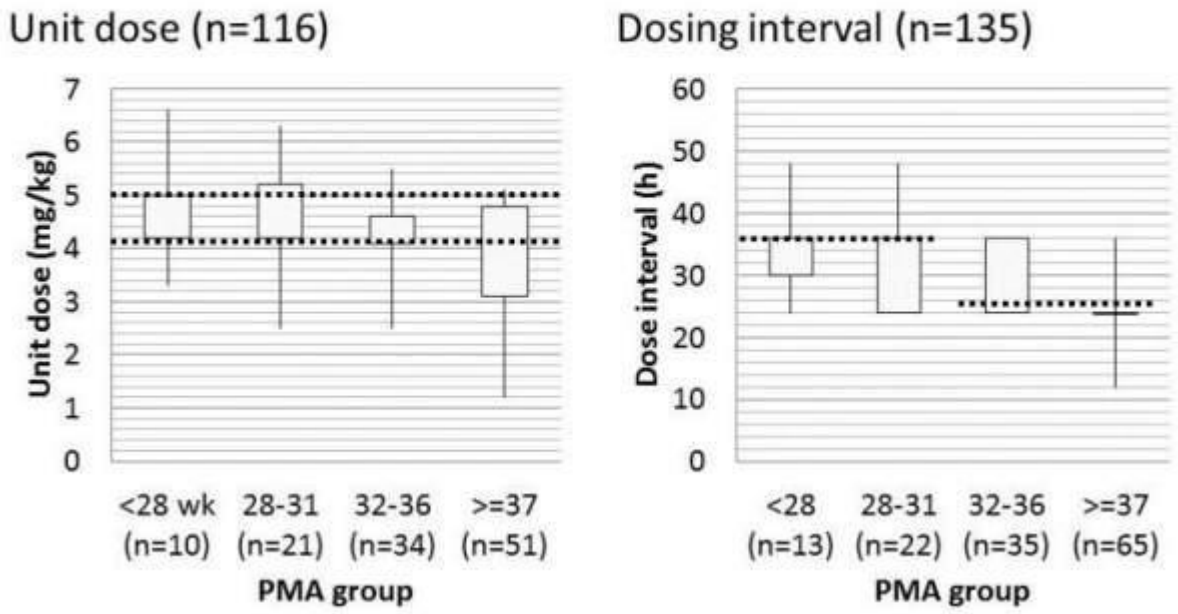
Background and aim: Little is known about dosing of the most frequently used drug class, antibiotics, in neonates. This analysis aimed to study dosing variations of frequently used antibiotics in European NICUs.

Methods: A point prevalence study reaching out to as many European NICUs as possible was performed. Demographic data of neonates receiving any drug on the study day morning chosen within one of three two-week study periods from January to June, 2012, and the dosing regimen and route of administration of each prescription was recorded.

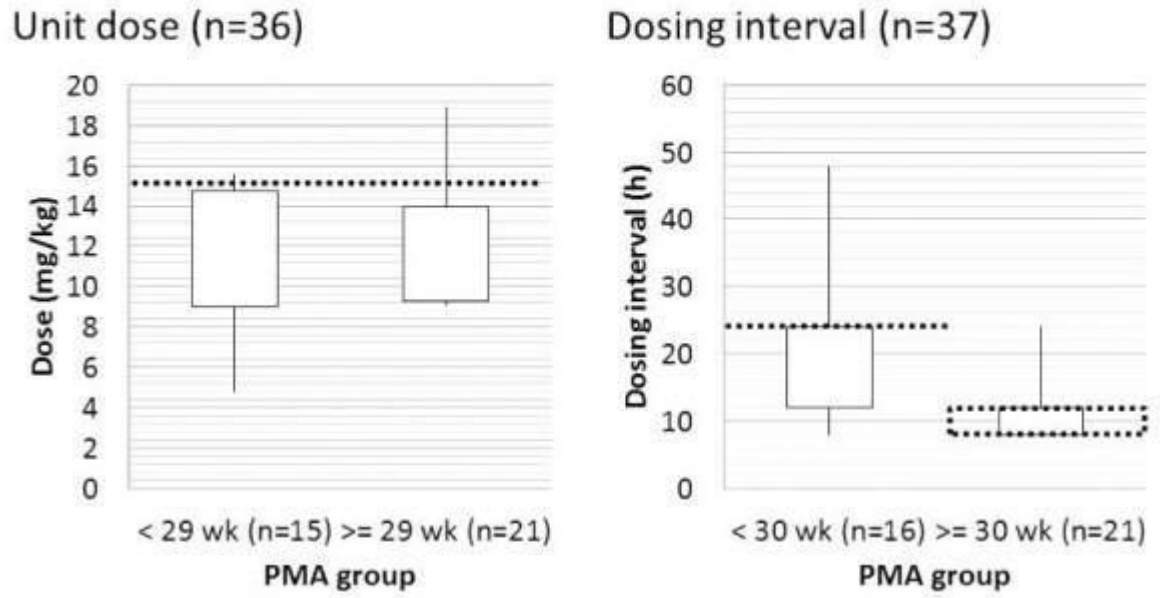
Results: In 21 countries 72 hospitals 824 neonates participated. Gentamicin, ampicillin, penicillin and vancomycin were used most frequently - in 138; 82; 73 and 36 neonates in 41; 31; 23 and 18 hospitals, respectively. Variability of gentamicin and vancomycin dosing by postmenstrual age is shown on Figures 1 and 2. Ampicillin was given in a median (IQR) dose of 52 (49;78); and penicillin 43 (30;51) mg/kg at median intervals of 12 (8;12) and 12 (12;12) h, respectively.

Figure 1. Gentamicin dosing in European NICUs. Data are presented as quartile range, min and max for dose and interval. BNFC recommended dose range and intervals are shown in dotted lines.



[Figure 1]

Figure 2. Vancomycin dosing in European NICUs. Data are presented as quartile range, min and max for dose and interval. BNFC recommended dose and intervals are shown in dotted lines.



[Figure 2]

Conclusion: While doses of gentamicin are within recommended ranges, the doses of penicillins are almost double of those in BNFC (30 and 25 mg, respectively). Vancomycin is given below recommended unit dose to ¾ of neonates. Variations in the dosing may rise from adjustments due to therapeutic drug monitoring of gentamicin and vancomycin but also from different recommendations in frequently used neonatal drug information sources.

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CRITICAL APPRAISAL OF WEB-BASED RESOURCES PROVIDING PROFESSIONAL EDUCATION ON ANTIBIOTIC PRESCRIBING IN CHILDREN: 10 MILLION HITS-ONLY 10 GOOD WEBSITES

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Background/aims: Web-based educational tools can provide easy-to-reach, regularly up-dated information to improve the knowledge about appropriate use of antimicrobials. We aimed to identify and appraise web-based educational resources for professionals on the optimal childhood use of antibiotics.

Methods: Websites of healthcare organizations and societies involved in infectious diseases and/or pediatrics and relevant international discussion forums were screened in May 2012 to identify online educational tools for childhood antibiotic prescribing. Two Google searches were conducted at the same time combining the following terms: “Antibiotics”, “Children”, “Education” and “Antibiotics”, “Children”, “Healthcare professionals”, “Website”. Identified resources were appraised using 6 criteria proposed for educational Internet resources (authority, objectivity/reliability, authenticity, timeliness, relevance for the targeted audience, accessibility/efficiency) with each criterion scored as met completely/met incompletely/not met.

Results: The two Google searches identified 9,700,000 and 2,790,000 results, respectively, with most of the websites excluded during title scanning leaving 10 and 12 websites, respectively, of potential interest. Targeted searching of institutional websites and discussion forums identified 31 further potentially relevant sites. On detailed review of the content only 10 websites addressed the relevant subject. Among these only APUA: Alliance for the Prudent Use of Antibiotics and Getsmart from the Centers for Disease Control and Prevention met all the quality criteria and provided relevant high-quality information.

Conclusion: Although a lot of material on improving childhood antibiotic prescribing targeting professionals is available online, only a very few websites provide high quality educational information. There is a need for improved evidence-based online educational material on this topic.

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ANTIBIOTIC PRESCRIPTIONS AMONG CHILDREN AGED BELOW 3 YEARS: TRENDS FROM 2006 TO 2012 IN SOUTHEASTERN FRANCE

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Background and aims: In France, pre-school children frequently receive antibiotics for respiratory tract infections, particularly 3rd generation cephalosporins (3GC), known to generate microbial resistance. Efforts to curb antibiotic prescriptions began in Southeastern France in 2000 and were later extended nationwide. Trends in overall and 3GC prescription for children < 3 years were monitored in the Alpes Maritimes area from 2006 to 2012 both yearly among the overall population and in daycare centres in 2006, 2008 and 2012.

Methods: Volume and type of ambulatory antibiotic prescriptions by general practitioners and paediatricians were obtained from the National Health Insurance (NHI) for children < 3 years for the first semesters of 2006 to 2012 per aged-matched overall population in the Alpes Maritimes. Between January and April 2006, 2008 and 2012, antibiotic prescriptions were documented by parents of a random sample of < 3 year-old day-care attendees, and compared using chi-square tests.

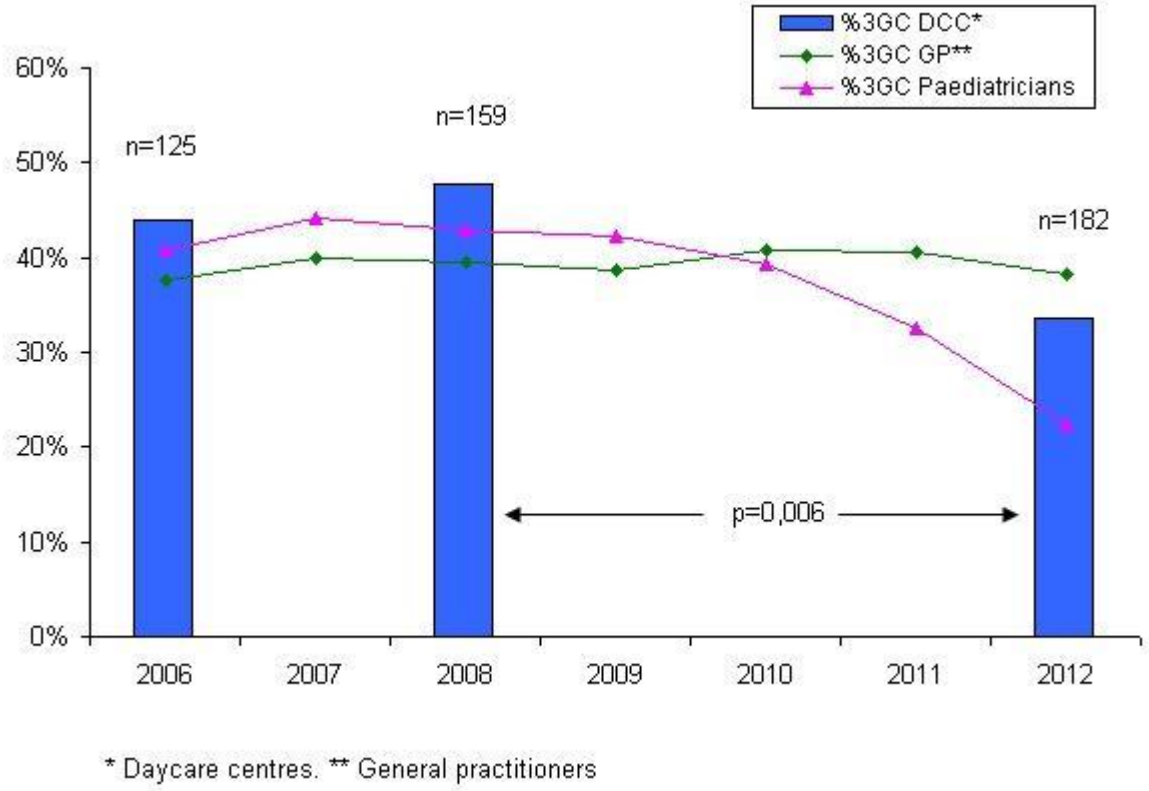
Results: Overall prescription/child peaked between 2009 and 2011 and was lowest in 2012. (Table1). Amoxicillin+/-clavulanate and 3CG accounted for over 80% of prescriptions. Compared to 2006, the study population increased by 5.3%, while prescriptions dropped by 4.5%. C3G prescriptions by paediatricians declined sharply as from 2011. Trends were similar in daycare centres (Figure 1).

Table 1: Population and antibiotic prescription trends for children < 3years of age in the Alpes Maritimes

	2006	2007	2008	2009	2010	2011	2012
# children < 3yrs*	34288	34898	35017	35662	35857	36481	36205
# prescriptions**	20215	20716	18945	22277	23688	22270	19345
% GP prescriptions***	57.7%	57.5%	56.2%	55.4%	54.6%	57.7%	60.5%
Prescriptions/1,000	590	594	541	625	661	610	534

*national population register (INSEE); ** national health insurance (AM PACA-Corse); ***general practitioners

[Table 1: Population and prescription trends]



[Figure 1: Trends in 3GC prescription]

Conclusions: Total antibiotic prescriptions decreased moderately over the 6-year period. Prescription of 3GC by paediatricians declined sharply. Reasons for the differences in prescription choices between GPs and paediatricians require investigation.

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TINN2: TREAT INFECTION IN NEONATES 2 AZITHROMYCIN FOR THE PREVENTION OF BRONCHOPULMONARY DYSPLASIA IN PRETERM NEONATES

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Background: In neonates, pulmonary Ureaplasma colonization, and inflammation may play a role in BPD development, a multifactorial disease of prematurity. The macrolide antibiotic azithromycin may be effective in reducing the severity of BPD as it is active against Ureaplasma and has anti-inflammatory properties.

Objectives and clinical trial design: Therefore, the TINN2-project (www.tinn2-project.org) was submitted and financed by the FP7 program in order to evaluate azithromycin in neonates and obtain a PUMA. The TINN2 Pediatric Investigation Plan has been approved by the PedCo in January 2013.

Within the PIP, the randomised, double-bind, placebo-controlled trial was designed to assess the efficacy of azithromycin in increasing the rate of survival without BPD in preterm infants of ≤28 weeks gestation ventilated within 48hours of birth. The trial will include 810 preterm neonates, born at ≤28weeks of gestation requiring respiratory support within 12hours of birth will be recruited. The drug will be given at the daily dose of 10mg/kg for 10days.

Among the main secondary objectives the trial will assess changes in the overall neonatal mortality rate, safety and pharmacokinetics of azithromycin, pulmonary colonisation by Ureaplasma, and Ureaplasma resistance to treatment.

Expected outcomes and potential implications: TINN2 will provide the required information on the pharmacokinetics, efficacy and safety, of azithromycin in the newborn to apply for a PUMA.

TINN2 currently benefits from various paediatric drug evaluation initiatives across Europe, including the ongoing TINN1-project consolidating a network of units with experience in clinical research that will be used for additional drug evaluation in neonates.

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POPULATION PHARMACOKINETICS OF CIPROFLOXACIN IN NEONATES AND YOUNG INFANTS LESS THAN 3 MONTHS OF AGE

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Background: In the absence of pharmacokinetic and pharmacokinetic / pharmacodynamic studies, ciprofloxacin is used off-label in neonates with suspected or proven gram negative infection. Within the FP7 EU project TINN (Treat Infection in NeoNates), our aim was to evaluate the population pharmacokinetics of ciprofloxacin in neonates and young infants < 3 months in order to optimize ciprofloxacin treatment.

Methods: Blood samples were collected from treated neonates and ciprofloxacin plasma concentrations were analyzed by HPLC-MS.. Population pharmacokinetic analysis used NONMEM software to optimize dosing.

Results: Ciprofloxacin was administered as an intermittent infusion over 30 minutes or 1 hour at the dose of 10 mg/kg/dose twice daily in neonates and three times daily in young infants. Sixty two babies were included in the pharmacokinetic analysis and a total of 480 concentrations (pharmacokinetic or scavenged samples) were available for modeling to determine population pharmacokinetic parameters. Simulation was used to determine ciprofloxacin dose required to achieve the adequate pharmacokinetic-pharmacodynamics target ($AUC_{0\text{-}24}$/MIC ratio).

Conclusion: This is the first report of the population pharmacokinetics of ciprofloxacin in neonates and young infants < 3 months. The developed model will be used to optimize ciprofloxacin treatment in neonates and infants.

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MANAGEMENT OF PAEDIATRIC TB IN LEADING UK CENTRES - UNVEILING CONSENSUS AND DISCREPANCIES

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Background and aims: National UK and international guidelines for the clinical care of children with TB differ in some fundamental aspects, with recommendations often based on expert opinion. We evaluated clinical practice in leading paediatric TB clinics in the UK.

Methods: A survey on diagnosis and management of latent and active TB was conducted in 12 specialist paediatric TB clinics in the UK using an electronic questionnaire.

Results: We had 100% response rate. Heterogeneous practice exists in use of IGRA and TST for screening (see table). Practice differs when choosing the age cut off for empirical TB prophylaxis for children: < 2yrs (69%) or < 5yrs (31%). In active TB, only 54% of clinicians do colour vision tests before prescribing ethambutol. Opinions divide on treatment duration of osteoarticular TB: 6 months (46%), 12 months (54%). There is consensus for conducting a routine HIV test, using drug doses recommended by British National Formulary (BNF) in treating active TB and monitoring MDR TB contacts without using chemoprophylaxis.

Conclusions: The survey shows marked variation in many aspects of clinical practice, highlighting the need to review their evidence base. Prospective paediatric studies are urgently required to unify clinical practice.

	TST alone	TST and IGRA	Either	Total
1mo-2yrs	4/12(33%)	8/12(67%)		12/12
2-5yrs	5/12(42%)	7/12(58%)		12/12
>5yrs	6/12(50%)	6/12(50%)		12/12
Immunocompromised		10/12(83%)	2/12(17%)	12/12

[Screening for latent TB in children, who had BCG]

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IMMUNITY LEVEL TO HAEMOPHILUS INFLUENZAE IN BETA-THALASSEMIA SPLENECTOMIZED CHILDREN

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Background: Patients with thalassemia and asplenia are at increased risk for infection. The aim of this study was to determine the Hemophilue influenza type b (Hib) antibody concentration among beta thalassemic patients with and without spleen.

Material and method: The Hib antibody concentration was investigated in 87 patients with thalassemia, 50 of who had undergone splenectomy. Hib antibody was determined by an ELISAmethod. Subjects who had Hib antibody level ≥1.0 µg/ml as long term protection, between 0.15 to < 1.0 µg/ml as short term protection and < 0.15 µg/ml as no protection. Also patients with Hib antibody concentration ≥0.15 µg/ml classified as protective and who had antibody level < 0.15 µg/ml as non protective. For the analysis we used SPSS 11.5 software. A two sided p-value less 0.05 was considered statistically significant.

Results: 83.8% (31) of non.splenectomized patients had protective antibody levels against Hib whereas among asplenic patients this rate was 32.0% (16) that there was significant differences (p< 0.001). Protection against Hib decreased with increase interval time after splenectomy from 64.7% in ≤60 months interval to 5.3% in >120 months interval (p=0.001). Thirty percent of the 50 splenectomized subjects had long term protection against hemophilus influenza type b where as 62.2 percent of 37 subjects with spleen had long term protection (p< 0.001).

Conclusion: Patients with splenectomy lower Hib antibody level than cases with spleen. Also antibody level decreased with time interval after splenectomy. Thus the vaccine recommendation seems essential for beta thalassemic splenectomized patients for increased serum Hib antibody concentration.

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PREVALENCE OF MENINGOCOCCAL CARRIAGE AMONG ADOLESCENTS IN CAMPINAS, BRAZIL

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Background and aims: Meningococcal disease is a rare consequence of N. meningitidis infection, with the highest incidence rates in young children. In contrast, meningococcal carriage is common, especially in teenagers. Taking in account the very limited published data currently available describing meningococcal carriage in Brazil, we performed a study to evaluate the prevalence of N. meningitidis carriage among adolescent students.

Methods: Cross-sectional study, including a representative sample of 1,208 adolescents attending 73 public and private schools in Campinas city. Oropharyngeal swabs were collected and phenotypic and genotypic characterization of carriage strains isolated among adolescents from 3 defined age subgroups: A(11-13y); B(14-16y) and C(17-19y) was performed. The effect of social behavior and previous vaccination against serogroup C were also analyzed.

Results: The overall carriage prevalence was 120 carriers per 1,208 subjects (9.9%), with the highest prevalence (12%) in older adolescents (17-19 years). The proportion of carriers was also higher among students attending public schools, sharing the dormitory with ≥ 2 people, or reporting passive smoking. Carriage of serogroup C dominated (1.3%), followed by serogroups B (0.99%), Y (0.49%), and W135 (0.16%). The most frequent strain isolated was C:23:P1.14-6. Previous vaccination did not interfere in the carriage rates.

Conclusions: The evidence gathered during this study in a representative Brazilian student cohort showed that the highest rates of carriage were observed in older adolescents, with an unusually high dominance of serogroup C. Social behavior was associated with increased risk of carriage. These results will have important implications in future vaccination strategies in Brazil.

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CHARACTERIZATION OF HUMAN IMMUNODOMINANT B-CELL EPITOPES WITHIN VIRULENT SURFACE PNEUMOCOCCAL PROTEINS (SPNPS)

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Background: We have previously identified 10 immunodominant B-cell epitopes within antigenic fragments of SPnPs (CbpD, PhtD, PhtE, ZmpB, PspA and PavB) with a potential role in host-pathogen interaction, by screening sera from patients with invasive pneumococcal disease (IPD) against 20-mer synthetic peptides covering the whole amino-acid sequence of previously defined antigenic regions. This work aimed to further characterize the selected epitopes regarding their specificity in patients with IPD and their immunoreactivity within each corresponding protein.

Methods: ELISA using selected B-cell epitopes, synthesized in their free soluble form, as capture antigens was applied to validate their immunoreactivity in sera from 35 IPD patients aged 2-16 years and 140 age-matched children with no history of IPD. Specific antibodies (eluents) against antigenic peptides were purified using sepharose B immunoaffinity columns. Antibody purification was confirmed by ELISA using the homologous peptide as capture antigen. Eluents' immunoreactivity was assessed against pneumococcal whole protein extract by Immunoblotting.

Results: Pep #4 derived from CbpD, pep #19 from PhtD and pep #40 from PhtE were consistently and specifically recognized by IPD patients' sera compared to controls' ($p < 0.0001$). Each eluent reacted with the homologous peptide in the confirmatory ELISA and recognized a protein band with a molecular mass matching to the corresponding parent protein, in whole pneumococcal cell lysates.

Discussion: Three of 10 previously identified B-cell epitopes reacted consistently and specifically with IPD sera. Purified anti-peptide antibodies recognized each corresponding parent protein in pneumococcal whole cell lysates, encouraging further investigation of their surface accessibility and opsonophagocytic function.

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HIGH RATES OF STREPTOCOCCUS PNEUMONIAE CARRIAGE DETECTED IN SALIVA OF CHILDREN

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Background and aims: With the introduction of pneumococcal conjugate vaccines, in-depth carriage studies are required to monitor the effects of vaccination. Here, we investigated saliva as a means of detecting Streptococcus pneumoniae colonization for potential use in surveillance studies.

Methods: Saliva was collected from 49 students (age 5 to 10 years, median 8) of a rural school near Utrecht. Samples were transported to the lab on ice, cultured and the remaining volume stored frozen. Cultures were inspected for S. pneumoniae colonies, then all bacterial growth was harvested and frozen. DNA was extracted from thawed raw and culture-enriched samples using a modified Agowa protocol, tested by quantitative-PCR (qPCR) targeting S. pneumoniae specific genes lytA and piaA and considered positive when both genes detected.

Results: Two children (4%) were culture-positive for S. pneumoniae. Thirty (61%) children were qPCR-positive for S. pneumoniae in raw saliva whereas 41 (84%) were q-PCR positive in culture-enriched samples. There was a negative correlation between age and quantity of lytA detected in raw saliva samples (Spearman's r=0.3, p=0.03).

Conclusion: Conventional culture detection of S. pneumoniae in saliva is extremely difficult due to saliva's polymicrobial nature. These limitations were addressed by combining culture-enrichment and sensitive molecular methods. This resulted in more than ten-fold higher rates of pneumococcal carriage detected in schoolchildren compared to results of conventional culture. The simplicity of sample collection and the high sensitivity of pneumococci detection suggest that saliva could be considered as an alternative to nasopharyngeal swab sampling in surveillance on pneumococcal carriage in children.

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THE ASSOCIATION OF GENETIC VARIANTS IN TOLL-LIKE RECEPTOR 2 SUBFAMILY WITH ALLERGY AND ASTHMA AFTER HOSPITALIZATION FOR BRONCHIOLITIS IN INFANCY

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Background and aims: Toll-like receptors (TLR´s) are a pivotal part of the innate immunity system. Despite of having a key role in pathogen defense, variations in TLR genes have also been connected to autoimmune conditions, such as allergy and asthma. TLR2 subfamily comprises TLR1, TLR2, TLR6 and TLR 10. We hypothesized that polymorphism of TLR2 subfamily may be associated with post-bronchiolitic asthma and/or atopy prevalence.

Methods: TLR1 rs5743618, TLR2 rs574308 and TLR6 rs5743810 SNP´s of 135 children who had been hospitalized for bronchiolitis at < 6months of age were analyzed. Present doctor-diagnosed asthma and allergic conditions were evaluated during a follow-up visit at preschool age, as well as asthma and atopy occurrence during first six years of life.

Results: Asthma was present in 17(12.6%), atopic dermatitis in 39(29%) and allergic rhinitis in 36(26.7%) children at the mean age of 6.3 years (SD). Children homozygous for the minor allele T at TLR6 rs5743810 were almost twice as likely to be present atopics (61% vs. 34% of allele C carriers, p=0.02). Further, those carrying the allele T at TLR2 rs574308 had asthma more often during first 6 years of life (41% vs. 24% of non-allele T carriers, p=0.05).

Conclusion: TLR6 rs5743810 and TLR2 rs574308 SNP´s were associated with asthma and atopy after severe bronchiolitis in infancy. Thus, TLR2 subfamily may be involved in childhood asthma.

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HIGH PROPORTION OF MANNOSE BINDING LECTIN (MBL) DEFICIENCY IN CHILDREN LESS THAN 2 YEARS OLD WITH INVASIVE PNEUMOCOCCAL DISEASE

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Background and aims: MBL is a serum protein of the innate immune system whose deficiency is observed in 15-25% of all human populations. Our objective is to evaluate the association of MBL deficiency in patients with invasive pneumococcal disease (IPD) according to age group and clinical manifestations

Methods: Prospective study including all patients with IPD (children and adults) in two Catalan Hospitals (period February/2011-October/2012). Demographic and clinical variables were registered. Immunocompromised patients or those with anatomic anomalies that predispose to meningitis were excluded. IPD was defined as isolation of S.pneumoniae or DNA detection by RT-PCR in any sterile fluid. Genotypic study of the MBL2 gene was performed and patients were classified as sufficient or insufficient MBL levels.

Results: 127 patients had IPD, 6 refused to participate. 69(57%) were male. 26(21.5%) were < 2 years of age, 35(28.9%) between 2-5yr and 60(49.5%) >5yr. Most frequent serotypes were 1(21.5%), 3(14%) and 19A(9.1%). Overall MBL deficiency was observed in 15.7% (IC95%,8.8-22.5) of patients but significant differences were observed comparing children < 2yr. vs. other patients (30.8% vs. 11.6%,P=0.02). Most frequent IPD was pneumonia 82.6%(IC95%,75.4-89.8) but a significant higher proportion of meningitis was observed in children < 2yr. vs. others (23.1% vs. 6.3%; p=0.01). MBL deficiency was more frequent in patients with meningitis vs. others (21.1% vs. 7.8%; p=0.07).

Conclusions: MBL deficiency is highly prevalent in children younger than 2 years with IPD. Additional studies are needed to evaluate this fact.

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DETECTION OF STREPTOCOCCUS PNEUMONIAE IN DRIED SALIVA SPOTS: EXPLORATORY STUDY ON ALTERNATIVE DIAGNOSTIC APPROACHES IN SURVEYS ON PNEUMOCOCCAL CARRIAGE

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Background and aims: Saliva is an easily accessible body fluid and was historically the method to test pneumococcal carriage in surveillance studies. The aim of this study was to determine the feasibility of using dried saliva spots (DSS) as an alternative to raw saliva collected on dry ice for pneumococcal carriage studies.

Methods: Saliva was collected from healthy volunteers and spiked with clinical S. pneumoniae strains applied to Whatman 903 Protein Saver cards (cotton fibers), and allowed to air-dry for 2 hours in ambient conditions. Dried saliva spots (DSS) were stored sealed with a desiccant pack at 30ºC, room temperature (RT), 4ºC, or -20ºC for up to 35 days. DNA was isolated from spots with a modified Qiagen DNeasy kit and tested in quantitative-PCRs (qPCR) targeting pneumococcal genes lytA and piaA.

Results: DSS processed immediately after drying showed equal quantity of pneumococcal DNA compare to raw saliva samples. The lower limit of detection of DSS was 10^4 CFUs per spot. Pneumococcal DNA was stable for up to 10 days in DSS stored $\leq$ RT and for up to 7 days in DSS stored at 30ºC. Presence of pneumococcal DNA was still detected in DSS stored up to 35 days at any temperature. There were no differences between various clinical strains.

Conclusion: Pneumococcal DNA is stable in DSS stored for up to one week. DSS may be considered as an attractive alternative to nasopharyngeal samples in surveillance studies on pneumococcal carriage, particularly in studies conducted in remote settings.

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M. TUBERCULOSIS VS. M. BOVIS BCG - ELUCIDATING DIFFERENCES IN THE HOST GENE RESPONSE BETWEEN PATHOGEN AND VACCINE STRAIN

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Background and aims: BCG is the only available vaccine against tuberculosis (TB). It is routinely administered to infants in many countries worldwide and provides protection against disseminating and meningeal forms of TB, however protection against pulmonary TB is sub optimal. In order to understand how the host response to M. bovis BCG (BCG) differs from that to M. tuberculosis (MTB), we compared genome wide RNA expression in human blood in response to in vitro infection with BCG or MTB compared to controls.

Methods: Whole blood from non-BCG-vaccinated healthy donors was infected with either MTB or BCG and RNA recovered at five sequential time points up to 96 hours. After amplification and labeling, RNA was hybridized to Illumina HT12 microarrays. Genes showing significant differential expression in the infected samples compared to controls over time were identified using a novel in-house statistical method.

Results: 2064 genes were significantly differentially expressed in response to both MTB and BCG compared to uninfected controls. However, genes uniquely differentially expressed in response to either MTB (2576) or BCG infection (1642) were also identified. Biological pathway analysis (using Ingenuity, IPA) of the host response to BCG and MTB revealed reduced expression of genes involved in cellular interactions, T-cell signalling as well as phagolysosome maturation.

Conclusion: Elucidation of differences in gene induction in response to BCG or MTB may help to better understand the specifics of MTB infection as well as the characteristics of vaccine response to BCG.

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RELATIONSHIP BETWEEN THE POLYMORPHISM OF IL28B AND RVR IN HCV INFECTED CHILDREN TREATED WITH PEGYLATED INTERFERON AND RIBAVIRIN

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Background and aims: Rapid virologic response (RVR) is defined as an undetectable hepatitis C virus (HCV) RNA at week 4 of treatment. RVR is used to predict 24-48 weeks therapy effectiveness.

Evaluation of relationship between the polymorphism of IL28B(rs12979860) and RVR in HCV infected children treated with pegylated interferon and ribavirin.

Methods: The study included 6 children (6,1-9,5 years): 4 girls, 2 boys, vertically HCV infected; 5 with genotype 1b(among them IL28B: CC-in 3, CT-1, TT-1) and 1 with genotype 4(IL28B: CT). All children underwent liver biopsy(LB), in 4 non-invasive FibroTest(FT) was performed. The baseline viral load (VL) and ALT activity was evaluated after 4 weeks of treatment. Therapy is continued in all children.

Results: High baseline VL(>600000IU/ml) was in 4/6 children, among them IL28B:CC-2,CT-1,TT-1. Low baseline VL(< 600000IU/ml) was in 2/6 children, among them IL28B: CC-1, CT-1. RVR was not attained. Decline of VL at 4 weeks was in all patients: < $2\log_{10}$ in 5(IL28B: CC-2, CT-2, TT-1), >$2\log_{10}$ in 1(IL28B-CC). Baseline ALT ranging from 46-85 UI/l(mean: 65) was elevated in all. At week 4 reduction of ALT was observed in 5/6 patients, among them normalization of ALT in 2(IL28B-CC). Girl with IL28B:TT, infected with HCV1b, had highest fibrosis score: LB(F2), FT(F1-F2), high baseline VL, at week 4 she declined VL< $1\log_{10}$ and did not normalized ALT.

Conclusions: RVR was not attained in any children, although half of them have IL28B:CC. The course of infection and response to therapy at week 4 were worse in girl with IL28B:TT.

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HEARING IMPAIRMENT AS A COMPLICATION OF ACUTE MENINGITIS

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Background and aim: Meningitis continues to result in substantial morbidity and mortality despite the availability of effective antimicrobial therapy. In survivors, neurologic complications can develop at any time during the course of meningitis and may be sudden or gradual in onset. Although many neurologic complications are severe and readily apparent, others, such as hearing loss, may be subtle or inapparent during the early phases of infection. The aim of the study was to determine the incidence of hearing loss in a pediatric population affected by meningitis.

Methods: We retrospectively reviewed the medical records of children 0-18 years old hospitalized at Infectious Diseases Unit, Bambino Gesù Hospital, Rome, Italy, for a laboratory confirmed meningitis between 1st January 2001 and 1st January 2013.

Results: We reviewed 214 cases of meningitis. The mean age was of 4,5 years (range 5 days-17.3 years). Neurologic sequelae occured in about 16,8% of children with meningitis; the distribution was as follows: hearing loss (22patients), cranial nerve palsy (3patients), paresis (3patients), visual field defects (3patients), ataxia (3patients) and aphasia (2patients). In two cases, a cochlear implantation was required.

Conclusions: The most common sequelae was hearing loss. In details, in this series, 22 (10,2%) children experienced hearing loss, consistent with previously reported rates of 5% to 35% within the pediatric population. In all but one children affected by hearing loss, no hearing impairment was clinically detached during hospitalization. Early prediction of an adverse outcome may help to determine which children require prompt surgical intervention or longer follow-up.

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ADHESION TO INFLUENZA VACCINATION AMONG MEDICAL STUDENTS DURING AND AFTER INFLUENZA A (H1N1) PANDEMIC

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Background and aims: Despite evidence that influenza vaccination reduces risk of infection and prevents transmission to patients, compliance to immunization guidelines is low among healthcare workers (HCW). We evaluate adherence to influenza vaccination among medical students in 2010 (during influenza pandemic) and in 2011 (post-influenza pandemic) and assessed their perception about influenza vaccination.

Methods: In a cross-sectional study just after the 2011 influenza season, medical students were asked if they had received influenza vaccine in 2010 and in 2011, and the reasons for vaccine acceptance or non-acceptance. First grade students in the year 2011 were excluded because they had not yet entered medical school when the pandemic occurred.

Results: 144 students were interviewed, varying from 39 from second grade to 25 in the fifth grade; 50% were male and median age was 23.3 years. In 2010, 131/144 (91.0%) medical students were vaccinated against influenza, while only 60/144 (41.7%) were vaccinated in 2011. This decay was observed in all grades. When inquired on the reasons for receiving influenza vaccine, the most frequently cited reason was “to be protected” in both years. The most cited reason for not receiving immunization was “because I forgot”. The knowledge about influenza vaccination being recommended for HCW increased from 59% for 2nd grade students to 96% among 6th grade students.

Conclusions: The adhesion to influenza vaccine was very high during the pandemic, but decreased significantly in the following season in all grades. Knowledge on immunization recommendations for HCW does not necessarily reflect higher adhesion to vaccination.

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NOSOCOMIAL INFECTIONS IN THE INTENSIVE CARE UNIT OF A PAEDIATRIC GREEK HOSPITAL IN ATHENS

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Aim: To monitor the nosocomial infection rate in our PICU and the risk factors that are associated with.

Methods and materials: A prospective observational study was carried out from January 2011 to March 2012, applying the methodology of the INICC and the definitions of the NHSN-CDC.

Results: During this period from 264 children that were hospitalized for 326 days in our PICU, 14 manifested nosocomial infections. Mean duration of hospitalization stay was 22 days (SD=23). Our patient's median age was 2,5 years, 50% were males. Nine children (64%) suffered from a severe underling disease and five of them from cancer. Six children (43%) had multiple previous hospitalizations in paediatric and surgical wards. Nine patients (64%) had central vascular catheter with a mean duration of catheterization 24 days, five (36%) had arterial catheters, nine (64%) were intubated and all of them had urinary catheter. The mean day presence of nosocomial infection was the 8^{th} day of hospitalization. Twelve children (86%) developed septicemia with positive blood culture, one pneumonia and another one urinary track infection. The causative microbial agent was: Candida albicans 21%, Enterobacter 21%, Enterococcus 14%, Serratia 14%, Klebsiella 14%, Staph. epidermitis 14%, Pseudomonas aeroginosa 7%. The mortality rate was 7%.

Conclusions: The incidence of nosocomial infection in our PICU is 5,3%. The most important risk factors for nosocomial disease are severe underling disease, multiple previous hospitalizations and the length of hospital stay rather than central vascular catheter and intubation.

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OPPORTUNITIES AND OBSTACLES TO THE ELIMINATION OF SCHISTOSOMIASIS FROM THE MIDDLE EAST: A CASE STUDY IN YEMEN

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Background and aims: Schistosomiasis, among the most prevalent neglected tropical diseases, is a life-threatening public health problem in Yemen especially in rural communities where schistosomiasis is still considered as the second cause of death, after malaria. This study aims to determine the current prevalence and distribution of schistosomiasis among rural communities under active schistosomiasis control and surveillances in Yemen.

Methods: A cross-sectional study was conducted among 399 children in 5 different governorates in Yemen namely, Taiz, Ibb, Thamar, Sana'a and Hodeidah. Urine and stool samples were collected and examined for the presence of Schistosoma haematobium and S. mansoni eggs. Demographic, socioeconomic and environmental information were collected by using a validated questionnaire.

Results: Out of 399 children (59.4% males and 40.6% females; aged ≤ 15 years) participated in this study, 127 (31.8%) participants were found positive for schistosomiasis. The overall prevalence of S. haematobium and S. mansoni infections were 23.6% and 9.5%, respectively. The highest prevalence of S. mansoni was reported in Ibb province while the highest prevalence of S. haematobium was in Taiz and Thamar. Among those infected, 38.4% and 14.6% were anaemic and had hepatosplenomegaly, respectively. Large populations of snails (both Bulinus and Biomphalaria species) were observed.

Conclusions: This study reveals an alarmingly high prevalence of schistosomiasis among rural communities in Yemen and this supports an urgent need to implement innovative and integrated control measures to save the lives and future of the most vulnerable children. A regional integration strategy is crucial to eliminate the disease from the region.

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PREVALENCE OF CHAGAS DISEASE IN BOLIVIAN PREGNANT PATIENTS (JUNE 2008-SEPTEMBER 2011) IN LA PAZ UNIVERSITY HOSPITAL. RISKS OF VERTICAL TRANSMISSION

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Background and aims: Due to migration, our country hosts numerous persons with Chagas disease. The risk of transmission in Spain is not vectorial, but from pregnant to new born. The aims is estimate the prevalence of Trypanosoma Cruzi infection in bolivian pregnant patients which gave birth at La Paz University Hospital; as well as to compared two different periods of screening before and after protocol implementation for bolivian pregnant patients in our hospital.

Method: Retrospective study selecting the data of bolivian pregnant patients which have given birth between June 2008 and September 2011. Data was collected from positive serology (two positive indirect determinations through quick test, ELISA or IFI) and controls on the new borns of these mothers (microhematocrit and PCR at bird and seried serologies (IFI) until 9 months of age). A statistic report analysis was elaborated through the SPSS program and a comparison analysis (test Chi squared) between the periods of June 2008-May 2010 (period 1) and from June 2010-September 2011 (period 2)

Results: A total of 693 bolivian patients gave birth. Serology was requested in 229 (33%), more serologies were requested in period 2 after protocol implantation (85=44,3%) than in period 1 (144=28,5%) p< 0,001. 43 (19,9%) of patients analysed were diagnosis. New born follow up was only in 33 cases (76,7%). None of the children controlled has been infected .

Conclusions: Adequate control is not being made of the vertical transmission of Chagas disease in our environment, even after proven results after protocol implantation.

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BURDEN OF VIRAL PATHOGENS ON SEVERE LOWER RESPIRATORY TRACT INFECTIONS AMONG PREMATURE INFANTS: PROSPECTIVE BIRTH COHORT STUDY IN BRAZIL

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Background and aims: Premature infants are at high risk for developing severe respiratory disease. Prospective studies on the role of viral pathogens on the burden of severe respiratory diseases are scarce, especially in developing countries. This 3-year study in Brazil (2008-2010) determined the incidence of severe respiratory syncytial virus (RSV)-related lower respiratory tract infections (LRTIs) requiring hospitalization in infants ≤35 weeks gestational age.

Methods: Infants identified as preterm births in 3 Brazilian referral hospitals were prospectively followed up from maternity hospital discharge for 1 year. Subjects were seen monthly for the first 6 months and bimonthly thereafter. Subjects with signs/symptoms of an LRTI were tested for respiratory viruses by real-time RT-PCR.

Results: The analysis population consisted of 303 preterm infants, including 246 who completed follow-up. At birth, 299 (98.7%) subjects were hospitalized an average (±SD) 36.4±26.9 days; 269 (88.8%) infants were admitted in the NICU (mean stay: 31.8±27 days). During follow-up, 432 LRTI episodes occurred in 176 subjects. RSV and human rhinovirus were each detected, alone or in combination, in 33.1% and 29.4% of these episodes, respectively (Table). Thirty subjects, representing 9.9% of the analysis population and 17.0% of subjects with an LRTI episode, experienced a severe RSV LRTI requiring hospitalization.

Conclusions: RSV is a substantial cause for hospitalization among premature infants in Brazil, resulting in hospitalization for approximately 10% of premature infants. RSV and human rhinovirus were the most frequently detected viruses in LRTI episodes.

Table. Viral Pathogens Identified by RT-PCR in Premature Infants With LRTI

Viral pathogen	Number (%) (N=432)
Respiratory syncytial virus (A and B)	143 (33.1)
Human rhinovirus	127 (29.4)
Human bocavirus	83 (19.2)
Metapneumovirus (A and B)	73 (16.9)
Influenza (A and B)	58 (13.4)
Parainfluenza virus (1 and 3)	39 (9.0)
Adenovirus	22 (5.1)
Coronavirus (OC43 and 229E)	21 (4.9)
Influenza (H1N1)	12 (2.8)

[Table]

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PROCALCITONIN LEVELS IN UMBILICAL CORD BLOOD REFLECT SEVERITY OF HISTOLOGICAL CHORIOAMNIONITIS AND ASSOCIATE WITH EARLY-ONSET NEONATAL SEPSIS

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Bacgroud and aims: Procalcitonin (PCT) levels in umbilical cord blood were investigated to determine associations of severity of chorioamnionitis (CAM) and clinical manifestations.

Materials and methods: The retrospective study was conducted for 143 pregnant women and neonates. PCT levels in umbilical blood were measured. The severity of CAM was classified according to the definition by Redline et al. PCT levels were evaluated the correlation with placental histological findings and clinical manifestations.

Results: The gestational age at birth and birth weight of study group were 32.2±5.0 weeks of gestation and 1802±885g, respectively. Twenty seven women had CAM. PCT of group with CAM was significantly higher than that without CAM ($p < 0.01$). PCT levels significantly rose with maternal or fetal stage. Ten of 11 neonates with ≥2ng/ml of PCT had early-onset sepsis (Table). In group without CAM, PCT levels had negative correlation with gestational age (n=116, r=0.72).

Conclusions: PCT levels in umbilical blood reflected severity of chorioamnionitis and influenced on neonatal outcomes.

PCT(ng/ml)	< 0.5	0.5 - 2	2 - 10	10≤
CAM(n=27)	**14**	**2**	**6**	**5**
Sepsis(n=12)	1	1	6	4
Intubation(n=21)	8	2	6	5
IVH(n=7)	0	1	3	3
Non-CAM(n=116)	**113**	**3**	**0**	**0**
Sepsis(n=0)	0	0	0	0
Intubation(n=44)	41	3	0	0
IVH(n=2)	2	0	0	0

[Table]

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EPIDEMIOLOGIC, CLINICAL CHARACTERISTICS, AND RISK FACTORS OF ADVERSE OUTCOME IN NEONATES WITH LATE ONSET SEPSIS

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Background: Late-onset sepsis (LOS) is a common complication in the neonatal intensive care unit (NICU). We aimed to describe the epidemiology, clinical characteristics, and risk factors for adverse outcome in neonates with LOS.

Methods: We conducted a cohort study of all neonates with LOS at the NICU of a Tertiary Taiwan Medical Center from January 2004 through December 2011 and used multivariate logistic regression to identify risk factors for final adverse outcome.

Results: Among 5010 neonates over 253,644 neonate-days, 713 (14.2%) experienced a total of 942 episodes of LOS (incidence rate [IR], 3.71 episodes per 1000 neonate-days). Although the rates of LOS were reversely proportional to birth weight and gestational age, the IRs were comparable between extremely preterm, late preterm and full term neonates. Fungemia was found to have significantly high rate of infectious complication (30.8%), persistent bloodstream infection (19.2%), and sepsis-attributable mortality (23.1%). The overall mortality rate was 12.6% (90/713), and sepsis-attributable mortality rate was 7.2% (68/942 episodes). Independent predictors of in-hospital mortality were Pseudomonas LOS (adjusted odds ratio [OR], 14.31; 95% CI, 3.87-53.0), fungemia (OR, 5.69; 95% CI, 2.48-13.01), presences of congenital anomalies (OR, 4.12; 95% CI, 1.60-10.60), neuromuscular comorbidities (OR, 3.34; 95% CI, 1.66-6.73), and secondary pulmonary hypertension with/without cor pulmonale (OR, 23.48; 95% CI, 5.96-92.49).

Conclusions: Late-onset sepsis predisposes NICU hospitalized neonates at risk of mortality or morbidity, especially caused by Pseudomonas aeruginosa or Candida spp. More aggressive treatment strategy is worth consideration in neonates with presumed LOS, particularly those with certain underlying chronic conditions.

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PROSPECTIVE ANALYSIS OF RISK FACTORS FOR GROUP B STREPTOCOCCAL COLONIZATION IN NEONATES AT TERTIARY CARE CENTRE IN NORTH INDIA

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Background and aims: Colonization with Group B Streptococcus (GBS) of birth canal and neonates plays a significant role in neonatal infections. Aim was to study the prevalence and risk factors associated with GBS colonization in neonates.

Methods: Swabs from mucus membranes and/or skin of external ear canal, anterior nares, umbilicus, throat and anorectal sites were obtained from neonates between 24 to 48 hours of delivery. Bacterial isolates including GBS were identified as per standard identification protocol.

Results: A total of 5250 samples were obtained from 1050 neonates enrolled in this prospective cross-sectional study. A total of 1375 bacterial isolates were obtained from 338 neonates, of these 49 were GBS from 34 neonates. GBS was isolated from all 5 body sites in 2.9%, from 3 in 5.9%, 2 in 20.6% and one in 70.6%. Among risk factors for colonization in neonates, maternal fever & prolonged labour were highly significant ($p < 0.001$), prolonged rupture of membrane (≥ 18 hrs) ($p < 0.01$), preterm birth, respiratory distress at birth, maternal medical illness and intrapartum antibiotics were significant ($p < 0.05$). Low birth weight, low apgar score (< 4 at 1 min.), sex, mode of delivery and meconium stained liquor were not found significant.

Conclusions: GBS colonization rate is low in institutional deliveries in a tertiary care centre in North India. To identify true GBS colonization rates and associated risk factors, multicentric and community based studies with cultures from multiple body sites are recommended.

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OBSERVATIONAL STUDY OF ROUTINE ENDOTRACHEAL TIP CULTURING IN NEONATAL INTENSIVE CARE UNIT

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Background and aims: Endotracheal(ET) tubes are routinely used for intubation in Neonatal Intensive Care Units(NICU). These tubes may become colonised or act as foci for respiratory infection / sepsis. At removal it is a common practice in many NICUs to send tips routinely for culture and sensitivity.

We examined the bacteriology associated with ET tube tips after removal.

Methods: Retrospective observational study in UK tertiary NICU of all ET tube tips from April 2012 to Sept 2012. All ET tube tips sent for culture during the 6 month period were analysed.

Results: 110 ET tube tips were sent during study period. 28(25%) had a positive culture. There were multiple tips from same patient, which grew the same bacterial growth because of colonisation.

Patient	A	B	C	D	E	F
Number of ET tips sent	6	4	3	2	2	2
Bacterial growth	Enterobacter	Coagulase Negative Staphylococcus (CONS)	CONS + E.Coli	Enterobacter	CONS + Acetobacter	CONS + Enterobacter

[ET tip culture in each patient]

In rest of the 9 patients only a single tip was sent which grew respiratory commensals and CONS.

None of the positive cultures led to antibiotic prescription.

Type of bacterial growth	CONS	Enterobacter	E.Coli	Enterococcus	Group B Streptococcus	Staph. aureus	H.influenza	Acetobacter	Candida
Number ET tips	10	7	7	1	1	1	1	1	1

[Type of bacterial growth]

30 bacterial growth from 28 tips.

Conclusions: Most of the positive ET tube tips were due to colonisation. None of them warranted antibiotic prescription.

Sending routine ET tube tips for culture is not beneficial.

ET secretions for culture may be more useful if clinical concern of respiratory infection in ventilated neonates.

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BEHAVIOUR OF PERTUSSIS IN CHILDREN LESS THAN 2 MONTHS IN ARGENTINA

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Incidence of pertussis increased during the recent years in Argentina. Clinical features in younger infants are atypical and the mortality risk high. Mothers are the most frequent source of infection.

Objectives: Identify epidemiology, clinical, and outcome of children less than 2 months old with Bordetella pertussis (B. pertussis) infection.

Material and methods: Prospective observational study. We included patients (p) ≤ 60 days admitted in the neonatal unit with B. pertussis infection confirmed by polymerase chain reaction from 2005 to 2012.

Results: We included 29 patients. Most of them, 28p (97%) diagnosed out of the winter season, more than half during summer. Twenty four (83%) were healthy term born. Mean age at diagnosis was 34 days (r:18-60d) and the most common chief complaints were paroxysmal cough and breathing difficulty (76% and 34%). Ten p (34%) were also febrile at admission. Eight p (28%) required mechanical ventilation, 2p (7%) ECMO. Twenty one (72%) had epidemiologic contact, 86% was the mother. Chest radiographs demonstrate pulmonary interstitial infiltrates in 17p (60%). White blood cell counts (WBC) mean 29.867 mm/3 (r: 8.700 - 102.000/mm3) and 75% lymphocyte count > 9.400 mm/3.

Coinfection was present in 5p (17%): adenovirus 2p, RSV 1p, pneumococus 1p and Chlamydia 1p. Four (90%) of them required Intensive Care Unit and mechanicalventilation. Three p (10, 3%) died. Mean WBC for those were 75.000mm/3 2p coinfected.

Conclusion: B. pertussis has a seasonal distribution. The mother is the main source of infection. Coinfection and leucocitosis were related with desfavorable outcome.

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CHARACTERISTICS AND RISK FACTORS IN VENTILATOR ASSOCIATED PNEUMONIA IN LEVEL III NEONATAL INTENSIVE CARE UNIT IN NEW DELHI

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Background and aims: Ventilator-associated pneumonia (VAP) is a serious problem in neonatal intensive care units (NICU). The objective was to find the incidence of VAP and identify factors associated with its development.

Methods: Medical records of newborns ventilated in the period between 1st October 2011 and 31st March 2012 were reviewed. Data on patient demographics, underlying diseases, medications, central catheters, nutrition, ventilator use etc. was retrieved. For patients with VAP, risk factors were evaluated from the time of admission until the onset of VAP and then throughout their NICU stay. For patients who did not develop VAP, risk factors were evaluated for their entire NICU stay. Data analysis was performed using SPSS Version 20.0. Risk factors were evaluated using Univariate and Multivariate Logistic regression Analysis.

Results: A total of 49 patients (9.7%) were ventilated during the study period. VAP incidence was 39 per 100 ventilated babies or 117 per 1000 ventilation days. Birth weight, Gestation, Duration of ventilation, Asphyxia, Surfactant administration, Antenatal Steroids, Central catheters, Total parenteral nutrition, or Blood transfusion had no influence on occurrence of VAP.

Table-1

Univariate Analysis

Variable	O.R.	Confidence Interval		p value
Gestation	1.053	0.858	1.292	0.622
Birth Weight	1.000	1.000	1.001	0.264
Duration of Ventilation	1.009	1.000	1.018	0.06
SGA	1.111	0.216	5.727	0.900
Apgar < 5 @ 5 min	2.222	0.462	10.682	0.319
Surfactant	3.667	0.636	21.147	0.146
Steroids	1.833	0.299	11.259	0.513
Central Catheter	0.500	0.117	2.132	0.349
TPN	0.686	0.158	2.985	0.615
Blood Transfusion	2.167	0.521	9.017	0.288
Breast Milk	0.149	0.026	0.852	**0.032**

[Table-1]

Multivariate logistic analysis revealed that Breast milk was protective.

Table-2

Logistic Regression Analysis

Factors	Odds Ratio	Confidence Interval		p value
Breast Milk	0.069	0.007	0.680	0.022

[Table-2]

Babies with VAP were significantly more likely to die (O.R. 6.6 , C.I. 1.3-34.1 $p< 0.05$).

Conclusions: VAP occurred at high rates in sick neonates in the NICU. Breast milk had protective effect. Patients with VAP were more likely to die.

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1-YEAR FOLLOW-UP AFTER NEONATES WITH URINARY TRACT INFECTION (UTI): EPIDEMIOLOGIC AND MICROBIOLOGIC CHARACTERISTICS, IMAGING FINDINGS, PROPHYLAXIS EFFICACY AND DISEASE RECURRENCE

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Background and aims: To analyze the epidemiologic/microbiological characteristics of 1st and recurrent UTI (R-UTI) episode in neonates < 2 months and antibiotic prophylaxis efficacy in prevention of further UTI.

Methods: A retrospective study including all neonates with UTI admitted between 2005-2009.

Results: 151 neonates were enrolled (2.7% of all 5617 neonates < 2 months of age, 2.1 cases/1000 live births); 56.3% were males and 5.9% had renal pathologies. One pathogen was isolated in 133 (88.1%) episodes. E. coli, Klebsiella spp., Enterococcus spp., M. morganii, Proteus spp. and Enterobacter spp. represented the most common pathogens (57.9%, 12.2%, 7.9%, 6.7%, 6.1% and 5% of all pathogens, respectively). Trimethoprim/sulfamethoxazole (TMP/SMX), ampicillin and cefuroxime-axetil were the most commonly used prophylactic antibiotics (45%, 13.2% and 8% of all enrolled patients). Ultrasound and VCUG examinations were abnormal in 18.1% and 21.2% patients, respectively. Twenty-three R-UTI episodes were recorded in 20 (13.2%) patients; 6/23 (26%) were diagnosed within 1 month following 1st episode. E. coli was the most frequent UTI pathogen recovered in R-UTI (12/23, 52.2%). No differences were recorded in E. coli distribution among the pathogens of first UTI vs. R-UTI. Seventeen (74%) of the 23 R-UTI episodes were caused by pathogens different (phenotypically) from those isolated in the 1st episode. R-UTI episodes occurred in 25.0%, 8.3% and 0 patients receiving TMP/SMX, cefuroxime-axetil or amoxicillin prophylaxis, respectively.

Conclusions: E. coli was responsible for the majority of 1st and R-UTI episodes. R-UTI was caused mostly by pathogens different than the pathogen isolated at the initial episode.

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NEONATE SKIN LACERATION AS IATROGENIC RISK FACTOR OF MOTHER-TO-CHILD HCV INFECTION DURING DELIVERY

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Background and aims: HCV mother-to-child transmission occurs mainly in the peripartum period. There is no information about association between neonate laceration during delivery and HCV infection.

The aim of the study was to establish the rate of neonate injury during delivery and the influence of this complication over the risk of HCV transmission.

Methods: We collected data of type and course of delivery in 392 children born to anti-HCV(+) mothers: 34 HCV infected children and 358 without HCV infection.

Results: 235/392(60%) were delivered vaginally, 157/392(40%) by cesarean section. Skin laceration was observed in 9(2,3%): 4/235 (1,7%) delivered vaginally, 5/157(3,2%) by cesarean section. In the group of HCV infected children 25/34(74%) were delivered vaginally, 9/34 (26%) by cesarean section. The rate of HCV infection in children delivered vaginally was 25/235(10,6%), by cesarean section 9/157(5,7%). Among children with skin laceration 5/9(55%) were HCV infected, without skin laceration HCV infection was recognized in 29/383(7,5%). Elective cesarean section as a standard procedure has lower risk of laceration than emergency. There were 43 children delivered by elective cesarean section in 38Hbd and none of them was injured, none of them was HCV infected.

Conclusions:

1. Iatrogenic exposure to HCV during delivery may increase the risk of HCV mother-to-child infection.

2. There is a higher risk of skin laceration during emergency cesarean section than during vaginal delivery or elective cesarean section.

3. Children born by elective cesarean section without skin laceration were not infected with HCV.

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VACCINATION OF THE LIVER TRANSPLANT RECIPIENTS IN HUNGARY HOW WE DO IT

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Strategies to win the war against transplant rejection will always be a priority, but battles against vaccine preventable infections must also be fought and won.

Hungarian Special Immunization Service increasingly emphasizes immunization of patients with special conditions, especially before and after solid organ transplant (SOT). According to vaccination guidelines for SOT candidates and recipients we apply our own experiences.

We report 85 liver transplant patients (77 children, 8 adults) between March 2004 and September 2012. Most patients have already been transplanted (55) at the first visit to our service and 80% of them were incompletely or not immunized at all. After screening their serostatus, immunstatus and vaccination records, patients received catch up immunization according to the national immunization calendar. The vaccinations were given by GP's except the live attenuated varicella and MMR vaccines. Patients with stable graft function and well documented immunfunction 2 years after the transplantation have been vaccinated at our department with Varilrix and received preparedness acyclovir prescription. After two-dose Varilrix schedule we tested VZV IgG (ELISA) and after successful seroconversion patients received MMR vaccine. 73% of all patients seroconverted. We did not detect vaccine disease, and breakthrough infections (in 6 cases) were mitigate varicella. 82% of our patients are followed up yearly and receive a booster dose if needed.

We know the patients are not fully protected but at the worst case they expected to have mitigated infection. Our goal is to continue the immunization procedure of SOT patients and maintain their protection with booster vaccination.

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SEROTYPE 19A AND THE 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE (PHID-CV): LESSONS LEARNED TO DATE

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Background and aims: After introduction of the 7-valent pneumococcal conjugate vaccine (7vCRM, Pfizer Inc.), significant reductions in invasive pneumococcal disease (IPD) incidence were observed. In some settings, this was followed by a rise in IPD caused by non-vaccine serotypes, mainly serotype 19A, suggesting that potential cross-protection against 19A disease by the 19F-containing 7vCRM may be limited. For PHiD-CV (GlaxoSmithKline Vaccines), a different method was used for 19F conjugation which positively affects its immunogenicity and immunological cross-reactivity against 19A. As it is unknown whether the heightened immune response is sufficient to provide any cross-protection against 19A IPD, we examined the data available to date from PHiD-CV post-marketing studies.

Methods: We summarized the occurrence of 19A IPD cases in the first 1-2 years after PHiD-CV introduction in infant immunization programs in Canada, Brazil and Finland in cohorts targeted for vaccination.

Results: Results from recent post-licensure epidemiological studies after introduction of PHiD-CV showed trends for reduced 19A IPD in children eligible for PHiD-CV vaccination, while increases in 19A IPD were observed over the same periods of time in non-vaccine-eligible individuals (Table). Results from double-blind randomized clinical trials assessing 19A nasopharyngeal carriage after PHiD-CV vaccination will also be presented.

Region	Age	Period assessed		Number of 19A IPD cases	
Vaccine-eligible cohorts					
		Pre-PHiD-CV implementation	Post-PHiD-CV implementation	Pre-PHiD-CV implementation	Post-PHiD-CV implementation
Quebec, Canada[1]	6-18m	Sep 2007-Dec 2008[a]	Sep 2009-Dec 2010[b]	15	9
	13-28m	Sep 2008-Dec 2009[a]	Sep 2009-Dec 2010[c]	12	8
Quebec, Canada[2]	6-11m	2008-2009[d]	2010[e]	12*	2
	12-23m	2008-2009[a]	2010[c]	24.5*	26
Ontario, Canada[3]	5-11m	Jan 2009-Jun 2009[d§]	Jan 2010-Jun 2010[e§]	1	1
	16-22m	Feb 2008-Aug 2008[e§]	Feb 2009-Aug 2009[c§]	1	1
Brazil (UH-USP)[4]	<2y	Jan 2006-Jun 2010[f]	Jul 2010-Jul 2012[g]	0.9*	0*
Brazil (SIREVAII)[5]	<2y	2008-2009[f]	2011[g]	8.5*	6
Finland[6]	0-11m	2004-2009[f]	2011[e]	2.7*	0
Non-vaccine-eligible cohorts					
Quebec, Canada[2]	0-6m	2008-2009	2010	4*	6
	2-5y	2008-2009	2010	19*	22
Brazil (SIREVAII)[5]	≥2y	2008-2009	2011	15.5*	30
Finland[6]	≥12m	2004-2009	2011	27.1*	31

*Average number of cases per year; §Birth cohort; observation period truncated for age to observe either priming or booster effect; [a]7vCRM priming + booster; [b]PHiD-CV priming + booster; [c]7vCRM priming + PHiD-CV booster; [d]7vCRM priming; [e]PHiD-CV priming; [f]no PCV in national immunization schedule; [g]PHiD-CV priming (+ booster) or catch-up; m, months; y, years; UH-USP, University Hospital of the University of Sao Paolo

References: [1]De Wals et al. *Vaccine* 2012; [2]Pneumococcal Surveillance Program Quebec, 2010 report, Laboratoire de santé publique du Québec; [3]Wong et al. *IDWeek* 2012, abstract 503; [4]Santos et al. *ICAAC* 2012, poster G-861; [5]SIREVAII annual reports 2008-2011; [6]Jokinen et al. *ISPPD* 2012, poster 165

[Table]

Conclusions: These findings may be consistent with the hypothesis that cross-reactive anti-19A antibodies elicited by PHiD-CV provide some protection against 19A IPD. However, the limited duration of surveillance and low numbers of cases warrant caution interpreting these results.

Funding: GlaxoSmithKline Biologicals SA.

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IMPACT OF TWO INFORMATION INTERVENTIONS IN MATERNITY HOSPITALS ON THE PERTUSSIS VACCINATION COVERAGE OF PARENTS

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Objective: The objective was to evaluate the impact of information interventions in maternity hospitals on pertussis vaccination coverage of young parents and their children, using standardised information.

Methods: A prospective, multicentre study was conducted between September 2011 and February 2012. The study was offered consecutively to all parents over the age of majority. After an observational phase (OP), an interventional phase (IP) was performed. Parent couples who were not up-to-date with vaccination were randomly enrolled in 1 of 2 groups, either with or without an added information letter to their general practitioner. Primary endpoint was parents' vaccination status, obtained by a follow-up telephone interview 3 months later.

Results: Enrolment included 453 subjects, 414 (91.4%) of whom were contacted. In maternity hospital, 18.8% of mothers and 19.7% of fathers, but only 7% of couples, were up-to-date with pertussis vaccination. For couples previously not up-to-date, 19.4% and 35.2%, respectively, achieved update 3 months following OP and IP, p=0.003. Added information to medical practitioners was not statistically significant, p=0.40. Parents were vaccinated earlier after IP and parental vaccination status significantly improved initiation of vaccination in infants (p=0.002).Vaccination was initiated in 92.5% of infants (median 65 days), predominantly with a hexavalent vaccine (83.8% of cases).

Conclusion: Providing standardised information on the importance of pertussis vaccination to an infant's immediate circle during maternity hospital stay has a considerable impact on the vaccination coverage of parents and their children.

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NASOPHARYNGEAL CARRIAGE OF STREPTOCOCCUS PNEUMONIAE IN HEALTHY CHILDREN AND ADULTS AFTER IMPLEMENTATION OF CONJUGATE-PNEUMOCOCCAL VACCINE IN NATIONAL IMMUNIZATION PROGRAMME

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This study was performed to determine the carriage rate of nasopharyngeal (NP) S. pneumoniae after implementation of the pneumococcal conjugate vaccine (PCV) in the national immunization program (NIP) of Turkey. Between may 2012 and August 2012, 1000 nasopharyngeal swabs were obtained from 500 children aged 1 month to 15 years and 500 adults aged 20 to 90 years without evidence of acute infection. The pneumococcal carriage rate was 10.2% in children and 1.6% in adults. S. pneumoniae NP colonization rates were similiar in all age groups of children (0-23 months [10.8% colonization rate], 24-60 months [12.7%] and > 60 months [8.8%]). Of the children included in the study, 19.4% had received PCV7 and 10.4% had received PCV13. Among all children 350 (70%) were not vaccinated with PCV. In children, only having 3 or more siblings under age 8 in the family and history of sinusitis were found to be risk factors for carriage ($p< 0.05$). The most common isolated serotypes were 23F (21%), 6A/B (16.3%), 19F (9.3%), 22F/22A (9.3%). Serotype covarege rates of PCV7, PCV10 and PCV13 were 62.7%, 67.4 and 72%, respectively. Serotypes 22F (9.3%), 15A/15F (6.9%) and 35A/35C (6.9%) were the most common isolated serotypes that was not existing in PCV13. This study provides data about the carriage rate and serotype distribution of S. pneumoniae strains in Turkish children and adults after introduction of PCV into the NIP.

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COMMUNICATION THROUGH NEW MEDIA: IS THERE A PLACE FOR PRO-VACCINE MESSAGES? EXPERIENCE OF VACCINEWSNET

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Background and aims: One-third of consumers now use the Internet to obtain health-related information, including information about vaccines. Vaccines, often seen as one of the greatest public health interventions, are recently losing a certain degree of public confidence. The internet and social media (e.g. Facebook, Twitter) have not only allowed for rapid sharing of information and misinformation, but also as forums for antivaccination groups.

Methods and results: VacciNewsNet (VNN) is a platform to provide up-to-date information to the public, media, health professionals and policy makers to help them understand the facts about vaccines. VNN uses the power of social media: the website www.vaccinews.net had more than 55,000 page views in 2012; the twitter account @VacciNewsNet is the most successful pro-vaccination account and reached more than 65,000 active followers in 2012. The Facebook page of VNN (www.facebook.com/VacciNewsNet) started on June 4th 2012 and has a weekly total reach going from 3,000 to more than 20,000 people. The Facebook page provides correct information on immunization and is used intensively by parents, health professionals and public health advocates to discuss news and views on vaccines.

Conclusions: Pro-vaccine initiatives can successfully make use of the online social media and can make evidence-based pro-vaccine messages 'go viral'. Social media can contribute to inform and educate the public about vaccinations.

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PNEUMOCOCCAL PNEUMONIA IN CHILDREN: A FRENCH PROSPECTIVE STUDY IN THE ERA OF 13 VALENT PNEUMOCOCCAL CONJUGATE VACCINES IMPLEMENTATION IN FRANCE

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Background and aims: Since the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7), serotype replacement has occurred, and non vaccine serotypes have increased particularly serotypes 1, 3 and 19A, which are major providers of empyema and pneumonia. In France the switch to PCV13, which includes additional serotypes 1, 3, 5, 6A, 7F, and 19A, occurred in june 2010. To analyze clinical and biological features of pneumococcal pneumonia before and after PCV13 implementation, the French Pediatric Infectious Diseases Group has set up an active surveillance network.

Methods: Observational prospective study performed in 7 French Pediatric Emergency Department, from July 2009 to December 2011. All children between 1 month and 15 years with radiographically confirmed pneumonia were included.

Results: 5174 patients were enrolled (median age 3.1 years). 342 pleural effusions were reported. 89.1% of children < 5 years were PCV7 vaccinated. 1610 patients had blood culture and 61 (3.8%) were positive. Pleural sample were obtained in 133 cases and 101 (75.9%) were positive. Pyogenic pneumonia was diagnosed in 147 cases (2.8 %): S. pneumoniae 123, S. aureus 16, and Group A S. pyogenes 8. Sp serotypes were available for 56 cases. Additional PCV13 serotypes were predominant (84%) and were: 1 (22 cases), 19A (13 cases), 7F (7 cases), 3 (5 cases).

Conclusion: Serotypes 1, 19A, 7F and 3 were the main serotypes of pneumococcal pneumonia in France before PCV13 implementation. Continuation of the study should assess the efficiency of PCV13 to prevent pneumonia in children and detect occurrence of serotype replacement.

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THE HEALTH AND ECONOMIC VALUE OF ROTAVIRUS VACCINATION IN KAZAKHSTAN

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Background and aims: Rotavirus-gastroenteritis (RV-GE) is a leading cause of morbi-mortality in Kazakhstan generating significant economic burden, including direct and indirect costs. We aimed to assess the public health and societal cost-effectiveness of universal rotavirus vaccination with RIX4414 (GlaxoSmithKline), a 2-dose human rotavirus vaccine, compared to no vaccination.

Methods: A static, deterministic, decision-tree previously described model was used to estimate direct/indirect associated costs and Quality-Adjusted Life-Years (QALYs) based on the number of RV-GE cases (mild, moderate and severe) and deaths, over a one year period for children under five-years of age in Kazakhstan. Country-specific epidemiological data and related costs recently published were used. Vaccine efficacy as reported from clinical trials and utility data from literature were included. Payer and societal perspectives were considered at 3% discount rate. Incremental cost-effectiveness ratio (ICER) was calculated defining threshold as per WHO-guidelines (1 GDP-per-capita for highly-cost-effective=1,933,100KZT). Sensitivity analysis was conducted on main parameters including an alternative scenario with a 3-dose regime.

Results: Rotavirus vaccination is expected to reduce rotavirus disease burden by preventing 95,008 mild, 25,116 moderate, 3,909 severe RV-GE cases and 63 deaths. Vaccination would be a cost-effective intervention from payer perspective (ICER= $KZT440,700-per-QALY-gained discounted and $KZT219,314-per-QALY-gained undiscounted) and from societal perspective would be cost neutral but generating additional QALYs. Additionally, a 2-dose program would be cost-saving as compared to a 3-dose program.

Conclusions: Our analysis indicates that universal rotavirus vaccination program would be a cost-effective intervention and would generate more value for money respectively from payer and from societal perspectives in Kazakhstan.

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SAFETY AND IMMUNOGENICITY OF A QUADRIVALENT INACTIVATED INFLUENZA VACCINE CONTAINING TWO A AND TWO B STRAINS IN CHILDREN/ADOLESCENTS AND ADULTS

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Background: Trivalent influenza vaccines (TIV) contain two A strain; H1N1, H3N2, and one B strain. Recently, 2 distinct B lineages (Victoria and Yamagata) have circulated worldwide, with neither providing good cross-protection against the other. Prediction of which B lineage would dominate during successive influenza seasons has been problematic, resulting in frequent mismatches. Quadrivalent influenza vaccine (QIV) was designed to address this issue by incorporating both B lineages.

Methods: A Phase III randomized, controlled, multi-center study, 385 children/adolescents and 1705 adults were randomized to receive one IM dose of QIV containing the B/Brisbane strain (Victoria lineage) and the B/Florida strain (Yamagata lineage), or the licensed TIV for the 2011-2012 season containing the B/Brisbane strain. Both vaccines contained the same H1N1 (A/California/07/2009) and H3N2 (A/ Perth/16/2009) strains. Safety was monitored and blood specimens for the immunogenicity assay (hemagglutination inhibition) were collected before and 21 days after vaccination.

Results: Overall, the safety profiles between QIV and TIV were similar in both age groups tested. A strong immune response was induced in both age groups following a single injection of either influenza vaccine. In adults, the three EMA criteria were met (95% CI inclusive) for each strain in the QIV group. In general, higher immune responses after QIV injection were observed in the children/adolescents than in adults against all strains.

Conclusions: QIV is well tolerated by adult and child/adolescent subjects and induces a strong immune response in both age groups following a single injection.

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RSV IMMUNOPROPHYLAXIS AT HOME VERSUS HOSPITAL SETTINGS: CLINICAL AND HEALTH ECONOMIC OUTCOMES- COMPARATIVE STUDY IN DEFINED BIRTH COHORT IN IRELAND

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Background and aims: Immunoprophylaxis (IP) has proved effective in reducing hospitalisation from respiratory syncitial virus (RSV) infection among high-risk infants. We aimed,

1. to compare the direct cost of RSV IP for high-risk infants allocated to monthly injections at home versus hospital settings,

2. to compare the compliance and 3. to analyse post-prophylaxis RSV hospitalisations.

Methods: Single-centre, multi-year retrospective review of RSV IP in defined birth cohort was undertaken. High-risk infants of Limerick university maternity hospital in Ireland, from 2003 to 2009 received IP through hospital and from 2009 to 2012 at home through a provider (TCP Healthcare®) purchased by the Health Service Executive (HSE) of Ireland. Compliance to IP was scored and post-IP follow-up conducted. Hospital Ethics Research committee approved the study.

Results: Unit cost of RSV IP session was € 300 and 520 for home and hospital groups respectively, taking into account IP failures and nosocomial admissions. Since introduction, home RSV IP programme prevented 12,700 hospital encounters in Ireland and under the base case assumptions a direct cost saving of €2.8 million for the HSE over 5 years. Compliance scoring was statistically significant for home group. Calculations are in addition to the drug cost of IP (Palivizumab®).

Conclusions: Significant professional hours in the hospital during winter time could be freed up by the 'outsourcing' of RSV IP to the 'home care'. In addition to the direct cost savings to the payer (Irish healthcare), prophylaxis at home offers significant indirect, opportunistic and societal cost savings as well.

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ASSESSMENT OF MF59-ADJUVANTED A/H1N1 INFLUENZA VACCINE

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Background and aims: Pandemic influenza causes clinical illness and hospitalization in all age groups; however, conventional inactivated vaccines have only limited efficacy in children. Vaccines against pandemic A/H1N1 influenza are required to protect all ages including children. We aimed to assess immunogenicity and safety of MF59-adjuvanted A/H1N1 influenza. vaccine in children.

Methods: We conducted a systematic review of the literature. Databases used were MedLine, Embase, Cochrane Library, CRD, Lilacs, ECRI, clinical trial register, and manual search in specialties journals. As MeSH terms we used “influenza A virus H1N1 subtype”, “influenza vaccines”, “efficacy”, and “safety”, and free terms “adjuvant vaccine” “influenza A-H1N1”, and “MF59”. Inclusion criteria were clinical trials with children vaccinated with MF59-adjuvanted influenza A/H1N1 vaccine, compared with other doses vaccines with/without MF59-adjuvanted. We registered results of immunogenicity and safety of the vaccine. The quality of included studies was assessed by CASP checklist.

Results: We found 142 references, and after title/abstract review, four clinical trials were selected, with moderate quality. The local and systemic adverse effects were rare and mild, without differences between groups. Seroconvertion and seroprotection levels were higher with MF59-adjuvanted vaccines. Antibody titers were higher too with the adjuvant vaccines.

Conclusions: The adjuvant vaccine has a good efficacy and safety profile. The adverse effects that may result are common and appear in similar way in both groups of vaccination.

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HEPATITIS B VACCINATION DURING MAINTENANCE CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Children with leukemia are at high risk of hepatitis B virus (HBV) infection. The aim of this study was to asses the immunogenicity of an intensified immunization schedule during maintenance chemotherapy for acute lymphoblastic leukemia (ALL).

Methods: Immunization against HBV was carried out in HBsAg negative and unvaccinated children receiving maintenance chemotherapy (week 28 to 99) of the Boston 2005-01 protocol.

Four doses of recombinant DNA vaccine were delivered at 0,1,2, 6 months.

The vaccine dosage was 5 µg for children less than 10 years of age, and 10 µg in the older children.

Anti-hepatitis B antibody level was measured by ELISA method 4 to 6 weeks after the fourth dose.

Seroconversion with protective rate was defined by the presence of antibody titers ≥ 10 UI/l.

Non-responders received a booster dose after completion of chemotherapy and anti-HBSAg titer was measured 4 to 6 weeks after.

Results: Immunization was initiated on average at week 46 (SD: 19.7) in 25 children with a median age of 4 years (IQR 1-14) .

Among them, 32% (8/25) achieved protective titers (GMT: 101.9 UI/l, 95% CI: 91.9-111.9 UI/l).

Responders were more likely vaccinated after week 40 of the protocol (OR: 9.7, 95%CI: 1.4-68.8).

Among non-responders, 10 received a booster dose and only 4 of them achieved protective titers.

Conclusion: HBV vaccination during maintenance chemotherapy is sub-optimal in children with ALL: only one third of children responded to vaccination.

Hepatitis B immunization should be started preferentially during the second year of the chemotherapy.

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CHANGES OF THE PNEUMOCOCCAL NASOPHARYNGEAL CARRIAGE FROM ERA OF PCV7 TO PCV10 OR PCV 13 IN KOREA

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Background and aims: S. pneumococcus (SP) is a known pathogen of invasive or non-invasive diseases in children. The introduction of protein-conjugated pneumococcal vaccine (PCV) since the year of 2000 reduced pneumococcal diseases. SP serotypes of nasopharyngeal colonization have been affected by PCV vaccination. We describe the change of SP serotypes colonized in Korean children.

Methods: Nasopharyngeal aspiration samples were obtained from children visited at Severance Children's Hospital from March 2009 to July 2012. We applied the multiplex PCR technique for the identification of pneumococci and determinations of their serotypes.

Results: Among the 2379 children enrolled, 84.2% were vaccinated with any type of PCVs and we checked vaccine type of 40.3% of them from Korean CDC databank. 19.0% of total samples were SP PCR positive and there was no difference by year (from 18.1% to 20.5%). Proportion of serotypes included PCV13 decreased from 58.9% in 2009 to 29.3% in 2012 (p-value = 0.002). Depending on the type of vaccination (PCV7, 10, and 13), SP positive rates were 22.2%, 23.5% and 17.0% respectively (PCV10 vs PCV13, p-value 0.258.). According to PCV vaccination types, 19A was present in 22.0% in PCV7, 12.5% in PCV10 and 24.0% in PCV 13 (PCV10 vs PCV13, p-value 0.365). The emerging of non-PCV13 serotypes since year of 2011 was remarkable.

Conclusion: In Korea, the overall pneumococcal carriage rate was 19.0% during recent 4 years and there was significant emerging in the serotypes not included in PCV13 after PCV10 or PCV13 implementation.

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FIFTH YEAR POST-ROTAVIRUS VACCINATION IN BELGIUM: DECREASE OF ROTAVIRUS-POSITIVE STOOL SAMPLES IN HOSPITALISED CHILDREN

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Background and aims: Rotavirus vaccination has been reimbursed in Belgium since November 2006 and vaccine coverage is about 85%. We assess and compare here the impact of mass rotavirus vaccination on rotavirus-related hospitalisations in children ≤5y old pre-vaccination and up to 5 years post-introduction of the vaccine in 9 paediatric wards in Belgium.

Methods: All rotavirus detection tests were collected from ≤5y old children. The absolute numbers of rotavirus-positive tests pre-vaccine (01/06/2004-31/05/2006) were compared with data at launch (01/06/2006-31/05/2007), and post-launch (01/06/2007-31/05/2012). Data are presented as % reduction (95% CI) per year post-vaccination considering the annual average pre-vaccination period as reference.

Results: The number of rotavirus-positive stool tests in hospitalised children ≤5y old decreased from an average of 917 (Table 1) pre-vaccination to 619 during vaccine launch, 399 in the 1st year post-launch, 229 in the 2nd year, 209 in the 3rd year, 212 in the 4th year, and 158 during the 5th year. An overall decline (-53%, 95% CI:50%-55%) in all-cause acute-gastroenteritis (AGE) related hospital admissions is observed, from 1,793 per year pre-vaccination to 850 during the 5thyear post-launch. The number of bed-days due to AGE has fallen from 9,100 pre-vaccination to 4,016 (-56%, 95% CI:55%-57%) post-vaccination. A reduction from 6,026 to 3,656 (-39%, 95% CI:38%-41%) is also seen amongst the non rotavirus-positive cases.

Conclusions: Significant declines in number of rotavirus and all-cause AGE-related hospitalisations are seen in young children after 5 years of mass rotavirus vaccination in Belgium.

	Pre-vaccine	Vaccine launch	1st year post	2nd year post	3rd year post	4th year post	5th year post
	Jun 04-May 06	Jun 06-May 07	Jun 07-May 08	Jun 08-May 09	Jun 09-May 10	Jun 10-May 11	Jun 11-May 12
	Average # of tests /year	% decline compared with pre-vaccination period (95% CI)					
Total # of positive tests	917	32% (29%-36%)	56% (53%-60%)	75% (72%-78%)	77% (74%-80%)	77% (74%-80%)	83% (80%-85%)
Community aquired	767	33% (30%-36%)	59% (55%-62%)	75% (72%-79%)	75% (72%-79%)	76% (73%-79%)	82% (80%-85%)
Nosocomial	150	30% (23%-37%)	45% (37%-53%)	73% (66%-80%)	86% (80%-92%)	82% (76%-88%)	85% (80%-91%)
# of AGE admissions	1,793	4% (3%-5%)	29% (27%-31%)	33% (31%-35%)	42% (39%-44%)	37% (35%-39%)	53% (50%-55%)
# of AGE hospitalisation days	9,100	7% (7%-8%)	27% (26%-28%)	34% (33%-35%)	44% (43%-45%)	43% (42%-44%)	56% (55%-57%)

[Table1]

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IMMUNOGENICITY AND SAFETY OF MENACWY-CRM, A QUADRAVALENT MENINGOCOCCAL CONJUGATE VACCINE, IN INFANTS

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Background and aims: MenACWY-CRM (Menveo®) is a quadrivalent meningococcal conjugate vaccine against serogroups A, C, W-135 and Y currently licensed in Europe, the US and many other countries worldwide for 2 years of age and above. Integrated immunogenicity and safety data in infants from 2 months of age have not been presented.

Methods: Results of 2 phase III immunogenicity and safety studies and 1 phase III safety study were evaluated to provide a clinical picture of MenACWY-CRM and co-administration of MenACWY-CRM with routine infant vaccines (DTaP-HBV-IPV, +HIB or DTP-HIB-IPV+HBV, +Rotavirus, +PCV7 or PCV13) and routine toddler vaccines (PCV7 or PCV13, +DTaP, + Hib, +MMR/MMRV). Primary immunogenicity was assessed one month postvaccination via serum bactericidal assays using human serum as the exogenous complement source (hSBA).

Results: Overall, 12,818 subjects were enrolled in clinical trials and randomized to receive study vaccines at clinical centers in the United States, Australia, Canada, Taiwan, and Latin America (LA). One month after receiving a 4-dose infant/toddler series (LA: 2, 4, 6, 16 months; elsewhere: 2, 4, 6, 12 months), 89-95%, 95-98%, 97-100% and 96-100% of subjects had hSBA titers ≥8 against serogroups A, C, W, and Y, respectively. Safety profiles and immune responses to concomitant vaccine antigens were similar in groups that received MenACWY-CRM plus routine vaccines or routine vaccines alone.

Conclusion: In a database of 12,818 subjects from 2 months of age, MenACWY-CRM was well tolerated and induced robust immune responses without evidence of clinically relevant interference when co-administered with routine infant vaccines.

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THE MEMORY B CELL RESPONSE TO A BOOSTER DOSE OF A 13-VALENT (PCV-13) OR 10-VALENT (PHID-CV) PNEUMOCOCCAL CONJUGATE VACCINE

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Background/aims: In the UK, children receive the 13-valent pneumococcal conjugate vaccine (PCV-13) at 2, 4 and 12 months of age. The purpose of this randomised controlled trial was to assess non-inferiority of a 10-valent pneumococcal conjugate vaccine (PHiD-CV) as an alternative 12-month booster. As a descriptive secondary objective, we assessed the memory B cell (MBC) responses to booster immunisation with either PCV-13 or PHiD-CV.

Methods: 178 children who had previously been vaccinated with PCV-13 at 2 and 4 months were randomised 1:1 to receive a booster dose of either PCV-13 or PHiD-CV at 12 months of age. Blood was taken before and 1 month following vaccination. MBCs were quantified using a cultured ELISpot assay for serotypes 1, 3, 4, 9V, 14 and 19A.

Results: 247 blood samples were available for analysis. A significant rise in MBC frequency was seen for 5 serotypes (1, 3, 4, 9V, 19A) in the PCV-13 group and 1 serotype (19A) in the PHiD-CV group. There was a particularly large increase in serotype 3-specific MBCs in the PCV-13 group (1.3 to 22.6 MBC/10^6 cells; $p< 0.0001$). Serotype 14 produced the smallest change in MBC frequency showing no significant increase in either group.

Conclusions: Following priming with PCV-13 in early infancy, a booster dose of PCV-13 results in a more pronounced peripheral blood MBC response than does a booster of PHiD-CV. However, correlation between MBC responses, (functional) antibody and clinical protection is unclear. Forthcoming IgG ELISA and OPA data may help further interpret these results.

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IMPACT OF PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINES ON NASOPHARYNGEAL CARRIAGE: EXPERIENCE FROM CLINICAL AND EPIDEMIOLOGICAL STUDIES

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Background/aims: We review the impact of the 10-valent pneumococcal non-typeable Haemophilus influenzae protein D conjugate vaccine (PHiD-CV, GlaxoSmithKline Vaccines) and its 11-valent predecessor (11Pn-PD) on S.pneumoniae (Sp) nasopharyngeal carriage (NPC).

Methods: We reviewed data from 3 randomised controlled trials (RCTs)[1-3], and 1 non-randomised controlled trial[4] assessing the impact of PHiD-CV on NPC, as well as 1 RCT assessing the impact of 11Pn-PD[5,6]. Trial characteristics are summarised in the table. Results from 2 recent PHiD-CV effectiveness studies (Brazil[7], Kenya[8]) were also assessed. NPC was analysed using standard culture methods, except in Brazil where PCR was used.

Results: A consistent decrease in vaccine serotype (VT) Sp NPC was seen after PHiD-CV/11Pn-PD vaccination compared to vaccination with a non-pneumococcal control vaccine, with a maximum reduction of 31 to 56% (Table). In some studies, the decline in VT Sp NPC was already noticeable post-priming. Trends for elevated NVT Sp NPC were seen at some time points post-booster but these increases did not lead to complete replacement and an overall reduction in Sp NPC was seen in each study (maximum reduction: 11-36%). Similarly, the effectiveness studies showed reduced VT and overall Sp NPC 6-9 months after PHiD-CV was introduced in these countries' routine immunisation schedules.

Conclusions: In these studies, PHiD-CV vaccination resulted in a consistent reduction in overall/VT Sp NPC suggesting that herd protection may be expected with PHiD-CV. Further studies are required to evaluate the public health implications of reduced overall Sp NPC.

Table: Trial characteristics and vaccine efficacy of PHiD-CV in reducing pneumococcal nasopharyngeal carriage

	POET[5,6] Czech/Slovak Republics NCT00119743	COMPAS[1] Panama NCT00466947	Study 053[2] Finland NCT00839254	Study 014[4] Czech Republic NCT00496015	Study 027[3] The Netherlands NCT00652951
Trial characteristics					
Trial design	Double-blind Randomised	Double-blind Randomised	Double-blind Cluster-randomised	Open-label Non-randomised	Single-blind Randomised
Vaccines	11Pn-PD vs. HepA	PHiD-CV vs. HepB or HepA	PHiD-CV vs. HepB	PHiD-CV vs. MenACWY-TT	PHiD-CV vs. 7vCRM
PCV included in NIP before study start?	No	No	No	No	Yes (7vCRM)
Vaccination schedule	Priming: 3, 4, 5 mo Booster: 12–15 mo	Priming: 2, 4, 6 mo Booster: 15–18 mo	Priming: 3, 4, 5 mo (3+1) or 3, 5 mo (2+1) Booster: 11–12 mo	Priming: 3, 4, 5 mo Booster: 12–15 mo	Priming: 2, 3, 4 mo Booster: 11–13 mo
NPC swab sampling schedule	6 swabs between 6 and 24–27 mo	6 swabs between 7 and 24–27 mo	5 swabs between 3 and 18–22 mo	5 swabs between 12–15 and 24–27 mo	5 swabs between 5 and 24 mo
N per group	11Pn-PD: 191 Control: 190	PHiD-CV: 955 Control: 966	PHiD-CV 3+1: 1849 PHiD-CV 2+1: 1316 Control: 1928	PHiD-CV[a]: 209 Control: 336	PHiD-CV: 520 Control: 260
Highest point estimates of vaccine efficacy[b] and time points with highest point estimates					
VE (95% CI) against VT *S. pneumoniae*	**43%** (-17; 72) at 15–18 mo	**31%** (5; 50) at 18–21 mo	3+1: **56%** (47; 64) at 18–22 mo 2+1: **38%** (25; 49) at 14–15 mo	**54%** (21; 74) at 12–15 mo	**0%** (-87; 45) at 11–13 mo
VE (95% CI) against any *S. pneumoniae*	**23%** (-17; 50) at 15–18 mo	**11%** (-7; 25) at 15–18 mo	3+1: **28%** (20; 36) at 18–22 mo 2+1: **15%** (4; 25) at 18–22 mo	**36%** (9; 54) at 12–15 mo	**3%** (-19; 21) at 18–20 mo

[a]Only includes subjects who had not received prophylactic antipyretics at vaccination; [b]Results for total vaccinated cohorts; [1-6], see references; POET, pneumococcal otitis efficacy study; COMPAS, clinical otitis media and pneumonia study; HepA, hepatitis A vaccine; HepB, hepatitis B vaccine; MenACWY-TT, quadrivalent meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine; PCV, pneumococcal conjugate vaccine; NIP, national immunisation programme; 7vCRM, 7-valent CRM_{197}-conjugated PCV; mo, months; NPC, nasopharyngeal carriage; N, number of subjects (per group) in total vaccinated cohort; VE, vaccine efficacy estimated as 1 minus relative risk; VT, vaccine type; CI, confidence interval. [1]Tregnaghi, ESPID2011, abs. 1411; [2]Vesikari, ECCMID2013; [3]van den Bergh, Clin Infect Dis 2012; [4]Prymula, Vaccine 2011; [5]Prymula, Vaccine 2009; [6]Borys, ISPPD2012, abs. 189; [7]Andrade, ISPPD2012, abs .211; [8]Hammitt, ISPPD2012, abs. 242

Funding: GlaxoSmithKline Biologicals SA

[Table: Trial characteristics and vaccine efficacy]

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LONG-TERM IMMUNOGENICITY, SAFETY AND EFFECTIVENESS OF GARDASIL® IN THE NORDIC COUNTRIES

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Objectives: To evaluate long-term effectiveness, safety and immunogenicity of the quadrivalent HPV (qHPV) vaccine GARDASIL®, a pivotal randomized, placebo-controlled, double-blind, 4-year study (protocol 015-21) was extended up to 14 years in 4 Nordic countries. Interim analyses were performed at 8 years of total follow-up.

Methods: Nordic citizens are assigned a unique personal identification number (PIN) at birth, and are registered in a Civil Registration System in each country. A total of 2,750 subjects receiving qHPV and 2,097 receiving placebo at the start of study 015-21 are included in effectiveness and safety analyses. 4,344 participants consented for long-term immunogenicity analyses. Neutralizing and total IgG antibody response to HPV 6/11/16/18 were detected by competitive Luminex immunoassay (cLIA) and VLP-specific total IgG Luminex immunoassay (total IgG LIA), respectively.

Results: There were no cases of HPV 6/11/16/18-related disease observed through the current follow-up. There was no specific pattern of new medical conditions in the two cohorts and no evidence of an increase above background. In addition, 94.4%, 95.5%, 99.1% and 60.0% of patients remained seropositive to HPV 6/11/16/18 at year 8, respectively in the cLIA and 97.6%, 96.4%, 100% and 90.8% respectively in the IgG LIA. There was no evidence of HPV type-replacement against non-vaccine HPV types in young women.

Discussion: No breakthrough cases of disease related to vaccine HPV types have been observed among young women vaccinated with GARDASIL® through year 8. GARDASIL® continues to be generally safe and well tolerated. Immunogenicity to vaccine HPV types remains high 9 years following vaccination.

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INVASIVE PNEUMOCOCCAL DISEASES IN BIRTH COHORTS VACCINATED WITH PCV-7 AND/OR PHID-CV IN QUEBEC: AN UPDATE

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Background: In the province of Quebec, the 10-valent pneumococcal conjugate vaccine (PHiD-CV) was introduced in the summer of 2009, replacing the 7-valent vaccine (PCV-7) according to a 2+1 doses schedule. Transition to the new vaccine was recommended regardless of the number of PCV7 doses already administered. The objective of the study was to compare rates of invasive pneumococcal disease (IPD) in children exposed to different vaccines.

Methods: IPD cases were identified by the reference laboratory collecting isolates and specimen from all microbiology laboratories in the province. IPD rates were computed in cohorts of children born in 2007-2011 and observed up to the end of 2011 (maximum age = 48 months). The main vaccine used for the infant primary immunization series and the toddler booster dose was inferred from the Quebec City Immunization Registry data.

Results: IPD rate was significantly lower in the cohorts exposed to PHiD-CV (31/100,000 person-years) as compared with those exposed to PCV-7 (56/100,000; p=0.02). This was explained by a reduced frequency of 7F, 19A and other non-vaccine types. IPD rate also tended to be lower in children who had received PCV-7 for the primary series and PHiD-CV for the booster dose (24/100,000) as compared to those who had received PCV-7 only (36/100,000; p=0.14).

Interpretation: Results of this ecological analysis are compatible with a high level of protection induced by PHiD-CV against IPD caused by homologous serotypes and some level of cross-protection against other serotypes.

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OBSTACLES FACTORS FACING ADEQUATE TUBERCULOSIS TREATMENT IN CHILDREN LIVING IN A DEVELOPING COUNTRY: A HOSPITAL-BASED STUDY

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Background and aims: Despite availability of antituberculosis treatment and application of Directly Observed Treatment Short-course (DOTS) strategy, default in tuberculosis (TB) treatment is still a problem, especially in TB high-burden countries. Defaulted TB treatment in children has not been much studied and reasons may likely be different. The aim is to determine factors influencing defaulted TB treatment and describe its reasons.

Methods: This retrospective cohort study was performed based on 1,350 documented TB in pediatric DOTS registry from January 2009-June 2012 in Hasan Sadikin General Hospital. We contacted by phone to parents of 102 identified defaulted TB treatment. Documented data covered the age, sex, distance of the patient's dwelling to hospital, payment methods, type of TB, and antituberculosis formula given. Chi-square analysis was performed to determine influencing factors of defaulted TB treatment with $P< 0.05$.

Results: Of the 102 parents of identified defaulted TB treatment consisting of 43 (44%) girls and 54 (55%) boys with median age 60 months presented with pulmonary TB (85%), there were five children who had completed TB treatment at their nearest health facility. Defaulted rate was 7.5%. The general problems encountered was financial (22.7%), time clash of working parents (16.5%), and far dwelling (16.5%). Far dwelling ($P=0.027$) and single drug formulations ($P=0.001$) are the significant factors influencing defaulted treatment.

Conclusions: Problems encountered in TB control may likely be different among countries as we find the urge to take into account using TB-9 form and fixed dose combinations.

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MONITORING OF STREPTOCOCCUS PNEUMONIAE STRAINS SEQUENCE TYPES (ST) ISOLATED FROM MENINGITIS PATIENTS AND CARRIERS

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Background: To conduct monitoring of S. pneumoniae strains sequence types.

Methods: Multilocus sequence typing (MLST) was performed for gene locus: aroE, gdh, gki, recP, spi, xpt, ddl of 23 S. pneumoniae isolates (serotypes: 1, 4, 17F, 14, 19F, 18C, 9N/9L, 6B, 6A). For investigation of STs UPGMA and eBURST were used.

Results: MLST allowed identifying allele profiles and STs for each profile. According to allele profiles of 23 isolates 19 closely related and belonging to one cluster STs were identified. eBURST analysis revealed 4 subcluster ST groups, closely related in origin. The group I included 2 isolates from nasopharynx and CSF (serotype 19F and 320 ST); group II-ST 3104 (from nasopharynx) and ST 517 (from CSF) which belonged to serogroup 9N/9L; in group III-3 isolates belonged to serotype 6A and 473 ST (2 isolates from CSF and 1 from nasopharynx); group IV- ST 246 and 244 ST (from CSF, serotype 4). When assessing the data on S. pneumoniae isolates in MLST base it was identified that the following STs were registered in Russia earlier: 423, 3104, 4841, 239. The STs: 490, 146, 7196, 473, 1227, 320, 3750, 517, 246 and 2436 were not registered in Russia, but were found in other regions.

Conclusions: S. pneumoniae strains, which cause of bacterial meningitis and those found in carriers belonged both to STs circulating on the territory of Russia and to STs which were not registered earlier. The data suggest that migration of STs from other regions take place.

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CURRENT PERTUSSIS EPIDEMIOLOGICAL SITUATION IN LATIN AMERICA AND ASSOCIATED VACCINATION STRATEGIES

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Background: Increasing pertussis in Latin America is affecting infant mortality rates (MR).

Methods: MEDLINES and National Ministry of Health websites were reviewed (2005-2012) epidemiological data.

Results:

Argentina: The incidence rate (IR) increased 46% in 6 years, ranging from 5.7/100,000 (2005) to 8.3/100,000 (2011), 374/100,000 < 1 year of age (MR=2.4%). A pregnant women vaccination strategy was implemented in 2012.

Brazil: 867 confirmed cases occurred in 2007, and 2,247 in 2011 (77% < 1 year of age) (MR=2.2%).

Chile: IR increased 275% in 2 years, (4.0/100,000 in 2009 and 15/100,000 in 2011). 50.2% of cases occurred in children < 1 year of age (MR=0.6%). A cocoon strategy was implemented in 2011.

Colombia: 1,720 cases reported in 2009, 1,325 in 2010 and 1,805 in 2011. 56% occurred in children < 6 months of age (MR=1.7%).

Costa Rica: In 2006-7 outbreaks caused 12 deaths. A post-partum vaccination strategy was implemented in 2007 with no deaths reported in 2010-11.

Mexico: 579 cases reported in 2009, 401 in 2010 and 495 in 2011. 85% occurred in children < 12 months of age.

Central America: El Salvador, Honduras and Guatemala reported very low IR.

Conclusions: Pertussis has been increasing in many Latin American countries in recent years, specifically in children < 1 year of age. Improvements in the sensitivity of surveillance and diagnostics might explain part of this increase. Nevertheless, this has lead to novel strategies like post-partum, cocoon, and pregnant women vaccination for which effectiveness studies should be put in place to measure their impact

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MYCOBACTERIUM PHOCAICUM BACTEREMIA: AN EMERGING INFECTION AMONG PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS

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Background and aims: Non-tuberculous mycobacteria (NTM), specifically the rapidly growing (RGM) are ubiquitous in soil, dust, bio-aerosols, and water. NTM may cause Central venous catheter (CVC) associated bacteremia. Heat-shock protein 65 (hsp65) and 16S rRNA genes sequencing is increasingly used for identification of these pathogens. Mycobacterium phocaicum (MPo) was first described in 2006, is closely related to M.mucogenicum. To our knowledge, no clinical cases were described so far. We describe hereby 4 cases of MPo bacteremia among pediatric hematology-oncology patients.

Methods: Cases with NTM bacteremia and clinical data were retrieved from hospital charts. Isolation of NTM was done using BACTEC 9240 and isolates identified by hsp65 and 16S rRNA genes sequencing.

Results: Between March 2011- October-2012, eight patients had NTM bacteremia. Four were from MPo. Ages were 3- 15.5 years. Primary diagnosis was leukemia, Burkitt, neuroblastoma and lymphoblastic lymphoma. CVC´s were inserted 14-63 days before bacteremia; duration of bacteremia was 1-15 days. Antibiotic treatment consisted of Meropenem, Clarithromycin and Ciprofloxacin. Lung CT scan was abnormal in 3/4 patients, mainly with ground glass appearance. All patients recovered. No positive blood culture was documented after removal of CVC. One patient died 2 months later from neuroblastoma.

Conclusion: MPo is an emerging RGM, may cause bacteremia in pediatric oncology patients with CVC as was previously described with other RGM. In our cases, possible pulmonary involvement was common. Removal of CVC seems important for clearance of bacteremia. More data is needed for the evaluation of the full pathogenic spectrum of these emerging pathogens.

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NOCARDIA ASTEROIDES PERITONEAL DIALYSIS-RELATED PERITONITIS; FIRST CASE IN PEDIATRICS, TREATED WITH PROTRACTED LINIZOLID. CASE REPORT AND LITRATURE REVIEW

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Background and aims: Peritonitis is a common problem in patients undergoing continuous ambulatory peritoneal dialysis (CAPD).Fungi and higher bacteria such as Nocardia asteroides as etiological agents have been infrequent in children undergoing CAPD.The predisposing factors,treatment protocol,and whether to treat with or without catheter in situ are unanswered questions in Nocardia peritonitis.

Material and methods: 13 years old female diagnosed with end stage renal failure on CAPD since 3 years.She presented with history of high grade fever leaking from the exit site of the peritoneal catheter,abdominal pain.On admission,patient started imprically on intraperitoneal (IP) Vancomycin,Ciprofloxacin.Initial peritoneal fluid examination was turbid appearance with white sediment and high WBC.Amphotricin-B was added after 4 days to cover for suspected fungal peritonitis.Peritoneal culture grew Candida Alberta and Nocardia after 12 days.Child went into cardiac arrest and septic shock.Catheter was removed.Child was managed in PICU with CVVH,ventilation and inotropic support.Case was complicated with peritoneal abscess that was evacuated by ultrasound guided aspiration.Jeujonal adhesions with some feeding intolerance were treated conservatively.

Results: Linizolid was given IV for 3 months in hospital then orally for 5 months with monitoring of side effects.Patient discharged home after 3 month on haemodialysis.

Conclusions: Nocardia peritonitis not reported before in pediatrics.It generally present as infection unresponsive to empirical treatment and initially an apparent 'culture-negative' peritonitis.Diagnosis and management can be problematic due to the slow growth and difficult identification.Duration of treatment for Nocardia peritonitis is not known.Linizolid can be used for prolonged period in trimethoprim-sulphamethoxazole resistant cases with close monitoring of side effect.

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INVASIVE STREPTOCOCCUS PYOGENES DISEASE IN THE PEDIATRIC DEPARTMENT OF A PORTUGUESE TERTIARY HOSPITAL, 2002-2012

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Introduction: Invasive Streptococcus pyogenes (iGAS) disease is associated with high mortality and morbidity. It has been documented a rise in its incidence.

Aims: Evaluate the epidemiology, diagnostic procedures, therapeutics and risk factors of iGAS disease in the Pediatric Department of a Portuguese tertiary hospital.

Material and methods: Retrospective analyses of the medical records of children admitted from January2002 to June2012.

Results: There were 26 cases, ages between 2 months and 9 years, 62% were boys and the majority of them occurred in the Winter-Spring months(65%), with a maximum of five cases/year. There was an 88% increase in the frequency of the disease in the last evaluated years. The most common signs and symptoms at admission were fever(88%), rash(50%), respiratory symptoms(50%) and articular pain(31%). The diagnoses were sepsis(7); necrotizing fasciitis(5); septic arthritis(5); otomastoiditis(3, 1 with meningitis and venous sinus thrombosis); toxic shock syndrome(2); periorbital cellulitis(2); bacteriemia(4) and a case each of septal pyohematoma, piomiositis, subperiosteal abscess, necrotizing pneumonia and osteomyelitis. Risk factors were identified in 15 cases: infected wounds(7), varicella(6, 1 with the consumption of NSAIDs) and viral infection(RSV/H1N1)(2). In 54%GAS was isolated from blood. A 3rd generation cephalosporin was the initial therapeutic choice in 20patients, and an association including clindamycin was the choice in 7(with cephalosporin/penicillin). Surgery was required in 14patients. There were no recorded deaths.

Conclusion: The number of cases is small but demonstrates the wide variety and severity of iGAS disease. We evidenced a significant increase in the frequency of the disease in the last evaluated years.

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SEROTYPE EVOLUTION AND ANTIMICROBIAL SUSCEPTIBILITY OF STREPTOCOCCUS PNEUMONIAE 2 YEARS POST INTRODUCTION OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN GREECE

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Background: The aim was to examine the evolving serotype epidemiology and antimicrobial susceptibility of Streptococcus pneumoniae isolates causing invasive pneumococcal disease (IPD) or acute otitis media (AOM) in children ≤14 y.o. following introduction of PCV13 to the Greek NIP in 2010.

Methods: Data from the 4th year of a prospective study initiated in September 2008 in 15 pediatric hospitals are presented. Serotyping was performed by latex agglutination and Quellung reaction using anti-sera (SSI, Denmark). Antimicrobial susceptibility was determined by E-test; isolates with MIC ≥2 μg/mL were considered resistant to penicillin.

Results: Among 94 isolates collected (37.2% ≤2 y.o.; IPD:11, AOM: 24) between November 2011-October 2012, the commonest serotypes for IPD were 19A (25.8%), 7F (25.8%) and 24F (9.7%) while for AOM 19A (17.5%), 3 (12.7%) and 11A (11.1%). A 43.9% reduction was noted in IPD cases in children ≤2 y.o. after PCV13 implementation (23 in 2010-2012 vs. 41 in 2008-2010). Theoretical coverage for PCV7, PCV10 and PCV13 in children 0-2 y.o. with IPD was 0.0%, 27.3% and 63.6% respectively whereas for AOM was12.5%, 12.5% and 29.2%. Resistance to penicillin exhibited 3.2% of IPD and 19.4% of AOM isolates, while rates for erythromycin resistance reached 25.8% and 38.7% respectively. The most prevalent resistant serotypes to penicillin and erythromycin were 19A and 19F.

Conclusions: Two years post PCV13 introduction, IPD cases in children ≤2 y.o have decreased but vaccine serotypes 19A and 7F remain the major cause for IPD in children ≤5 y.o, while non-vaccine serotypes are predominant in AOM cases.

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INDICATIONS FOR OSELTAMIVIR TREATMENT IN HOSPITALIZED CHILDREN WITHOUT UNDERLYING DISEASES. IS IT ALWAYS NECESSARY?

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Aims: To analyze if treatment with oseltamivir in hospitalized children without underlying diseases and influenza confirmed infection improved the outcome of the diseases.

Methods: Multi-centric, retrospective study was performed in Madrid between September 2010-June 2012. Children admitted with confirmed influenza infections were included. Children with underlying diseases were excluded. Patients who received and who do no received treatment with oseltamivir were compared. Fever duration, oxygen support, antibiotics administration, length of hospital stay, intensive care admission and bacterial complications were analyzed. To compare variables Chi-square, Fisher´s exact test, ANOVA or Mann Whitney U were used.

Results: 287 children were included, 93 of them treated with oseltamivir (32%). There were no significantly differences among treated and untreated patients in most clinical data studied. Patients with asthma presented no differences in the outcome variables between both groups.

	Treated (n=93)	No treated (n=194)	p
History of asthma	34 (36.6%)	49(25.5%)	NS
Antibiotic treatment	41 (44%)	98(51%)	NS
Hospital stay	4.7± 3.6	4.9 ± 3.2	NS
Fever duration	1.2 ± 2	1.6 ± 2.4	NS
Hypoxia duration	1.6 ± 2.3	2.1 ± 2.9	NS
Intensive care admission	6(6.5%)	3 (1.6%)	NS
CRP > 60 mg/L	10/69 (14.5%)	21/113 (18.1%)	NS
Typical pneumonia	5/45 (10%)	13/76 (17%)	NS

[Clinical characteristics of the groups]

Conclusions: We have not found benefit in treating with oseltamivir any hospitalized pediatric patient without underlying diseases or risk factor for developing a serious illness.

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DISTRUBUTION OF RHINOVIRUS GENOTYPES IN NASOPHARYNX AMONG SYMPTOMATIC CHILDREN WITH ACUTE OTITIS MEDIA OR UNCOMPLICATIED RESPIRATORY TRACT INFECTION

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Background and aims: Rhinoviruses are the most common respiratory viruses which have recently been classified into A, B, and C genotypes. Our aim was to investigate if the distribution of these genotypes is similar or different between symptomatic young children diagnosed with acute otitis media (AOM) and uncomplicated respiratory tract infection.

Methods: We enrolled children (6-35 months) with acute symptoms suggestive of AOM. AOM group showed middle ear effusion and acute inflammatory signs in pneumatic otoscopy along with acute symptoms, while non-AOM group had no abnormal otoscopic signs or only middle ear effusion.

We took nasopharyngeal samples from each child and analyzed the samples for rhinovirus by PCR and further sequenced the rhinovirus positive samples to determine if the rhinovirus genotype was of A, B, or C.

Results: We sequenced altogether 202 samples which had been positive for rhinovirus by PCR. Sequencing gave genotype result from 137/202 samples (68%), 77 samples in AOM group and 60 samples in non-AOM group. The distribution of rhinovirus genotypes A, B, and C was following: 33/77 (43%), 4/77 (5%), and 40/77 (52%) in AOM group and 25/60 (42%), 5/60 (8%), and 30/60 (50%) in non-AOM group, respectively (p=0.763).

Conclusions: The distribution of rhinovirus genotypes is similar in symptomatic young children diagnosed with acute otitis media and uncomplicated respiratory tract infection suggesting that each rhinovirus genotype similarly predisposes young children to the development of AOM.

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SEVERITY OF RESPIRATORY TRACT DISEASE IN PEDIATRIC PATIENTS POSITIVE FOR HUMAN RHINOVIRUS/ENTEROVIRUS IN RESPIRATORY SPECIMENS

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Background and aims: Human rhinovirus/enterovirus (HRV/ENT) is commonly identified in acute respiratory infections (ARIs) in children, although data on its clinical severity remains limited. We aimed to compare clinical severity between HRV/ENT, respiratory syncytial virus (RSV), influenza A/B (FLUA/B) and other common respiratory virus infections in children.

Methods: Retrospective study of children presenting in a tertiary care hospital with ARIs and confirmed single positive viral infections on mid-turbinate swabs by molecular assays. Outcome measures for clinical severity included hospital admission and, for inpatients, a composite end-point consisting of intensive care admission, hospitalization greater than 5 days, oxygen requirements and death.

Results: A total of 118 HRV/ENT, 104 RSV, 104 FLU A/B and 65 other common respiratory viruses were identified. Compared to children with RSV, FLUA/B and other common respiratory viruses, those positive for HRV/ENT were more likely to have underlying cardiorespiratory comorbidies (respectively 32.2% vs 14.4%, $p< 0.001$; 32.2% vs 9.6%; $p< 0.001$; 32.2% vs 16.9%, $p< 0.001$). In multivariable analysis adjusting for underlying diseases and age, children with HRV/ENT infections had increased odds of hospitalization compared to those with RSV (OR 2.6, 95% CI 1.37-4.76, p=0.003) and FLU A/B (OR 2.6, 95%CI 1.37-5.0, p=0.003) infections and increased odds of severe clinical disease (OR 2.39, 95% CI 1.28-5.0, p=0.006) only when compared to those with FLUA/B infections.

Conclusions: Children presenting with HRV/ENT had a more severe clinical course than those with RSV and FLUA/B infections, thus suggesting the importance to consider HRV/ENT infections in children with severe ARTIs.

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IMMUNITY AGAINST POLIOMYELITIS IN THE NETHERLANDS

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Background and aims: In the Netherlands, a poliomyelitis epidemic occurred in 1956. Routine childhood vaccination using inactivated polio vaccine (IPV) was introduced in 1957. Thereafter, three outbreaks occurred that were restricted to Orthodox Protestant individuals, refusing vaccination and living in a socio-geographically closely-knit network. We estimated age-specific antibody titers against poliomyelitis in the general population (NS) and religious groups.

Methods: We used a serum bank, established in 2006-2007 to estimate seroprevalence of diseases, targeted by the National Immunisation Programme (NIP).

We used Sabin-strain viruses as challenge viruses and determined neutralizing antibodies against poliovirus types 1, 2, and 3 in the NS and religious groups refusing vaccination. Results were given as ^{2}log reciprocal titers (GMT), cut-off for seroprotection was GMT = 3.

Results: Overall seroprotection in the NS (n=6386) was 94.6% (95%CI 93.9-95.3), 91.8% (95%CI 90.9-92.6) and 84.0% (95%CI 82.9-85.1) for the three serotypes. In 0-7-month-olds, eligible for 3 IPV-doses, mean seroprevalence was ≥ 80% for all serotypes. Seroprotection reached the highest level in 5-year-olds (100%, type1 and 2) and 9-10-year-olds (96%, type3). After a completed NIP, high and long-lasting GMTs were found.

For orthodox protestant people (n=326), seroprotection was 46.4% (95%CI 29.7-63.2), 38.4% (95%CI 26.9-49.9) and 44.6% (95%CI 35.7-53.9) for the three serotypes.

Within the NS, risk factors for non-protection were less than 6 IPV-doses, adherence to orthodox protestant religion, not traveling and a Dutch ethnicity.

Conclusions: A completed NIP results in high protection against all three poliovirus-types. However, people, refusing vaccination on religious grounds, remain at risk.

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ROTAVIRUS EPIDEMIOLOGY AND GENOTYPES AFTER MONOVALENT VACCINE INTRODUCTION IN ARACAJU, BRAZIL (2006 - 2012)

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Background and aims: Rotavirus diarrhoea is still an important cause of children mortality worldwide. Vaccine introduction can lead to a reduction in the mortality and morbidity and in Brazil, Rotarix®, a monovalent rotavirus vaccine, was introduced since March 2006. This study describes the epidemiology of rotavirus diarrhoea after the vaccine introduction; the current incidence; age groups distribution; seasonality; predominant rotavirus genotypes and vaccine efficacy.

Methods: In a cross sectional survey, children with acute diarrhoea were enrolled prospectively from October 2006 to April 2012 at Emergency Hospital of Sergipe (HUSE), in Aracaju, Brazil. A questionnaire with clinical and epidemiological information and stool samples were obtained. ELISA tests were carried out to detect rotavirus infection and positive samples were genotyped. Descriptive statistic calculations were carried out to define rotavirus epidemiology.

Results: ELISA positive results were found in 231 of 1881 specimens. Overall incidence was 12.2% (95%CI, 10.7-13.7%). Rotavirus positive cases were more severe and in older patients (p=< 0.01). They circulated throughout the year with some increase in June and September. The most frequent genotype were G2P[4] with 167 cases (71.4%) and G1P[8] with 29 cases (12.4%). During 2006-2008 G2P[4] was predominant, during 2009-2010, G1P[8] has reappeared, and in 2012, G8 and G3 genotypes were the most frequent.

Conclusions: Rotavirus incidence in all causes diarrhoea remains low after Rotarix® introduction in Brazil, confirming the success of the programme. Nevertheless, new rotavirus strains associated to severe diarrhoea are emerging. Surveillance is needed to monitor the shifts in rotavirus epidemiology.

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POTENTIAL IMPACT OF TEMPORARY WITHDRAWAL OF ROTAVIRUS VACCINES IN ACUTE GASTROENTERITIS HOSPITALIZATIONS IN NORTH-WEST SPAIN (GALICIA)

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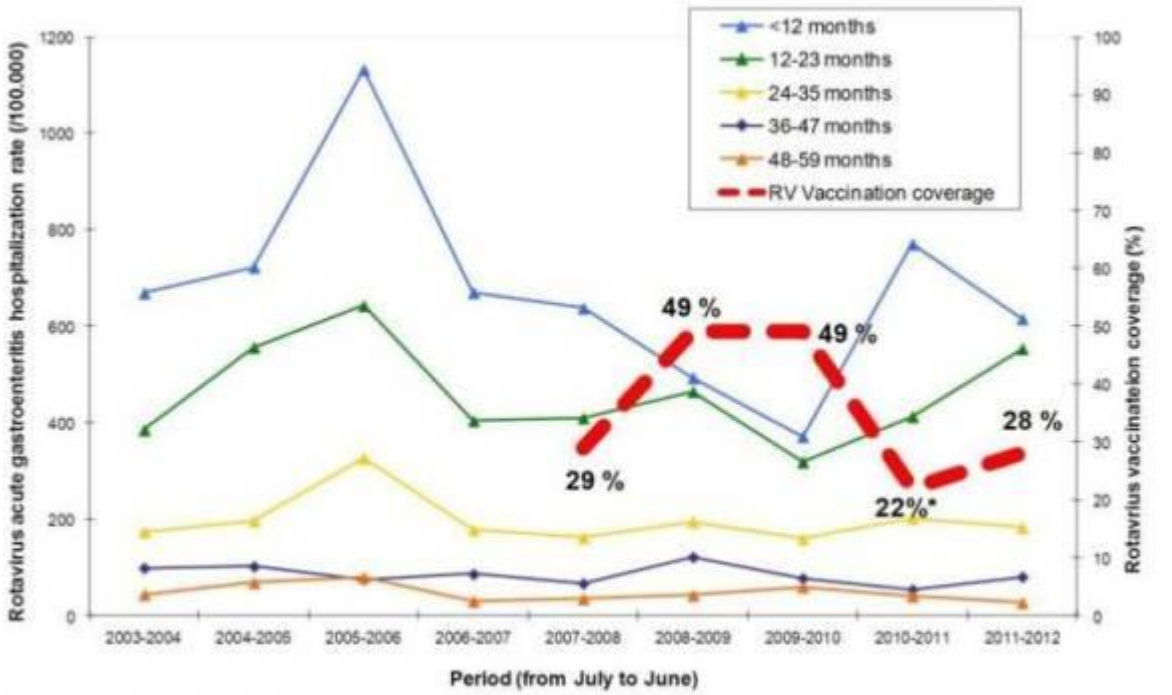
Aims: In 2010, rotavirus vaccination (RV) was held in Spain during 5 months June, due to a quality problem identified in the vaccine manufacture. Our study aims to evaluate the impact of this RV cease on rotavirus acute gastroenteritis (RAGE) hospitalizations in children< 5 years.

Methods: The annual hospitalization rates of RAGE were calculated by using the official surveillance system for hospital data for the Autonomous Region of Galicia (CMBD) and the population census (INE). Rotavirus vaccination coverage was estimated using sales data provided by IMS Health.

Results: In the 5-yearly periods pre-vaccination, the median RAGE hospitalization rate was of 696.2/100.000 children ≤1 years. Hospitalization rates in post-vaccination period July 2009-June 2010 decreased by 47% (371.3/100.000). Rates in the period just after vaccination cease -i.e., July 2010-June 2011- increased by 11% (771.1/100.000). In the period July 2011-June 2012, with rotavirus vaccination resumed, RAGE hospitalization rate decreased by 12% (615.5/100.000) as compared to the median AGE-rotavirus rate for the pre-vaccination period. A similar pattern was found on all-cause AGE hospitalization rates, correlating well again with vaccine coverage variation.



(*) 22% is the mean RV vaccine coverage for that period. However, for 5 months within that period, no new batches of vaccine were released onto the market, and the coverage estimated for those months was 0-5%.

[Rotavirus hospitalization rate]

Conclusions: A rebound increase in the rates of hospitalization for rotavirus AGE just after vaccination cease has been observed in Galicia. This increase is more pronounced in children for whom the vaccine was indicated

(< 12 months). Although other factors might contribute to explain this variation in rotavirus incidence, our data points out changes in vaccination coverage as a main determinant.

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PERSISTENT EPSTEIN-BARR VIRUS DNA DETECTION IN CHILDREN WITH INFECTIOUS MONONUCLEOSIS AND COINFECTION BY CYTOMEGALOVIRUS AND HUMAN HERPESVIRUS-6

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Background and aims: Infectious mononucleosis (IM) is a clinical syndrome caused by primary infection with Epstein-Barr virus (EBV). We evaluated the possible role of coinfections by cytomegalovirus (CMV) and/or human herpesvirus 6 (HHV6) as enhancing factors of persistent EBV DNA detection.

Methods: Forty-seven children (27 males) aged 0.8 to 15.3 years (mean: 5.8) were admitted with typical IM signs. All were examined for antibodies and specific DNA detection in saliva blood and/or urine on admission and every 3 to 9 months; follow-up was 1.1-12 years (mean: 5.4). Based on the detection of different viral DNA detected on admission, the patients were grouped in: 1)EBV only; 2)EBV+HHV6; 3)EBV+CMV; 4)EBV+CMV+HHV6.

Results: Thirty-five children (74%) had coinfections. Mean persistence of EBV DNA occurred for 8 months (range 2-14) in children with only EBV, 26.7 months (4-87) in EBV-HHV6 group, 31.1 months (7-89) in EBV-CMV group, 47.2 months (13-120) in children with EBV-CMV-HHV6 coinfections. A statistically longer persistence of EBV DNA occurred in coinfected children than in only EBV infected (EBV vs EBV-HHV6 p=0.016, EBV vs EBV-CMV p=0.007, EBV vs EBV-CMV-HHV6 p=0.001). No statistical difference was observed among the groups of coinfected children.

Conclusions: In our hospital-based study, the great majority of children admitted with IM had a herpesvirus coinfection, which enhanced EBV replication and persistence of EBV DNA, presumably by transacting genes.

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SEROCONVERSION AFTER QUADRIVALENT HUMAN PAPILLOMAVIRUS VACCINE IN HIV-INFECTED GIRLS

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Background and aims: HIV-infected women have an increased prevalence of human papillomavirus (HPV) infections and a higher risk of cervical cancer. The quadrivalent HPV (QHPV) vaccine is effective in preventing genital precancerous lesions and warts in immunocompetent people. We aim to describe the immunogenicity of the QHPV vaccine in HIV-infected girls.

Methods: Cross-sectional study in a series of 27 HIV-infected girls who received a complete QHPV (types 6, 11, 16 and 18) vaccination series. Serum antibodies against QHPV antigens in the first 6 months after the third vaccine dose were measured by an enzyme immunoassay (DRG Diagnostics, Germany). Seropositivity was defined as an anti-HPV index > 1.00 and results were analyzed according to different clinical and immunovirological variables.

Results: Twenty-seven girls were included (median age: 15 years; 26 and 16 vertically-infected and with AIDS, respectively). Only one remained antiretroviral naive, 10 (37%) had received HAART as first treatment (median number of regimens: 3.5), and 13 (48%) had interrupted HAART at least once for a median time of 26 months.At the time of vaccination and assessment all patients were symptom-free, none of them presented with severe immunosuppression and viral load was undetectable in 19 (70%) and 16 (59%), respectively. Seroconversion occurred in 25 (93%) vaccinees with no differences based on clinical and immunovirological variables.

Conclusions: QHPV was highly immunogenic in this series of HIV-infected adolescent girls. Long term antibody levels need to be mesured to assess the durability of the protection.

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PEDIATRIC HERPES ZOSTER HOSPITALIZATION RATES REMAIN UNCHANGED DURING THE FIRST DECADE POST INTRODUCTION OF THE VARICELLA VACCINE IN GREECE

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Background and aims: The varicella vaccine was introduced in the Greek National Immunization Program (NIP) in 2004. Toddler vaccination and catch-up of susceptible older children, adolescents, and adults was implemented. The study examined time trends in pediatric herpes zoster (HZ) hospitalizations following vaccine implementation.

Methods: A retrospective study was conducted among all pediatric HZ patients hospitalized at a pediatric referral hospital in Greece during 1999-2011. Time trends in the occurrence of pediatric HZ cases were evaluated with ARIMA modeling. HZ hospitalization rates prior and following the introduction of the varicella vaccine in the NIP were compared with the Rao-Scott test.

Results: During the study period, 9647 pediatric patients were admitted to the study site, while 134 (1.4%) patients were hospitalized for HZ. The rate of HZ hospital admissions increased from 1999 (12.67 cases/1000 admissions) to 2011 (17.12 cases/1000 admissions). However, no significant increase in the rate of HZ cases was detected over time (p=0.673). Moreover, no significant decrease in the rate of HZ admission prior to and following the introduction of the varicella vaccine in the NIP was identified (p=0.680). However, the mean age of study participants increased significantly during the study period (2.53±1.8 years in 1999 to 14.00±0.01 years in 2011; p=0.006).

Conclusions: The rate of hospitalized pediatric HZ patients remains unchanged following the introduction of the varicella vaccine in the Greek NIP. The present evidence may serve as a baseline to detect future changes in HZ hospitalization rates. Ongoing surveillance of HZ hospitalization rates is deemed necessary.

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LIPOSOMAL AMPHOTERICIN B VERSUS PENTAVALENT ANTIMONY SALTS FOR VISCERAL LEISHMANIA IN CHILDREN

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Objective: The aim of this study was investigate the efficacy of a 21 day schedules of Liposomalamphotericin B, compared to pentavalent antimony salts for the first episode of visceral leishmaniasis.

Methods: seventeen cases of visceral leishmaniasis who were admitted to Dr Behcet Uz Children's Hospital between January 2005 to April 2012 were retrospectively reviewed. One group included eleven patients who were treated with pentavalent antimony salts, sodium stibogluconate or meglumineantimoniate, intramuscularly for 28 Days. Second group was treated with amphotericin B intravenously at a dosage of 3 mg/kg on 1-5,10 and 21^{th}days (a cumulative dose of 21 mg/kg/day).

Results: The mean duration of hospital stay was 16 ± 2,7 days in liposomalamphotericin B group, while it was 30,18 ± 0,98 days in pentavalent antimony salts group and significantly longer in pentavalent antimony saltsgroup (p=0,000). The mean time required for recovery of fever in amphotericin B was 2.17 ± 0,753 days and 4,45 ± 1,508 days in pentavalent antimony salts group and significantly longer in pentavalent antimony salts group (p=0,000). Statistically significant durational increase was present in Hemaglobin levels in both of the drug groups; however significant durational difference was present in white blood cell, platelet counts and albumin levels only in pentavalent antimony salts.

Discussion: While pentavalent antimony salts were found to increase biochemical and haematological findings; liposomal amphotericin B was responsible for rapid recovery in fever and shorter hospital stay. As a result, our study shows the advantages of both medications independent of their costs.

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BRAIN ABSCESSES IN CHILDREN: THE EXPERIENCE OF AN ITALIAN PAEDIATRIC CENTER

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Background and aims: Brain abscess (BA) is an uncommon but potentially life threatening infection in paediatric population. The objective of this case series is to describe management and outcomes of BAs in a single Paediatric Tertiary Referral Center.

Methods: We retrospectively reviewed medical records of children with BA admitted to Regina Margherita Children's Hospital, Turin, Italy, from 1998 to 2012.

Results: Eighteen children (12 M, 6 F) were included. Age ranged from 2 weeks to 16.5 years (mean 8.1 ± 5.6 years). Contiguous infections, especially otitis, were the most frequent predisposing factors (10/18 patients). At presentation, 9 patients had headache and 8 fever. Seizures occurred in 6 children. Neuroimaging consisted in CT in 14 patients and MRI for 4. Fourteen children had a single BA;16 abscesses were located in the cerebral hemispheres and 2 in the cerebellum.

Antimicrobial therapy was administered for a mean of 53.2 days (range 13-117 days). Ceftriaxone plus metronidazole and meropenem plus vancomycin were the most frequent combinations. Fourteen patients underwent surgery and consequent microbiologic examination. Gram positive bacteria, in particular Streptococcus intermedius, were the predominant isolated pathogens; four cultures were sterile. No death was recorded. Six children presented neurological sequelae, including motor deficits (3), hydrocephalous (2), visual impairment (1).

Conclusions: Despite the advances in surgical and diagnostic techniques, and the availability of new antimicrobials, BA in children remains associated with a high morbidity rate and may cause relevant neurological damage. Along with an appropriate antimicrobial treatment, neurosurgical intervention is often crucial in BAs' management.

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SPINAL EPIDURAL ABSCESS IN CHILDREN

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Background and aim: Spinal epidural abscesses (SEA) are rare but serious infections that require prompt diagnosis and treatment to avoid complications.

Methods: Retrospective review of all cases of SEA admitted to a tertiary paediatric hospital in the last 6 years.

Results: A 43-day-old girl was admitted with a 2-day history of low-grade fever and irritability. A dorsal spinal mass was noticed. WCC=29560/µL and CRP=90mg/L. Spinal MRI showed posterior SEA from T6-T11. Surgical drainage was performed and vancomycin and cefotaxime started, later switched to flucoxacillin when MSSA was isolated. A 4-year-old boy, one day after minor facial trauma, presented with high fever, abdominal pain and meningeal signs. WCC=15470/µL, CRP=380mg/L and ESR=78mm/h. Abdominal and heart ultrasounds and CSF were normal. Three days later a scarlatiniform rash and worsening back pain were noted. Bone cintigraphy scan was normal. Spinal MRI showed SEA from C7-T10. Ampicillin+clindamycin were started. S. pyogenes was isolated in the blood culture. A 14-year-old girl presented with an 8-day history of worsening back pain, with an episode of bladder dysfunction and lower limbs paresthesia. WCC=24580/µL, CRP=512mg/L and ESR=103mm/h. Spinal CT was normal. Ceftriaxone and flucloxacillin were started. Spinal MRI showed SEA from C7-L5, with subcutaneous infiltration. Surgical aspiration of the subcutaneous collection grew MSSA. All responded well to treatment and repeat MRI showed residual collection.

Conclusions: The initial clinical manifestations were nonspecific, leading to a delayed diagnosis in 2 cases. Spinal MRI was the best imaging tool. A conservative approach was adopted in 2 patients with good outcome.

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MULTIPLE ERYTHEMA MIGRANS AS A MANIFESTATION OF EARLY STAGE LYME BORRELIOSIS IN CHILDREN

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Background: Multiple Erythema Migrans is rare in early stage of Lyme borreliosis in European children.

Patients and methods: During 2011 we have diagnosed and cured 34 children with Erythema Migrans. Demografic,clinical,ECG and borrelial serum ELISSA antibody titers were obtained.Patients were followed up clinically and serologically one year after a tick bite.

Results: All patients developed Erythema Migrans 7-10 days after a tick bite.Multiple EM occured in 94% of patients. Skin lesions were more frequently presented with a ring -like lesion (94%) than mixt lesions (6%).

All patients had normal ECG.Systemic symptoms were reported by two patients (6%);local symptoms were reported by 41% of patients. Four weeks after a tick bite 97% of patients were borellial serum ELISSA antibody titers positive.

All patients had a good response to antibiotic therapy.Clinical and serological findings were normal in all one year after a tick bite.

Conclusion: Analysis of our group of children showed that the predominant skin lesion was Multiple EM which is not characteristic of early stage of the disease. Response to antibiotic therapy was good similarly solitary EM.

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LIFE-THREATENING KINGELLA KINGAE ENDOCARDITIS IN A 13-MONTH-OLD HEALTHY BOY

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Introduction: Kingella Kingae (Kk) is increasingly reported in childhood. It is a common etiology of osteoarticular infections in young children. However this germ can be responsible of more aggressive clinical picture.

Clinical case: We report the case of a 13-month-old boy admitted for fever, vomiting, photophobia and deterioration of the general state. The diagnosis of aseptic meningitis was done, based on laboratory findings and lumbar puncture. A treatment with cefotaxime and aciclovir was initiated with improvement of the patient´s general condition and resolution of the fever over 24hrs. However, on day 2, blood culture grew for Kk. An echocardiogram showed the presence of a wide vegetation (10x9 mm) on the posterior mitral valve leaflet with moderate regurgitation. A cerebral scan showed a right-frontal hypodense lesion. The diagnosis of bacterial endocarditis with frontal septic embolization and reactive meningitis was made.

A mitral plasty was complicated by an embolization in the LAD coronary artery with myocardial ischemia. The patient needed ECMO during 4 days. Eventually, the cardiac function improved dramatically and the final evolution was excellent with IV ampicilline continued for 6 weeks.

Conclusion: Kingella Kingae is included in the HACEK group that causes 5% of the endocarditis, even on healthy heart. Some authors recommend an echocardiogram in case of bacteremia.

Our case demonstrates that endocarditis can be associated with infected material embolizations, including in the cerebral and coronary territories. Amazingly, this case also shows the impressive recovery potential of children after an acute ischemic event in a peripheral circulation.

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CHRONIC COUGH FOLLOWING ACUTE RESPIRATORY ILLNESS IN CHILDREN

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Introduction: Despite chronic cough being a substantial cause of childhood morbidity and associated costs, data on its prevalence following acute respiratory illness (ARI) in children are scarce.

Aim: To determine the prevalence and predictors of chronic cough (>4 weeks duration) amongst children following presentation to a tertiary paediatric emergency department (ED) with ARI.

Methods: A cohort study of children aged < 15 years attending the Royal Children's Hospital ED, Brisbane, Australia with cough as a symptom. Children participate for 28 (±3) days following enrolment. Demographic, epidemiological, risk factor, microbiological and clinical data are collected at enrolment. Daily diary cards and weekly contacts are used to ascertain cough persistence. Children with persistent cough at day 28 are reviewed by a paediatric respiratory physician.

Results: We report preliminary data on 248 children (median age 30.3 months, range 1.02 months - 13.9 years, male: 62.1%) enrolled between December 2011 and August 2012, contributing a total of 5663 child-days of follow-up. The prevalence of chronic cough at day 28 was 20% (95% CI 14.8, 24.7); wet cough (37%), dry cough (22%), variable cough (18%), unsure (22%). At baseline, 41.6% of all children were virus positive on nasal swab, 81% bacteria positive and 36% both virus and bacteria positive.

Conclusions: The prevalence of chronic cough in these children following ARI is the highest yet reported. Our ongoing study will comprehensively describe the natural history, aetiology and outcomes of cough during and after ARI.

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PEDIATRIC PROFILE OF FIRST HUMAN TRICHINELLOSIS OUTBREAK IN INDIA

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Background: Trichinella infection is extremely uncommon in India with the diagnosis being even more difficult because of the non specific symptoms of the disease. We report an outbreak of human Trichinellosis in India.

Methods: Two children, belonging to the same community, presented as acute onset fever with generalized myalgia and eosinophilia, after consumption of uncooked pork in a common gathering. Trichinellosis was suspected in both index cases and was confirmed on muscle biopsy. A detailed epidemiological survey was carried out in the affected community and 54 people including 8 children, who participated in the gathering, were subjected to Proforma based assessment and blood investigations after informed consent.

Results: Out of 8 children, 1 had consumed pork in uncooked form, 4 in open fire roasted form and 3 in fried form. Clinical symptoms were found only in children who consumed pork in uncooked or open fire roasted form (n=5). These included fever with chills(100%), myalgia(100%) and periorbital edema(80%). One child developed dysphagia and breathing difficulty. Laboratory parameters studied in both symptomatic and asymptomatic patients showed eosinophilia in 75%(n=6), raised ESR in 50%(n=4), and an elevated creatinine phosphokinase enzyme levels in 37.5%(n=3). The analysis revealed milder severity of symptoms in children as compared to the adult population of the community. All symptomatic patients were treated with a short course of oral steroids and albendazole therapy.

Conclusion: In areas with high prevalence of raw meat consumption, infection due to Trichinella should be suspected in children presenting with eosinophilia myalgia syndrome.

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CLINICO- LABORATORY PROFILE OF CHILDREN WITH NEUROBRUCELLOSIS IN BIKANER, NORTHWEST INDIA

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Background and aims: Neurological manifestations of Brucellosis are rare. The aim of this observational study is to establish the evidence of neurobrucellosis in children in Bikaner.

Methods: The study is related to patients with brucellosis whose principal presenting features were neurological symptoms (headache, vertigo, dizziness, vomiting, seizure, altered sensorium and encepalopathy) along with fever. The diagnosis of active brucellosis was confirmed by raised brucella agglutination titre of 1:320 or more in the serum and confirmation of neurobrucellosis was done by raised brucella agglutination titre of 1:640 or more in the cerebrospinal fluid.

Results: This study included 11 children out of 68 having active brucellosis. The median age was 5 years. Median duration of fever was 15 days. Fever with seizures was the most common presentation (100%). Other associated neurological manifestations included irritability (88.9%), headache (77.8%), neck rigidity (77.8%), vomiting (66.7%), upper motor neuron signs (44.4%) and impaired consciousness (33.3%) with median GCS scale 9 (range 2-15). Hepatosplenomegaly and joint pain were found in 88.9% and 33.3% children respectively. CSF lymphocytosis was observed in seven (77.8%) cases. CSF Culture and staining was negative in all the cases. The response to treatment started within 10-15 days and all the children became symptom-free at the end of six weeks.

Conclusions: Neurobrucellosis is an uncommon but serious manifestation affecting central and peripheral nervous system. Treatment combination of cotrimoxazole, rifampicin and doxycyclin showed marked clinical and radiological improvement. All children were completely disease-free at the end of one year follow up.

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CASPASE 3/7 ACTIVITIES MEASUREMENT OVER A RANGE OF CYAA TOXINS CONCENTRATIONS ON DIFFERENT CELLS

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Introduction: Adenylate cyclase toxin (CyaA) toxin is an important virulence factor of Bordetella pertussis, the causative agent of whooping cough, and a potential component of acellular pertussis vaccine.

Materials and methods: The work involved the production of three purified forms of CyaA with different enzymic and invasive properties. These were: the native enzymatically-active, invasive toxin (CyaA), an invasive derivative lacking AC enzymic activity (CyaA*) and a non-acylated, non-invasive form of CyaA (proCyaA). These were expressed in E. coli BL21/DE3 as recombinant proteins. After purification by a combination of chromatographic methods (Q-and Butyl-Sepharose) their properties were investigated by several assays.

Results: The AC enzymic activity was assayed by a conductimetric method. CyaA and pro-CyaA had a high level of enzymic activity but that of CyaA* was very low. Caspase 3/7 activities were measured over a range of toxin concentrations. At these concentrations, neither urea buffer alone nor CyaA* induced any significant increase in caspase 3/7 from different mammalian cells. The greatest effect of CyaA was observed on J774.2 and RBL-2H3 cells where increasing concentration of toxin gave increasing activity.

Coclusions: regard to the results of this the study showed that both enzymatic and invasive functions are required for the cytotoxic effects of adenylate cyclase toxin.

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AETIOLOGICAL DIAGNOSIS OF BLOODSTREAM INFECTIONS THROUGH A MULTIPLEX REAL-TIME POLYMERASE CHAIN REACTION TEST IN PAEDIATRIC AGE: PRELIMINARY RESULTS

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Background and aims: Outcome of bloodstream infections (BSIs) is strongly related to microbiological diagnosis. Molecular methods may be useful in children as they can speed up pathogen identification and require smaller blood amounts than blood cultures (BC).

Methods: Medical records of patients who underwent a multiplex real-time Polymerase Chain Reaction (PCR) test (Septifast test - SF - Roche Diagnostics) in the tertiary Regina Margherita Children's Hospital (Turin, Italy) from September 2009 to September 2011 were retrospectively revised. Results of SF were compared with BC (automated Bact/Alert 3D, BioMérieux) closely collected.

Results: 307 SF were collected from 166 patients: 112 males, median age 9.11 years (range 0-26.8). 109 had immunodeficiency and 16 were newborns. Clinical and laboratory data led to a BSI diagnosis in 174 cases (57%). At the time of sampling, all patients were receiving empirical chemotherapy. SF resulted positive in 34 cases, 3 interpreted as contaminants. Aetiological definition was achieved simultaneously by SF and BC in 17 cases: 15 were monomicrobial and 2 polymicrobial infections. BC failed microbiological identification in 11 cases (with SF identifying more than one pathogen in 2), and was not performed in 3. Conversely, BC alone resulted positive in 18 septic episodes, although 3 isolates were not included in the SF master list (Fusarium, Ralstonia mannitolytica, Sphingomonas paucimobilis). A 31% increasing of bacteria identification chances due to SF was documented.

Conclusions: PCR methods can't replace BC, but they are a valuable adjunctive diagnostic tool for aetiological BSIs definition, especially in children receiving empirical chemotherapy.

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THE CHALLENGE: PCT VS CRP PREDICTING INVASIVE BACTERIAL INFECTIONS IN YOUNG FEBRILE INFANTS

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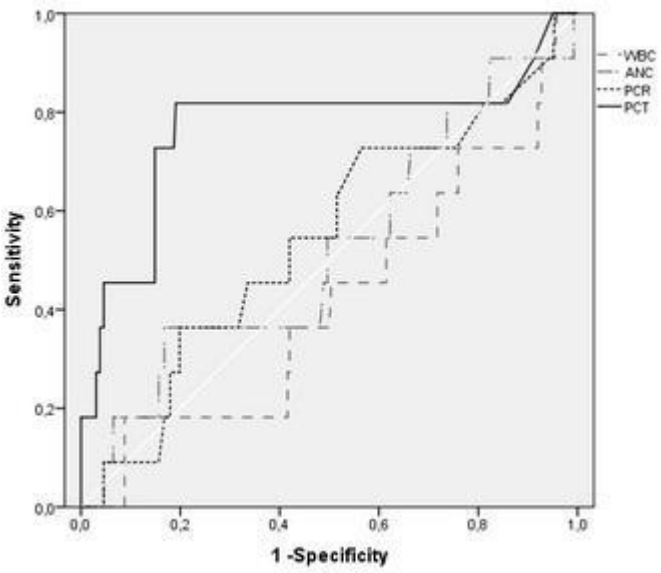
Fever without source (FWS) is one of the most common presenting complaints to pediatric ED. The aim of this study was to determine the accuracy of C-reactive protein (CRP) and procalcitonin (PCT) to rule out invasive bacterial infections (IBI) in these children.

We conducted a retrospective study among children < 90 days of age with FWS admitted to our ED during July/2008-January/2012 with at least one blood culture and RCP/PCT determination. IBI was defined as the isolation of a bacterial pathogen from the blood or cerebrospinal fluid (CSF).

During the study period 454 children were evaluated and 176 did not met inclusion criteria. Potentially severe bacterial infection was documented in 75 patients (27%): 64 UTI and 11 bacteremias (2 Pneumococcus, 5 GBS, 2 E.faecalis, 1 S.mitis and 1 E.coli).

PCT showed larger area in the ROC curves (0,767 (0.573-096)) than CRP (0,544 (0.36-0.72)) to detect IBI.



[ROC FWS]

Positive likelihood ratios for PCT (>0.5 ng/ml) and CRP (>3 mg/dl) were 4.8 (95% CI: 3-7.7) and 1,1 (95% CI: 0.27-3.36), respectively. Negative likelihood ratios for PCT and CRP were 0.32 (95% CI: 0.12-0.84) and 0.97 (95% CI: 0.76-1.3) respectively. Clinical appearance presented higher positive LR and lower negative LR than CRP in IBI detection.

Conclusions: PCT is a better marker than CRP for identifying children with IBI. CRP showed low sensitivity in young febrile infants. We should not underestimate other markers as clinical appearance in children with FWS.

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MOLECULAR SURVEILLANCE OF ROTAVIRUS INFECTIONS IN FRENCH INFANTS: TOWARDS THE EMERGENCE OF G12P[8] EPIDEMIC STRAINS?

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Background and aims: Rotaviruses are the major cause of acute gastroenteritis in young children worldwide, and require careful surveillance, especially in the context of vaccination programs (current vaccination coverage is under 10% in France) to characterize circulating rotaviruses and detect the emergence of potentially epidemic strains.

Methods: From 2005 to 2012, stool samples were collected from 5080 children under 5 years old with acute diarrhea admitted to the pediatric emergency units of 15 French large public hospitals. Rotaviruses were detected, then genotyped by RT-PCR for G (VP7) and P (VP4) types.

Results: The genotyping of 4643 rotaviruses showed that G1P[8] strains (62.1% [53.0-75.0]) were predominant, G9P[8] (17.0% [7.3-25.1]) still had a high circulation although declining, G2P[4] (7.9% [0.9-17.9]) were very variable, and G3P[8] (5.1% [1.7-15.1]) and G4P[8] (2.8% [0.9-5.6]) were mostly circulating locally. G12P[8] were progressively increasing over time from 0.4% to 3.3% in the last season. Most strains were associated with P[8] (87.5% [76.3-94.1]). Overall, 96 uncommon strains or possible zoonotic reassortants (2.1% [0.7-4.5]) were also detected such as G8 and P[6] strains.

Conclusions: The relative stability of rotavirus genotypes may ensure vaccine effectiveness in the short and medium terms in France. But, the recent increase in G12P[8] strains circulation might prefigure their emergence during the next seasons. Finally, the unusual strains should be monitored during ongoing and future vaccination programs, especially as all genotypes can cause severe infections. Special attention should be paid to the emergence of new rotavirus reassortants not included in current rotavirus vaccines.

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EXTERNAL VALIDATION OF THE REFINED LAB-SCORE, FOR IDENTIFICATION OF SEVERE BACTERIAL INFECTION IN FEBRILE CHILDREN UNDER THREE MONTHS

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Background: The identification of severe bacterial infection (SBI) in children with fever without source (FWS) remains a diagnostic problem. A risk index score, the Lab-score, associating CRP, procalcitonin and urinary dipstick (UD) to predict SBI was derived and recently refined and re-validated, providing a 94% [90-100] sensitivity and 70% [66-74] specificity. We aimed to validate it on the particular and problematic population of children ≤3-months of age.

Methods: Data from multicentre cohort study of children with FWS. The refined Lab-Score was calculated for each children.

Results: 1098 children (28% SBI) were included. The refined Lab-Score yielded a 0.86 [0.82-0.89] AUC ROC, significantly higher than the one of all biomarkers (CRP, Procalcitonin, neutrophil count - $p < 0.0001$), as well as the Lab-Score one ($p=0.0007$). According to a decision curve analysis, the refined Lab-Score performed better than biomarkers and the original Lab-Score in children ≤3-months of age, for all thresholds. The cut-offs previously chosen offered 77% [72-82] sensitivity, with 87% [84-89] specificity. The second threshold identified led to 67% [62-72] sensitivity, and 92% [90-94] specificity. Both sensitivities were lower than the original ones (98% and 94% respectively); however specificities were higher (53% and 70% respectively). A new threshold yielded a 80% [75-84] sensitivity, with 81% [78-84] specificity.

Conclusion: The refined Lab-score demonstrated higher specificities in children ≤3-months of age, but with decreased sensitivities. This could be problematic given that clinicians would not accept to misdiagnose SBI in this particular population of infants, and specific thresholds for this age were warranted.

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THREE-WAY COMPARISON OF THE PERFORMANCE OF THE TUBERCULOSIS SKIN TEST AND INTERFERON-GAMMA ASSAYS FOR DETECTING TUBERCULOSIS INFECTION AMONG CHILDREN

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Background and aims: Limited evidence exists regarding the comparative performance of interferon gamma release assays (IGRAs) for detecting TB infection in children. We compared the performance of the tuberculosis skin test (TST) with the QuantiFERON-TB Gold-In-Tube (QFT-IT) and TSPOT-TB assays for detecting TB infection in children.

Methods: A cross-sectional study was conducted among 153 children evaluated for active TB disease (n=63) and for latent tuberculosis infection (LTBI; n=90) (mean age±SD:7.8±4.7 years). Participants were assessed with the TST, QFT-IT and TSPOT-TB concomitantly. Comparisons of tests were evaluated with the kappa statistic.

Results: Among children with active TB disease, TST was positive in 95.2% (n=60), while QFT-IT and TSPOT-TB were positive in 84.1% (n=53) and 74.6% (n=47), respectively. The concordance between tests was highest between TST and QFT-IT (82.5%) and lowest between TST and TSPOT-TB (73.0%). Moreover, the concordance between QFT-IT and TSPOT-TB was 77.8% (κ=0.33). In contrast, in children evaluated for LTBI, TST was positive in 64.4% (n=58) while QFT-IT and TSPOT-TB were positive among 51.1% (n=46) and 45.6% (n=41), respectively. In this group the agreement between QFT-IT and TSPOT-TB was good (κ=0.62; concordance:81.1%), while it was limited to moderate between TST and TSPOT-TB (κ=0.50; concordance:74.4%).

Conclusions: A lower proportion of positive results were obtained with IGRAs as compared to TST in children with either active TB or LTBI. Agreement between the TST and QFT-IT exceeds that with TSPOT-TB among children with active TB disease. In contrast, good agreement between the QFT-IT and TSPOT-TB was observed among children with LTBI.

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CAN ABNORMAL IMAGING FINDINGS IN CHILDREN AFTER FIRST URINARY TRACT INFECTION (UTI) PREDICT RECURRENCE OF UTI? A 4-YEAR FOLLOW-UP

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Background/aim: The aim of this study was to examine the association of imaging findings after the first episode of UTI with the risk of recurrent UTI.

Methods: We retrospectively examined the imaging findings regarding ultrasound(US), voiding cystourethrography (VCUG) and DMSA of 357 children who admitted at 'Aghia Sophia' Children's hospital with a first episode of UTI during 2008. A four-year follow-up took place for 259 children and analysis regarding risks for recurrent UTI was performed.

Results: Positive findings in US, VCUG and DMSA were found in 32/320 (10%), 93/330 (30.8%) and 18/163 (11%) respectively. In 152 children who had undergone all 3 exams, US was abnormal in 18 (11.8%), VCUG in 63 (41.2%) and DMSA in 15 (9.9%). 52/152 children were detected with severe Vesicoureteral reflux (VUR) (grade III-V) and 10 of them had abnormal US (positive predictive value (PPV) (55.6%). Of 15/152 children with renal scarring, 1 had abnormal ultrasound (PPV:5.6%) and 8 had VUR in VCUG (PPV:12.7%). Recurrent UTI during follow-up had 45/259 (17.4%) and 23 (51%) experienced it in the first 12 months. Abnormal US, renal scarring, VUR and chemoprophylaxis after first UTI episode were not associated with risk of recurrence ($p>0.05$).

In line with recent guidelines, if VCUG had not been performed to children with normal ultrasound, in 63/74 (85.1%) VUR would have not been detected and 11/63 (17.4%) children had recurrent UTI.

Conclusion: Data of our study indicate that neither initial radiographic findings nor chemoprophylaxis can be associated with the risk for UTI recurrence.

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CONTRIBUTION OF (1-3)-B-D-GLUCAN TO THE DIAGNOSIS OF INVASIVE CANDIDA INFECTION IN NEONATE

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Introduction: Candida species are the third most common cause of late onset sepsis in patients hospitalized in Neonatal Intensive Care Unit. The incidence is 3 % in premature infant < 1500g. The diagnosis of neonatal invasive Candida infections (ICIs) is difficult because the clinical signs are not specific and sensibility of blood cultures is less than 40 %.

Objective: To assess the contribution of serum (1-3)-ß-D-glucan (BDG) levels to the diagnosis of neonatal ICIs.

Methods: This retrospective study was performed at Amiens University Medical Center (Amiens, France) during the period December 2010 - March 2012.

Newborns in whom a BDG assay was performed for a suspected ICI are included in our study. Two groups of patients were constituted: the infected group (n = 18) and the non-infected group (n = 43).

Results: Sixty-one premature infants were included. Patients were (median (25^{th}-75^{th} p)) 28.5 weeks (26.7-30.6) gestational age and 1000 g (910-1440) birth weight.

The BDG level was higher in the infected group (364 pg/ml (131-976) vs. 89 pg/ml (30-127); $p < 0.001$).

The optimal BDG cut-off for distinguishing between non-infected and infected patients was 125 pg/ml (Se = 84%, Sp = 75%).

Conclusion: Our study results suggest that BDG levels were increased in neonatal invasive Candida infections (cut-off for BDG positivity > 125 pg/ml).

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THE ANALYSIS OF VANCOMYCIN SERUM TROUGH CONCENTRATION IN NEONATES AND INFANTS

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Background: Vancomycin (VCM) serum trough concentrations of 15-20 mg/L were recommended to improve clinical outcome for Staphylococcus aureus complicated infections by practice guidelines from Infectious Diseases Society of America. In newborn and infant patients, however it is unclear whether the current VCM dosages are enough to achieve this target concentration.

Methods: We analyzed the correlation of VCM dosages and trough concentrations , and the ratio of achievement for target trough in NICU of Juntendo University Hospital, Japan. Medical records of neonate and infant inpatients with VCM treatment were investigated from January 2010 to October 2012. Cases such as insufficient for duration of the treatment before the monitoring, changed dosage, and serum creatinine levels were > 0.5 mg/dL were excluded. Current dosages were based on Nelson Textbook, Red book and Sanford Guide (Neonates, 20-30 mg/kg/day; Infants with mild to moderate and severe infection, 30-40 and 60 mg/kg/day).

Results: Subjects were 69 patients, twenty of whom were excluded. Trough concentrations were 13.2 ± 3.5, 7.9 ± 4.2 and 9.1 ± 4.7 mg/L, for neonates, mild to moderate and severe infants. The ratios of achievement for trough concentrations 10-15 mg/L were 83.3%, 29.2% and 55%, and for 15-20 mg/L were 33.3%, 4.1% and 0%. In addition, trough concentrations correlated negatively with postnatal age and weight in neonates with dosages 20-30 mg/kg/day.

Conclusions: It was difficult for neonates and infants to achieve the target trough concentrations by current initial dosages. Further research is required to confirm the appropriate VCM dosing regimen.

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VENTRICULOPERITONEAL SHUNT INFECTION AND TREATMENT IN PEDIATRIC PATIENTS WITH HYDROCEPHALUS: SINGLE CENTER EXPERIENCE

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Infection remains the most significant complication of ventriculoperitoneal (VP) shunt surgery and the reported rates of VP shunt infection vary widely across studies in patients with hydrocephalus. The objective of this study is to review and evaluate the infections complicating VP shunt surgery in pediatric patients with hydrocephalus.

Children who underwent VP shunt surgery for hydrocephalus between 2010 and 2012 were evaluated. Medical charts and clinical follow-up evaluations were reviewed and analyzed retrospectively. Between 2011 and 2012, 36 patient who were between 3 days of age and 16 years old have followed with VP shunt infections. Among them 24 boy and 12 girl. The most frequent indications for VP shunt surgery were conjenital malformations-myelomeningocele, tumor and intraventriculer hemorrhage. Among 36 patients bacteria grew in CSF culture of 19 patients and others were consistent for cerebrospinal fluid (CSF) inflamation. The most common growing bacteria was coagulase negative staphylococcus (%78). The other microorganism grew in culture were Staphylococcus aureus, Enterococcus faecalis, Enterococcus gallinarium, Pseudomonas stutzeri, Candida albicans, Streptococcus mitis, and ESBL (-) Klebsiella pneumonia. Among 36 patients VP shunt were removed and external ventriculer drainage was replaced in 24 patients and in 12 patients VP shunt were not removed. The mean duration of treatment was 14.7 days (range:4-56 days). Only one patient died during the treatment and others were fully recovered with treatment. In a case of a shunt infection the timely usage of appropriate antibiotics and removal of the shunt appear to be essantial for successful treatment of VP shunt infections.

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THE USE OF INTRAVENOUS COLISTIN AMONG CHILDREN: SINGLE CENTER EXPERIENCE

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Multidrug-resistant (MDR) gram-negative infections recently increasing thus leads to usage of colistin. Although it is well described in adults, tocixities of colistin in children are not well known. We report findings of pediatric intravenous colistin usage. We evaluated 28 children prescribed intravenous colistin. The mean age of children was 5.5 years (range: 4 days to 17 years). The most commonly targeted organisms were MDR Acinetobacter baumanii (82%) and MDR Pseudomonas (18%). MDR Acinetobacter baumanii growth were detected in blood culture in 15 patients, urine culture in one patient, wound culture in one patient, and endotreacheal aspiration fluid culture in one patient, respectively. MDR Pseudomonas growth were detected in respiratuar cultures in 4 patients, and blood cultures in one patient. The median duration of intravenous colistin therapy was 11 days. Additional antimicrobial therapy was given to all children, the most common given concomitant antibiotics were carbapenems in 13 children, sulbactam-ampicilin in 5 children, ciprofloxacin in 4 children and aminoglycosides in 3 children. During the intravenous colistin therapy one patients died due to infection. None of the children developed nephrotoxicity. This study showed that effectiveness and safety of intravenous colistin therapy in MDR gram-negative infections in children. Moreover, we found that nephrotoxicity in children may not be as high as described in adults.

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IMMUNOMODULATORS TO TREAT ATOPIC DERMATITIS AND VACCINATION: REVIEW

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Background and aims: Immunomodulators creams used to treatment of atopic dermatitis, inhibit the synthesis and release of inflammatory cytokines. Our interest is to evaluate its action on the vaccine response.

Methods: Literature review of period 2003-2013 using the keywords “vaccine” and “tacrolimus” or “pimecrolimus” in databases: CINAHL, CUIDEN, DOCUMED, EMBASE, ERIC, IBECS, IME, LILACS, MEDLINE, OvidMD, PubMed, SciELO.

Results: We found three published clinical trials:

· A 7-month, multicentre, randomised, controlled trial[i] investigated the equivalence of response to vaccination against meningococcal serogroup C disease in children (2-11 years) with moderate to severe atopic dermatitis, by applying either 0.03% tacrolimus ointment (N=21) or a hydrocortisone ointment (N=111), versus control group (N=44) non-atopic dermatitis children.

· In a open-label, noncomparative study[ii], 23 children aged 2 to 12 years with moderate to severe atopic dermatitis were treated with tacrolimus 0.03% ointment for 7 weeks, immunized with a pneumococcal polysaccharide vaccine, and had their antibody response measured before and 4 weeks after vaccination.

· A 2-years prospective study[iii] investigated whether treatment with pimecrolimus cream 1% in 91 infants with mild to severe atopic dermatitis (aged 3 to 23 months), affects the development of a normal antibody response to vaccinations againts tetanus, diphtheria, measles, and rubella.

Conclusions: Topical application of tacrolimus 0.03% ointment doesn't affect response to vaccination against neither meningococcal serogroup C nor pneumococcal.

Treatment of atopic dermatitis with pimecrolimus cream 1% in early childhood doesn't appear to interfere with the development of a normal immune response to vaccinations.

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THE NEONATAL AND PAEDIATRIC ANTIMICROBIAL POINT PREVALENCE SURVEY: ANTIMICROBIAL USAGE IN LATVIAN HOSPITALS IN 2012

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Background and aims: The Point Prevalence Survey (PPS) was conducted as part of the Antibiotic Resistance and Prescribing in European Children (ARPEC) Project. The study aimed at analyzing paediatric and neonatal antimicrobial prescribing patterns in Latvian hospitals, to identify targets for quality improvement.

Methods: A one-day PPS on antibiotic use in hospitalised children was conducted in November 2012 in 10 Latvian hospitals, using a validated and standard method. The survey included all inpatient paediatric and neonatal beds and identified all children receiving an antimicrobial treatment on the day of survey.

Results: There were 448 paediatric and 101 neonatal (< 29 days) inpatients reported. 169 (38%) paediatric patients and 23 (23%) neonates received at least one antibiotic. Overall, 8 antibiotics accounted for 75% of total paediatric use (DU75%). Paediatric top one antimicrobial was ceftriaxone (20% prescriptions). Top three classes were third-generation cephalosporins (27% prescriptions), broad-spectrum penicillins (15%), first generation cephalosporins (13%). Antibiotics were most predominantly used intravenously (78% of 207 prescriptions). Bacterial lower respiratory tract infections (LRTI) were the most common indication for antibiotic use (23% of all prescriptions). Neonatal DU75% included 5 antibiotics; top one antibiotic - benzylpenicillin (33% of 36 prescriptions). Top three classes were beta-lactamase sensitive penicillins (33%), aminoglycosides (25%), broad-spectrum penicillins (14%). LRTI were the most common indication for antibiotic use (39% of all 36 prescriptions).

Conclusion: We identified three problem areas for improvement: high use of third-generation cephalosporins for paediatric patients, prescription of antibiotic combinations with broad-spectrum antibiotics for neonates and predominant use of parenteral antibiotics.

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IS LINEZOLID AN EFFICIENT AND SAFE ALTERNATIVE TO VANCOMYCIN IN VERY PREMATURE INFANTS WITH LATE-ONSET INFECTION?

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Background: Glycopeptide is the usual probabilist treatment in coagulase-negative staphylococcus late-onset sepsis in premature infants, but provides renal toxicity. Linezolid is effective in gram-positive cocci infection, and devoid of renal side-effects. Its efficacy and safety in premature population is unknown.

Aim: To determine whether linezolid is a possible alternative to vancomycin in very premature infants with late-onset infection.

Methods: We conducted an observationnal retrospective study including infants born before 37 weeks of gestation (WG), hospitalized in neonatal intensive care unit from January 2008 to September 2010, treated by i) linezolid in continous infusion in case of renal failure or ii) twice a day oral treatment if intravenous access was no more available.

We assessed clinical and microbiological efficacy and safety of treatment.

Results: 35 treatments were studied among 33 infants aged 27.9 +/- 3.4 WG, treated during 7.6 +/- 3 days. Bacteria were isolated mainly from blood cultures (staphylococcus epidermidis, haemolyticus…). 8 children died (25%) in context of sepsis and renal failure. Clinical and biological efficacy were observed in 78% (18/23) and 79% (27/34) cases, respectively. No renal toxicity, no anemia, but 17% thrombocytopenia and 5.7% lactic acidosis were observed.

Conclusions: Whatever the global clinical efficacy observed in this newborn population, this study reports serious concerns about possible side effects like thrombocytopenia and lactic acidosis, even if imputability seems difficult to affirm in this septic context. This underlines the need for controlled randomized studies before using linezolid safely in this high-risk population.

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MULTIDRUG RESISTANT BACTERIA IN A TERTIARY CARE CHILDREN'S UNIVERSITY HOSPITAL

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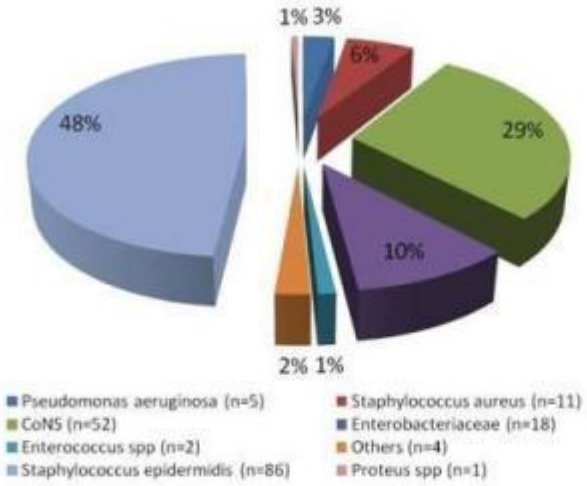
Background and aim: To describe frequency and pattern of multidrug resistant (MDR) pathogens in a tertiary care children's hospital.

Methods: All bacterial isolates of children admitted from January 1st, 2006 to December 31st, 2007 and from January 1st, 2011 to December 31st, 2011 were collected. Clinical records were retrospectively reviewed to identify children's characteristics.

Results: 1028 bacterial isolates were collected from 523 children [median age: 18.6 (2.3-88.1) months]. On the whole, 41.9% of isolates were MDR, with no significant difference during the 3-year observations. The incidence of MDR bacteria was 3.9/1,000 patient-days. On the whole MDR bacteria, 41.5% were isolated from blood (table 1), 25.3% from respiratory specimens (table 2), 24.6 from pus and wound samples (table 3) and 8.6% from invasive device. The wards with higher incidence were Neonatal Intensive Care Unit (24.8%), Intensive Care Unit (21.8%) and Haematology/Oncology ward (16.7%). 70.3% of infections caused by MDR bacteria were healthcare-associated. Antimicrobial resistance for sentinel pathogen were: Extended-spectrum β-lactamase Enterobacteriaceae: 20.9%, Vancomycin-resistant Enterococci: 9.8%, Methicillin-resistant Staphylococcus aureus: 19.9%, Carbapenem-resistant Enterobacteriaceae: 1.1%, Carbapenem-resistant Pseudomonas aeruginosa: 28.4%.

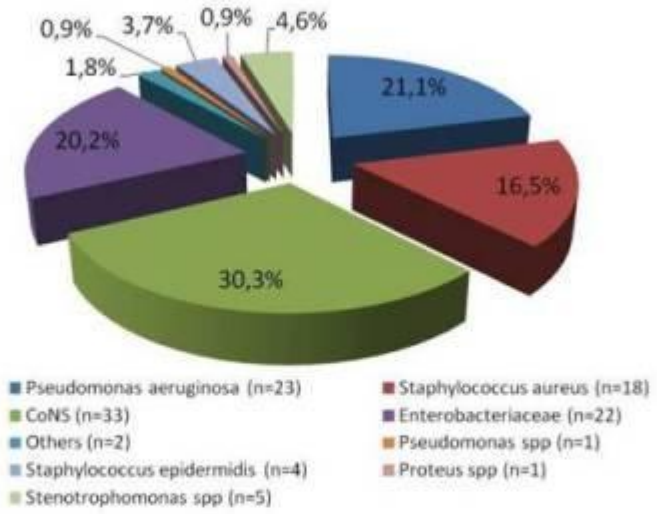
Conclusion: The high diffusion of MDR bacteria in a tertiary care children's university hospital and their elevated association to healthcare practice suggests the need of more attention in antimicrobial drugs use and preventive strategies.

Table 1: Distribution of MDR bacteria from blood (n=179)



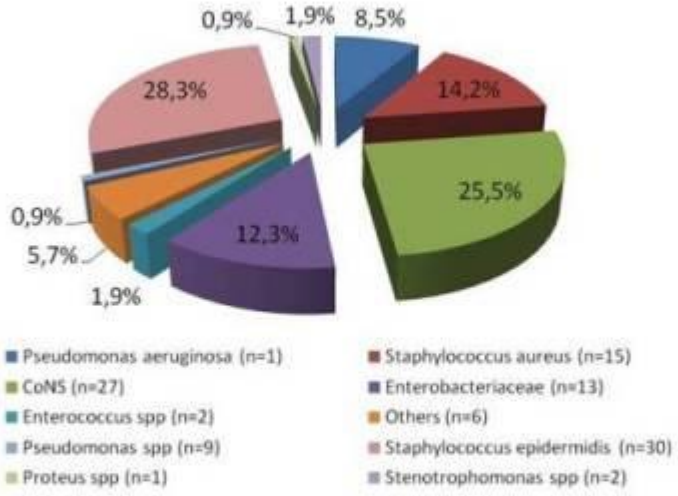
[Table 1]

Table 2: Distribution of MDR bacteria from respiratory specimens (n=109)



[Table 2]

Table 3: Distribution of MDR bacteria from pus and wound samples (n=106)



[Table 3]

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RISK FACTORS IN CHILDREN WITH MULTIDRUG RESISTANT BACTERIA INFECTIONS IN A THIRD CARE UNIVERSITY ITALIAN HOSPITAL

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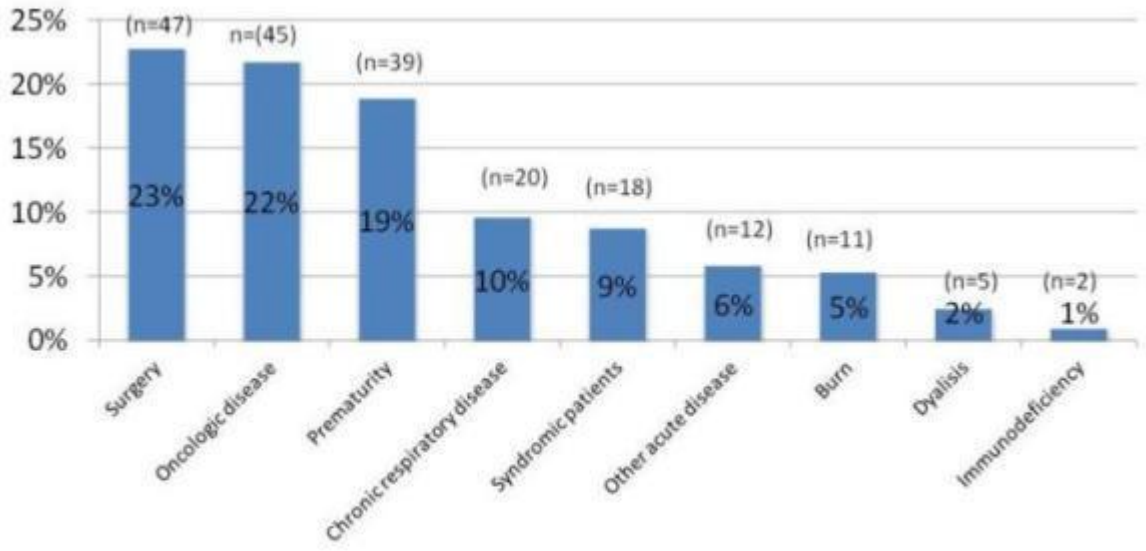
Background and aim: Multidrug resistance (MDR) is the most actual emergency among hospitalized patients, especially in children. Compared to adults, children have different risk factors linked with MDR, but studies focused on this topic haven't been published yet. Our aim was to identify the most frequent risk factors in hospitalized children with MDR bacterial infections.

Methods: All bacterial isolates of children admitted from January 1st, 2006 to December 31st, 2007 and from January 1st, 2011 to December 31st, 2011 were collected. Clinical records were retrospectively reviewed to identify children's characteristics. Multidrug-resistant bacteria were identified with the more recent CDC and ECDC definitions.

Results: 1028 bacterial isolates were collected from 523 children [median age: 18.6 (2.3-88.1) months]. On the whole, 41.9% of isolates were MDR, with no significant difference during the 3-year observations. The 88.3% of all the hospitalized children with MDR infection presented at least one risk factor, and the most common found were recent surgery (22.8%), oncologic disease (21.8%) and prematurity (18.9%) (Table 1). The 67.9% had at least one invasive device: the 77.1% of blood samples MDR positive were found in children with implanted CVC, and 75.2% of MDR isolated from bronchial aspirate were obtained in ventilated patients.

Conclusion: With the spread of MDR bacteria in hospitalized children, identification of main risk factors in pediatric patients is now becoming increasingly urgent.



[Risk factors in hospitalized children with MDR.]

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ANTIMICROBIAL TREATMENTS FOR ESBL PRODUCING-ENTEROBACTERIACEAE RELATED URINARY TRACT INFECTIONS: RESULTS OF A FRENCH NATIONAL SURVEY

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The emergence of ESBL producing-enterobacteriaceae (ESBL-PE) is an increasing problem.

Aim: to evaluate the medical practices in French institutions when an ESBL-PE related urinary tract infection (UTI) is identified.

Methods: A survey that should involve 26 paediatric hospitals has been performed. The last five cases of ESBL-PE/centre and the answers to two simulated clinical cases of ESBL-PE related non septic pyelonephritis (7 months-old girl without underlying diseases) and cystitis (30 months-old girl) should be collected.

Results: 83 cases of ESBL-PE related UTI (E. coli 90%, K. pneumoniae 8%) in 21 participating centres have been collected. Antimicrobial susceptibility was 100% for penems, 88% for amikacine, 52% for fluoroquinolone and 41% for trimethoprim. For acute pyelonephritis (n=53, mean age: 29 months, M/F sex ratio=0.33), ESBL adapted antibiotic treatment was intravenous in 81% of cases with 55% bi-therapy. Penems were used in 53% and aminosides in 36% of cases. For cystitis (n=26, mean age: 61 months, sex ratio=0.33), 22 were treated with antibiotics. An intravenous treatment was used in 3 (penems=2).

For the simulated clinical cases (85 answers), the pyelonephritis would have been treated with penems (76%) and/or aminosides (80%). A bi-therapy would have been used in 71% of cases. Intravenous antibiotic treatment would have been used in 29% of the cystitis case with 8% bitherapy including 16% penems and 11% aminoside prescriptions.

Conclusion: This survey highlights the heterogeneity of antimicrobial treatments in ESBL-PE related UTI and the overuse of penems. There is an urgent need of specific guidelines for ESBL related infections.

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SINGLE NUCLEOTIDE POLYMORPHISM OF IL-10 AND IL- 28B AS PREDICTORS TO THE RESPONSE OF INTERFERON THERAPY IN HCV INFECTED CHILDREN

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Background and aims: We aim to detect the relation between SNPs of IL-10 (-1082, -819, and -592) and IL28B gene (rs12979860) and prediction of response to Pegylated interferon (PegIFN) plus Ribavarin (RBV) in Egyptian pediatric subjects with genotype 4.

Methods: A RFLP-PCR and Real time PCR techniques were used to genotype 34 pediatric patients with HCV for IL-10 SNPs and IL-28B SNP respectively. Patients received (PegIFN) and (RBV) for 48 weeks subdivided according to their response to treatment into responders (20) and non-responders (14), and 20 healthy subjects.

Results: A significant difference ($p < 0.005$) was observed in IL-28B rs12979860 genotype frequencies between responders and non-responders. In responders CC genotype had greater frequency than CT and TT genotypes (60%, 30%, 10%) respectively with C allele in its wild genotype more likely to respond to treatment than in its mutant types. IL-10 at -819 showed significant difference in its genotype frequencies between responders and non-responders, TT genotype had greater frequency in responders than CT and CC (55%, 20%, 25%) respectively. Subjects with T allele (CT/TT) showed higher rates of response than those with no T allele (CC), its protective effect in both recessive and dominant forms.

Conclusion: Il-28B CC genotype as well as the IL-10 (-819) TT genotype are significantly associated with response to PegIFN and RBV for pediatric patients with HCV infection genotype 4. These SNPs can be used for predicting response to treatment before patient is prescribed to the expensive PegIFN-RBV therapy.

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ENGINEERED LACTOBACILLUS RHAMNOSUS GG CAPTURING ROTAVIRUS-SPECIFIC HYPERIMMUNE BOVINE COLOSTRUM ANTIBODIES PROTECT AGAINST DIARRHEA IN AN INFANT ROTAVIRUS INFECTION MODEL

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Background and aims: Rotavirus-induced diarrhea cause more than 500,000 deaths annually in the world and new effective treatment strategies should be considered due to the partial protection of current therapies in developing countries. Purified antibodies derived from hyperimmune bovine colostrum (HBC) of cow immunized with rotavirus were previously used for treatment of rotavirus diarrhea in children. A combination of HBC antibodies and the probiotic strain of Lactobacillus rhamnosus GG (LGG) was also found to be more effective than HBC alone in reducing diarrhea in a mouse model of rotavirus infection. In order to further improve the treatment, LGG was engineered to display IgG-binding domains of protein G which capture HBC-IgG antibodies and target rotavirus.

Methods: The expression of IgG-binding domains on the surface of LGG, their binding activity to HBC-IgG and to rotavirus (simian strain RRV) was assessed by western blot, flow cytometry and EM. The prophylactic activity of modified LGG and HBC was evaluated in the neonatal mouse model of RRV infection.

Results: Efficient binding of modified lactobacilli to HBC and rotavirus was observed. Compared to HBC alone or a combination of wild type LGG and HBC, a combination of LGG expressing IgG-binding domains and HBC was significantly more effective in reducing the prevalence, severity and duration of diarrhea.

Conclusions: The combination therapy with engineered LGG and HBC reduces the effective dose of HBC by nearly 100-fold and could decrease treatment costs considerably. This antibody capturing platform strategy could also be used to target other gastrointestinal pathogens.

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«HALO» PHENOMENON (PHENOMENON "STEFANIS") IN RELATION WITH ANTIMICROBIAL COPPER IMPLEMENTATION

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Aim: The aim of this study was to evaluate the antimicrobial action of copper alloys in the form of a 'circle' ("halo" phenomenon), resulting in a further reduction of microbial loads in non antimicrobial copper implemented multi-touch surfaces.

Method - Material: In a Neonatal Intensive Care Unit (NICU) with the capacity of 26 beds (boxes) of a pediatric hospital implemented with antimicrobial copper Cu^+ (Cu^+63% Zn - 37% low lead) and certified for the antimicrobial activity of objects and surfaces, samples and cultures were taken within 50cm distance from the Cu^+ implemented objects and surfaces, in order to measure the microbial flora. This process took place the period before, during and 2 months after Cu^+ implementation. Parameters such as Operational Protocols and staffing of the NICU during the research were not differenciated.

Results: The reduction of microbial load on multi-touch surfaces of Cu^+ was recorded at 90%, and at a distance of 50 cm from the Cu^+ implemented objects or surfaces the reduction of microbial loads (cfu / ml) was recorded at a rate of 70-75% ($N = 36$-$P < 0,05$). Microbial strains found were: Klebsiellaspp., Staph. Epidermidis, Staph. Aureus, Sphingomonaspaucimobilis.

Conclusions: The recorded 'radial action' of the Cu^+ alloys in a circular form ("halo" phenomenon) provides further confirmation of copper's antimicrobial ability. The «halo» phenomenon enables Cu^+ to reduce microbial flora and increase its beneficial effects on health sector and sets the bases for further comparative.

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METABOLIC ACTIVITY OF INTESTINAL MICROFLORA WHILE ANTIBACTERIAL THERAPY

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Background and aims: To evaluate the effect the antibiotic therapy on the metabolic activity of intestinal microflora depending on the use of probiotics.

Methods: 74 children receiving antibiotic therapy (ABT) were included into the study. Children were divided into 2 groups. The 1st group of 25 children received probiotic (B.bifidum, B. longum, L. casei) from the first day of ABT. Patients from the 2nd group (21 children) received ABT without probiotics. Metabolic activity of intestinal microflora wasevaluated based on the level of short chain fatty acids (SCFA) with gas-liquid chromatography analysis on the first and 21st days.

Results: At baseline, children from the 1st and 2nd groups showed increasing level of propionic acid (0,222±0,009 U and 0,219±0,009 U respectively) and butyrate (0,103±0,006 U and 0,108±0,007 U respectively), as well as decrease in acetic acid (0,675±0,011 U and 0,673±0,010 U respectively). Anaerobic index (AI) was changed to negative values (-0,481 ±0,014 U in the 1st and -0,486 ±0,015 U in the 2nd groups).

Three weeks later, a group of children who received probiotic from the first day of ABT showed a normal level of C2-C4 fatty acids due to the stabilization of microflora content and removing the negative impact of antibiotic therapy. In the 2nd group changes in SCFA worsened due to microflora disorders while antibiotic therapy.

Conclusion: SCFA levels in stool can be an objective marker of the state of intestinal microflora. Preventive use of probiotics to protect against activation of proteolytic microorganisms.

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THE ROLE OF IL-17 ON OCCURENCE OF PLASMA LEAKAGE IN DENGUE HAEMORRHAGIC FEVER THROUGH ACTIVATION OF PRO INFLAMATORY CTYTOKINE

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The role of IL-17 in virus infection has been evaluated, but there is no data its role in dengue hemorhagic fever. First aim was to evaluate the effect of shock in dengue hemorhagic fever into Th17 and IL-17 level. Second aim was to known the effect of IL-17 recombinant exposure on macrophage activation through expression of TNF-a, IL-8 and MMP-2. Third aim was to analysis an effect of activated macrophage by IL-17 on plasma leakage on human umbilical vascular endothelial cells (HUVECs) culture marked by albumin level.

Methode: Expression of Th17 was done by flow cytometry. Expression of IL-17 was done by ELISA. Expression of TNF-a, IL-8 and MMP-2 from activated macrophage exposed to IL-17 recombinant was evaluated by ELISA. Albumin level was evaulated by spectroscopy.

Results: There are significant increase on Th 17 and IL-17 in DHF with shock than without shock ($p< 0.000$). There is significant increase on TNF α between group in IL-17 recombinant exposure on macrophage at 16. 24 and 48 hour. There are significant different of MMP-2 between groups in IL-17 recombinant exposure macrophage 16. 24 and 48 hour. Post hoc test showed significant different of IL-8 between exposures 16. 24 and 48 hours; ($p< 0.000$), There is significant different of albumin level between 2. 4 and 8 ng/mml dose of IL-17 and time of exposure 48 hour ($p< 0.000$).

Conclusion: There is role of Th17 in pathomechanisms of plasma leakage in dengue hemorhagic fever via macrophag activation and secretion proinflammatory cytokine.

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THE CONTRIBUTION OF NON-CONVENTIONAL T CELLS AND NK CELLS IN THE MYCOBACTERIAL-SPECIFIC IFNΓ RESPONSE IN BCG IMMUNISED INDIVIDUALS

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Background: BCG vaccine is given to >120 million infants each year worldwide. The key components of a protective immune response against TB remain incompletely understood. The importance of γδ T cells and natural killer (NK) cells in the mycobacterial-specific immune response has recently been recognised.

Methods: Participants in four age-groups (birth, 2 months, 10-24 months and adults) were BCG-immunised. Ten weeks later, in vitro BCG-stimulated blood was analysed for NK and T cell markers (CD3, CD4, CD8, CD56, TCRγδ) and intracellular IFNγ by flow cytometry. Total functional IFNγ response was calculated using integrated mean fluorescence intensity (iMFI).

Results: In infants and children, $CD4^+CD8^-$ and $CD4^-CD8^-$ (double negative (DN)) were the main IFNγ-expressing cells. In adults, $CD4^-CD8^+$ cells were the main IFNγ-expressing cells, followed by $CD4^+CD8^-$ and DN T cells. The iMFI was higher in DN T cells compared to CD4 T cells in all age groups; most significant differences in infants immunised at birth ($p=0.002$) or 2 months of age ($p< 0.0001$). When NK cells were included for analysis, they accounted for the majority of total IFNγ-expressing cells and, together with γδ T cells, had the highest iMFI in infants immunised at birth or 2 months of age.

Conclusion: In addition to CD4 T cells, NK cells and DN T cells including γδ T cells are the key cell populations producing IFNγ in response to BCG in infants and children. This suggests that the innate immune response and unconventional T cells play an important role in protection against TB.

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WHOLE-BLOOD CYTOKINE RESPONSES TO QUANTIFERON PEPTIDES IN PEDIATRIC TUBERCULOSIS ACCORDING TO INFECTION STAGES AND SEVERITY

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Background and aims: The primary aim of this study was to explore cytokine/monokine responses to Mycobacterium tuberculosis (M.tb) peptides that would aid in diagnosing and staging M.tb infection. The secondary objective was identification of host immune responses to M.tb that help to contain the pathogen by comparing cytokine/monokine profiles in LTB versus non-severe Tuberculosis (TB) versus severe TB.

Methods: 15 cytokines/chemokines were quantified in a multiplexed microsphere-based assay following whole blood stimulation with M.tb antigens in 47 children (median age: 8 years). Cytokine/chemokine concentrations were compared in latent-TB infection (LTBI n=12) versus TB-disease (n=28) and in non-severe pulmonary TB (non-severe PTB, n=11) versus severe-TB (complicated PTB or disseminated TB n=17). Seven non-infected children were simultaneously analysed as controls.

Results: Beside IFNg, the most sensitive marker to diagnose M.tb infection was IP-10 with 560 pg/ml optimal sensitivity cut-off as determined by area under ROC curve (95% CI: 83%-99%). None of the 15 studied analytes could distinguish LTBI from TB disease. Finally, TB-disease severity was associated with moderately decreased M.tb antigen-induced Th1 cytokines (IL-12: p=0.09; IFNg: p=0.07) but with clearly defective Th2 cytokine levels (IL4: p=0.08; IL5: p=0.02; IL13: p=0.02). Also IL17, IL10 and MCP-1 levels appeared depressed in severe TB (p=0.08, 0.07 and 0.08 respectively).

Conclusion: This study confirms that IP-10 should aid in diagnosing M.tb infection though as the 14 other cytokines/monokines it did not allow TB staging. Severe TB-disease in children appears related to defective mixed cytokine responses but not to the presumed unbalanced Th1/Th2/regulatory cytokine network.

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COMPARISON OF INTERFERON-GAMMA RELEASE ASSAY (IGRA) AND TUBERCULIN SKIN TEST (TST) FOR DIAGNOSIS OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

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Background and aims: There is still no gold standard for diagnosis of tuberculosis. We compared IGRA (Quantiferon, QTF) with TST for diagnosis of tuberculosis in children/adolescents.

Methods: Records of children/adolescents of tuberculosis clinic for evaluation of latent/active tuberculosis from 2007 to 2012 were analyzed. The study population was tested with QTF and TST and divided in three groups based on final diagnosis: active tuberculous disease (TD), latent tuberculous infection (LTBI) and controls (CT). Mann-Whitney U test, $\chi 2$ test and kappa (κ) coefficient were used to analyze and compare QTF and TST results.

Results: 331 children/adolescents (161 male) were included with median age 7yrs (range 0.3-17); TD, LTBI and CT were recorded in 4.8%, 40.5% and 54.7%, respectively. QTF was positive in 117 (35.3%) and TST in 140 (42.3%) children. Eleven (8.2%) LTBI cases presented negative TST and positive QTF results. Overall, median IFN-gamma concentration achieved was 0.05IU/ml (range 0-79.3) with no significant difference between children (0-10yrs) and adolescents (>10yrs); in TD, median concentrations were 23.1IU/ml and 11.3IU/ml for ≤2yr-old and >2yr-old patients respectively (p=0.638). In LTBI, IFN-gamma values tended to be higher in children than adolescents (4.9 vs 0.8IU/ml, p=0.1). Median ages and IFN-gamma values but not TST sizes differed between LTBI and TD (7 vs 5.5yrs, p=0.003 and 4.5 vs 15.6IU/ml, p=0.001), respectively. TST and QTF results were concordant in 274 of cases (91%) (κ=0.639).

Conclusions: IFN-gamma values of QTF are higher in TD than LTBI and tend to be higher in younger age. QTF and TST show concordant results.

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POPULATION PHARMACOKINETICS AND DOSING OPTIMIZATION OF VANCOMYCIN IN CHILDREN WITH MALIGNANT HEMATOLOGICAL DISEASE

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Background: Vancomycin is widely used for the treatment of moderate to severe infections that are caused by vancomycin susceptible bacteria, and primarily coagulase-negative Staphylococci and methicillin-resistant Staphylococcus aureus species. Its systemic clearance was reported to be higher in adults with malignant hematological disease compared with non-oncology adults and an increased dosing regimen has been proposed in these patients. In the absence of data, an optimal dosing regimen is not available in children. The aim of this work was to evaluate the population pharmacokinetics of vancomycin in children with malignant hematological disease and to optimize vancomycin therapy.

Methods: Vancomycin therapeutic drug monitoring (TDM) concentrations were collected prospectively in children with malignant hematological diseases. Population pharmacokinetic analysis was performed to optimize dosing using NONMEM software.

Results: One hundred and two serum vancomycin concentrations from 70 children were analyzed. The concentrations ranged from 2.3 to 36.4 mg/L using empirical dosing regimen (40-60 mg/kg/d). A one-compartment pharmacokinetic model was developed. Body weight and creatinine clearance were identified as significant covariates. Vancomycin clearance was higher in children with malignant haematological disease than that in non-oncology children. Model-based optimized dosing was tested in simulated clinical trials, which achieved the adequate pharmacokinetic-pharmacodynamics breakpoint ($AUC_{0\text{-}24}$/MIC ratio).

Conclusion: An optimized dosing regimen, taking into account bodyweight, creatinine clearance and susceptibility of the pathogens involved, could be used in routine to individualize vancomycin therapy in children with malignant haematological disease. A prospective study is warranted to evaluate its potential clinical benefits and safety.

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THE INFLUENCE OF MATERNAL HIV AND MYCOBACTERIUM TUBERCULOSIS ON INFANT RESPONSES TO BCG VACCINATION

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Background and aims: Altered immune responses might contribute to the high morbidity and mortality observed amongst uninfected infants exposed to human immunodeficiency virus-1 (HIV) in utero. This study examined the influence of maternal HIV and Mycobacterium tuberculosis (Mtb) infection on infant immune responses to BCG immunisation.

Methods: 109 mother-infant pairs were enrolled from Khayelitsha, Cape Town, South Africa, and were followed for four months. Peripheral blood samples were collected from the mother-infant pairs at delivery and from the infant at 16 weeks of age. Responses to BCG antigens were measured using multi-parameter flow cytometry and multiplex enzyme-linked immunosorbent assays.

Results: At birth, HIV-exposed, uninfected infants had increased frequencies of BCG-specific proliferating T cells expressing TNF-α and increased levels of TNF-α protein in cell culture supernatants; levels were highest amongst HIV-exposed infants born to Mtb sensitised mothers. IFN-γ levels were lower amongst HIV-exposed, uninfected infants compared to unexposed infants. Maternal Mtb sensitisation was associated with increased infant IFN-γ levels; infants born to HIV-infected, Mtb sensitised mothers had similar levels compared to unexposed infants.

Following BCG vaccination at 6 weeks of age, the immune response to infant BCG vaccination was unaffected by maternal HIV infection or Mtb sensitisation.

Amongst mothers, Mtb sensitisation significantly influenced the response to BCG-antigens in HIV-infected, but not in HIV-uninfected mothers.

Conclusions: Antenatal HIV exposure was associated with some alteration in immune response to BCG antigens at birth, however HIV-exposed, uninfected infants had comparable potential to respond to BCG immunisation as HIV-unexposed infants.

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HIV1 VPR POLYMORPHYSMS ASSOCIATED WITH AA 77: A VIRUS HOTSPOT?

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Background: There are several HIV-1 Vpr polymorphisms that have been involved in biological functions of this viral protein that include replication and pathogenesis of virus, with direct influence in AIDS progression, namely in infants with perinatal acquired HIV-1 infection. The aim of this ongoing work was to study HIV1 Vpr polymorphisms at the position 77 in an HIV1-infected family, prompted by a clinical case of a perinatal-infected-5-year-old boy with repeated ear infections, but otherwise healthy.

Methods: Since July 2012, an HIV1-infected family (father, mother and son) has been studied in what regards HIV1vpr gene polymorphisms. The family members were clinically evaluated studying several clinical markers and other pathophysiological conditions.

Results: The analysis of HIV1 vpr sequences revealed two different mutations at the sequence that codes for amino acid position 77. Both parents were infected with virus carrying R77H mutation, while the child's-virus had R77Q variant. Both parents and child were considered asymptomatic, although the child had very high viral load (1,073,899 RNA copies/ml). Following therapeutic period to decrease the child's viral load, the child continues with no clinical signs of disease and interrupts therapy.

Conclusions: Our results show that different mutations associated with the aa 77 lead to non-progressive phenotypes. More, we identified a clinical case where the patient, a 5-year old child, remained with no visible signs of disease regardless of high viral load. With this study we aim to study Vpr not only as a bio-marker of disease progression, but also as an evolution flag of HIV1.

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CLINICAL FOLLOW-UP OF CHILDREN WITH VERTICALLY-ACQUIRED HIV/HCV CO-INFECTION IN SPAIN- A CROSS-SECTIONAL STUDY

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Background and aims: Little data exist regarding the clinical evolution of patients with HIV/HCV co-infection acquired by vertical transmission. This study aims to give further information on the current clinical situation of this patient group and alert about the liver damage.

Methods: A cross-sectional study was performed to describe vertically-acquired HIV/HCV co-infected children, included in Node 1 of the Spanish Paediatric HIV Cohort (CoRISpe-1). Data collected included the clinical state, diagnostic procedures and treatment.

Results: Information was obtained from 26 patients, of whom 19 are still being followed in pediatric units. The median age at the last visit was 16,5 years (IQR 14-19.25); 58% were female. All patients received HAART. The median CD4 count was 761 cel/mm3 (IQR 492-929), 76% had >500 cel/mm3 CD4 and 88% more than 25% of CD4. 69% have undetectable HIV viral load. HCV genotypes were: 46% genotype 1, 15% genotype 3 and 27% genotype 4 (11% unknown). 42% had increased ALT (> 40 U / L). 15% were seronegative for HCV antibodies. Liver biopsy was performed in 8 of 26 patients, 5 of whom had some degree of fibrosis. FibroScan was performed in 20 patients being abnormal in 40% (stiffness >7.6 kpa). One patient died of hepatic cirrhosis. 8 patients were treated for HCV infection (RBV+Peg-IFN); virological response was sustained in only 2 of them.

Conclusions: Whilst HIV infection in vertically-acquired HIV/HCV co-infected children appears to be well controlled, an important proportion of these patients suffer from progressive liver disease at adolescence or young adulthood.

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PREVENTING MOTHER TO CHILD TRANSMISSION OF HIV PAEDIATRIC AUDIT CYCLES BETWEEN 2004 - 2010

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Aim: This audit was undertaken firstly to look at the performance of a local regional Paediatric team over a 6 year period and secondly to estimate the impact of several service changes.

Methods: Three cycles of retrospective case note audit of all babies exposed to HIV and followed up in a large Regional Centre were performed using a near identical standard proforma.

Results:

	2004 - 2005	**2008**	**2010**
Number included	57	30	24
New Maternal Diagnosis	54%	26.7%	30%
Maternal VL < 40 copies/ml before delivery	75%	76.7%	89%
Baby's sample documented	49%	75%	96%
Care Plan filed?	26%	85%	100%
Transmission Rate *	1.7% (n=1)	0%	0%

[Audit Results]

*Two confirmed detectable DNA PCT at the age 6 weeks and 3 months

Discussion: In line with the data from NSHPC we have also seen a higher proportion of mothers diagnosed before conception and a decreasing delivery rate of babies exposed to HIV in 2010. It has been noted that most of the significant outcome measures have improved over the audit period. As the care of HIV in Pregnancy requires a multidisciplinary approach the improvements have to be attributed to the joint effort of the whole team involved. Some of the improved outcome measures are also related to the Paediatric service changes as shown in the selected outcome measures above.

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3-YEAR OBSERVATION OF MINERALIZATION DISORDERS AND VITAMIN D3 LEVELS IN VERTICALLY HIV-INFECTED CHILDREN

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Background and aims: To assess prevalence of densitometric disorders and vitamin D3 deficiency in HIV-infected children treated with antiretroviral therapy and to estimate efficiency of vitamin-calcium supplementation.

Methods: Threefold (0-1-2years) densitometric measurements with simultaneous vitamin D3 level evaluation were performed in 50 vertically HIV-infected children aged 4-16 years, receiving cART. All children with impaired DEXA results and those with lower range were given supplementation of calcium and vitamin D3 (31/50). Age at DEXA measurements, cART duration, level of vitamin D3 in group with impaired DEXA result, administered supplementation and its influence on DEXA result were recorded. Regardless of DEXA results, cART was not modified.

Results: 25/50 (50%) children presented impaired 1st DEXA result of lumbar spine, among which 13 had incorrect results in total spine. Vitamin D3 level was low in 19/25 (76%), of which 4 had extremely low level. Measurements performed after 1 year showed DEXA improvement in 3 children (with supplementation) and deterioration in 3 children with previously correct DEXA (without supplementation). Results after the next year showed that 7 children with primarily impaired results improved to have no abnormalities, none subject worsened previous result. Level of 25OHD3 increased in consecutive years. Children with and without supplementation presented improvement and stability, respectively.

Conclusions: Impaired results of densitometry and 25OHD3 level were observed in significant percentage of vertically HIV-infected children receiving cART. Introducing supplementation of vitamin D3 and calcium improves bone mineralization and increase vitamin D3 level.

EFFECT OF NUTRITIONAL STATUS ON CLINICAL SPECTRUM OF SEVERE MALARIA IN CHILDREN

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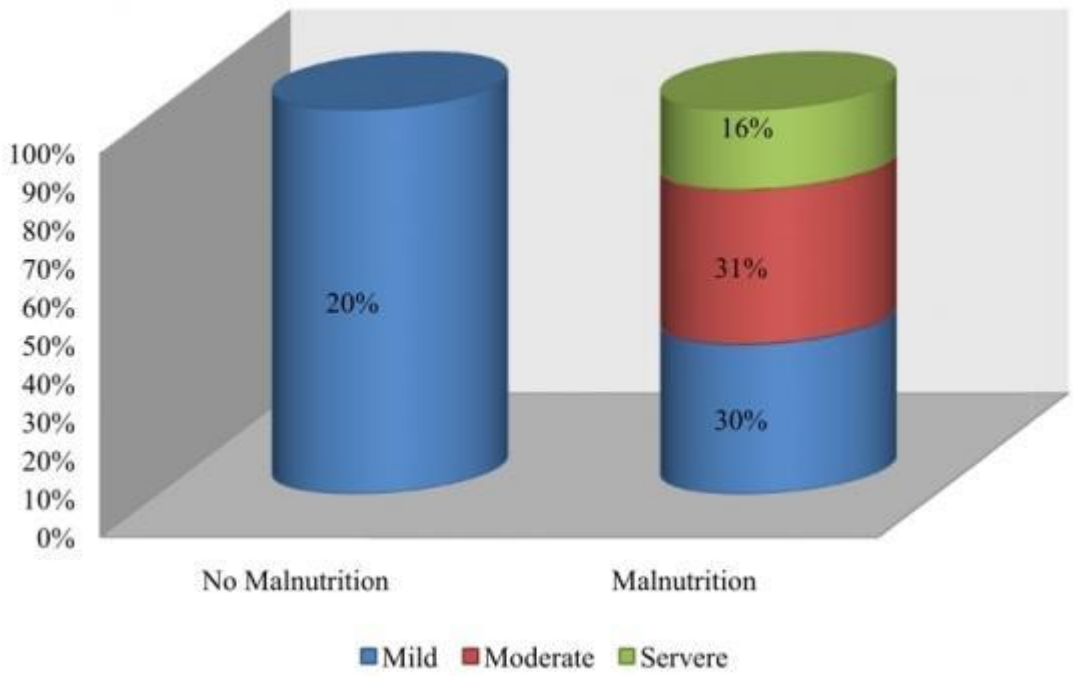
Background and aims: Malnutrition may play important role in various systemic complications observed in severe malaria. This clinico-observational study describes the effect of nutritional status on clinical spectrum of severe malaria in children.

Methods: This study was conducted on 95 admitted children with malaria in department of pediatrics, S.P.Medical College, Bikaner from January 2012 to December 2012. The species diagnosis was done by peripheral blood smear and rapid diagnostic test. Severe malaria was defined as per WHO criteria for Severe Malaria (2000). The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently. Children were grouped according to their nutritional status based on WHO/UNICEF classification.

Results: Majority of cases of severe malaria (80%) had malnutrition (figure 1).

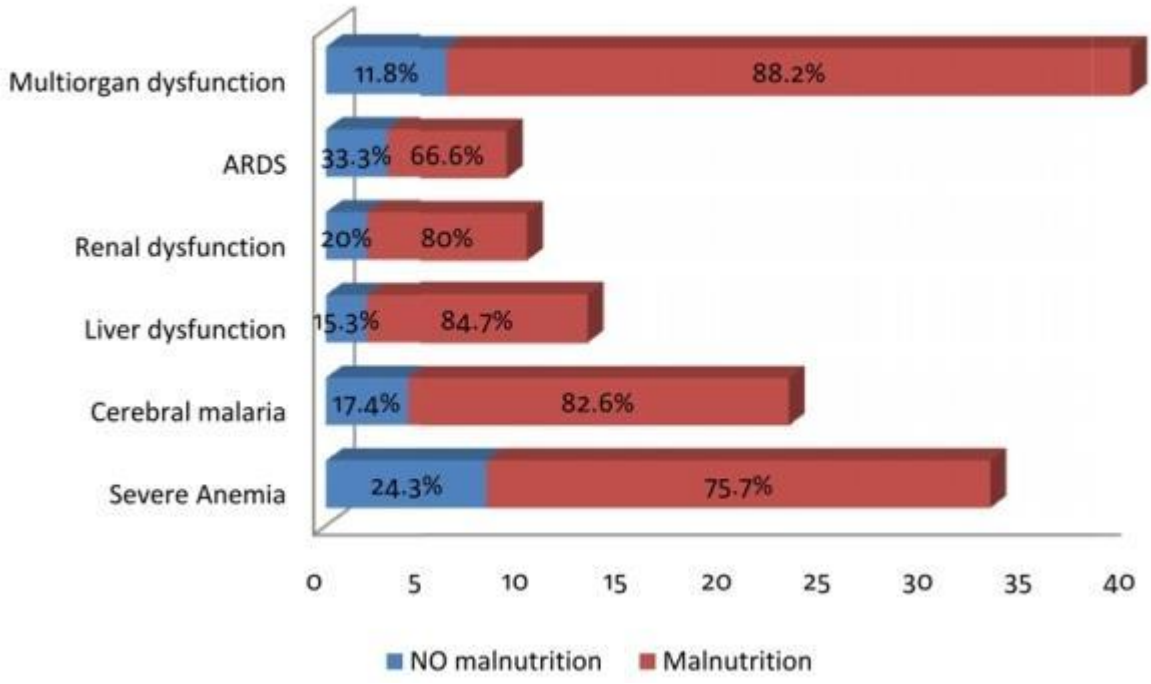
Figure 1: Incidence of severe malaria in association with nutritional status



[Figure 1: Incidence of severe malaria in associati]

Severe anemia (34.7%) was the most common severe manifestation followed by cerebral malaria (24.2%), hepatic dysfunction (13.6%), renal dysfunction (10.5%), acute respiratory distress syndrome (9%) and multiorgan dysfunction (42.1%) (figure 2).

Figure 2: Manifestations of severe malaria in association with malnutrition



[Figure 2 Manifestations of severe malaria in assoc]

Conclusions: This study affirms the association of malnutrition with severe malaria.

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POSITIVE PREDICTIVE VALUE OF THE ROTAVIRUS ICD-9 DISCHARGE CODE IN SPAIN

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Aims: To determine the positive predictive value (PPV) of the ICD-9-CM code for rotavirus disease in the Spanish hospital discharge database (CMBD) in order to estimate vaccine effectiveness.

Methods: Retrospective study conducted in Valencia, Spain. Children under 3 yoa born during 2007-12, admitted to public hospitals during January 2008-June 2012, with a discharge code of intestinal infection (001-009). We analysed the PPV of: rotavirus code (008.61) as first discharge diagnosis (A), as first/second diagnosis (B), as any diagnosis (C), or codes 001-009 (excluding 008.61) in first position with 008.61 as second (D).

PPVs using data from the regional laboratory database (RedMIVA) as gold standard were calculated using two definitions:

1) rotavirus test positive vs. negative; or

2) rotavirus test positive vs negative or untested.

Results: There were 4,295 hospitalized cases of intestinal infections, 1,877 (43.7%) were coded as rotavirus. Of all admissions, 3,046 (70.9%) were tested for rotavirus. Of the rotavirus gastroenteritis coded, 1,411 (75.2%) had a positive test result, and 59 (4.2%) had a negative result.

PPVs ranged between 95.9% and 46.5% (Table).

	1	2
A	95.9% (95%CI: 94.5-97.0)%	73.3% (95%CI: 70.8-75.6)%
B	95.9% (95%CI: 94.6-96.8)%	73.8% (95%CI: 71.6-75.9)%
C	96.0% (95%CI: 94.9-96.9)%	75.2% (95%CI: 73.2-77.1)%
D	95.2% (95%CI: 77.3-99.2)%	46.5% (95%CI: 32.5-61.1)%

[PPV]

Conclusion: The moderate-high positive predictive value of the rotavirus discharge code grants the use of CMBD database for analysis of rotavirus vaccine effectiveness and impact.

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INTESTINAL PARASITIC INFECTION AMONG PRE-SCHOOL CHILDREN

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Background: Intestinal parasites are common in children. The aim of the study was to determine the prevalence of intestinal parasites in pre-school children, brought to Pediatric Clinic in Prishtina with complaints of gastrointestinal symptoms.

Methods: Fecal samples were taken from 350 children and brought to National Institute of Public Health laboratory. Lugol solution was used during microscopic examination. Statistical significance was analyzed by using Chi-Square test.

Results: Intestinal parasitic infections were identified in 40 children (11.5%). In the total sample, the most frequent parasites found was Giardia lamblia 24 (60%). The second frequency was for Ascaris lumbricoides 15 (37.5%), and the third one for Enterobius vermicularis 1 (2.5%). There is no stastistical difference related to sex.

Conclusions: There is e low prevalence of intestinal parasitosis among pre-school children even though this study emphasizes the need for improved environmental hygiene and health education of the population.

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PREVENTION OF INFECTIONS ASSOCIATED WITH INTRAVENOUS CATHETERS IN VLBW-INFANTS: SURVEILLANCE OF SKIN DISINFECTION VIA PUNCTION SWABS

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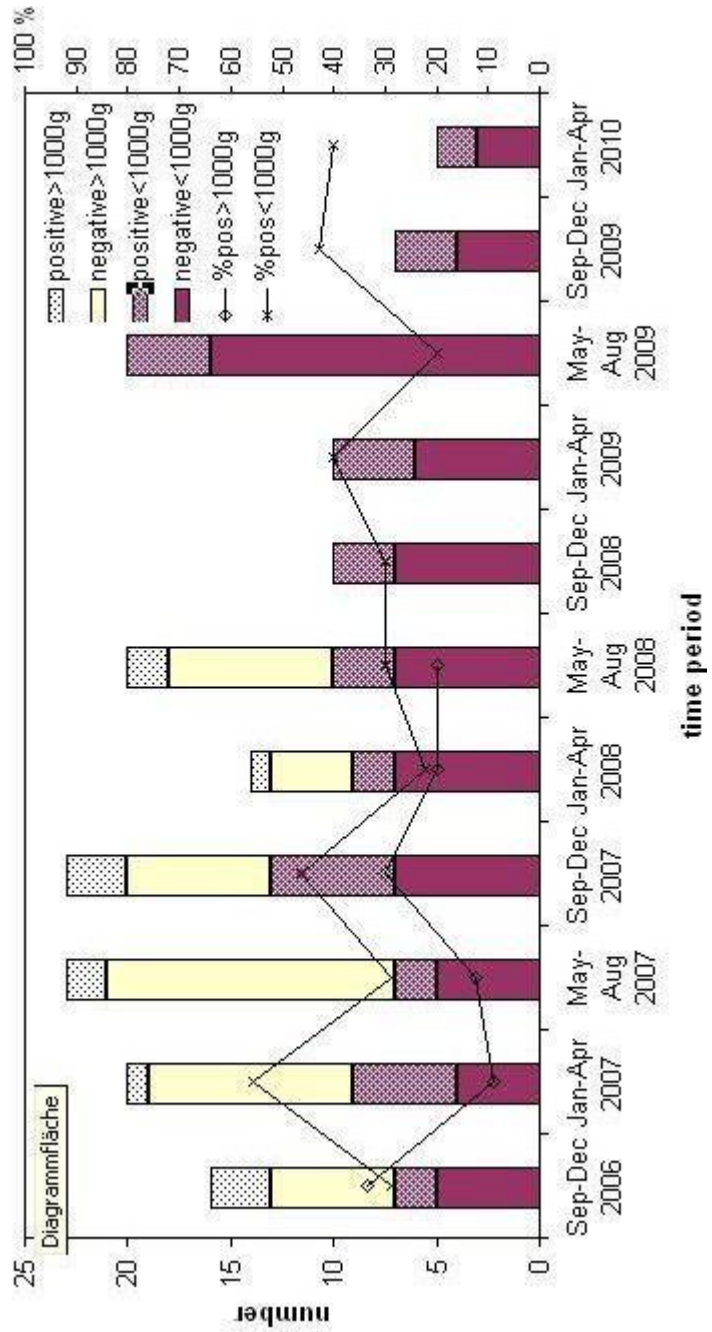
Background and aims: Premature infants with a birth weight under 1500g are at high risk to suffer from septic infections, mostly device associated. Our department participates in the german nosocomial infection surveillance system NEOKISS. Interpreting our outcome data of the years 2000-2005, our aim was to reduce the rate of intravascular catheter associated infections by checking adherence to line insertion practices. We chose post puncture skin smears as key indicator.

Methods: From Sept. 2006 to April 2010 170 VLBW-infants (after 09.2008 ELBW) were included in the study. After skin disinfection with Octenidin 0.1% or Octenisept and successful insertion of a peripheral intravascular cannula (PVC), before fixation a skin smear from the puncture site was drawn and cultured.

Results: In 68 from 911 swabs (7.5%) of 48 children (28.2%) smear germs were detected, most frequently (69%) coagulase-negative staphylococci. In 3 ELBW infants sepsis was diagnosed directly after a positive skin swab with the same germ, 2 children died.

There is no linear relationship between the smear result, the infants age when the smear was drawn, the infants maturity (gestational age), singleton or multiple birth, punction area location and antibiotic pretreatment.

Among children with a positive smear PVC-associated infections occurred significantly more frequent than in children without a germ in the punction swab. We observed no significant decrease of swab contamination during the observation period.



[Skin swab results]

Conclusion: Continuous education and surveillance of venipuncture hygiene is necessary. Coagulase-negative staphylococci are the most common contaminants.

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SCREENING NEWBORNS FOR CONGENITAL CHAGAS DISEASE (AMERICAN TRYPANOSOMIASIS) IN GENEVA, SWITZERLAND

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Chagas disease is caused by Trypanosoma cruzi. Vector-borne transmission occurs exclusively in the Americas, where millions are infected. Transmission can occur vertically with a risk of mother-to-child transmission of 1%-10%. Children are often asymptomatic at birth. The risk of developing cardiac or gastrointestinal disease in their life time is estimated between 20% and 30%. In Europe, vertical transmission of Chagas disease has recently emerged in the context of international migration.

Since 2008, a Chagas screening program is performed in our institution. All pregnant women followed in our hospital and coming from an endemic area are tested. If the mother is positive, neonates are screened at birth (direct exam and PCR on cord blood) and at nine months (serology). Treatment is started if any test is positive.

Between January 2008 and December 2011, 22 pregnant women were tested positive. We tested 26 children (4 of the mothers had 2 children each). Four (19%) were positive for Chagas disease. Two children were treated with nifurtimox and two with benznidazole. Both were well tolerated. Two patients were not tested at nine months (lost to follow-up). The serology will be repeated in two other children because of unclear results.

The Chagas disease screening program allowed treating mothers, detecting and treating four vertically infected children, and screening previously born children from infected mothers. Pediatric Chagas disease in non-endemic countries is an under recognized entity. Most of the patients are asymptomatic but can develop serious complications later in life; therefore, a mother-baby screening program is warranted.

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PHARMACOKINETICS OF CIPROFLOXACIN (FLUOROQUINOLONE) IN NEONATES ADMINISTERED FOR SUSPECTED GRAM NEGATIVE SEPSIS (TINN TREAT INFECTION IN NEONATES EUROPEAN CONSORTIUM)

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Background: Ciprofloxacin is prescribed off-label in 25% of European neonatal units for suspected sepsis particularly if known resistance to first line antibiotics. There is insufficient data to define a rational neonatal dose regimen.

Aim: To obtain neonatal pharmacokinetic data of ciprofloxacin for preterm to term neonates.

Methods:

Design: A population PK study with sparse informative sampling supplemented by scavenged clinical samples. Recruited on neonatal and paediatric intensive care units/ wards at Liverpool Women´s and Children´s Hospitals UK.

Eligibility - administered ciprofloxacin for clinical care for suspected sepsis 24-52 weeks PMA.

Sampling schedule: 3 samples day 1 and 5 within 3 to 10 minutes of 3 set times following the infusion (6 per baby plus scavenged). **PK parameters** - AUC, Cmax/Cmin, volume of distribution and clearance).

Results: 62 recruits stratified into 4 week age bands between 24-48 weeks PMA.

A minimum of 7 babies per age group (except PMA 48-52 as none were eligible).

36 recruits completed both day 1 and 5 samples (42% day 5 samples missing as treatment had stopped or mortality). These were supplemented by 183 scavenged clinical bloods with exact times (4.3 on average per recruit).

10 samples from clinically required LP were obtained to determine the CSF level of ciprofloxacin.

6 /62 babies had confirmed Gram negative infection in blood cultures.

52 DNA buccal or blood samples were obtained for pharmacogenomic analysis.

Conclusion: A pharmacokinetic sampling strategy was achieved that will capture changes in absorption, distribution, metabolism and excretion throughout neonatal age range.

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IMPLEMENTATION OF ANTIMICROBIAL COPPER IN NEONATAL INTENSIVE CARE UNIT (NICU)

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Aim: The aim of this study was to investigate the effectiveness of the application of antimicrobial copper alloys (Cu +) in a Neonatal Intensive Care Unit (NICU) in relation to the reduction of microbial flora.

Materials and methods: At a Level III Neonatal Intensive Care Unit of a pediatric hospital, with the capacity of twenty-six (26) incubators, antimicrobial copper (Cu +) was implemented on touch surfaces and objects. The copper alloy contains Cu 63% - Zn 37% (Lead Low). Microbiological cultures were taken in three different time periods, before and after the application of Cu^{+}, using dry and wet method technique.

Results: In the above NICU, the reduction of microbial flora after the implementation of the antimicrobial copper (Cu +) on the selected surfaces and objects was statistically significant ($n = 15$, $p < 0,05$) and was recorded at 90%. The pathogens isolated at high rates (CFU / ml) prior to copper implementation were as follows: Klebsiella spp., Staph. Epidermidis, Staph. Aureus, Enterococcus spp.

Conclusions: This study highlights the positive impact of antimicrobial copper (Cu +) and demonstrates that copper implemented surfaces and objects are effective in neutralizing bacteria, which are responsible for Health Care Acquired Infections in the nosocomial environment (HCAIs).

The innovative implementation of antimicrobial copper in the NICU and the significant reduction of microbial flora heralds the reduction of antimicrobial drugs use, and a possible reduction of hospital acquired infections and hospitalization time.

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PATTERN AND RESISTANCE RATES OF BACTERIA ISOLATED FROM BLOODSTREAM INFECTIONS IN A TERTIARY LEVEL NICU: COMPARISON OF TWO PERIODS

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Background and aims: Knowledge of incidence and antimicrobial susceptibility patterns of bacterial pathogens is essential for empirical antimicrobial treatment in NICU.

Methods: Retrospective analysis of bacteria isolated from blood cultures of neonates hospitalized in a NICU between 2 periods (A:1/2007-12/2008 and B:1/2011-10/2012).

Results: Among 228 and 116 pathogens isolated during period A and B, Gram-positive bacteria constituted 80% and 72.4%, respectively. Coagulase-negative staphylococci (CoNS, 89.9% vs 84.5%) were the most frequent Gram-positive bacteria followed by Staphylococcus aureus (2.8%vs 2.4%), Enterococcus faecalis (2.8% vs 3.6%), E. faecium (2.8% vs 3.6%) and group B streptococci (GBS, 1.7% vs 1.2%) in both periods. 1/3 of S.aureus and >60% of CoNS were methicillin resistant whereas all staphylococci were vancomycin-sensitive. All GBS and E. faecalis isolates were susceptible to ampicillin and vancomycin. Resistance rates of E. faecium to vancomycin were 60% vs 50% in period A and B, respectively. Table 1 depicts the most frequent Gram-negative bacteria.

Susceptibility %	Amikacin		Ceftazidime		Imipenem		Ciprofloxacin	
Gram-negative bacteria (N of isolates in period A and B)	A	B	A	B	A	B	A	B
Klebsiella pneumoniae (21 vs 14)	80.6	85.7	23.8	0	100	92	100	28.5
Enterobacter cloacae (9 vs 6)	66.7	83.3	55.6	66.6	88.9	83.3	66.7	83.3
Escherichia coli (5 vs 3)	100	100	80	100	100	100	100	100
Acinetobacter baumannii (4 vs 6)	75	16.6	50	16.6	75	16.6	75	16.6

[Table 1]

Conclusion: CoNS are the most frequent bloodstream isolates demonstrating high-level resistance to beta-lactams. Resistance of E. faecium to vancomycin and of Gram-negative bacteria to third-generation cephalosporins are of concern. Emerging carbapenem resistance further limits available therapeutic options.

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TRENDS IN INCIDENCE AND ANTIMICROBIAL RESISTANCE OF LATE-ONSET SEPSIS: 5 YEARS OF EXPERIENCE

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Background and aims: Late-onset sepsis (LOS) continues to be a challenging complication, especially in very low birth weight infants, increasing morbidity, mortality and medical costs. **Aim:** to evaluate clinical data of newborns with LOS and trends in causative microorganisms and their antimicrobial susceptibility.

Methods: Retrospective analysis of medical records and microbiological data of all newborns with LOS, defined by signs/symptoms compatible with positive blood culture or with laboratory studies suggestive of infection (WBC>30.000/µL or < 5.000/µL, platelet count< 100.000/µL, CRP>2mg/dL), after 72hours of life. Study period: January08-December12.

Results: Among a total of 14950 live births (LB), we identified 76 newborns with LOS (5,1 per 1000LBs), with median gestational age 28weeks (99% preterm, 11%>32 weeks) and median birth weight 975g. Fifty-five had positive blood cultures (3,7 per 1000 LBs). Forty-four percent started symptoms in the 2nd week of life, with respiratory distress being the major sign identified. Necrotizing enterocolitis was associated in 7 cases, meningitis in 2 and pneumonia in 1.Coagulase-negative staphylococci (CoNS) predominated (33; 2.2 per 1000LBs) followed by E. coli (6; 0.4 per 1000LBs). Among major pathogens identified, CoNS showed no resistance to vancomycin as well as E. coli to gentamicin. Methicillin resistant Staphylococcus aureus was isolated in just 1 case (5 S. aureus in total).Vancomycin and 3rdgeneration cephalosporins were the main antibiotics used. Lethality occurred in 7 cases.

Conclusions: CoNS remain the leading cause of LOS, as described in previous studies. In vitro susceptibility test of isolates showed low levels of resistance to commonly used antibiotics.

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DIAGNOSTIC VALUE OF PROCALCITONIN IN PREDICTING INVASIVE BACTERIAL INFECTIONS IN NEONATES WITH FEVER WITHOUT SOURCE

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Background and aims: Procalcitonin (PCT) value in management of neonates with fever without source (FWS) is still lacking. Our aim is to assess the diagnostic accuracy of PCT in detecting invasive bacterial infections (IBI) in neonates with FWS.

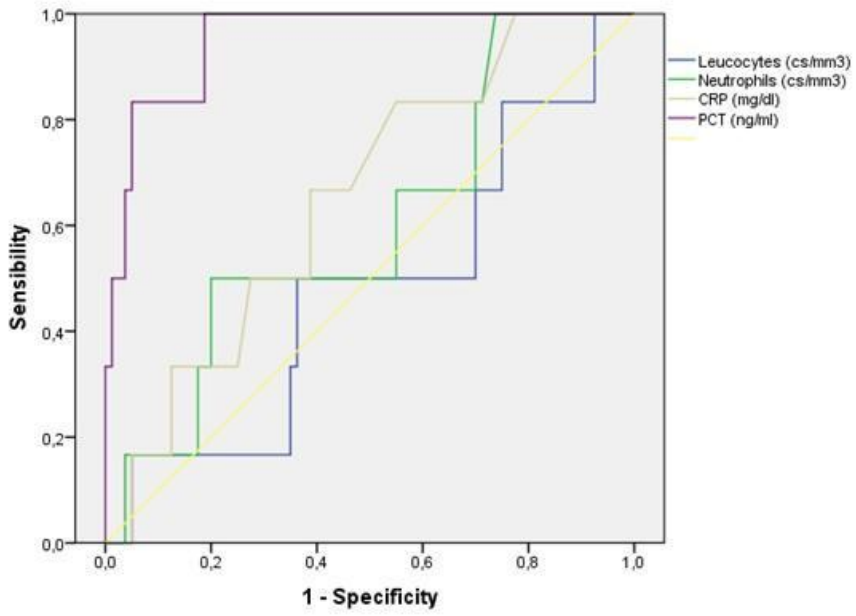
Methods: A retrospective study was conducted on previously healthy neonates with FWS admitted to a tertiary care Pediatric Emergency Department between August 2008 and August 2012. Children born preterm, with underlying diseases or without available blood culture, c-reactive protein value (PCR) and PCT value were excluded. An IBI was defined by isolation of a bacterial pathogen in blood or cerebrospinal fluid culture.

Results: 129 neonates were admitted during the study period and 88 children met the study inclusion criteria. IBI was diagnosed in 6 children (6.8%). Negative likelihood ratio (LR-) for IBI and PCT 0.5 ng/mL was 0 (IC95% 1.35-3.07). Positive likelihood ratio (LR+) for IBI and PCT 2 ng/mL was 11.38 (IC95% 4.87-26.62) (Table1). AUC for PCT, CRP, neutrophils and leucocytes were 0.952 (0-1), 0.654 (0.453-0.855), 0.602 (0.374-0.830) and 0.477 (0.231-0.723) respectively (Graphic1).

Conclusions: PCT is an accurate marker of IBI in healthy neonates with FWS. It´s better test than CRP for ruling out or suspect IBI in newborns.

	Sensitivity	Specificity	LR +	LR -
IBI PCR 3 mg/dl	16.67% (3-56.35)	89,02%(80,44-94,12)	1.51(0.22-10.07)	0.94(0.64-1.34)
IBI PCT 0.5 ng/ml	100% (60.97-100)	81,71%(71.99-88.59)	5.45(3.45-8.63)	0(1.35-3.07)
IBI PCT 2 ng/ml	83.33%(53.51-100)	92.68%(87.04-98.31)	11,38(4.87-26.62)	0,17(0.03-1.07)

[Table 1]



[Graphic1]

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BACTEREMIA ASSOCIATED COMPLICATIONS AND MORBIDITIES IN NEONATES: THE CHARACTERISTICS, INCIDENCE AND RISK FACTORS

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Background: Few data are available on the clinical characteristics and morbidities of neonates who had complications after bacteremia, understood as any newly infectious focus or organ dysfunction directly related to bacteremia but not occur concurrently.

Methods: All neonates hospitalized in our neonatal intensive care unit (NICU) with bacteremia between 2004 and 2011 were reviewed, and those who developed bacteremia associated complication (BAC) were analyzed to identify the clinical characteristics and outcomes. Logistic regression was used to identify independent risk factors for BAC.

Results: Of 975 episodes of bacteremia, 101 (10.4%) in 93 neonates were followed by BACs with a median interval of 3 days (range, 0-17 days) after onset of bacteremia. The major BACs consisted of newly infectious focuses (n=40, 39.6%), major organ dysfunctions after septic shock (n=36, 35.6%), and neurological complications after meningitis or septic shock (n=34, 33.7%). All patients with BACs after bacteremia suffered from various morbidities, including 30 (32.3%) neonates finally died, 4 (4.3%) discharged with family requested cessation of all treatment, 17 (18.3%) with persistent sequelae, and 42 (45.2%) were stable. Independent risk factors for BACs included initial inappropriate antibiotics (odds ratio [OR], 5.7; 95% CI, 3.49-9.32), bacteremia with septic shock (OR, 5.35; 95% CI, 3.23-8.86), meningitis (OR, 8.9; 95% CI, 4.18-18.95), and group B streptococcus sepsis (OR, 3.1; 95% CI, 1.12-8.13).

Conclusions: A worth noting percentage of neonates with bacteremia suffered from sequelae or died of infections complications. Further studies regarding avoidance of infectious complications and better treatment strategies to optimize outcome are worth consideration.

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OUTBREAK OF ECHOVIRUS 11 FULMINANT NEONATAL HEPATITIS IN BELGIUM DURING SPRING 2012

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Nonpolio enterovirus infections are common during summer and fall. Among neonates clinical presentation varies from asymptomatic viral shedding and non-specific febrile illness to sepsis-like syndrome and severe liver, cardiac or cerebral diseases. Echovirus 11 is the most frequent cause of serious neonatal morbidity and mortality, often presented as fulminant hepatitis. Mortality rates are greater for infections that appear during the first week of life, probably through vertical transmission.

We report four cases of echovirus 11 neonatal infections between April and June 2012. All children were admitted during the first week of life, day 4 to 6, with sepsis-like syndrome. All the cases were biologically characterized by marked transaminase elevation (GOT >> GPT), hemolytic anemia, thrombocytopenia, and severe coagulopathy. Diagnosis was confirmed by positive polymerase chain reaction on blood, stool or cerebro-spinal fluid samples. Among them three were born by vaginal delivery and one deceased. All were treated by intravenous immunoglobulins (IVIG) within 7 days of admission (1 to 2g/kg). Contact history was only documented in the patient delivered by caesarian. Portal blood flow inversion was found in three of the reported cases, which is a marker of portal hypertension commonly reported in fulminant hepatitis.

This study shows that outbreak of enterovirus is still associated with severe infection and fulminant hepatitis in newborns. Clinical presentation is aspecific although early diagnosis and rapid treatment is mandatory to avoid fatal evolution. There was rational to administer IVIG, and positive outcome in 3 patients out of 4 might have been favored by this treatment.

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ABSOLUTE EFFECTIVENESS OF ACELLULAR PERTUSSIS VACCINE AND RELATIVE EFFECTIVENESS IN COMPARISON TO WHOLE-CELL VACCINE DURING EPIDEMIC YEARS IN QUEENSLAND, AUSTRALIA

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Background and aims: In Queensland, Australia, 2009-2011 were epidemic years for pertussis with notification rates highest in late childhood. Peak notifications coincided with the first birth cohorts primed with acellular pertussis vaccine, which replaced whole-cell pertussis vaccine in 1999. We investigated the relative effectiveness of acellular to whole-cell pertussis vaccine by comparing notification rates of children born in 1998, primed with either, or a mixture of, acellular and whole-cell pertussis vaccine. We also assessed acellular pertussis vaccine effectiveness (VE) against hospitalisation and notification in Queensland children in 2009 and 2010.

Methods: Queensland notification, hospitalisation and vaccination register data were linked.

Among children born in 1998, notification rates during 2009-2011 were calculated by receipt of ≥3 doses of either purely acellular, purely whole-cell, or mixed pertussis vaccine, before the first birthday.

VE was calculated using the screening method, for 3, 4, or 5-doses of pertussis vaccine among children aged 1-3, 5-7, and 7-11 years, respectively, by year of birth. Population vaccination coverage figures were provided from the Australian Childhood Immunisation Register.

Results: Notification rates were higher in children primed with acellular compared to whole-cell pertussis vaccine: IRR 3.29 (95%CI:2.44-4.46).

VE point estimates against hospitalisation and notification in 1 to 3-year-olds were 84%-89% in 2009 and 2010. VE point estimates against notification among 5 to 11-year-olds were 71%-88% in 2009, and 36%-71% in 2010.

Conclusions: Although less protective than whole-cell vaccine, acellular pertussis vaccine provided very good protection against pertussis in 1 to 3-year-olds, and, generally, good-to-moderate protection in 5 to 11-year-olds.

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PERSISTENCE TO 12, 18 AND 24 MONTHS OF BACTERICIDAL ANTIBODIES INDUCED BY INFANT IMMUNISATION WITH A SEROGROUP B MENINGOCOCCAL VACCINE

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Background: We evaluated the persistence of antibodies beyond 12 months of age following infant immunisation with 4CMenB (a serogroup B meningococcal vaccine recently recommended for European licensure).

Methods: In this follow-on study, children previously receiving 4CMenB at 2, 4, 6 or 2, 3, 4 months of age with routine vaccines (M246R and M234R, respectively) and without routine vaccines (M246), received 4CMenB at age 12, 18 or 24 months. 4CMenB-naive controls received 4CMenB at 12 and 14, 18 and 20 or 24 and 26 months. Serum bactericidal activity was determined before and one month after each immunisation using human complement (hSBA, protective correlate ≥1:5).

Results: At 12 months, prior to any booster doses, 116/157(74%: 95% CI 66%-81%) of the M246R group had hSBA ≥ 1:5 for strain H44/76 compared to 121/143 (85%: 78%-90%) for M246, 50/87 (57%: 46%-68%) for M234R and 25/199 (13%: 8%-18%) for controls. For 5/99 these proportions were ≥ 95% for all 4CMenB recipients compared with 1% for controls. For NZ98/254 these were 21% for M246R, 19% (M234R), 35% (M246) and 1% for controls. By 24 months these proportions in 4CMenB recipients were 11% - 21% for H44/76, 83% - 96% for 5/99 and 7-9% for NZ98/254, and in control participants were ≤4%.A booster dose of 4CMenB resulted in ≥ 97% of participants having hSBA ≥1:5 for H44/76 and 5/99, and 77%- 97% for NZ98/254.

Conclusions: A booster dose of 4CMenB is required to maintain elevated hSBA titres. The persistence of the post-booster hSBA increase is being evaluated.

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KNOWLEDGE OF TURKISH FEMALE UNIVERSITY STUDENTS ABOUT HPV INFECTION AND HPV VACCINATION

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Background and aims: Female students are supposed to have sufficient knowledge about HPV infection and HPV vaccination because they are in the risk group for HPV infection and the related complications. This study was descriptively conducted in order to determine knowledge of female university students about HPV infection and HPV vaccination.

Methods: This study was conducted with 380 female students of Bozok University, Yozgat, Turkiye during September-December 2012. All of the female students were informed verbally and they participated voluntarily. A questionnaire was used to collect data. Percentage distributions and Chi-square test were used to evaluate data.

Results: Mean age of the participant students was 20.17±1.84. It was found out that 60.0% of students had an income equal to expenses, 49.2% lived city center most and 56.3% stayed at public university dormitories.

It was discovered that 59.5% of the students did not hear about HPV infection, 72.4% did not know how HPV infection was transmitted, 90.0% did not know health problems caused by HPV infection, 23.4% heard about HPV vaccination but nearly all of them did not have HPV vaccination.

In this study, there was statistically significant difference between mothers' educational level, school, class and living-place, and HPV infection and HPV vaccination; and between transmission ways, knowing probably health problems and wish to have vaccination ($p < 0.05$).

Conclusions: In light of our study results, it was determined that female students did not have sufficient knowledge about HPV infection and HPV vaccination.

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BCG HEALING AND TETANUS ANTIBODY LEVELS AFTER PRIMARY IMMUNIZATION IN INFANTS EXPOSED TO IMMUNOSSUPRESSORS DURING GESTATION

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Background and aims: Immunosuppressors used during gestation are known to interfere with the fetus' immune system development. However, little is known regarding their influence on the response to the infant's immunization. We evaluated BCG adverse events and scar development as well as tetanus antibodies in children born to renal transplant women.

Methods: 24 renal transplant women and neonates and 30 healthy women and neonates at term (Control) were studied. All transplant mothers received azathioprine, prednisone and either tacrolimus (71%) or cyclosporin (29%). T, B and NK cells were evaluated at birth in 17 neonates of transplant group and from all controls. BCG was administered at birth or as early as when they reached 2Kg; DTwP vaccine was administered at 2, 4 and 6 months of age. Children were followed up and the evolution of BCG scar was registered. At 7 months of age, tetanus antibodies were measured by ELISA.

Results: Infants of transplant group had lower median CD4 T cells/mm3 (1238x1646, p=0.037) and B lymphocytes/mm3 (119x517,p< 0.001) than controls, but similar CD8 T cells/mm3 (633x667,p=0.288) and NK cells/mm3 (774x764,p=0.432). No BCG adverse events were observed. Median time for BCG scar development was 1.8 months in both groups(p=0.919). All children had protective tetanus antibodies (>0.1 IU/mL) and similar tetanus antibody levels (1.680 IU/mL in transplant and 1.609 IU/mL in control group, p=0.553) after vaccination.

Conclusions: Despite low numbers of CD4 T and B cells at birth, children exposed in utero to immunosuppressors have adequate BCG healing and response to tetanus vaccine.

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HIGH COVERAGE OF RECOMMENDED INFANT VACCINES IN FLANDERS (BELGIUM) CONTRASTS WITH LOW COVERAGE OF PERTUSSIS BOOSTER IN THEIR PARENTS

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Background and aims: Previous infant surveys in Flanders demonstrated a high coverage but delay in age at vaccination. A new EPI-based survey (2012) ordered by the Flemish government evaluated timeliness and incomplete vaccination in infants, and assessed uptake of the recommended pertussis-containing booster vaccine (dTpa) in their parents (cocoon strategy, since 2009).

Methods: Through a randomized cluster design 946 toddlers were selected from 105 municipalities in Flanders. After consent of the parent(s), 874 (91%) families were interviewed at home. The requested information included socio-demographic characteristics and documented vaccination history. Infants' vaccination data were updated from medical files when incomplete. We assessed coverage of poliomyelitis (mandatory), tetanus-diphtheria-pertussis, H. influenzae type b, hepatitis B, measles-mumps-rubella (MMR), pneumococcal (PnC), and meningococcal C vaccines in infants, and dTpa vaccine in their mother or father.

Results: Coverage rates at 18-24 months of age were high at 97% for MMR and PnC and 93% for all other vaccines. Though 75% of infants had received their first vaccine dose at the recommended age of 8 weeks, only 25% received the third pertussis-containing dose at the recommended age of 16 weeks. Infants who were not immunised in well-baby clinics or who had more siblings or a younger or non-working mother were more at risk for not being fully vaccinated. Only 35% of mothers and 27% of fathers remembered having received dTpa booster.

Conclusions: Though infant vaccination rates meet high standards in Flanders, timeliness of infant vaccination and parent compliance to pertussis cocoon strategy leave room for improvement.

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TWO-DOSE TODDLER VACCINATION WITH INVESTIGATIONAL MENINGOCOCCAL B RECOMBINANT VACCINE - ANTIBODY PERSISTENCE AND RESPONSE TO BOOSTER AT 24 MONTHS

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Background: A two-dose catch-up immunisation with the investigational multicomponent serogroup B meningococcal vaccine, 4CMenB, was highly immunogenic in 12−15 month-old toddlers. We examined antibody persistence and response to a booster dose one year later (NCT01139021).

Methods: Participants in this extension study, who originally received two doses of 4CMenB at 12/14 or 13/15 months of age, received a booster dose 12 months after their last dose. Serum bactericidal activities with human complement (hSBA) against four serogroup B strains representative for individual vaccine antigens - factor H binding protein (fHbp), Neisserial adhesin A (NadA), Neisseria heparin binding antigen (NHBA) and New Zealand strain outer membrane vesicles (NZOMV) - were measured before, one month and six months after the booster.

Results: Of the 85 exposed subjects, 100% originally displayed seroprotective hSBA titres (≥ 5) against fHbp and NadA, 71% against NHBA and 99% against NZOMV one month after their primary immunisations. One year later the respective proportions were 71%, 96%, 37% and 15%, rising to 100%, 100%, 99% and 100% one month after a 4CMenB booster dose. GMTs after the booster were higher than after the primary series, indicating a true booster response. Six months after the booster these levels were 99%, 100%, 93% and 75%, respectively.

Conclusions: Two doses of 4CMenB, administered as a catch-up vaccination in toddlers, induced a response against all antigens in the majority of subjects. Levels remained high for 12 months against fHbp and NadA, and were boosted for all antigens by a third dose.

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CLIMATIC EFFECTS ON THE SEASONALITY OF RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN HOSPITALISED WITH LOWER RESPIRATORY TRACT INFECTIONS IN MALTA

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Background and aims: Respiratory Syncytial virus (RSV) is a major cause of hospitalisation in small children. We aimed to study the influence of meteorological factors on the onset of RSV related hospitalisations in children < 2 years old.

Methods: A prospective study was performed from October 2009 to September 2011. RSV was cultured from nasopharyngeal swabs. Daily readings of temperature, relative humidity, rainfall and wind speed and direction were recorded. Spearman correlation was used to analyse any relation with meteorological factors whilst climatic differences were analysed using Student t-test.

Results: The first season lasted from February till May 2010, during which 30 of 134 children admitted with bronchiolitis (22%) had RSV infection. The subsequent season started in December 2010 and ended in March 2011 during which 49 of 144 children (34%) had positive RSV cultures.

RSV hospitalisations were negatively correlated with a decreasing wind chill index

(p=< 0.01). Comparison of the climatic factors only revealed significant differences in relative humidity. January 2010 (weeks 1-5) was significantly less humid during the day (72.87% vs 82.48%;p=0.0001) and night (76.16% vs 88.07%;p=0.0001) compared to January 2011. Similarly, November 2010 (weeks 46-47) was significantly less humid during the day (70.67% vs 79.87%; p=0.0009) and night (74.33% vs 87.87%;p=0.0001) than November 2009. These periods preceded exactly the onset of the RSV seasons.

Conclusion: Relatively lower humidity, on a background of cold temperature, was conducive to the different onset of the RSV seasons possibly from its effect on the stability and transmissibility of RSV.

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INVASIVE PNEUMOCOCCAL DISEASE IN PICU PATIENTS BEFORE AND AFTER INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN THE NETHERLANDS

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Background: Invasive Pneumococcal Disease (IPD) continues to be a major cause of morbidity and mortality worldwide, especially in children under 5 years of age. The 7-valent pneumococcal conjugate vaccine (PCV7) was included in the national immunization program in the Netherlands in 2006. We compared patient and disease characteristics in patients with IPD admitted to the Paediatric Intensive Care Unit (PICU) before and after PCV7 introduction.

Methods: IPD patients admitted to the PICU of the Radboud University Medical Centre (1991-2010) were identified via electronic hospital registries. Clinical and laboratory findings of patients were collected by retrospective chart review. Differences were analyzed by Fisher's exact test.

Results: A total of 52 patients was included (36 patients diagnosed in the pre-vaccination era). The percentage of PCV-7 serotypes in IPD patients decreased following introduction of PCV7 (62,1% vs 10,0% ; $p< 0.05$)). No significant changes were observed in the percentage of patients older than 5 years (22.2% vs 18,8%), mortality (33.3% vs. 25.0%), or the percentage of patients with an IPD predisposition (36,1% vs. 31,3%).

Conclusions: National infant PCV-7 vaccination in the Netherlands caused a decrease in the percentage PCV-7 serotype strain related IPD in patients admitted to PICU. This decrease in PCV serotype strains related IPD was not associated with a decrease in percentage mortality. Most IPD cases requiring PICU admission are < 5 year of ages. One third of IPD PICU patients occurs in patients with a predisposition for IPD.

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ESTIMATING THE PNEUMOCOCCAL VACCINE COVERAGE AND VACCINE SCHEDULE ADHERENCE IN 5 EUROPEAN COUNTRIES

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Introduction: Pneumococcal conjugate vaccine (PCV) is part of national immunization program (NIP) in children in most European countries since 2006-2008 with 2+1 or 3+1 schedules. The aim of this study was to describe the pneumococcal vaccination coverage and schedule adherence in 5 European countries.

Methods: Web-based survey was conducted in September - October 2012 to mothers having at least one child of 9 to 30 months of age with available vaccination booklet in France, Germany, Spain (excepting Madrid and Galicia regions) and Switzerland and face to face interview survey in Portugal.

Results: In children 9-18 months of age, total of 57 to 85% received at least one dose of PCV. Among those children, 54 to 98% had completed the full primary series according to country recommended schedule (Table). Regarding other childhood vaccine DTP, 94 to 97% of children received at least one dose. In children 19-30 months of age with completed full primary series, only 43 to 92% had received the booster dose.

Conclusions: Pneumococcal vaccination coverage of pneumococcal vaccination is considerably low compared to that of other childhood vaccine, DTP. The adherence to full primary series and booster administration is suboptimal. In general, the vaccine coverage and schedule adherence is higher in countries where PCV was in NIP with 2 + 1 schedule. Adherence to recommended vaccine schedule should be a public health priority.

	France 2+1 (NIP)	Switzerland 2+1 (NIP)	Germany 3+1 (NIP)	Spain 3+1	Portugal 3+1
9-18 months of age					
≥ 1 dose of PCV*	85 % N=232	69% N=95	73% N=199	78% N=212	57% N=157
Full PCV series**	90% N=143	98% N=74	66% N=132	54% N=114	68% N=107
≥ 1 dose of DTP	97% N=265	94% N=130	95% N=259	95% N=258	94% N=259
19-30 months of age					
1 booster dose***	81% N=150	92% N=89	66% N=121	63% N=112	43% N=68

[The adherence to pneumococcal vaccination schedule]

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RANDOMIZED CLINICAL TRIAL TO EVALUATE THE IMPACT OF A FACT SHEET ABOUT INFANT VACCINATION PAIN MANAGEMENT ON PARENTAL KNOWLEDGE UPTAKE

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Background: Vaccination injections are the most common painful medical procedure that infants experience. We developed a fact sheet for parents summarizing evidence-based strategies for managing pain during vaccination.

Purpose: To determine maternal knowledge uptake from the factsheet; and the additional impact of administering the factsheet with a baseline knowledge test (i.e., pre-test).

Methods: New mothers at Mount Sinai Hospital, Toronto, Canada, were randomized to two study groups (factsheet) and two control groups (information on another new baby health topic). A pre-test was given to one of the study groups and one of the control groups. Following review of the fact sheet/control sheet, post-tests were administered to all four groups. The test consisted of 10 true/false questions about the effectiveness of various strategies for reducing pain and distress during infant vaccination injections and the level of confidence in the response (5-point likert scale: very sure, sure, a little sure, neither sure nor unsure, a little unsure, very unsure).

Results: 120 mothers participated. There were no significant differences ($p>0.05$) in maternal characteristics among groups. Mean knowledge test scores were higher in the intervention groups: 5.6 (SD=2.0) and 6.9 (1.6) compared to the control groups 3.2 (2.2) and 3.4 (2.5). A 2-way (study group, pre-test group) ANCOVA revealed a significant ($p< 0.05$) main effect of the study group and an interaction between the study group and pre-test group.

Conclusion: The factsheet improved maternal knowledge about effective pain management strategies for vaccination injections. Knowledge was augmented by the use of a pre-test.

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COMPARISON OF VIRUS SHEDDING AFTER VACCINATION WITH LIVED ATTENUATED HUMAN ROTAVIRUS VACCINE AND PENTAVALENT HUMAN-BOVINE REASSORTANT ROTAVIRUS VACCINE

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Background: Transmission of rotavirus vaccine or vaccine-reassortant strains to unvaccinated contacts has been reported. Therefore, it is essential to evaluate and characterize the nature of vaccine-virus shedding among rotavirus vaccine recipients.

Material and methods: Two groups of healthy infants who received a complete course of RotaTeq or Rotarix were enrolled (between March 2010 and June 2011) to compare fecal shedding for one month after each vaccine dose. Shedding was assessed using both enzyme immunoassay (EIA) and real-time reverse transcription-polymerase chain reaction (RT-PCR).

Results: Eighty-seven infants (34 girls and 53 boys) were enrolled in the study. After the first vaccine dose, the peak time of virus shedding occurred between day 4 and day 7, with positive detection rates of 80-90% by real-time RT-PCR and 20-30% by EIA. The shedding rate detected by real-time RT-PCR was higher than that detected by EIA. Mixed effects logistic regression analysis of real-time RT-PCR data showed no significant differences between infants receiving RotaTeq and Rotarix when shedding rates were compared after the first vaccine dose (P=0.71) or after the second vaccine dose (P=0.99). However, infants receiving Rotarix shed significantly higher viral loads than those receiving RotaTeq when compared after the first vaccine dose (P=0.001) and after the second dose (P=0.039).

Conclusions: In terms of shedding rates detected by real-time RT-PCR, vaccine uptake of RotaTeq or Rotarix among infants in Taiwan was comparable. Clinical significance of higher shedding viral loads in Rotarix should be further observed.

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SAFETY OF PENTAVALENT ROTAVIRUS VACCINE IN HEALTHY PREMATURE INFANTS: AND OBSERVATIONAL STUDY

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Background and objectives: Premature infants (PI) seem to be at greater risk of severe forms of rotavirus (RTV) gastroenteritis and hospitalization. The risk increases as the lower gestational age (GA) and lower weight. To date, studies on safety and efficacy of the pentavalent vaccine against RTV reflect similar results in preterm and term infants, which has led to the different societies to recommend.

Methods: Longitudinal observational epidemiological study to assess the safety of Rotavirus Pentavalent Human-Bovine vaccine in premature infants less than 32 weeks GA by studying the occurrence of adverse effects in the vaccinated population. All infants were to be followed for clinical adverse events for 42 days after each dose.

Results: The vaccine has been administered to 186 infants under 32 weeks. First dose was administered at 6 or more weeks of life, after discharge, and ended before 22 weeks.

There were no serious adverse events. No case of intussuspection occurred.

There have been mild side effects as: 2 vomiting, 4 irritability / crying , 2 bronchiolitis VRS negative, similar rate to control groups prior published in clinical trials. There have been no hospital admissions or emergency room visits for gastroenteritis so far.

Conclusions: Vaccination against RTV has shown to be as safe in prematures than in term infants.

Vaccination should be considered as an option in neonatal units after discharge.

We need to have more experience in real life data substantiating the safety and efficacy that trials have provided.

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IMPACT OF THE PNEUMOCOCCAL CONJUGATE VACCINE 13 (PCV13) IN THE INVASIVE PNEUMOCOCCAL DISEASE (IPD)

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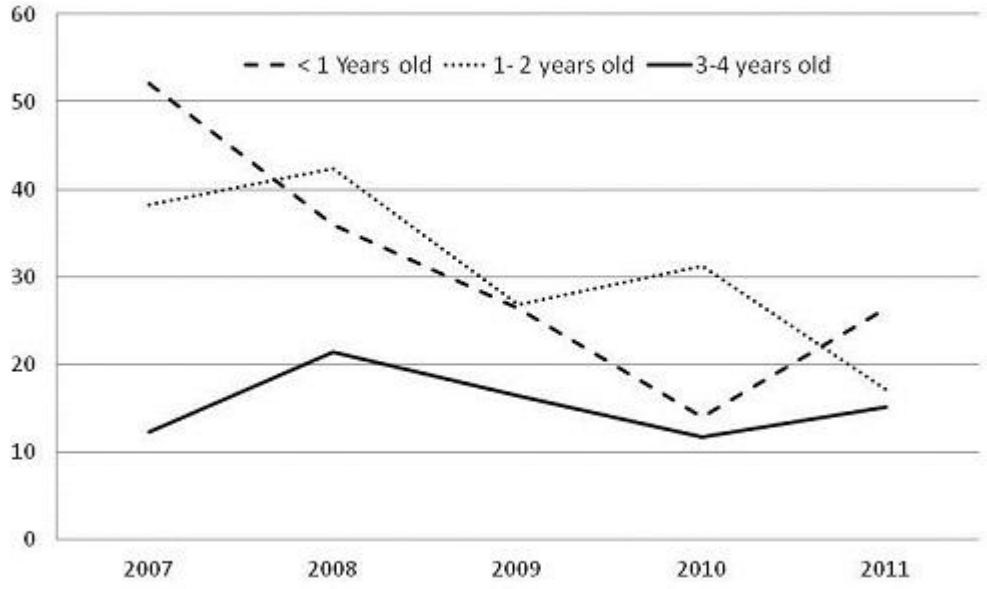
Background and aims: The strectocuccus pneumoniae (SP) is able to produce a range of infections including invasive diseases (IPD). The PCV13 can help to reduce these diseases. The epidemiological information system (AVE) and the Vaccine Information System (SIV) allow to evaluate the impact of PCV13 in the IPD. The aim of this paper is to evaluate the situation of the IPD before and after the introduction of the PCV13 in the Valencian Community (VC).

Methods: The frequency and distribution of pneumococcal serotypes was obtained from AVE. The information related with vaccination was obtained from SIV. All data correspond to the VC for the period 2007-2011.

Results: On Graph 1 it is show the IPD evolution by age.

Graphic 1.- IPD INCIDENCE (X 10^5)



[Graph 1]

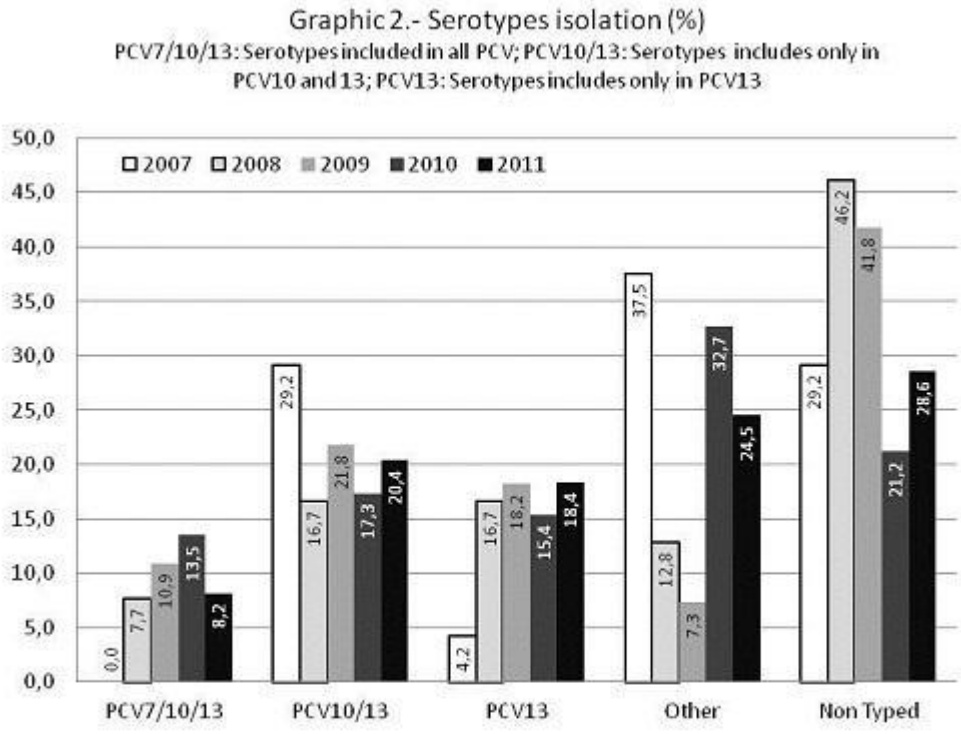
Vaccine coverage and the proportional distribution of the different types of PCV are showed on table 1.

	2007	2008	2009	2010	2011
Coverage 1 years old	45,9	52,34	57,24	65,03	70,05
Coverage 2 year old	50,99	50,73	56,06	62,8	73,32
% PCV7	97,13	98,60	99,09	40,16	0,55
% PCV10	0,05	0,05	0,70	18,78	5,07
% PCV13				40,93	94,31
% Other /unknow	2,83	1,36	0,21	0,13	0,08

Table 1.- Vaccine coverage and distribution of PCV types (%)

[Table 1. Vaccine coverage and distribution of PCV]

Graph 2 shows the evolution of serotypes isolated during the study period.



[Graph 2]

Conclusions: The incidence of IPD has been reduced to half in children less than two years, but not in older.

Vaccine coverage has been increased during the study period. The PCV13 have replaced to other vaccines.

It has not already seen an impact in the isolated serotypes, although the high percentage of nontyped SP can mask the results.

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UNIVERSAL VARICELLA VACCINATION PROGRAMME IN TUSCANY REGION (ITALY), 2008-2011: IMPACT ON DISEASE INCIDENCE, IMMUNIZATION COVERAGE AND ADVERSE REACTIONS

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In Italy, the majority of vaccine-preventable diseases are subject to mandatory notification. Varicella is an important cause of morbidity in Italy, where 500,000 cases were notified each year. Starting from July 2008, Regional Tuscany authorities recommended universal varicella vaccination with two doses of MMRV (measles-mumps-rubella-varicella) vaccine for children aged 13 to 15 months and 5-6 years. The aim of this work is to describe the results of the adoption of universal varicella immunization during the first three years of implementation.

Mandatory notifications in subjects under 15 years, immunization coverage and adverse reactions to MMRV vaccine were obtained from the regional archives. Incidence rates were calculated by age group and a comparison between the pre-vaccine period (2005-2007) and the vaccination-period (2009-2011) was also performed, excluding the 2008 transition year from the analysis.

After three years of varicella immunization implementation the incidence rates have been halved in each age group target of the program. In the vaccination period, the notification system recorded 8,547 cases less than in the previous period, in subjects under 15 years. In 2011, immunization coverage with one dose of MMRV vaccine reached 82.2%. An overall adverse reaction reporting rate of 6/10,000 doses was registered (45 cases). Only 15 cases out of 77,938 doses were classified as severe without permanent damage.

The impact of the immunization strategy in Tuscany was very positive in terms of incidence reduction. High immunization coverage with MMRV was achieved in a very short time with a low reporting rate of adverse reactions.

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IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINES ON ACUTE OTITIS MEDIA AMONG CHILDREN IN GERMANY

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Background: Routine infant immunization with the pneumococcal conjugate vaccine PCV7 started in Germany in 2007. Although substantial decline of invasive pneumococcal diseases has been observed, the effect of PCVs on non-invasive disease is unknown so far. Therefore, we assessed in these analyses the impact of PCVs on otitis media (OM) in children in Germany.

Methods: Data from IMS-Health-VIP® were used for uninterrupted time series analyses that used ICD-10 diagnosis rates as main outcomes (H66=suppurative OM, H65=non suppurative OM). The pre-vaccine period 2003-2006 provided baseline values and was compared to the single years 2007-2011 characterized by a rapidly growing vaccination rate with 7-valent and higher-valent PCVs in children < 2 years of age. Percentaged reduction rates were adjusted to the size of the corresponding age cohorts; the Poisson model was used for statistical analysis.

Results: During baseline period an average of 1,403,497/391,828 episodes of suppurative/non-suppurative OM occurred annually in children aged 0-4 years. In 2011, the episodes had reduced significantly by 19.3%/25,9% (p-value for both < 0.0001) for suppurative/non-suppurative OM representing a reduction of 270,875/101,483 cases in 2011 compared to baseline. During the 5 years from 2007 to 2011 the cumulated numbers of reduced episodes were 833,677/346,483 for suppurative/non-suppurative OM. Analysis among children aged 5-10 years showed similar trends.

Conclusion: A significant reduction in otitis media diagnoses among children in Germany after introduction of PCVs was demonstrated. Our results contribute to the growing body of evidence supporting the beneficial impact of pneumococcal conjugate vaccines in children also in non-invasive disease.

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BCG ADVERSE EVENTS: OUTCOME WITH ISONIAZID TREATMENT

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Background and aims: There is no consensus regarding the best treatment for BCG adverse events (BCG-AE). Herein we describe clinical characteristics and outcome of BCG-AE in São Paulo city, Brazil.

Methods: From January 2009 to December 2011, patients identified from the surveillance data or spontaneous demand to the Immunization Reference Center were evaluated, treated and follow-up monthly until 3mo after lesion involution. All individuals were immunized with BCG Moreau-Rio de Janeiro strain. Treatment was performed mainly with isoniazid in accordance with the Brazilian guidelines.

Results: Among the 163 patients evaluated, 31 had normal reaction, 130, locoregional adverse events and 2, other diagnoses. None of the children had HIV-seropositive mothers. No cases of BCG dissemination were identified. Six patients had more than one clinical manifestation. Clinical presentations of the 136 locoregional BCG-AE were: suppurative lymphadenitis,52.2%; injection-site abscess,26.5%; ulcer>1cm,2.9%; lymph nodes>3cm,3.8%; BCG-induced lupus vulgaris,0.7%; infected wound,0.7%; warts-like lesion,5.1%; BCG scar reactivation,5.9%; vasomotor phenomenon,0.7%, and other skin lesions,1.5%. Isoniazid was used in 96 patients and multiple drug treatment, in 3. Median period of treatment was similar between the two most common types of BCG-AE (injection-site abscess: 2.8mo, suppurative lymphadenitis: 3.2mo, p=0.450). Most warts-like lesions and BCG reactivation had spontaneous regression. Regarding the outcome, 93.9% patients had healing, 4.5% were lost for follow-up, 2 died of causes not related to BCG-AE and 3 patients are still on follow-up.

Conclusion: BCG-AE following BCG Moreau-Rio de Janeiro strain has usually favourable outcome. In cases of treatment failure, other differential diagnosis or antimicrobial resistance should be considered.

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OROPHARYNGEAL SWABS FOR NEISSERIA MENINGITIDIS (NM) TAKEN INTO ENRICHMENT BROTH, STORED FROZEN AND BATCH CULTURED SHOW LITTLE LOSS OF SENSITIVITY

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Background and aims: It is currently recommended that oropharyngeal swabs obtained in investigation of meningococcal carriage should be plated onto agar immediately or, if taken into transport medium, plated within 5 hours. This makes such studies expensive and logistically complex. It would be useful if swabs could be frozen and batch processed in a single laboratory later.

Methods: Oropharyngeal (OP) swab samples collected from healthy school students, were plated immediately onto agar plates and then placed into vials of STGG broth, held at 4°C for up to 3 hours, vortexed and frozen at -80°C. Subsequently 100µl of broth from all vials holding swabs identified to be Neisseria sp. on immediate plating were plated and cultured using the same standard methods employed for the direct plates.

Results: Of 1069 swabs collected, immediate plating yielded 107 Nm isolates. Of these 107 samples, 96 frozen swab-in-broth were also positive for Nm (sensitivity 90% vs. gold standard). A subset of these isolates were genotyped and where the genotype was resolved were found to be the same isolates identified by direct plating. Corresponding results for N. lactamica were 30/35 (86%).

Conclusions: Meningococcal carriage studies are important because conjugate meningococcal vaccines' effectiveness can be enhanced by their impact on transmission; the impact of newer protein-based meningococcal vaccines on carriage therefore needs to be investigated. The scientific, logistic and economic gains resulting from rapid sampling and batch processing may outweigh the losses resulting from 10% reduction in sensitivity particularly for populations where carriage rates are high.

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ABSCESS IN THE THIGH - A CLINICAL CASE

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Introduction: The BCG vaccine is a live attenuated vaccine of Mycobacterium Bovis. In Portugal this vaccine is inoculated intradermally, on the left arm, of all newborns in nursery at the same time that the anti-HBV is administrated in the right thigh.

Case report: 6 months old infant, male, caucasian race, with irrelevant personal background that came to the Emergency Room presenting a swelling in the right thigh, since 1 month and a half, which has gradually increased, had scarce local inflammatory signs and with no significant changes in the overall state. Performed an ultrasound which showed a "massive collection in the topography of the rectus femoris with about 6x3,5x2cm." About 20cc of purulent content were drained, whose microbiological study revealed "several acid-fast bacilli resistant", and the polymerase chain reaction for Mycobacterium tuberculosis complex tested positive. No signs of systemic disease were found nor any deficiency in the Immunological status. Taking into account the good general health of the infant, the location and progress of the lesion, it was concluded that the abscess resulted from accidental inoculation of the BCG vaccine, intramuscularly, in the thigh, probably by switch with anti B Hepatitis vaccine. He began treatment with Isoniazid and Rifampicin with total recovery.

Conclusion: The BCG vaccine is tested to be inoculated intradermally and in the arm. The inoculation at any other location may arise complications. We want to stress the need to bee rigorous in the technique of BCG vaccination.

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LEISHMANIA DONOVANI: CD2 BIASED IMMUNE RESPONSE SKEWS THE SAG MEDIATED THERAPY FOR A PREDOMINANT TH1 RESPONSE IN EXPERIMENTAL INFECTION

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We have evaluated the effect of combining CD2 with conventional antimonial (sb) therapy in protection in BALB/c mice infected with either drug sensitive or resistant strain of Leishmania donovani with 3 107 parasites via-intra-cardiac route. Mice were treated with anti CD2 adjunct SAG sub-cutaneously twice a week for 4 weeks. Assessment for measurement of weight, spleen size, anti-Leishmania antibody titer, T cell and anti-leishmanial macrophage function was carried out day 0, 10, 22 and 34 post treatments. The combination therapy was shown boosting significant proportion of T cells to express CD25 compared to SAG monotherapy. Although, the level of IFN-c was not statistically different between combination vs monotherapy ($p = 0.298$) but CD2 treatment even alone significantly influenced IFN-c production than either SAG treatment ($p = 0.045$) or with CD2 adjunct SAG treatment ($p = 0.005$) in Ld-S strain as well as in Ld-R strain. The influence of CD2 adjunct treatment was also documented in anti-leishmanial functions in macrophages. Our results indicate that CD2, which can boost up a protective Th1 response, might also be beneficial to enable SAG to induce Macrophages to produce Leishmanicidal molecules and hence control the infection in clinical situation like Kala-azar. Drug resistance is the major impedance for disease control but the encouraging results obtained after infecting mice with resistant strain of the parasite strongly imply that this drug can be effective even in treating resistant cases of Kala-azar.

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GENETIC CHARACTERISTICS OF ENTEROVIRUS 71 IN 2011 IN GUANGZHOU

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Objective: To study the aetiological agent of hand-foot-mouth disease, and the genetic characteristic of EV7 l of Guangzhou in 2011.

Methods: 63 blood, pharynx swab and stool samples of hand-foot-mouth disease were collected from Guangzhou women and children medical centern in 2011. 12 EV7l positive samples were used to isolate the virus and EV7l strains'VPl were sequenced and phyletic evolution was analysed.

Results: The affinities of 12 clinical isolates of Guangzhou area in 2011were far from A, B subtype, and the affinities of nucleotide homology and amino acid homology were less than 85% and 96.5%. With the C subtype genetic type is relatively close, nucleotide, amino acid homology over 88.5% and 97.5%, especially with the C4 subtype affinities of recently, the nucleotide and amino acid homology were 92.9% ~ 94.6% and 97.9% ~ 98.9%.

Conclusions: 12 EV71 isolates strains of Guangzhou area in 2011 belong to subtype C4a, and the choice of the evolutionary process.

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PRESENCE OF STAPHILOCOCCUS AUREUS IN NEWBORNS WITH MECONIAL AMNION FLUID

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Aim: The aim of this study is to show the percentage of Staphilococcus aureus in smirches of newborns, from mothers with meconial amnion fluid after 48 hours of delivery.

Material and method: Newborns from mothers with meconial amnion fluid in 2010 year were analysed.

Microbyologic findings from ear, pharynx and nose were analysed, taken randomly at our Department of Neonathology. They were processed at the Institute of Virusology and Microbyology in Skopje.

Results: In Special Hospital for Gynecology and Obstetrics”CAIR”, Skopje, in the course of 2010 year, 3290 newborns were born live. 530 (16,1%) of them were born from mothers with meconial amnion fluid.

Bacterial flora were analysed in 273 (51,5%) of newborns with meconial amnion fluid. 216 (79,12%) of them were sterile and 57 (20,87%) were positive.

Staphilococcus aureus was isolated in 24 (42,1%), Streptococcus beta haemoliticus in 4 (7,01%), Klebsiella aerogenes in 4 (7,01%), Acinetobacter species 6 (10,52%), Enterococcus in 3 (5,3%), E.coli in 13 (22,8%), Streptococcus pneumoniae in 2 (3,07%) and Pseudomonas aeruginosa in 1 (1,75%).

Conclusion: The analysis showed that the most frequent bacterial flora in newborns from mothers with meconial amnion fluid, after 48 hours of delivery is Staphilococcus aureus, followed by E.coli and Streptococcus species.

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MEDITERRANEAN SPOTTED FEVER (MSF) IN CHILDREN IN ORAN, ALGERIA

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We report prospective study conducted on MSF in children. Our cases were confirmed to be caused by R. conorii using immunofluorescence methods completed by Western blot and cross-absorption. Cases were encountered in the summer. Two children presented with two eschars. This is quite unusual in MSF. However, particular climat, including higher temperature, reported in Oran in recent years, may have led to an increased proclivity of ticks to bite. Although 62.5% of the children, were hospitalised, only two (with seizures). Cases were particularly severe in adults; 49% of 167 patients diagnosed with MSF were hospitalised with a severe form. Cases of MSF seem to be milder in children than in adults. In adults, the eschar is most often observed on the trunk and legs. Herein, the eschar is frequently localised on the cephalic area. When they initially sought medical care, children were prescribed drugs that were ineffective to treat rickettsiosIs. It should be remembered that doxycycline remains the treatment of choice for all patients. The risk of dental staining by doxycycline is negligible when a single (short course of therapy). Chloramphenicol continues to be used as the empirical parenteral treatment of severe cases if presence vomiting and lack of intravenous doxycycline. Josamycin can be used in children, but newer macrolides are also of interest, particularly azithromycin. MSF seems to be still misdiagnosed in children as other eruptive febrile diseases. The consequences of this include delays in appropriate therapy and a risk of a severe form and even a fatal outcome.

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CHARACTERISTICS OF CHILDHOOD TUBERCULOSIS IN TAIWAN, 2002-2009

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Background and aims: The current nationwide burden of TB continues to be a public health problem in Taiwan. The purpose of this study was to assess the epidemiology of childhood TB in Taiwan between 2002 and 2009.

Methods: We analyzed data reported as part of surveillance programs run by the Taiwan Center for Disease Control.

Results: The overall annual incidence rate during the entire data collection period was 3.04 per 100,000 population for children. For children, there was a 46% decrease in the incidence of TB, a decrease from 4.82/100,000 population in 2002 to 2.60/100,000 population in 2009. The annual incidence by age group presented a decline in the most recent years, demonstrating a peak incidence rate in the 10-14-year age group (3.63 per 100,000 population), followed by the 0-4-year age group (3.18 per 100,000), and the 5-9-year age group (2.27 per 100,000). Females had higher incidence rate than males (3.18 vs. 2.91 per 100,000 population). The incidence pattern was different among the four regions studied between 2002 and 2009. The eastern region had the highest rate of all of the studied regions (16.2 per 100,000), followed by the southern region (3.00/100,000).

Conclusions: Maintaining a vigilant surveillance system and effective application of DOTs strategy is needed for elimination of childhood TB in Taiwan.

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MOLECULAR DIAGNOSIS OF STRONGYLOIDES STERCORALIS IN FECAL SAMPLES BY PCR COMPARED TO CONVENTIONAL TECHNIQUES

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Strongyloides is the most neglected of tropical diseases and is considered an extremely common cause of morbidity and mortality worldwide. Approximately, 100-200 million persons are infected worldwide in 70 countries.Conventional diagnostic techniques don´t efficiently detect the parasite. Therefore, the need for more efficient methods that improve diagnosis particularly in those at risk to develop the severe disease is warranted.

Stool samples were collected from 115 patients of all age groups living in rural areas in Ismailia governorate, Egypt. All samples were subjected to agar plate culture (APC), Harada-Mori culture, Baermann concentration, formalin ethyl acetate concentration (FEAC), and real-time PCR targeting the small subunit of the rRNA gene.

Among the total of 115 stool samples, S. stercoralis was detected by the four conventional methods. Harada-Mori detected 11 positive samples (9.6%), FEAC detected 13 (11.3%), Baermann concentration detected 16 (13.9%) and APC detected 18 (15.7%) samples. Real-time PCR assay detected S. stercoralis DNA in 23 (20%) samples. Threshold cycles (Ct-values) of S. stercoralis positive samples were found to be between 24.45 and 40.35 with a median threshold of 29.59 cycles.

Real-time PCR is a very sensitive and specific method, offering a two-fold increase in the detection rate of S. stercoralis by FEAC. It doesn´t require much time to perform, has the ability to detect dead larvae and easy to perform and interpret the data, but it still the most expensive method. On the other hand, PCR has the ability of detecting multiple pathogens simultaneously in one test using multiplex real-time PCR.

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THE HUMAN BOCAVIRUS IS ASSOCIATED WITH LUNG- AND COLORECTAL CANCERS AND PERSISTS IN SOLID TUMOURS

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The human bocavirus (HBoV) is the second human pathogenic parvovirus. It causes respiratory infections and gastroenteritis. Some autonomous animal parvoviruses and also some human non-autonomous parvoviruses are known to persist and even integrate into the host genome resulting in transformation of the infected cells and eventually contribute to the multi-step development of cancer. Surprisingly, also HBoV persists in a so far unknown percentage of patients without causing clinical symptoms beyond those of the primary infection.In total, 11 of 60 (18.3%) lung and 9 of 44 (20.1%) colo-rectal tumors were tested positive for HBoV DNA, confirmed by sequencing and/or Southern-blotting. HBoV DNA thereby is present in the nuclei of infected cells, either in single or multiple copies, and appears also to form filaments. The data show that HBoV is present in lung and colorectal cancers. This gives rise to the hypothesis that the virus plays an active role in cancer by interactions with the host genome, or contributes to cancer development indirectly by inducing a persisting inflammation, as other DNA viruses like the human hepatitis B virus do. The occurrence of HBoV-DNA-filaments could confirm the postulated sigma- or rolling- hairpin replication mechanism. Moreover it must be concluded that it should be our foremost challenge to avoid human bocavirus infections to convert to a persistent form. This has to be done in childhood, when the majority of HBoV infections occur, e.g by development of novel vaccines.

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CLINICAL CHARACTERISTICS OF CHILDREN WITH VIRAL SINGLE- AND CO-INFECTIONS AND A PETECHIAL RASH

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Background: Children with petechial rash are more likely to undergo invasive diagnostics, to be treated with antibiotics for potential bacterial infection and be hospitalized. However, viruses have also been associated with petechial rash. Nonetheless, a systematic analysis of viral infections with modern available techniques as quantitative real time polymerase chain reaction (q-PCR) in the context of petechial rash is lacking. The purpose of this study was to prospectively uncover viral pathogens that may promote the emergence of petechiae in children and analyse the correlation with the clinical characteristics and course.

Methods: We conducted a prospective study in children (0 to 18 years) presenting with petechiae and suspected infection at the emergency department between November 2009 and March 2012. In nasopharyngeal aspirates the following viruses were analysed by q-PCR: Cytomegalovirus, Epstein-Barr virus, parvovirus B19, Influenza A and B, parainfluenza viruses, human respiratory syncytial virus A and B, human metapneumovirus, rhinovirus, enterovirus, adenovirus, human coronavirus OC43, 229E, NL63 and human bocavirus.

Results: A viral pathogen was identified in 67% of the analysed 58 cases with petechial rash. Virus positive patients showed a significant higher incidence of lower respiratory tract infections. Forty-one percent were viral co-infections, which were significantly younger than virus negative patients, had a higher leukocyte count and were longer hospitalized.

Conclusions: A petechial rash is frequently caused by viral single- and co-infections and can rapidly be identified via q-PCR. The specific role of viral pathogens in children with a petechial rash has further to be clarified in future studies.

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CHLAMYDIA PNEUMONIA INFECTION ASSOCIATED WITH UNCONTROLLED ASTHMA: A HOSPITAL BASED STUDY

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Background and aims: Asthma is a common chronic childhood diease whose prevalence is increasing. Number of asthmatics admitted with exacerbations are also increasing, and may be associated with infections. The aim off this work was to evaluate the proportion of anti- Chlamydia pneumoniae (Cp) IgM positivity in patients with uncontrolled asthma and partly controlled childhood asthma and their clinical correlates.

Methods: This was a hospital based cross sectional study. Children aged 1 to 12 y suffering from asthma were included after written informed parental consent. For diagnosis and classification of uncontrolled and partly controlled asthma, GINA guidelines 2009 were used. Anti-Cp IgM was tested by using an enzyme linked immunosorbent assay (ELISA) and value of antibody index ≥ 0.90 was considered positive. Data was collected on demographic, clinical and investigative variables including chest radiograph posterior-anterior view.

Results: From August 2010 through August 2011 44 patients hospitalized with uncontrolled asthma in exacerbation and 45 patients with partly controlled asthma from ambulatory care settings were included. Anti-Cp IgM was positive in 25 % (n = 11/44) and 6.7 % (n = 3/45) patients with uncontrolled and partly controlled asthma, respectively (Odds ratio = 4.67, χ (2) = 5.64, 95 % CI 1.20-18.10, p 0.0 17). Among the patients of uncontrolled asthma, duration of hospital stay was longer in anti-Cp IgM positive patients (9 ± 2.19 vs. 7.19 ± 2.10 d, p 0.02).

Conclusions: Since anti-Cp IgM positivity was associated with age >5 y and radiological consolidation in uncontrolled asthma in exacerbation, specific treatment of Chlamydia pneumoniae must be actively considered.

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THERAPY FOR CHILDREN WITH LUNGS PNEUMOCOCCAL INFECTIONS IN BOSNIA

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Background: Unfortunatly and today, lower respiratory tract infections caused by Streptococcus pneumoniae are a major source of morbidity among children in Bosnia and Herzegovina. Widespread use of broadspectrum antibiotics contributes to increasing rates of bacterial resistance to antibiotics. Resistance of pneumococcal strains to penicillin, cefotaxime, and ceftriaxone has increased over the past decade.

Objective: To estimate the initial and follow-up antibiotics of treatment of lower respiratory infections among pediatric patients and the relationship between type of antibiotics and outcomes, and benefits of vaccination in future and resistence of antibiotics therapy.

Methods: Prescribing data and microbiological data were analyzed for 19 (65.5%) of 29 primary care pediatricians in the intervention Sarajevo Canton region, and 18 (52,9%) of 34 pediatricians clinicians in the same region as control group. Results were stratified and reported by age, sex, and level of lungs infection to detect effects of different antibiotics on pneumonia treatment and microbiological resistence.

Results: The incidence resistence of penicillin , cefotaxime and ceftriaxone on Streptococcus pneumonia isolates has increased to 23% in Sarajevo Canton areas of Bosnia and Herzegovina. Although uncommon, resistance also has been described for clindamycin, macrolids, and imipenem. Second-generation macrolide use among children with pneumonia increased greatly during the late 2010s, in contrast to the nationwide decrease in antibiotic use.

Conclusions: Streptococcus pneumonia is the most common cause of lungs bacterial infections . Inappropriate use of antibiotics is common in primary care, and effective interventions are needed to promote judicious antibiotic use and reduce antibiotic resistance.

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DIFFERENT PERCENTAGE OF REDUCING CRP LEVELS AFTER THREE DAYS THERAPY OF SIX GROUPS DIFFERENT ANTIBIOTICS IN CHILDREN WITH PNEUMONIA

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Introduction: Well-known laboratory parameters indicating infection such as C-reactive protein (CRP) are either unspecific but sensitive biomarkers useful for the early diagnosis and therefore can be recommended to guide the initiation of empiric antibiotic therapy, but with caution and monitoring other laboratory data and diagnostic procedures and pediatrics experience.

Aims: To determine whether C-reactive protein (CRP) can be used as a parameter to identify the time point when antibiotic treatment pneumonia in children can safely be discontinued.

Methods: Authors made a restrospective study of 1600 children ages from 12 months to 7 years old with two CRP data and x-ray of lungs confirmation of pneumonia during five years period from 2007 to 2011. We measured C-reactive protein (CRP),in first and control data after 3 days antibiotics therapy comparing six groups antibiotics as separate single therapy.

Results: Mean CRP levels for definite possible serious bacterial lungs infections (19.11± 2.10mg/L) and plus definite serious bacterial infections (58.18±3.19mg/L) were significantly higher than that for no serious bacterial infection (7.18±1.91 mg/L). There was higher statistical difference in serum CRP values among the therapy with different six groups of single antibiotics in children with bacterial pneumonia after three days management as different percentage of reducing CRP levels.

Conclusions: The principle of using CRP parameters that reflect the individual balance between the host and the pathogen as well as the effects of antibiotic treatment should provide a rational basis for studying appropriate individualized durations of antibiotic treatment.

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DEFINING THE CURRENT CAUSES AND CLINICAL FEATURES OF CENTRAL NERVOUS SYSTEM INFECTION IN CHILDREN IN THE UK

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Background and aims: In UK children with meningitis or encephalitis, a pathogen is identified in only half of cases. Furthermore there are few data defining clinical and laboratory features of central nervous system (CNS) infection by diagnosis or aetiology. This study aimed to identify causes together with clinical and laboratory features of childhood CNS infection.

Methods: We undertook a prospective study recruiting children having a lumbar puncture for suspected meningitis who presented to 3 UK teaching hospitals between June 2011-June 2012. Data collected included clinical features, laboratory findings and treatment. Meningitis was defined as isolation of a pathogen from CSF ± a CSF WBC>4/µL and encephalitis by supportive neuroimaging.

Results: Of 375 children enrolled, 13(3%) had bacterial meningitis, 26(7%) had viral meningitis, 2(0.5%) had meningitis caused by atypical organisms, 8(2%) had encephalitis, 35(9%) had CSF pleocytosis with no cause identified and 203(54%) had non-CNS infection. Enterovirus was the most commonly isolated CNS pathogen occurring in 18/84(21%) cases. In infants, respiratory abnormalities and reduced feeding were more frequent in bacterial versus aseptic meningitis. In children >1 year, rash and reduced GCS were more common in bacterial meningitis. Overall, children with bacterial meningitis had higher CSF and blood WBCs and a higher CRP, compared to aseptic meningitis.

Conclusions: In the UK, aseptic meningitis accounts for most (83%) childhood meningitis. No pathogen is identified in 56% of aseptic meningitis cases. Larger studies are needed to confirm clinical differences between CNS infections and better diagnostic methods are required to inform prevention and management guidelines.

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NEONATAL APENDICITIS: AN UNCOMMON INFECTION

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Neonatal appendicitis is a very rare clinical entity but it has a high mortality (28-90%). This usually devastating ending of the disease is due, firstly, to the delayed diagnosis with the consequent delayed surgical treatment, because of the low suspicion and the atypical symptoms of the disease and secondly, to the early perforation and peritonitis, typical of this age group. Abdominal radiograph and ultrasonography is very helpful for the diagnosis.

We present a case of a 15 day old girl with acute appendicitis witch, despite treatment, died at the postoperative period. The particularities of the disease and the diagnostic questioning are also discussed, according to the international litterature, in order to remind and sensitize the clinicians to this unexpected situation.

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VARICELLA ZOSTER AND ARTERIAL ISCHEMIC STROKE IN CHILDHOOD

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Introduction: Varicella is a common childhood illness predominantly affecting children under the age of 10 years.Central nervous system complications are well recognized and include reports of ischemic stroke affecting both adults and children.

Aim: We report an three year old Irish caucasion girl, immunologic-ally healthy who presented with acute left hemiparesis two months after otherwise uncomplicated varicella zoster infection.

Methods: History, Examination, Clinical features, Investigations, Management and outcome.

Results: A 3 year old Irish caucasian girl admitted with acute left hemiparesis 8 weeks after the onset of uncomplicated chickenpox. The neurological deficit resolved within 72hrs after the onset. Magnetic resonance imaging(MRI) of the brain showed infarction in the territory of the internal capsule. A full prothrombotic screen(levels of proteinC,S antithrombin III,heparin cofactor II, plasmingoes, activated protein c resistance ratio,and investigation to detect the factor V leiden mutation or an antiphospholipid antibody)at the time of admission was normal.She has been treated with low dose of asprin with no recurrent events.She is been followed up regularly in paediatric out patient and had a repeat MRI 12 months after the stroke and the infarct is completely resolved.

Conclusion: In young children with arterial Ischemic Stroke,there is a threefold increase in preceding varicella infection compared with published population rate. Varicella associated with arterial ischemic stroke account for nearly one-third of childhood stroke and has a characteristic features,including a two fold risk of recurrent arterial ischemic stroke and transient ischemic attacks.this may be prevented by introduction of varicella vaccine in Ireland.

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ENDEMIC KAPOSI'S SARCOMA IN THE GAMBIA

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Background and aims: Infectious diseases are a common cause of malignancy in Sub-Saharan Africa (SSA). Human Herpes Virus-8 (HHV8) is endemic in Africa, with high rates of childhood infection. It is the aetiologic agent of Kaposi's sarcoma (KS), which accounts for 26% of all childhood malignancies in Africa; particularly in East and Southern Africa where it is commonly associated with HIV. In West Africa, where HIV seroprevalence is low, there is little data on its prevalence and presentation and diagnosis is easily confused with neglected tropical diseases such as podoconiosis and mycetoma.

Method: A teenage farmer presented with foul-smelling, fungating masses on his right hand and a nodular eruption of his left ankle. Both upper and lower limbs were oedematous. X-ray of his hands revealed bony erosions. Biopsies were sent for histology and microbiology, and bloods for haematology, biochemistry and HIV. Diagnosis of mycetoma was made on appearance and the occupational risk factors.

Results: Blood tests were unremarkable and HIV serology negative. Proteus and pseudomonas were isolated from the swabs but no fungal filaments or grains were seen on macerated tissue. Histology demonstrated a spindle cell tumour and immunostaining HHV8, consistent with endemic KS.

Conclusion: KS-associated herpesvirus is a common pathogen is SSA. However, there is no prevalence data on infection in The Gambia and no documentation of endemic KS in the national cancer registry. Improved access to diagnostic services will increase awareness, inform epidemiological studies and improve availability of treatment.

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INVASIVE GROUP A STREPTOCOCCAL INFECTIONS IN CHILDRENS ADMITTED WITH VARICELLA IN MIDWESTERN REGIONAL HOSPITAL

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Introduction: Group A streptococci(GAS) are bacteria commonly found in the throat and on the skin. The vast majority of Group a Strep infections are mild illnesses, such as strep throat and impetigo. Occasionally however, these bacteria can cause much more severe and even life-threatening diseases, such as necrotizing fasciitis and Streptococcal Toxic Shock Syndrome (STSS). the risk of invasive GAS infection during the varicella zoster infection is much higher.

Aim: To audit number of childrens admitted in Mid western regional hospital with varicella infection complicated by group a streptococcal infection.

Methods: Number of childrens admitted with varicella and associated complication with group A stertococal infections in Midwestern Regional Hospital from June 2002-June2012 from HIPE search,Microbiology laboratory data search,Canvasing the paediatrics consultant about children admitted under their care. Chart review of the admissions, Date of birth, Gender, Date of admission, Date of discharge, Area infected by group A streptococcal infection.

Results: 193 children admitted with varicella during this study period. 94(48%) female and 99(52%) male median length of stay in hospital was 5.5 days ranges from 1-12 days.9 children that is 3% of the total admission with varicella had necrotizing fascitis secondary to invasive group a sterptococcal infection at various different sites of the body.

Conclusion: This study provides a minimum estimate of severe complications resulting from varicella in children in the midwetern region. Most complications, excluding the death, occur in otherwise healthy children and thus would be preventable only through a universal childhood immunisation programme in Ireland.

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ETIOLOGICAL STRUCTURE OF ACUTE OBSTRUCTIVE BRONCHITIS IN CHILDREN

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Acute obstructive bronchitis are one of the most widespread forms of diseases of the bottom respiratory ways in children of early age (till 3 years) that is caused as anatomo-physiological features of respiratory ways in children of this age, and action of the viruses causing these diseases.

Definition of etiological structure of acute obstructive bronchitis in children was the **purpose** of our work.

Methods: Nasal swabs samples from 115 children hospitalized at Children Infection Diseases Hospital (Minsk) for acute obstructive bronchitis (AOB) were studied for the detection of influenza virus A and B, parainfluenza virus 1-4 types, respiratory syncytial virus (RSV), adenovirus, rhinovirus, human coronavirus (HCoV), human bocavirus (HBoV), human metapneumovirus (HMPV) by multiplex PCR assay.

Results: One or more respiratory viruses were detected in 96 of 115 (83,5%) cases. Mono-infection was diagnosed in 90% cases and at 12 (10%) patients were proved mix-infection. The most often etiological agents of AOB were RS-virus (41%), Rhinovirus (14%) and Influenza virus 1-4 types (14%). Parainfluenza virus was detected in 5%, HBOV - 7%, HMPV - 9%. Among mix-infections were HBoV+Rhino (3 cases), HboV+HMPV (1), HBoV+Adeno (1), HBoV+Parainfluenza (2), Parainfluenza+RSV (3), Influenza A (H1N1) pdv-09+RSV (1), InfluenzaB+HMPV (1).

Conclusions: This study demonstrates that main etiological agents of acute obstructive bronchitis in children are respiratory viruses among which PSV belongs the most important role.

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DIAGNOSIS OF PAEDIATRIC COMMUNITY- ACQUIRED LOWER RESPIRATORY TRACT INFECTION CAUSED BY MYCOPLASMA PNEUMONIAE BY POLYMERASE CHAIN REACTION

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Background and aims: Mycoplasma pneumoniae(M.pneumoniae) has been frequently implicated in the pathogenesis of acute respiratory tract infections. Symptomatic disease may be manifested in the upper respiratory as pharyngitis, otitis or in the lower respiratory tract as tracheobronchitis, bronchopneumonia or may remain totally asymptomatic. The aim of our study was to detect IgM and IgG antibodies to M. pneumoniae by enzyme immunoassay, Myocplasma pneumoniae DNA in nasopharyngeal aspirates by polymerase chain reaction (PCR) and to correlate clinical, serological and PCR findings for establishing diagnosis of Mycoplasma pneumonia infection.

Methods: The present study evaluated sixty-two children hospitalised for community-acquired lower respiratory tract infection (n=62) using IgM and IgG enzyme immunoassay (ELISA) and PCR assay to amplify a 345 base pair fragment on P1 adhesin gene of M.pneumoniae, employing nasopharyngeal aspirates (NPA).

Results: Serology was found positive in 18(29%) cases. PCR was positive in 3(4.8%) of the 62 cases with serologically proven M.pneumoniae infection. None of the demographic, clinical or radiological findings were significantly associated with M.pneumoniae infection.

Conclusion: Mycoplasma pneumoniae should be considered as a potential etiological agent in paediatric lower respiratory tract infections. The detection must be performed by a combination of serology and PCR.

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ENCEPHALITIS DUE INFLUENZA A (H1N1) IN A SEVEN YEAR-OLD GIRL WITH GOOD RESPONSE TO OSELTAMIVIR

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Background and aims: Human infection with the novel H1N1 influenza virus was first reported in April 2009. Novel Influenza A (H1N1) virus produces higher mortality in young people. Different clinical manifestation of Influenza A (H1N1) has been reported. We present encephalitis due influenza A (H1N1) with good response to oseltamivir.

Patient: The patient was a seven year-old girl presented with mood change and gait ataxia from 5 days before admission. She also had fever, delusion, and lethargy. She had history of common cold several days before admission. She was treated with acyclovir with impression of encephalitis without improvement. In physical examination (P/E) she was febrile, there was no nuchal rigidity. P/E of chest, abdomen and extremities were normal. Lumbar puncture was performed. Cerebrospinal fluid (CSF) was normal. CSF culture showed no growth after 48h. CBC, FBS, BUN, Cr, Na, K, ALT, AST, CRP and procalcitonin were all normal. HSV PCR was negative. Elecroencephalography (EEG) was done that suggested encephalitis. Brain MRI was normal. Throat culture was obtained for the diagnosis of influenza A (H1N1) that was positive. The patient was treated with oseltamivir. The patient recovered after treatment and tests for equilibrium became normal.

Conclusions: Encephalitis due to influenza A (H1N1) should be considered in every patient with signs and symptoms of encephalitis during influenza A (H1N1) pandemy.

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IMMUNITY LEVEL TO HAEMOPHILUS INFLUENZAE IN BETA-THALASSEMIA SPLENECTOMIZED CHILDREN

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Background: Patients with thalassemia and asplenia are at increased risk for infection. The aim of this study was to determine the Hemophilue influenza type b (Hib) antibody concentration among beta thalassemic patients with and without spleen.

Material and method: The Hib antibody concentration was investigated in 87 patients with thalassemia, 50 of who had undergone splenectomy. Hib antibody was determined by an ELISAmethod. Subjects who had Hib antibody level ≥1.0 µg/ml as long term protection, between 0.15 to < 1.0 µg/ml as short term protection and < 0.15 µg/ml as no protection. Also patients with Hib antibody concentration ≥0.15 µg/ml classified as protective and who had antibody level < 0.15 µg/ml as non protective. For the analysis we used SPSS 11.5 software. A two sided p-value less 0.05 was considered statistically significant.

Results: 83.8% (31) of non.splenectomized patients had protective antibody levels against Hib whereas among asplenic patients this rate was 32.0% (16) that there was significant differences (p< 0.001). Protection against Hib decreased with increase interval time after splenectomy from 64.7% in ≤60 months interval to 5.3% in >120 months interval (p=0.001). Thirty percent of the 50 splenectomized subjects had long term protection against hemophilus influenza type b where as 62.2 percent of 37 subjects with spleen had long term protection (p< 0.001).

Conclusion: Patients with splenectomy lower Hib antibody level than cases with spleen. Also antibody level decreased with time interval after splenectomy. Thus the vaccine recommendation seems essential for beta thalassemic splenectomized patients for increased serum Hib antibody concentration.

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EBV-ASSOCIATED LYMPHOPROLIFERATIVE DISORDERS (EBV-LPD) ARE A SIGNIFICANT PROBLEM AFTER HEMOPOIETIC STEM CELL TRANSPLANTATION

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During eight years, 2002 through 2010, thertione patients with thalassemia major received an HLA-haploidentical transplant. The patients were conditioned with 60 mg/kg hydroxyurea , 3 mg/kg azathioprine from day -59 to -11, 30 mg/m^2 fludarabine from day -17 to -11, 14 mg/kg busulfan on day -10, 200 mg/kg cyclophosphamide, 10 mg/kg Thiotepa, 12.5 mg/kg anti-thymocyte globulin daily from day -5 to -2,following by CD34$^+$ mobilized peripheral and bone marrow progenitor cells infusion and 2 .10^5/kg T-cell by fresh marrow addback.

Six patients developed EBV positive expression between days 100-150 post transplant and were treated with pathology documentation, fever and lymph node enlargement. One of them ,at that time had mixed chimerism, (65% donor). We infuse unmanipulated donor lymphocytes at the dose of CD3+ 5 x 10 ^{4} /kg (UDLI). Twenty days after the first infusion the PCR EBV became negative, the chimerism analysis showed 92% donor.Three of the six patients developed a post-transplant lymphoproliferative disorder (PTLD).

All of them, despite receiving the anti -CD20 monoclonal antibody, had a rapidly progressive course. One patient affected by diffuse large cerebral B cell lymphoma died in 15 days. The second patient, affected by PTLD cervical lymphadenopaties, received eight Rituximab infusions and reached complete remission.The last patient, 3 year old boy, despite 8 weekly doses of rituximab, showed a large abdominal lymphoadenopathy. The child underwent surgical intervention in another institution.He received 3 doses UDLI, after the third dose the EBV PCR was negative, the chimerism was complete and PTLD in remission.

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BURDEN OF VIRAL PATHOGENS ON SEVERE LOWER RESPIRATORY TRACT INFECTIONS AMONG PREMATURE INFANTS: PROSPECTIVE BIRTH COHORT STUDY IN BRAZIL

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Background and aims: Premature infants are at high risk for developing severe respiratory disease. Prospective studies on the role of viral pathogens on the burden of severe respiratory diseases are scarce, especially in developing countries. This 3-year study in Brazil (2008-2010) determined the incidence of severe respiratory syncytial virus (RSV)-related lower respiratory tract infections (LRTIs) requiring hospitalization in infants ≤35 weeks gestational age.

Methods: Infants identified as preterm births in 3 Brazilian referral hospitals were prospectively followed up from maternity hospital discharge for 1 year. Subjects were seen monthly for the first 6 months and bimonthly thereafter. Subjects with signs/symptoms of an LRTI were tested for respiratory viruses by real-time RT-PCR.

Results: The analysis population consisted of 303 preterm infants, including 246 who completed follow-up. At birth, 299 (98.7%) subjects were hospitalized an average (±SD) 36.4±26.9 days; 269 (88.8%) infants were admitted in the NICU (mean stay: 31.8±27 days). During follow-up, 432 LRTI episodes occurred in 176 subjects. RSV and human rhinovirus were each detected, alone or in combination, in 33.1% and 29.4% of these episodes, respectively (Table). Thirty subjects, representing 9.9% of the analysis population and 17.0% of subjects with an LRTI episode, experienced a severe RSV LRTI requiring hospitalization.

Conclusions: RSV is a substantial cause for hospitalization among premature infants in Brazil, resulting in hospitalization for approximately 10% of premature infants. RSV and human rhinovirus were the most frequently detected viruses in LRTI episodes.

Table. Viral Pathogens Identified by RT-PCR in Premature Infants With LRTI

Viral pathogen	Number (%) (N=432)
Respiratory syncytial virus (A and B)	143 (33.1)
Human rhinovirus	127 (29.4)
Human bocavirus	83 (19.2)
Metapneumovirus (A and B)	73 (16.9)
Influenza (A and B)	58 (13.4)
Parainfluenza virus (1 and 3)	39 (9.0)
Adenovirus	22 (5.1)
Coronavirus (OC43 and 229E)	21 (4.9)
Influenza (H1N1)	12 (2.8)

[Table]

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EVALUATION OF THE INDICATION AND COMPLICATION OF HICKMAN CENTRAL VENUS CATHETER INSERTION IN PAEDIATRIC POPULATION DURING LAST 5 YEARS

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Aims of the study: The study was designed in order to evaluate the clinical data, indications and complications related to Hickman Central Venus Catheter (CVC) insertion to all paediatric patients, between 2008-2012.

Methods: The records of all patients ≤14 years of age underwent Hickman CVC insertion were assessed.

Results: The study population consisted of 24 patients. Out of them 16 were neonates (mean age 0.2±0.1 years) and 8 were children (mean age 4.8±1.9 years). The majority were males (17;70%). Among neonates, main indications for Hickman insertion were NEC (9;56%), feeding disorders (5;31%), encephalopathy (1;6%) and biliary atresia (1;6%). Children required Hickman due to ALL's (2;25%) or solid tumor's (4;50%) chemotherapy, encephalopathy (1;12.5%) and feeding disorder (1;12.5%). The main insertion site was right jugular vein (20;77%). Hickman remained for 15±7 days in neonates and for 135±130 days in children (p=0.005). Total CVC-days were 1008.

The main complication was CRBSI (4;15%) and colonization (4;15%). Rupture, thrombosis and malposition were recorded in 1 case each (4%). CONS was responsible for the majority (6;75%) of the colonization. The above complications indicated the Hickman removal in 28% of the cases, while the rest CVCs were removed as not longer needed. Comparing patients that developed CRBSI vs those that didn't, the length of hospitalization was the main risk factor (OR 0.673, CI 95% 0.233-0.870, p=0.002).

Conclusion: Hickmans are indicated for neonates undergoing surgical procedures or facing feeding problems as well for children with malignancies. Main complication remains infection related to the hospitalization length.

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SYSTEMATIC REVIEW OF HERD IMMUNITY BY VACCINATING CHILDREN AGAINST SEASONAL INFLUENZA

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Background: Population-based influenza vaccination of children has been recommended in some countries on the basis of conferring both direct protection and possible indirect benefits to the community. We aim to systematically assess the evidence on herd immunity from influenza vaccination of children.

Methods: A systemic review of published studies, as well as grey literature, in any language to December 2012, that examined indirect protection by vaccinating children against seasonal influenza. Risk of bias assessments and data extraction were performed independently by two authors.

Results: In total, 25 studies were identified: 13 of them examining trivalent inactivated influenza vaccine (TIV); 12 assessing live attenuated influenza vaccine (LAIV). Seven of 13 TIV studies and 3 of the LAIV studies were randomised controlled trials. Despite substantial heterogeneity in study characteristics and difficulty in generating quantitative estimates, it was evident that vaccinating children aged 0.5-15 years against influenza conferred indirect protection to the community, especially to older adults and to those with limited contact with wider populations. The indirect benefit of vaccinating school children was supported by:

(1) the Japanese program of vaccinating school children (aged 3-15 years) with TIV that reported a 36% reduction in adjusted-mortality among seniors aged ≥65 years, and

(2) US school-based programs using LAIV prior to universal vaccination recommendations.

Conclusions: Our review suggests that vaccinating healthy children against influenza has indirect protective effects to the community. These findings should be considered as an essential component in informing decision making about universal influenza vaccination in children.

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CARBAPENEM RESISTANT BACTERIA; THE IN HOUSE BEAST!

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Introduction: Gram negative bacteria are important cause of neonatal sepsis carrying highest morbidity and mortality. Development of multidrug resistance is a major challenge. Carbapenems have been the saviors for years. The recently description of Carbapenem resistant gram negative bacteria (CRB) in neonatal units is the worst nightmare.

This study reports the microbiological distribution of (CRB), clinical presentation, risk factors and outcome. Comparing them to other gram negative bacteria.

Method: A retrospective hospital based study. At level 3 neonatal unit at the university of Jordan hospital.

Results: 28 (CRB) were identified out of 99 cultures with gram negative bacteria. Most of it were late septic episodes. 57% of them were CLABSI. The average age of sepsis was 12.5 days. 71.4% of newborns affected with (CRB) were premature and low birth weight infants (< 2500g).

Acintobacter was the only (CRB) identified. Fever was the most common presenting symptom (28.6%).Followed by respiratory symptoms (21.4 %). Then hematologic abnormalities in asymptomatic newborns (17.9%).Mortality rate was 10.7%.66% of babies who died were female newborns ,received IVIG and had shock as the presenting symptom. None of the newborns who died had fever at presentation.

Conclusion: In units where (CRB) is an issue, we suggest implementing skin colonization screening and cohorting policies. Colonized newborns who develop laboratory abnormalities should be given empirical treatment until primary blood culture results are available .IVIG use doesn't improve survival. Fever at presentation is a good prognostic sign. Further prospective studies are needed to identify risk factors and best preventive measures.

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PROCALCITONIN LEVELS IN UMBILICAL CORD BLOOD REFLECT SEVERITY OF HISTOLOGICAL CHORIOAMNIONITIS AND ASSOCIATE WITH EARLY-ONSET NEONATAL SEPSIS

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Bacgroud and aims: Procalcitonin (PCT) levels in umbilical cord blood were investigated to determine associations of severity of chorioamnionitis (CAM) and clinical manifestations.

Materials and methods: The retrospective study was conducted for 143 pregnant women and neonates. PCT levels in umbilical blood were measured. The severity of CAM was classified according to the definition by Redline et al. PCT levels were evaluated the correlation with placental histological findings and clinical manifestations.

Results: The gestational age at birth and birth weight of study group were 32.2±5.0 weeks of gestation and 1802±885g, respectively. Twenty seven women had CAM. PCT of group with CAM was significantly higher than that without CAM ($p < 0.01$). PCT levels significantly rose with maternal or fetal stage. Ten of 11 neonates with ≥2ng/ml of PCT had early-onset sepsis (Table). In group without CAM, PCT levels had negative correlation with gestational age (n=116, r=0.72).

Conclusions: PCT levels in umbilical blood reflected severity of chorioamnionitis and influenced on neonatal outcomes.

PCT(ng/ml)	< 0.5	0.5 - 2	2 - 10	10≤
CAM(n=27)	**14**	**2**	**6**	**5**
Sepsis(n=12)	1	1	6	4
Intubation(n=21)	8	2	6	5
IVH(n=7)	0	1	3	3
Non-CAM(n=116)	**113**	**3**	**0**	**0**
Sepsis(n=0)	0	0	0	0
Intubation(n=44)	41	3	0	0
IVH(n=2)	2	0	0	0

[Table]

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INTERFERON GAMMA AND INTERFERON GAMMA RECEPTOR-1 GENE POLYMORPHISMS IN CHILDREN WITH NON-RESPONDERS TO HEPATITIS B VACCINATION

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Objective: The variations of genes involved in processes such as pathogen recognition, antigen processing and maturation of lymphocytes may affect the develop of immune response to the hepatitis B vaccine. The aim of the study were to investigate the +874 T/A polymorpism in the first intron of interferon gamma (IFNG) gene and intronic (CA)n polymorphic microsatellite marker of the interferon gamma receptor 1 (IFNGR1) gene in children with non-responders to hepatitis B vaccination, and to determine whether vaccine responce is influenced by these gene polymorphisms.

Material and method: A total of 200 children (109 males and 92 females) between 9,2±1,6 years of age were included in this study. One hundred healthy children who had anti-HBs antibody < 10 mIU/mL levels after vaccinated against hepatitis B according to a standardized schedule were included in this study as non-responder group. One hundred healthy children who had anti-HBs antibody >10 mIU/mL levels after vaccinated against hepatitis B were included as responder group. These polymorphisms were genotyped by using amplification refractory mutation system-polymerase chain reaction.

Results: The frequency of TT genotype of IFNG (+874 T/A) gene polymorphism was higher in non-responders (p=0,003). The frequencies of allele 170 and 182 for (CA)n alleles for the intronic (CA)n microsatellite of IFNGR1 gene were significantly higher in non-responders (All of them, p< 0,05).

Conclusion: The TT genotype of IFNG (+874 T/A) gene, allele 170 and 182 for (CA)n alleles for the intronic (CA)n microsatellite of IFNGR1 gene may be associated with non-responders to hepatitis B vaccination.

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SENSITIVITY OF TORCH SCREEN VS URINE FOR CMV IN DIAGNOSING INTRAUTERINE INFECTION IN MIDWESTERN REGION

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Introduction: The TORCH screening is a blood tests that is used to check for several different infections in a newborn. TORCH stands for **toxoplasmosis**, **rubella**, cytomegalovirus, herpes simplex, and HIV.Many infants with intrauterine growth retardation (IUGR) are screened for TORCH infections. A diagnosis of Congenital CMV can be made if the infant urine is tested with in one week after birth.The yield and costs of TORCH screen may not be justifiable.

Aim: The aim of the study was to determine the number of congenital infections detected with the current use of the TORCH screen Vs urine for CMV.

Methods: A review of all TORCH screen results and urine for CMV results were undertaken in a 10 year period from January 2002 to December 2012 by serology laboratory results with subsequent review of relevant medical charts.Canvasing the neonatologist about the babies admitted under their care.

Results: During this study period there where 54231 live births out of which 2964 babies were born below tenth centile out of that 419 with symmetrical IUGR for which TORCH screen was sent and only five are positive that is 1.1% of the total blood test and in comparison to that only 77 urine test was sent for CMV and 17 are positive that is 20% of the total test.

Conclusion: The yield and costs of TORCH screen may not be justifiable but CMV diagnosis can only be made if the virus is detected in infants urine during the first week of life.

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WHAT IS THE NORMAL INCIDENCE OF RESPIRATORY COMPLAINTS IN CHILDREN? FIRST RESULTS OF THE CHILD-IS-ILL STUDY ('KIND-EN-ZIEKMETING')

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Background and aim: Many children with respiratory tract infections (RTI) are referred to a paediatrician because they are ill 'too often'. But what is too often? And when should investigations into potential underlying disease be undertaken? In the Child-is-ill study respiratory tract symptoms (RTS) matching possible RTI are studied in 2-18-year-old children from the Dutch general population.

Methods: In an online prospective 2-year cohort study parents are weekly asked about RTS in their child(ren) during the preceding week; if present, additional questions about complaints, doctor visits and use of antibiotics are asked. The study was advertised through social media and the internet.

Results: During 2012, parents enrolled 749 children (376 boys; 1/3< 4yrs, 1/3=4-9yrs, 1/3>9yrs; families: 640 non-smoking, 283 non-atopic); 24,033 childweeks were reported, with 'no complaints' in 84% of them. The number of weeks with 'no complaints' increased in spring and summer, and with decreasing age. Cough, stuffy nose, runny nose, throatache and headache were reported most often (1581x, 1093x, 966x, 798x, 728x); earache, hoarseness and dyspnea were reported 312x, 302x and 213x. Rather unexpectedly, ear discharge was seldom reported (74x). Often, several complaints were concomitantly reported.

Conclusion: The - preliminary - results may be 'stating the obvious'. However, it is important to collect solid evidence to support clinical experience; this will help to identify children who are 'different'. Also, these data can be used to compare with groups of children with identified underlying disease. The Child-is-ill study aims to reach 1000 inclusions (100,000 childweeks) to help solve these clinical questions.

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THE UNPLEASANT COMPANY ENTEROVIRUS KEEPS: UNINVITED ROTAVIRUS

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Background: Enteroviruses are the most common causative agents of aseptic meningitis. Clinical suspicion of enterovirus etiology is strong in an epidemic setting and if characteristic manifestations are present.

Aims: We present a case of enterovirus meningitis, complicated with rotavirus co-infection during the summer meningitis outbreak 2012, Plovdiv, Bulgaria.

Materials and methods: A 21-month-old boy was admitted to the Infectious Diseases Department for treatment of meningitis. Improvement was rapid on day 3. Simultaneously, a 5-month-old boy was accommodated in another room because of fever, vomiting and diarrhea. On day 2, due to signs of meningeal irritation a lumbar puncture was performed, indicative of meningitis. The child was transferred to meningitis ward. He was without fever and vomiting but diarrhea persisted. His mother declined accommodation in a separate room and the 2 infants remained together. On day 6, before arranged discharge, the older boy presented with intractable vomiting and became lethargic. On the following day, vomiting quickly abated but diarrhea developed. His general condition rapidly improved. Both children were discharged fully recovered. In a week's time, virological test results were as follows: the older boy- spinal fluid culture negative with stool culture positive for Echovirus-30, confirming the enterovirus etiology of his meningitis. Regarding the infant - his stool culture was enterovirus negative but rotavirus positive (ELISA). No virological tests were performed on his spinal fluid.

Conclusion: Our case provides further evidence for the nosocomial potential of the rotavirus and stresses the importance of contact precautions to prevent secondary diarrhea cases.

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QUANTITATIVE AND QUALITATIVE IMMUNE RESPONSES TO THE 13 PNEUMOCOCCAL SEROTYPES IN ADULTS AFTER IMMUNIZATION WITH 23-VALENT PNEUMOCOCCAL POLYSACCHARIDE VACCINE

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Objective: To evaluate the quantitative and qualitative immune responses to the 23-valent pneumococcal polysaccharide vaccine (PPV23), this study was done at the Ewha Center for Vaccine Evaluation and Study (ECVES).

Methods: A total of 30 healthy Korean adults were immunized with one dose of PPV23. Sera were collected just before vaccination and after 4 weeks. Anticapsular IgG antibody concentration and opsonic index to the each 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) were measured with ELISA and multiplexed opsonophagocytic killing assay (MOPA), respectively.

Results: ELISA and MOPA for 13 serotypes were performed successfully. Geometric mean antibody concentration (GMC) and geometric mean opsonic indices (GMI) with 95% confidence interval (CI) were measured. The percent of IgG Ab concentration ≥0.35 ug/mL to 13 serotypes were 86 -100% and the percent of opsonization indices ≥8 to 13 serotypes were 33 -100% and 90-100% before and after immunization, respectively.

Conclusions: The quantitative and qualitative immune response studies to the 13 pneumococcal serotypes were performed successfully in ECVES. The PPV23 was highly immunogenic for the 13 serotypes in Korean adults. ELISA and MOPA can be applied for the evaluation of pneumococcal conjugate vaccine as well as PPV23 for the evaluation of immune response to vaccination for all age groups.

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INVASIVE BACTERIAL INFECTIONS AT A UNIVERSITY HOSPITAL FOR 15 YEARS, 1996-2011

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Backgrounds: Despite of effective antibiotics and newly developed vaccines, bacterial infection is still the most important cause of morbidity and mortality in children. The purpose of this study is to describe the etiology of invasive bacterial infections in children in recent decades.

Methods: We retrospectively collected the data of invasive bacterial infections in children ≤ 18 years of age at Ewha Womans University Hospital from 1996 to 2011.

Results: A total of 159 cases were noted. In all ages, S. agalactiae (41/159, 25.8%), S. aureus (38/159, 23.8%), and S. pneumoniae (32/159, 20.1%) were the most common pathogens. S. agalactiae was a common etiology of meningitis (31/39, 79.5%), bacteremia without focus (8/39, 20.5%), and septic arthritis (2/39, 5.1%). S. aureus was a common etiology of septic arthritis and osteomyelitis (27/38, 71.1%) and bacteremia without focus (7/38, 18.4%). S. pneumoniae was a common etiology of meningitis (12/32, 37.5%) and pneumonia (11/32, 34.4%). S. agalactiae (39/65, 60.0%) and S. aureus (8/65, 12.3%) were most common bacterial pathogens in infants younger than 3 months. S. pneumoniae (21/57, 36.8%) and H. influenzae (14/57, 24.6%) were common in children from 3 months to 5 years of age. S. aureus (21/37, 56.8%) and S. pneumoniae (9/37, 24.3%) were common in children beyond 5 years of age. Through the fifteen years, yearly frequency of invasive bacterial disease was similar, however invasive diseases caused by H. influenzae have decreased, especially since 2001.

Conclusion: S. agalactiae, S. aureus and S. pneumoniae are important causative organisms of invasive bacterial infections.

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INCIDENCE OF RESPIRATORY SYMPTOMS IN CHILDREN WITH DOWN SYNDROME: FEASIBILITY OF A WEB-BASED PARENT-REPORTED PROSPECTIVE STUDY

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Background and aims: Respiratory tract symptoms (RTS) are common in children with Down syndrome (DS), they are often, but not always, the result of respiratory tract infection (RTI). We designed a web-based study to determine the rate of RTS in DS children in relation to common comorbidity ('KiDS-dagboekstudie').

Methods: Parents were informed about the study through social media. Upon enrollment, parents weekly receive a web-based questionnaire for two years. When the child has had symptoms in the preceding week, additional questions about the type of complaints, doctor visits and use of antibiotics are shown. Additionally, parents receive three questionnaires (t=0,1&2yrs) on the family situation, comorbidity and daily (school) activities. The results will be compared to the Child-is-ill study ('Kind-en-Ziekmeting') that is being run in an identical fashion in children that are considered to be 'normal as to being ill' by their parents.

Results: Between January-August 2012, 98 DS children were enrolled (mean age 6yrs, range 0.1-17.6; 57% boys). Table 1 shows comorbidity; Table 2 shows data on RTS. In the first 3 months, the weekly response rate was stable and remained high at 89% (range 84.7-92.9%).

Conclusion: We designed a feasible web-based study to collect prospective data on parent-reported RTS in DS children. The preliminary results show that parent-reported RTS are a considerable problem in DS children that warrants further study.

TABLE 1 ***Comorbidity in DS children***		***TABLE 2*** ***RTS in children with DS***	
Congenital heart disease	37%	History of suffering from frequent serious RTI	73%
Hypothyroid disease	15%	History of RSV infection	25%
Diabetes mellitus	0%	History of wheezing	29%
Celiac disease	2%	≥6 courses of antibiotics for RTI	52%
Hearing loss	41%	History of antibiotic prophylaxis	18%
Chronic snoring	13%	History of inhaled corticosteroids	31%

[Tables]

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CROSS-REACTION OF 6B/19F ANTIBODIES TO SEROTYPES 6A, 6C, AND 19A AFTER IMMUNIZATION WITH PCV7 IN KOREAN CHILDREN

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Purpose: This study was aimed to investigate the serological properties of cross-protective antibodies against vaccine-related serotypes 6A, 6C, 19A induced in young children after booster of PCV7.

Methods: IgG and IgM concentrations and opsonic index (OI) against vaccine serotypes 6B and 19F and vaccine-related serotypes 6A, 6C, and 19A was measured by ELISA and multiplexed opsonophagocytic killing assay (OPA). The serological properties and antigenic specificity of protective antibodies were determined by IgM depletion of immunesera, OPA, competition OPA against serogroup 6 and 19 pneumococci.

Results: In 4 selected immunesera, the concentration of serum for 6B ranged from 5.6 to 57.4ug/ml in IgG and from 3.61 to 26.49ug/ml in IgM, respectively; as for 19F, from 13.4 to 156.1ug/ml (IgG) and from 10.43 to 64.61ug/ml (IgM), respectively. Compared to pre-IgM depleted immune sera, OI of IgM-depleted immunesera against 6B and 19F decreased 67-97% (6B), 0-85% (19F), respectively, whereas OI against 6A, 6C, and 19A decreased 87-100%(6A), 49-100%(6C), and 89-100% (19A), respectively. In competition OPA, free 6B and 19F polysaccharide completely inhibited the immune protection against serotypes 6A, 6C, and 19A as well as 6B and 19F.

Conclusions: The booster of PCV7 certainly induced cross-protective antibodies against serotypes 6A, 6C, and 19A with both IgG and IgM isotypes. Furthermore, IgM-type protective antibodies are more highly contributed to opsonophagocytic activity against vaccine-related serotypes as well as most of vaccine types than do IgG-type antibodies.

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ANTIMICROBIAL RESISTANCE PATTERN IN ETHIOPIAN CHILDREN WITH BLOOD STREAM INFECTIONS AT BLACK LION AND YEKATIT 12 HOSPITALS

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Bloodstream infection is a common cause of hospitalization, morbidity and death in children. It is a serious problem that needs immediate attention and treatment. The aim of this study was to determine the pattern of bacterial agents responsible for blood stream infection and to get an updated knowledge about their antibiotic resistance pattern. A cross sectional study involved about 201 pediatric patients (≤12 years) was conducted from October 2011 to February 2012 at pediatric units of Tikur Anbessa Specialized Hospital and Yekatit12 Hospital. Standard procedure was followed for blood sample collection. Among 201 study subjects 110 (54.7%) were males. Majority 147 (73.1%) of them were neonates (≤ 28 days). The mean length of hospital stay before sampling was 4.29 days. Out of the 201 tested blood samples, blood cultures were positive in 56 (27.9%).Gram negative and Gram positive bacteria constituted 29(51.8%) and 26(46.4%), respectively. The most frequent pathogen found was Staphylococcus aureus 13 (23.2%), followed by Serratia marcescens 12(21.4%), CoNS 11(19.6%), klebsiella spp 9(16%), Salmonella spp 3(5.4%) and Enterobacter cloacae 2(3.6%). Majority of bacterial isolates showed high resistance to Ampicillin, Penicillin, Co-trimoxazole, Gentamicin and Tetracycline. Ciprofloxacin and Nalidixic acid were the most effective antimicrobial agents for Gram negative bacteria while Vancomycin and Clindamycin for Gram positive bacteria. In conclusion the present study revealed that majority of the isolates was multidrug resistant. These alarmingly higher percentages of multi-drug resistant emerged isolates urge us to take infection prevention measures and to conduct other large studies for appropriate empiric antibiotic choice.

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EPIDEMIOLOGIC, CLINICAL CHARACTERISTICS, AND RISK FACTORS OF ADVERSE OUTCOME IN NEONATES WITH LATE ONSET SEPSIS

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Background: Late-onset sepsis (LOS) is a common complication in the neonatal intensive care unit (NICU). We aimed to describe the epidemiology, clinical characteristics, and risk factors for adverse outcome in neonates with LOS.

Methods: We conducted a cohort study of all neonates with LOS at the NICU of a Tertiary Taiwan Medical Center from January 2004 through December 2011 and used multivariate logistic regression to identify risk factors for final adverse outcome.

Results: Among 5010 neonates over 253,644 neonate-days, 713 (14.2%) experienced a total of 942 episodes of LOS (incidence rate [IR], 3.71 episodes per 1000 neonate-days). Although the rates of LOS were reversely proportional to birth weight and gestational age, the IRs were comparable between extremely preterm, late preterm and full term neonates. Fungemia was found to have significantly high rate of infectious complication (30.8%), persistent bloodstream infection (19.2%), and sepsis-attributable mortality (23.1%). The overall mortality rate was 12.6% (90/713), and sepsis-attributable mortality rate was 7.2% (68/942 episodes). Independent predictors of in-hospital mortality were Pseudomonas LOS (adjusted odds ratio [OR], 14.31; 95% CI, 3.87-53.0), fungemia (OR, 5.69; 95% CI, 2.48-13.01), presences of congenital anomalies (OR, 4.12; 95% CI, 1.60-10.60), neuromuscular comorbidities (OR, 3.34; 95% CI, 1.66-6.73), and secondary pulmonary hypertension with/without cor pulmonale (OR, 23.48; 95% CI, 5.96-92.49).

Conclusions: Late-onset sepsis predisposes NICU hospitalized neonates at risk of mortality or morbidity, especially caused by Pseudomonas aeruginosa or Candida spp. More aggressive treatment strategy is worth consideration in neonates with presumed LOS, particularly those with certain underlying chronic conditions.

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ACUTE RHEUMATIC FEVER FOLLOWING ACUTE POST-STREPTOCOCCAL GLOMERULONEPHRITIS SECONDARY TO GROUP G STREPTOCOCCAL INFECTION

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Background: Group G streptococcus (GGS) have been reported to cause acute post-streptococcal glomerulonephritis (APSGN) or acute rheumatic fever (ARF). Our patient is the first case to be reported for having both ARF and APSGN secondary to GGS.

Methods and Results: A 6-year-old girl, presented with facial puffiness for 3 weeks and tea-colored urine and oliguria for 2 days. she received antibiotics 4 weeks earlier for sore throat. No history of skin rash or joints pain . She was afebrile with generalized edema, blood pressure of 137/81mmHg while other examinations were unremarkable. Complete blood count, renal function and C4 level were normal but C3 was low with high Anti-streptolysin O (ASO) titer. Throat culture and Antinuclear antibody were negative. Urinalysis showed hematuria and proteinuria. Electrocardiogram was normal. She was diagnosed as APSGN and treated with Furosemide and Amlodipine. Two weeks later she presented with right knee pain but she was afebrile. Examination revealed grade 3/6 pan-systolic murmur, right knee swelling, tenderness with restricted range of movement. Throat culture came positive for GGS. ESR ,CRP and ASO titer were high while rheumatoid factor was negative. Echocardiogram revealed severe mitral and aortic regurgitation with pericardial effusion . ARF diagnosis was established with dramatic response upon starting Aspirin. On Subsequent 2 weeks follow-up she was symptoms free and maintained on Benzathine penicillin prophylaxis.

Conclusion: In our case the association between ARF following APSGN secondary to GGS infection suggests some GGS stains might have both nephritogenic and rheumatogenic features though pathogenesis yet to be understood.

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BLOOD STREAM INFECTIONS AMONG NEONATES ADMITTED TO A VIETNAMESE PAEDIATRIC HOSPITAL

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Background and aims: Blood stream infections (BSI) causing septicaemia are among the major causes of neonatal morbidity and mortality globally, but have not been described in Vietnam previously.

We describe positive blood cultures (BSI) and septicaemia related death among hospitalized neonates in Vietnam.

Methods: Among all neonates admitted to a tertiary paediatric hospital in South Vietnam in a 12 month period in 2009-10, data on positive blood cultures were obtained. For neonates with positive culture, data were retrieved on isolate, antibiotics susceptibility, basic demography and clinics. Each neonatal death occurring was audited to determine septicaemia relation.

Results: Among 5802 neonates admitted, 2220 blood cultures were performed, of which 399 were positive (18%). Among these, 3% had central venous catheters, 16% were early onset (≤3 days old), and 62/64 deaths were septicaemia related. Among BSI, 66% were known pathogenic and the remainder potential pathogenic Staphylococcus Coagulase Negative. Gram-negative bacteria accounted for almost half, Klebsiella spp (n=78), Acinetobacter spp (n=58) and E. Coli (n=21) were the most frequent. Only 3 Streptococus spp were isolated. Further, antibiotic resistance was common, including resistance towards antibiotics empirically applied in the hospital.

Table 1
Distribution of 399 blood stream infections (BSI) among all 385 neonates and 62 neonates dying in relation to septicemia

14 duplet BSI culture samples with different organisms isolated at different times

Pathogenicity	Isolate	All BSI	Deaths
Known	*Klebsiella* spp	78	19
	Acinetobacter spp	58	10
	Escherichia coli	21	5
	Other Gram-neative bacteriae	35	8
	Streptococus spp	3	1
	Other Gram-positive bacteriae	16	3
	Candida spp	13	3
Potential	*Staphylococcus coagulase negative*	175	13
Total		399	62

Other Gram-negative bacteriae: spp *Enterobacter, Morganella, Pseudomonas, Proteus* and *Burkholderia*

Other Gram-positive bacteriae: *Staphylococcus aureus* and *Enterococcus* spp

[Distribution of 399 blood stream infections (BSI)]

Conclusion: Among BSI in hospitalized Vietnamese neonates, the majority was known pathogenic and Gram-negative. Streptococus spp were rare, in contrast to developed countries. The vast majority of deaths occurring were septicaemia related. Further, antibiotics resistance was common towards the antibiotics empirically used. Systematic surveillance should be considered to guide future BSI prevention and management.

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EFFICACY OF MUMPS COMPONENT OF MMR VACCINE IN KOREA; A CASE CONTROL STUDY

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Background and aims: Although mumps vaccine coverage has reached to> 95%, the disease has continuously occurred. We studied the effectiveness of the mumps component of the MMR vaccine in recent mumps outbreak of 2008-2009 in Korea.

Methods: We evaluated the efficacy of mumps vaccine through the retrospective case-control studies (case: control= 1:3) in four university hospitals from January 2008- December 2009. Mumps cases included hospitalized patients for characteristic swelling of the parotid or other salivary glands or mumps related complications. We collected demographic and clinical data including vaccination status by medical records, and if needed, by contacts through the telephone.

Results: One hundred twenty two cases of mumps were identified and 449 controls were selected. Most of cases were born before 1994, aged 15-19. Ninety-eight percent (57/58) among cases whose vaccination status were available had at least one MMR vaccination, and 35 cases (60.3%) had received one dose mumps vaccine and 22 cases (37.9%) two doses.Estimated risk for disease is OR 0.33 (95% CI 0.02-5.33) in vaccinated that is lower than in non-vaccinated. Risk for mumps is OR 0.33 (95% CI 0.02-5.33) for 1 dose and OR 0.11 (95% CI 0.01-2.12) for 2 doses.

Conclusion: We evaluated the efficacy of mumps vaccine. Mumps vaccine had preventive effect and two-dose vaccination had superior effect than one dose, even though there was no statistically significant difference. In addition to the efficacy of the vaccine, it is needed to consider other factors that are involved in occurrence of mumps outbreak.

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PERSISTENCE OF VACCINE-INDUCED MUMPS ANTIBODY

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Backgrounds and aim: Despite of high vaccination rate, mumps still occurs as small outbreaks. Waning immunity has been considered as a potential factor on mumps outbreak. The purpose of this study is to identify the relation of vaccination status and persistence of vaccine-induced mumps antibody.

Methods: From healthy children and young adults aged 7-25 years, we collect sera for determining mump antibody (IgG) level and the information of mumps vaccination status from their vaccination cards or medical records.

Results: A total of 79 subjects were enrolled (male= 40, female=39). Mean age of subjects was 12.3 ± 3.6 years (median= 12 years, 7- 22 years). According to vaccination status, one-, two-, and three- dose vaccinee were 11.4% (n=9), 87.3% (n=69), and 1.3% (n=1), respectively. Time interval from last vaccination to sera collection were 7.9± 4.3 years (median= 7.2 years, 2.5-21.0 year). Geometric mean titers of mumps-IgG was related with vaccination count (P=0.005), but not related with time interval from last vaccination (P=0.053). Among the 2-dose vaccines, there was no relation between geometric mean titers of mums-IgG and time interval from last vaccination. Mumps-IgG antibody decreased 0.5% as time interval from last vaccination increased per month in linear regression (P= 0.01).

Conclusion: We identified that mumps antibody decreased as time interval from last vaccination increased, especially one-dose vaccinee. Preventive measures could be necessary for adolescents and young adults who got only one-dose mumps vaccination if mumps outbreaks will occur.

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PROSPECTIVE ANALYSIS OF RISK FACTORS FOR GROUP B STREPTOCOCCAL COLONIZATION IN NEONATES AT TERTIARY CARE CENTRE IN NORTH INDIA

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Background and aims: Colonization with Group B Streptococcus (GBS) of birth canal and neonates plays a significant role in neonatal infections. Aim was to study the prevalence and risk factors associated with GBS colonization in neonates.

Methods: Swabs from mucus membranes and/or skin of external ear canal, anterior nares, umbilicus, throat and anorectal sites were obtained from neonates between 24 to 48 hours of delivery. Bacterial isolates including GBS were identified as per standard identification protocol.

Results: A total of 5250 samples were obtained from 1050 neonates enrolled in this prospective cross-sectional study. A total of 1375 bacterial isolates were obtained from 338 neonates, of these 49 were GBS from 34 neonates. GBS was isolated from all 5 body sites in 2.9%, from 3 in 5.9%, 2 in 20.6% and one in 70.6%. Among risk factors for colonization in neonates, maternal fever & prolonged labour were highly significant ($p < 0.001$), prolonged rupture of membrane (≥ 18 hrs) ($p < 0.01$), preterm birth, respiratory distress at birth, maternal medical illness and intrapartum antibiotics were significant ($p < 0.05$). Low birth weight, low apgar score (< 4 at 1 min.), sex, mode of delivery and meconium stained liquor were not found significant.

Conclusions: GBS colonization rate is low in institutional deliveries in a tertiary care centre in North India. To identify true GBS colonization rates and associated risk factors, multicentric and community based studies with cultures from multiple body sites are recommended.

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USE OF PROCALCITONIN IN THE DIAGNOSIS OF TUBERCULOSIS IN THE PEDIATRIC AGE

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Background and aims: Procalcitonin (PCT) is a protein used as a biomarker of inflammatory response to infection. We investigated the utility of PCT in the diagnosis of tuberculosis (TB) in the pediatric age in Spain, a country with a low-intermediate TB burden.

Methods: Cross-sectional study in a consecutive case series of children diagnosed with TB (n=23; 9 females, median age: 62 months). At diagnosis, white blood cell count (WBC), eryhtrocyte sedimentation rate (ESR), serum PCT and C-reactive protein (CRP) were measured. PCT and CRP values were determined by the LUMItest PCT immunoluminometric analysis (ATOM SA, Brahms Diagnostica, Germany; normal ≤0.5ng/ml) and an immunoturbidimetric procedure (Cobas Integra, Roche, Spain; normal < 15mg/l), respectively. Two control groups were used: healthy children (n=60) and patients diagnosed with pneumococcal pneumonia (n=35). Appropriate non-parametric statistical tests were used.

Results: Among TB cases, 11 (48%) were culture-confirmed and 6 (26%) were extra-pulmonary; median (range) WBC, CRP, PCT and ESR values were 8700/mm3 (5000-19900), 5mg/L (0-116), 0.05ng/ml (0-0.23) and 10mm/h (2-43), respectively. A correlation was found only between WBC and CRP levels (r=0.42, p=0.045).

PCT values remained within normal ranges in all TB cases and significant differences were only observed with children with pneumococcal infection (p< 0.0001), who showed as well higher CRP (p< 0.0001) and WBC (p=0.025) values. When compared to healthy controls, only CRP levels were higher in TB patients (p=0.012).

Conclusions: In our study, PCT was not elevated in children with TB at diagnosis and differed significantly with patients affected with pneumococcal pneumonia.

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SYSTEMIC LUPUS ERYTHEMATOSUS DIAGNOSED WITH MACROPHAGE ACTIVATING SYNDROME TRIGGERED BY ACUTE HSV INFECTION

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Background and aim: Patients with systemic lupus erythematosus(SLE) exhibit unique immune reactions to viral infections. Latent EBV infection has been suspected to be involved with SLE disease course. Generally, HSV infection influences macrophages to enhance antiviral activities and interfere with innate immunity. Sometimes HSV infection in SLE patients is confused with symptom aggravation of SLE. Macrophage activating syndrome(MAS), a rare complication in SLE can be triggered by infections.

It is not easy to find the cases have reported infections as a cause of MAS or MAS as the first presentation of SLE.

Case presentation: A-14-year-old female came to hospital with fever and painful facial skin rash for 2 weeks. Splenomegaly was observed. Viral markers of latent EBV and acute HSV infection were positive. Pancytopenia, mild liver function abnormality, prolonged PT, hyponatremia and hyperferritinemia were reported, but bone marrow biopsy revealed normocellular. Concerning laboratory findings with the ongoing fever, it was thought to be a mild form of MAS activated by acute HSV infection.

Given positive ANA and anti-SS-Ab, low C3, C4 and hemolytic anemia findings with the history of arthralgia, photophobia, and later-revealed malar rash, we diagnosed her as SLE with latent EBV infection. After given steroid, the fever and skin rash are vanished, and the abnormal laboratory findings became normalized.

Conclusion: We report a very rare case of MAS triggered by acute HSV infection as the first manifestation of SLE.

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ISOLATION OF A UNIQUE CONJUGATIVE PLASMID DNA FROM MULTIPLE ANTIBIOTIC RESISTANCE PSEUDOMONAS AERUGINOSA ISOLATED FROM ICU PATIENT IN KERMAN, IRAN

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Background: Emergence of antibiotic resistance plasmids among the nosocomial bacteria created huge burden in treatment of patients across the world. Our aims were to isolate a plasmid from drug resistance nosocomial pathogens and to study it´s conjugation, transformation, curing and stability in the recipient cells.

Methods: Antibiotic sensitivity was performed by paper disk diffusion and E-test. Plasmid was isolated using alkaline lysis technique and confirmed by conjugation and transformation. Curing of the plasmid was done by replica plate method after exposing to different curing agents.

Results: Two Pseudomonas aeruginosa, two Escherichia coli, and a Klebsiella pneumoniae were isolated from intensive care unit (ICU) of Afzalipoor hospital. The isolates exhibited various degrees of susceptibility 13 antibiotics. Plasmid isolation revealed that only P.aeruginosa isolate 1 carried a high molecular weight plasmid. The isolated plasmid was named as pKUM. Conjugation and transformation showed co-transfer of gentamicin, kanamycin, cefotaxime, ceftazidime and piperacillin/Tazobactam resistant phenotypes to E.coli ATCC25922 (Rifʳ) at frequencies of 3.13×10^{-5} and 5.3×10^{-7} respectively. Plasmid pKUM was cured using different curing agents and was stable in both donor cells and the transconjugants.

Conclusion: From above results it can be concluded that only P.aeruginosa isolate1 carried a plasmid encoding multiple antibiotic resistant genes. The results were further suggests the role of plasmid in dissemination of antibiotic resistance genes in the ICU of the hospital environment.

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NEONATAL MENINGITIS CAUSED BY NEISSERIA MENINGITIDIS-CASE REPORT

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Neisseria meningitidis is a major cause of meningitis in children and adults, but very rare in neonatal period. 0,54% of nenatal meningitis is meningococcal etiology. More resent data from U.S. (Cove Bacterial Survallance Program) gives a frequency of 9 per 100000 births. Low incidence of infection during the neonatal period is probably in relation to the transfer of maternal protective antibodies. Fulminanat course is typical of meningococcal meningitis. Purpura is unusual in the neonatal period. It is a manifestation of vascular inflammation and antigen-antibody reaction, the newborns are not able to respond because thay are imunologicly immaturity.

Case presents rare situation: an unusal etiology and favorable course of neonatal meningitis without neurological sequels despite describing literature. Fullterm newborn in 28th day of life developed symptoms and sings of meningitis, with purpuric changes in the skin. CSF analysis confirmed bacterial meningitis, bacterial isolate Neisseria meningitidis serogroup B. Blood culture remains sterile after the prescribed incubation. After twentyone-days dual antibiotic therapy recived positive response, with no neurological effects.

Need to improve the prevention of neonatal exposure to patological agents, in this case at home, at time of reduced immune capacity.

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SURAMIN INHIBITS ENTEROVIRUS 71 REPLICATION IN VIVO BY BLOCKING VIRUS ENTRY INTO TARGET CELLS THROUGH BINDING OF THE NAPHTHALENE TRISULFONIC ACID GROUP TO THE VIRAL CAPSID

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Background: Enterovirus 71 (EV71) is the causative of Hand Foot and Mouth Disease, which caused diseases in millions of children. There is no approved anti-viral nor vaccine. The aim of our study is to identify therapeutics to treat and prevent severe EV71 infections.

Methods: A clinically approved drug collection was screened in a quantitative RT-PCR based platform. Potency of hits was evaluated by plaque assay. Time of addition (T.O.A.) test was used to identify the target steps in viral life cycle. The binding between Suramin and EV71 viral particle was evaluated by STD-NMR. In vivo efficacy was tested in EV71 infected 10-day-old ICR mice and adult rhesus monkeys.

Results: IC_{50} and IC_{90} of suramin in rhabdomyosarcoma cells are 0.08 µM and 0.49 µM, and CC_{50}>1mM. Treatment with Suramin at 50 mg/kg/day in EV71 infected 10-day-old mice reduced the mortality for 30% and in monkey peak viral load was reduced. Suramin blocks the virus-cell attachment in T.O.A.. Inhibition by a set of poly-sulfonated and poly-sulfated compounds indicates that sulfur groups are involved in the mechanism of action. STD-NMR analysis confirmed the binding between Suramin and EV71 particle on sulfonate groups.

Conclusions: We identified suramin as EV71 entry inhibitor both in vitro and in vivo, which sulfonated groups bind to EV71 particle and compete with cellular receptors or attachment factors. Suramin is an approved pediatric drug with a long history of clinical using, and represents a promising candidate for therapy and prevention of severe EV71 infections and HFMD.

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EMERGENCE OF PLEURAL EMPYEMA BY STREPTOCOCCUS PNEUMONIAE SEROTYPES 3 AND 19A IN NORTHERN MEXICAN CHILDREN FOLLOWING PNEUMOCOCCAL HEPTAVALENT CONJUGATED VACCINE

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Background: Publications of pneumococcal pleural empyema in children (PPEC) in Mexico and Latin America are limited. We have published serotype replacing in Mexico after implementation of PCV-7 on invasive pneumococcal disease, but emphasis on PPEC was not established.

Aims:

1. To describe clinical and microbiological characteristics of PPEC, and

2. To recognize emergent pneumococcal serotypes causing PPEC following PCV-7 vaccination.

Methods: Based on a 7 years of active surveillance (Oct/2005 - Sept/2012) all children < 16 years old with culture-confirmed pneumococcal pleural empyema were admitted at the General Hospital of Tijuana, Mexico, on the US-Mexico Border (the most transited frontier in the world). Following isolation, pneumococcal serotype identification was performed, along with clinical analysis.

Results: A total of 35 pleural empyemas were admitted, from which 23 (65.7%) isolation was successful. S. pneumoniae was isolated in 21 (91.3%). Median age at admission was of 4.25 years, with 66.6% of patients < 5 years old. Pleural decortication was performed in 8 patients, median hospitalization days was of 17, and only one patient died. Before PCV-7 implementation, serotype coverage was of 57% (serotype 14 the most prevalent), while following PCV-7 vaccination vaccine-serotype coverage decreased to 14.2%, with emergence of serotypes 3 and 19A (these two serotypes accounted for 53.8% of all emerging serotypes causing PPEC).

Conclusions:

1. PPEC is a common health problem in children, with a rate in < 5 years old of 3.75/100,000.

2. Replacement with non-PCV-7 covered serotypes is present, with predominance of serotypes 3 and 19A as emerging pathogens.

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DIAGNOSIS OF GASTROINTESTINAL VZV INFECTION BY IDENTIFICATION OF VZV DNA IN SALIVA BY NESTED PCR

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Background: DNA and transcripts encoding VZV gene products as well as immediate early proteins are found in the human enteric nervous system (ENS) after episodes of varicella or administration of varicella vaccine. Little is known about the consequences of VZV reactivation in the gut; however, it might boost viral immunity and/or cause enteric zoster (HZ).

Methods: To identify putative enteric reactivation, we screened saliva of subjects complaining of abdominal pain or other symptoms for the presence of VZV DNA.

Results: This study enabled VZV to be demonstrated as the cause of massive gastric ulceration and hemorrhage in a 16 year old male, necessitating partial gastric resection. VZV DNA was found in the resected stomach and VZV glycoproteins, indicative of lytic infection, were found in cells of the ulcer margin. We examined 32 saliva specimens from 22 patients. Nested PCR was used to identify DNA encoding VZV genes. VZV DNA was identified in 8/9 saliva specimens from patients with clinically diagnosed zoster but no GI symptoms; 5/5 cleared the DNA after convalescence. No VZV DNA was detected in 6/6 saliva specimens from healthy controls. VZV DNA was found in 5/7 saliva specimens from patients with unexplained (helicobactor negative) severe abdominal pain. VZV DNA disappeared from the saliva of these 5 patients (in 2 following treatment with valacyclovir) after abdominal pain relented.

Conclusions: Endoscopic exploration is needed when VZV DNA is detected in saliva of patients with unexplained abdominal pain and/or GI bleeding. Such patients might benefit from early antiviral therapy.

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USE OF DAPTOMYCIN IN TREATING PERSISTENT BACTERAEMIA FROM COAGULASE NEGATIVE STAPHYLOCOCCI IN NEONATES

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Background and aims: Daptomycin is currently licensed for the management of Staphyloccoccus aureus bacteraemias, endocarditis and skin and soft tissue infections in adults. Few paediatric and neonatal data are available. We aim to describe the use of daptomycin in neonates with persistent coagulase negative staphylococci (CONS) bacteraemia.

Methods: We reviewed the medical records of two neonates with persistent CONS bacteraemia treated successfully with daptomycin.

Results: The first neonate was a full term boy with a birth weight of 3800 grams. The baby developed pyrexia on day 14 of life and blood cultures grown Staphylococcus Epidermidis sensitive to vancomycin. However blood cultures remained repeatedly positive during treatment and vancomycin was stopped. Daptomycin was then used successfully for two weeks. The second neonate, a full term girl with a birth weight of 2380 grams, developed clinical sepsis one day post operatively for correction of oesophageal atresia. Blood cultures grew Staphylococcus Hominis sensitive to vancomycin. Despite treatment cultures remained positive and linezolid was then used with no success. The bacteraemia resolved eventually with a 10 day course of daptomycin. Both neonates tolerated the treatment well with no side effects. The dose used in both cases was 6mg/kg twice daily.

Conclusions: Daptomycin may be considered for treatment of persistent CONS bacteraemia in neonates if treatment with other antibiotics is proven unsuccessful. Further studies are urgently needed to determine dosing, efficacy and adverse effects in the neonatal population.

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ACUTE BACTERIAL MENINGITIS IN CHILDREN - FINDINGS FROM THE EMERGENCY DEPARTMENT OF A TERTIARY CARE HOSPITAL

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Objectives:

1) To determine the signs and symptoms of acute bacterial meningitis (ABM) in different age groups.

2) To determine the role of CT scan in children with ABM.

Methods: This study is a retrospective study of patients who had been admitted through the Emergency Department (ED) of AKUH, Karachi with the diagnosis of ABM. Data collected using variables such as age, sex, presenting complaints, clinical signs and symptoms, CT scan findings and final outcome of patients.

Results: A total of 192 patients were admitted. The presenting complaint in 86% patientswere fever, vomiting was present in 48%, among them 52.68% were more than 5 years. Irritability was present in28.12%, of whom 50% were less than one year. Fits were present in 24.47% out of which 44.68% were less than one year. Neck stiffness and signs of meningeal irritation, Kerning's sign and Brudzincski's sign, were present in 27.60%,13.54% and 9.3% respectively. On presentation headache was found in 40.10% amongst which 72.72% were over 5 years. CT-scan was performed on 59.4%. Positive findings on CT scan were present in 21.0% which showed cerebral oedema in66.66%, hydrocephalus in 8.3% and cerebral infarct in 25% of patients . Almost 20.8% were admitted in HDU. Adverse outcome was observed in 3.12% patients.

Conclusion: Younger children with ABM present with nonspecific signs and symptoms. Headache and signs of meningeal irritation are common findings in children over 5 years. CT-scan may have a beneficial role in diagnosis of ABM.

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LYMPHOPENIA IN CHILDREN - IS POTENTIAL SUSCEPTIBILITY TO INFECTIOUS DISEASE BEING IGNORED?

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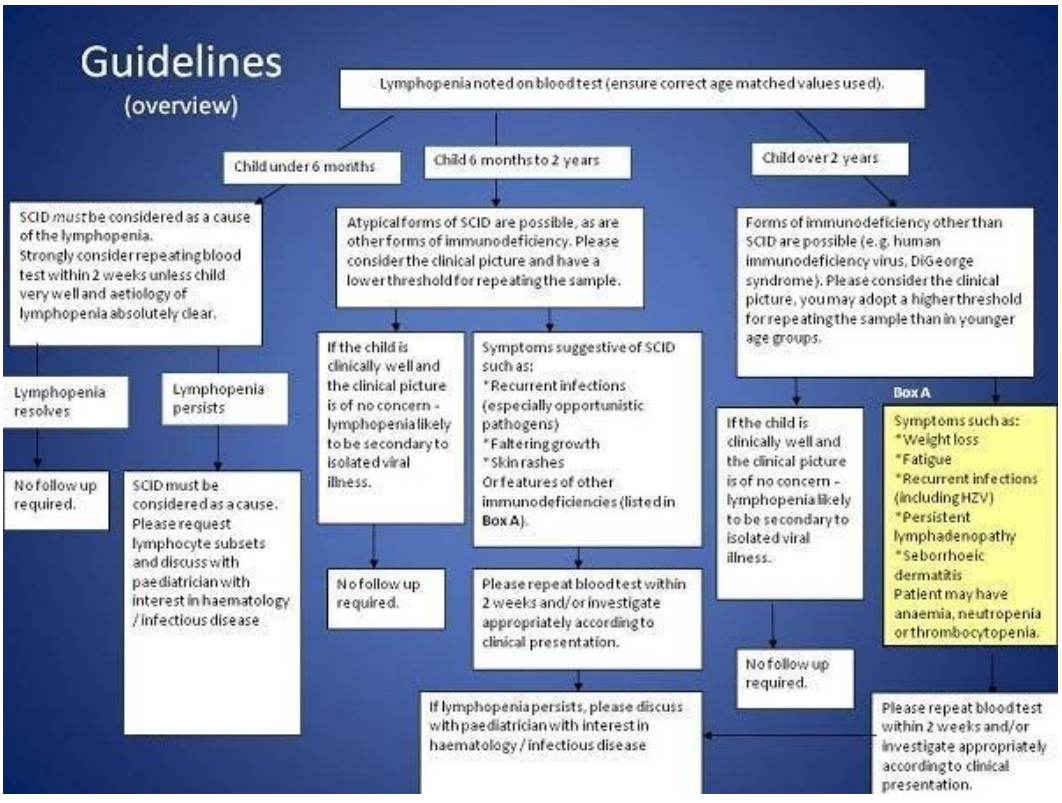
Background and aims: Paediatric lymphopenia may reflect immunodeficiency and therefore susceptibility to Infectious Disease. A systematic approach is required to manage lymphopenia. The only UK guideline is the archived primary immunodeficiency network guideline which recommends that lymphopenic infants should be followed-up and severe combined immunodeficiency (SCID) considered if lymphopenia persists. A retrospective audit was conducted at Sandwell Hospital UK to assess if paediatric lymphopenic patients were appropriately identified, investigated and referred. The standards used were best practice recommendations from immunologists.

Methods: All paediatric patients >28 days with lymphopenia were identified from laboratory records over a period of 11 months. The group was divided into those < 1 year (age group at greater risk of SCID) and ≥1 year. Data regarding diagnosis, lymphocyte counts, further investigations and referrals was analysed.

Results: 209 lymphopenic patients were identified. 26 were < 1 year; 27%(7/26) had their lymphocyte count re-checked within 2 weeks. The lymphopenia had resolved in 71% (5/7), the remaining 2 patients died shortly after the abnormal result. 183 patients were ≥1 year old. 18%(33/183) had their lymphocyte count re-checked within 2 weeks. Lymphopenia had resolved in 85%(28/33). In no cases were further investigations performed or referrals made. In 4 cases the lymphopenia was commented upon in the discharge summary, although no plan documented.

Conclusion: The best practice recommendations for lymphopenic patients were not followed. It is important to identify children who may have underlying immunodeficiency. We have drafted guidelines for managing lymphopenia.



[A Guideline to Managing Paediatric Lymphopenia]

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COMPLICATIONS OF EPSTEIN BAR COUSED MONONUCLOEOSIS INFECTIOUS AMONG HOSPITALIZED CHILDREN

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Background and aims: Infectious mononucleosis (IM) is mostly caused by Epstein-Barr (EBV). Primary EBV infection in children is usually asymptomatic, in young adults is manifested us mononucleosis. In industrialized countries disease occurs in the second decade of life. Complications of disease are rare (hematologic, neurologic, respiratory), potentially fatal complication is splenic rupture.

The aim of this work was to describe complication among hospitalized children with EBV IM.

Methods: We analyzed clinical manifestations and complications among hospitalized children in Infectious disease Clinic in Podgorica, from January 2011 y with verified positive ELISA test against EBV VCA IgM antibody.

Results: In Infectious disease Clinic from January 2011 year were hospitalized 48 patients from 3-16 years old with EBV MI, preschool group from 3-6 years 15 patients (31.25%) and school group from 7-16 years old 33 (68.7%). All patients had symptoms of fever and tonsillopharyngitis, splenomegaly occurs in 34, hepatomegaly in 15, lypmhadenopathy in 44 patients. Streptococcal throat infection occurs in 14 patients In the first group: interstitial pneumonia occurs in 2, mild thrombocytopenia in 2, mononucleous hepatitis in 3, parotitis in one patient. In the second group: mild thrombocytopenia occurs in 3 hemolytic anemia in one, mononucleous hepatitis in 5, aseptic meningitis in one patient.

Conclusions: Our results revealed that IM appeared in earlier ages compared with industrialized countries. Complications were mild and all patients recovered to normal range up to 3 weeks after admission.There was no splenic rupture and death among patients.

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DISEASE SEVERITY AND PRESENTATION IN CHILDREN WITH RECENT MEASLES EPIDEMIC: KARACHI, PAKISTAN

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Introduction: Measles is an important vaccine preventable infection. Despite immunization the reported measles related deaths are increased globally. An estimated 164 000 people died from measles in 2008 - mostly children under the age of five.

Objective: To determine the clinical features and disease severity of measles in children during recent epidemic, presenting to emergency department.

Methods: The study was conducted at Emergency department of AKUH from February - August 2012.The charts of the patients with the diagnosis of “measles” or “suspected measles” were reviewed retrospectively. All the signs and symptoms like fever, rash, vomiting, irritability, drowsiness, and decrease intake were recorded. The duration of hospital stay and rate complications were recorded. Data was analyzed using SPSS version 19.0.

Results: During the study period total 170 children presented to emergency department with suspected measles. The median age of presentation was 22 months, with mostly children (76%) who are more than 9 month of age. Males were 53.5% with peak in the month of May (27%). More than half were unvaccinated (53%). History of contact with measles was positive in 9.4% of children. Fever (67%) and cough (22.4%) were the most common presenting complaints. From the ED 77% got admitted, with 15% being admitted in high dependency unit. Complications observed were acute gastroenteritis (48%), pneumonia (31.6%) , otitis media(3%) and encephalitis(2.2%) respectively .

Conclusion: Measles is still a common reason for Emergency department visits in children. Improving vaccination in children can prevent morbidity and mortality related to this communicable disease.

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THE DIFFERENCE OF THE NON-MALIGNANCY HEMOPHAGOCYTIC SYNDROME IN CHILDREN WITH ADULTS IN A SINGLE TERTIARY INSTITUTION

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Background: Hemophagocytic lymphohistiocytosis is a disorder that is characterized by the activation of non-neoplastic mononuclear phagocytic system leading to marked histiocytic proliferation, hypercytokinemia and T-cell immunosuppression.

Methods: We retrospectively collected data on 20 patients diagnosed with hemophagocytosis from 2005 to 2011 at the Taichung Veterans General Hospital. Inclusion criteria were presence of haematological abnormalities on CBC and pathological evidence of hemophagocytosis on biopsy specimen and the cases of HLH associated with malignancy were excluded.

Results: A total of 20 patients (11 children as age under 18 year-old, 9 adults) were included in this analysis. The median age at diagnosis was 23.8 (children 5.9, adults 46.2; overall range, 0.3-86 years). Only two children (18%) had underlying disease (SCIS and SLE) but five adult cases (55.5%) had underlying disease (2 hepatitis C virus, 2 systemic lupus erythematosus, 1 Still's disease). The clinical presentations of jaundice, hepatomegaly and ascites were predominant in children. The high level of GPT and bilirubin were found in children. Most of the children cases received IVIG (100% cases) and etoposide (91%) but few of adult cases received IVIG (0%) and etoposide (33.3%).Overall survival rate was 55% but higher in children (64%) than adults (45%). The most common reason of death was septic shock in both groups.

Conclusions: In our study, liver function impairment with jaundice and ascites were found frequently in children group than adults. Otherwise, lower incidence rate of association with underlying disease, higher survival rate were also noted in children group compared with adults.

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PERFORMANCES OF THE CEPHEID GENEXPERT MTB/RIF ASSAY IN DIAGNOSIS OF PULMONARY TUBERCULOSIS AMONG CHILDHOOD TB SUSPECTS IN THE GAMBIA

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Background and aims: Clinical presentation of tuberculosis (TB) in children is non-specific and microbiological confirmation of disease is rare; treatment in children is therefore mostly commenced on the basis of clinical signs and symptoms. We assessed the utility of GeneXpert MTB/Rif assay (GX) in diagnosis of pulmonary TB and Rifampicin resistance in a West African childhood TB clinic.

Method(s): Induced sputum samples were obtained from all TB suspects aged < 15 years seen at the childhood TB clinic of MRC Unit, The Gambia. Samples were tested by smear microscopy for AFB, liquid culture and GX.

Results: Between April and December 2012, 27 (22.9%) of 118 childhood TB suspects investigated were diagnosed with active TB (6 culture positive; 21 culture negative). 2 (33.3%) and 4 (66.7%) of the 6 culture positive TB cases had positive smear microscopy and GX test respectively.

The GX was positive in the 2 smear +ve/culture +ve cases and in 2 of 4 smear -ve/culture +ve cases and negative in all of the 21 culture negative TB cases. The GX was negative in all of the samples obtained from children who did not have TB (n=91). There was no evidence of rifampicin resistance in any of the samples analyzed.

Conclusion: This preliminary result suggests that GX offers a more sensitive method for detection of M. tuberculosis in children compared with sputum smear microscopy but cannot be recommended to replace culture methods where available. There is need for additional methods to improve diagnosis of TB in children.

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ANTIBODY PERSISTENCE UP TO 4 YEARS AFTER VACCINATION WITH A QUADRIVALENT MENINGOCOCCAL ACWY TETANUS TOXOID CONJUGATE VACCINE IN ADOLESCENTS

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Background and aims: Long-term protection against meningococcal disease relies on antibody persistence after vaccination. We report the persistence of antibodies up to 4 years after vaccination of adolescents aged 11-17 years with meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (MenACWY-TT, GlaxoSmithKline Vaccines) compared with MenACWY polysaccharide vaccine (MenACWY-PS, GlaxoSmithKline Vaccines).

Methods: This phase III, open, controlled, multi-centre persistence study in India and the Philippines (NCT00974363) included healthy subjects previously randomized 3:1 (NCT00464815) to receive a single dose of MenACWY-TT or MenACWY-PS (Year 3 and 4 Total Persistence Cohorts, N=643 and 541, respectively). Persistence was assessed 3 and 4 years post-vaccination by serum bactericidal antibody assay using rabbit complement (rSBA) (clinical cut-offs assessed: 1:8 and 1:128). Vaccination-related serious adverse events (SAEs) were recorded.

Results: The According-to-Protocol (ATP) cohorts for persistence included 626 and 536 subjects at Year 3 and 4, respectively. Percentages of subjects retaining rSBA titres ≥1:8 and ≥1:128 and geometric mean titres (GMTs) are presented in the table. Exploratory analyses suggested that for each serogroup percentages of subjects retaining rSBA titres ≥1:8 and ≥1:128 (except for MenC at Year 3) and GMTs (except for MenC at both time points) were statistically significantly higher with MenACWY-TT than with MenACWY-PS. No vaccination-related SAEs were reported.

Conclusions: Overall, ≥72.6% of recipients of MenACWY-TT retained rSBA titres ≥1:128 for each serogroup up to 4 years later.

Funding: GlaxoSmithKline Biologicals SA

Table: Percentage of subjects with rSBA titres ≥1:8 and ≥1:128 and GMTs (ATP cohort for persistence at each time point)

Antibody	Time point	MenACWY-TT				MenACWY-PS			
		N	% ≥1:8 (95% CI)	% ≥1:128 (95% CI)	GMT (95% CI)	N	% ≥1:8 (95% CI)	% ≥1:128 (95% CI)	GMT (95% CI)
MenA	Y3	472	93.2 (90.6; 95.3)	89.2 (86.0; 91.8)	470.2 (402.1; 549.8)	154	83.1 (76.2; 88.7)	79.2 (72.0; 85.3)	211.9 (152.7; 294.1)
	Y4	403	90.1 (86.7; 92.8)	85.4 (81.5; 88.7)	375.7 (312.4; 451.7)	133	80.5 (72.7; 86.8)	75.9 (67.8; 82.9)	171.4 (119.6; 245.6)
MenC	Y3	472	91.5 (88.6; 93.9)	85.0 (81.4; 88.1)	375.6 (314.8; 448.1)	154	86.4 (79.9; 91.4)	78.6 (71.2; 84.8)	407.0 (275.7; 600.8)
	Y4	402	94.3 (91.5; 96.3)	89.3 (85.9; 92.2)	376.7 (319.6; 444.0)	133	87.2 (80.3; 92.4)	80.5 (72.7; 86.8)	368.7 (248.0; 548.2)
MenW-135	Y3	472	82.4 (78.7; 85.7)	78.6 (74.6; 82.2)	352.6 (282.0; 440.9)	154	30.5 (23.4; 38.4)	24.7 (18.1; 32.3)	16.4 (11.2; 24.1)
	Y4	402	77.4 (73.0; 81.4)	72.6 (68.0; 76.9)	208.2 (163.3; 265.3)	132	27.3 (19.9; 35.7)	19.7 (13.3; 27.5)	12.0 (8.4; 17.2)
MenY	Y3	472	93.4 (90.8; 95.5)	89.4 (86.3; 92.0)	752.3 (633.3; 893.6)	154	57.8 (49.6; 65.7)	51.3 (43.1; 59.4)	68.5 (44.2; 106.1)
	Y4	400	89.5 (86.1; 92.3)	85.8 (81.9; 89.0)	545.0 (440.7; 673.9)	132	48.5 (39.7; 57.3)	46.2 (37.5; 55.1)	49.5 (30.6; 79.9)

Y3 = 3 years after vaccination; Y4 = 4 years after vaccination; N = number of subjects with available results; 95% CI = 95% confidence interval; GMT = geometric mean antibody titre; ATP = according-to-protocol
rSBA carried out at the UK Health Protection Agency, Manchester

[Table ACWY-TT 043]

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ANTIBODY PERSISTENCE 4 YEARS AFTER VACCINATION WITH A QUADRIVALENT MENINGOCOCCAL ACWY TETANUS TOXOID CONJUGATE VACCINE IN HEALTHY TODDLERS

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Background and aims: We evaluated antibody persistence 4 years after a single dose of a meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (MenACWY-TT, GlaxoSmithKline Vaccines), compared with a meningococcal serogroup C conjugate vaccine (MenC-CRM_{197}, Pfizer), in toddlers aged 12 to 23 months.

Methods: This phase III, open-label, controlled, multi-centre persistence study in Finland (NCT00955682) enrolled children previously randomized (3:1) as toddlers (NCT00474266) to receive 1 dose of either MenACWY-TT or MenC-CRM_{197} (Year 4 cohort, N=294). Serum bactericidal antibody assay using rabbit (rSBA) (cut-off 1:8) and human complement (hSBA) (cut-off 1:4) were used to assess immunogenicity. Vaccination-related serious adverse events (SAEs) reported since vaccination were recorded.

Results: At Year 4, 270 children were included in the according-to-protocol (ATP) cohort for persistence (MenACWY-TT: N=225; MenC-CRM_{197}: N=45). In the MenACWY-TT group, for serogroups A, C, W-135, and Y, respectively, 29.3%, 73.7%, 81.2%, and 65.4% of children retained hSBA antibody titres ≥1:4, and 74.1%, 40.4%, 49.3%, and 58.2% of children retained rSBA antibody titres ≥1:8. Exploratory analysis between the 2 groups suggested that percentages of children retaining hSBA-MenC titres ≥1:4 and hSBA-MenC GMTs were statistically significantly higher with MenACWY-TT than with MenC-CRM_{197}. No vaccine-related SAEs were reported.

Conclusion: Four years after MenACWY-TT vaccination, hSBA antibodies persisted for all serogroups and levels for MenC were higher with MenACWY-TT than with MenC-CRM_{197}.

Funding: GlaxoSmithKline Biologicals SA

Table: Percentage of children with rSBA titres ≥1:8 and GMTs and hSBA titres ≥1:4 and GMTs (ATP cohort for persistence at Y4)

		rSBA			hSBA		
Antibody	**Group**	**N**	**% ≥1:8 (95% CI)**	**GMT (95% CI)**	**N**	**% ≥1:4 (95% CI)**	**GMT (95% CI)**
MenA	**MenACWY-TT**	224	74.1 (67.9; 79.7)	107.3 (77.6; 148.3)	198	29.3 (23.1; 36.2)	4.9 (4.0; 6.0)
MenC	**MenACWY-TT**	225	40.4 (34.0; 47.2)	12.3 (9.8; 15.3)	209	73.7 (67.2; 79.5)	32.0 (23.8; 43.0)
	MenC-CRM_{197}	45	35.6 (21.9; 51.2)	13.5 (7.4; 24.5)	32	46.9 (29.1; 65.3)	11.3 (4.9; 25.6)
MenW-135	**MenACWY-TT**	225	49.3 (42.6; 56.1)	30.5 (22.4; 41.5)	165	81.2 (74.4; 86.9)	47.1 (35.7; 62.2)
MenY	**MenACWY-TT**	225	58.2 (51.5; 64.7)	36.2 (27.1; 48.4)	130	65.4 (56.5; 73.5)	29.8 (20.2; 44.1)

Y4 = 4 years after vaccination; **N** = number of children with available results; **95% CI** = 95% confidence interval;
GMT = geometric mean antibody titre; **ATP**= according-to-protocol
rSBA testing performed at the UK Health Protection Agency, Manchester (HPA) and hSBA performed at GlaxoSmithKline Vaccines

[Table ACWY-TT 048 Persistency]

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ANTIBODY PERSISTENCE AND SAFETY 3 YEARS AFTER A SINGLE DOSE OF MENACWY-TT VACCINE IN HEALTHY INDIVIDUALS AGED 10-25 YEARS

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Background and aims: This phase II, open, controlled, multi-center study in the US (NCT00715910) assessed year 3 antibody persistence in subjects aged 10-25 years who previously (NCT00454909) received 1 dose of Neisseria meningitidis serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine (MenACWY-TT, GlaxoSmithKline Vaccines) or MenACWY diphtheria toxoid conjugate vaccine (MenACWY-DT, Sanofi Pasteur Inc.).

Methods: 431 subjects aged 11-25 years previously randomized 3:1 to receive MenACWY-TT or MenACWY-DT, and 56 non-randomized subjects aged 10 years, who received MenACWY-TT (MenACWY-TT<11), participated in the persistence assessment. Immunogenicity was measured by serum bactericidal antibody assay using human complement (hSBA) with 1:8 cut-off (primary endpoint). Serious adverse events (SAEs) related to vaccination or study procedures since primary vaccination were recorded.

Results: The according-to-protocol cohort for persistence included 473 subjects (MenACWY-TT: 335; MenACWY-DT: 84; MenACWY-TT<11: 54). Antibodies persisted for serogroups C, W-135 and Y in terms of hSBA titers ≥1:8 and geometric mean titers (GMTs); fewer subjects retained hSBA-MenA titers ≥1:8 and hSBA-MenA GMTs decreased to almost baseline levels (Table). Exploratory analyses suggested higher proportions of subjects (11-25 years) with hSBA titers ≥1:8 and higher GMTs for serogroups C, W-135 and Y with MenACWY-TT than with MenACWY-DT; hSBA-MenA GMTs were higher with MenACWY-DT than with MenACWY-TT. No related SAEs were reported.

Antibody	Group	N	Titers ≥1:8				GMTs		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
MenA	MenACWY-TT	316	118	37.3	32.0	42.9	6.2	5.2	7.3
	MenACWY-DT	79	38	48.1	36.7	59.6	10.0	6.5	15.3
	MenACWY-TT<11	52	23	44.2	30.5	58.7	9.6	5.6	16.4
MenC	MenACWY-TT	319	297	93.1	89.7	95.6	119.3	95.5	149.0
	MenACWY-DT	81	66	81.5	71.3	89.2	54.4	33.8	87.6
	MenACWY-TT<11	54	52	96.3	87.3	99.5	140.0	84.5	232.0
MenW-135	MenACWY-TT	323	308	95.4	92.5	97.4	143.9	124.7	166.2
	MenACWY-DT	80	68	85.0	75.3	92.0	79.4	50.9	123.9
	MenACWY-TT<11	54	52	96.3	87.3	99.5	139.2	99.8	194.0
MenY	MenACWY-TT	321	308	96.0	93.2	97.8	209.2	180.1	242.9
	MenACWY-DT	80	71	88.8	79.7	94.7	145.5	97.6	216.9
	MenACWY-TT<11	52	50	96.2	86.8	99.5	188.0	132.6	266.7

Table: Percentage of subjects with hSBA antibody titers ≥1:8 and GMTs 3 years after primary vaccination (ATP cohort for persistence at year 3)

N, number of subjects with available results
n/%, number/percentage of subjects with titer equal to or above specified value
GMT, geometric mean antibody titer
ATP, according-to-protocol
CI, confidence interval; LL, lower limit; UL, upper limit

[Graph1]

Conclusions: Three years after MenACWY-TT or MenACWY-DT vaccination, ≥81.5% of subjects had hSBA titers ≥1:8 for serogroups C, W-135 and Y, with lower persistence for serogroup A.

Funding: GlaxoSmithKline Biologicals SA

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IMMUNOGENICITY AND SAFETY AFTER BOOSTER VACCINATION WITH A QUADRIVALENT MENINGOCOCCAL ACWY TETANUS TOXOID CONJUGATE VACCINE IN HEALTHY CHILDREN

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Background and aims: We evaluated booster vaccination with a meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (MenACWY-TT, GlaxoSmithKline Vaccines) compared to a meningococcal serogroup C conjugate vaccine (MenC-CRM$_{197}$, Pfizer), in healthy children aged 5 to 6 years.

Methods: In this phase III, open-label, controlled, multi-centre study (NCT00955682), Finnish children, previously randomized (3:1) as toddlers (NCT00474266) to receive a single dose of MenACWY-TT or MenC-CRM$_{197}$, received a booster dose of the same vaccine, 4 years post-priming. Immunogenicity was evaluated before and 1 month post-booster vaccination with serum bactericidal antibody assays using rabbit (rSBA; cut-off 1:8) and human (hSBA; cut-off 1:4) complement. Serious adverse events (SAEs) were recorded for 31 days post-vaccination.

Results: Of 293 children in the booster total vaccinated cohort, 258 were included in the according-to-protocol immunogenicity cohort (MenACWY-TT: N=215; MenC-CRM$_{197}$: N=43). After MenACWY-TT booster vaccination, all and ≥99.5% of children had rSBA titres ≥1:8 and hSBA titres ≥1:4, respectively for each serogroup, with a ≥64-fold increase in geometric mean titres compared to pre-booster values. After MenC-CRM$_{197}$ booster vaccination all children had rSBA titres ≥1:8 and hSBA titres ≥1:4 for serogroup C. Exploratory analyses showed that hSBA GMTs for serogroup C were statistically significantly higher after MenACWY-TT than after MenC-CRM$_{197}$ booster vaccination (Table). No vaccine-related SAEs were reported.

Conclusion: Booster vaccination with MenACWY-TT induced robust immune responses to each meningococcal serogroup included in the vaccine and was well-tolerated in children.

Funding: GlaxoSmithKline Biologicals SA

Table: Percentage of children with rSBA titres ≥1:8, hSBA titres ≥1:4 and GMTs at pre- and post-booster vaccination (Booster ATP cohort for immunogenicity)

			rSBA			hSBA		
Antibody	Group	Time point	N	% ≥1:8 (95% CI)	GMT (95% CI)	N	% ≥1:4 (95% CI)	GMT (95% CI)
MenA	MenACWY-TT	Pre	212	74.5 (68.1; 80.2)	111.9 (80.3; 156.1)	187	29.4 (23.0; 36.5)	4.8 (3.9; 5.9)
		Post	214	100 (98.3; 100)	7173.3 (6389.2; 8053.5)	202	99.5 (97.3; 100)	1343.2 (1119.3; 1612.0)
MenC	MenACWY-TT	Pre	213	39.9 (33.3; 46.8)	12.1 (9.6; 15.2)	200	73.5 (66.8; 79.5)	31.2 (23.0; 42.2)
		Post	215	100 (98.3; 100)	4511.9 (3935.9; 5172.3)	209	100 (98.3; 100)	15831.4 (13625.8; 18394.0)
	MenC-CRM$_{197}$	Pre	43	37.2 (23.0; 53.3)	14.3 (7.7; 26.5)	31	48.4 (30.2; 66.9)	11.9 (5.1; 27.6)
		Post	43	100 (91.8; 100)	3718.4 (2596.0; 5326.0)	33	100 (89.4; 100)	8646.1 (5886.6; 12699.3)
MenW-135	MenACWY-TT	Pre	213	48.8 (41.9; 55.7)	30.2 (21.9; 41.5)	158	82.3 (75.4; 87.9)	48.3 (36.5; 63.9)
		Post	215	100 (98.3; 100)	10949.7 (9531.4; 12579.1)	192	100 (98.1; 100)	14411.2 (12971.8; 16010.2)
MenY	MenACWY-TT	Pre	213	58.2 (51.3; 64.9)	37.3 (27.6; 50.4)	125	65.9 (56.8; 74.2)	30.2 (20.2; 45.0)
		Post	215	100 (98.3; 100)	4585.3 (4128.6; 5092.5)	173	100 (97.9; 100)	6775.5 (5961.3; 7700.9)

rSBA testing was performed at the UK Health Protection Agency, Manchester (HPA) and hSBA performed at GlaxoSmithKline Vaccines
Pre = pre-booster vaccination; **Post** = one month post-booster vaccination; **N** = number of children with available results; **95% CI** = 95% confidence interval; **GMT** = geometric mean antibody titre; **ATP** = according-to-protocol

[Table ACWY-TT 048 Booster]

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A 3 YEAR RETROSPECTIVE REVIEW OF VIRAL RESPIRATORY ISOLATES IN PAEDIATRICS INTENSIVE CARE ADMISSIONS

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Introduction: During the H1N1 2009 Pandemic season, all children ventilated on Paediatrics Intensive Care (PICU) for respiratory failure had respiratory samples taken for virology screen.H1N1 (2009) was declared eradicated both national and internationally in August 2010.We reviewed results of samples taken during and beyond this period and compared the respiratory isolates.

Methods: All Nasopharyngeal Aspirates, Non -direct bronchoalveolar lavage or tracheal secretions from admissions in the months of September to April of 2009/2010, 2010/2011and 2011/2012 was reviewed. The months of May to August of each year were regarded as 'offpeak' and so left out of the study. PICU admissions, discharges and death notifications records werecorrelated with virology reports.

Results: Samples were processed from 287 PICU patients/episodes. 192(67.1%) of the children were ages 0-2 years.(154)53.8% of the patients were male. One or more Respiratory viruses was isolated in 159 samples(55%). RSV accounted for 77(48.4%) of the positive samples, Rhinovirus 45(28.6%), Para-influenza Virus Type1-4, 14(8.8%), Adenovirus 9(5.7%), Pandemic H1N1 (2009) 8(5.1%) and HumanMetapneumovirus 2(1.3%) . Coinfection was found in 12 (7.5%) of the positive samples. There were ten(3.4%) mortalities from the study population. A serious co-morbidity was present in all10(100%) mortalities. A respiratory virus was isolated in 7/10 (75.%) of the deaths. No positive swabs for H1N1 (2009) was found afterJanuary 2011.

Conclusion: With the Pandemic H1N1 (2009) truly over, resources needs to be devoted to common viruses with greater burden of disease.

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IMPROVEMENT OF DIAGNOSIS IN CHILDREN WITH PARASITIC INFECTIONS

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Background: Toxocariasis is a disease caused by roundworms larvae. Immunoglobulin E (IgE) and eosinophils play roles in allergy and defense against parasites.

Aims: 1.To evaluate Toxocara canis seroprevalence in our county; 2.To establish correlations between Toxocara infection from one side and IgE levels, eosinophils count and haemoglobin from other side; 3.To improve parasitic infection diagnosis.

Methods: We've analyzed every 10th patient admitted in pediatric department during 4 weeks period. Inclusion criteria: children between 1-15 years of age. Blood tests included: haemoglobin, total IgE (nephelometry), Toxocara canis IgG (ELISA), eosinophils counts. Stool samples were examined using Kato-Miura method. Data was statistically analyzed (independent T test).

Results: 47 children were included in study: 12 of them had positive IgG Toxocara canis serology, 38 of them had elevated IgE levels and 6 of them had parasitic co-infections (ascaridiasis, trichuriasis). 9 of 38 patients with elevated IgE had positive serology for Toxocara. In order to compare IgE levels of Toxocara seropositive patients with IgE of seronegative ones, we didn't observe significant difference (p value= 0.354). There wasn't statistical difference between mean haemoglobin value of seropositive patients versus seronegative ones (p value= 0.597). We noticed statistical difference between eosinophils counts and Toxocara serology: seropositive patients had significant eosinophilia as compare to seronegative patients (p value= 0,002).

Conclusions: 1. In our county every 4th child is Toxocara seropositive and every 8th child has parasitic co-infections; 2. Eosinophilia represents more specific indicatory than total IgE for Toxocariasis; 3. Kato-Miura / eosinophils are useful investigations for parasitic infections diagnosis.

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SCREENING OF FAMILY MEMBERS OF ACUTE BRUCELLOSIS IN ENDEMIC AREAS OF TURKEY

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Background: The aim of this study is to examine if additional serological screening of the family members of acute brucellosis patients that have been diagnosed by our clinic will help detect previously unrecognized cases.

Method: In the period between January 2009 and September 2010, pediatric patients with acute brucellosis and their family members were enrolled and analysed. They were serologically screened for brucellosis using the standard serum tube agglutination test (SAT).

Results: Twenty-four acute brucellosis index pediatric cases and their 99 family members were enrolled from January 2009 to September 2010. Twentyfour index cases' median age was 103.5 months. Elapsed median time until brucella diagnosis was 17 days. The most common symptom was fever that was observed in 23 (95.8 %) patients. Ingestion of unpasteurized cow milk was reported by 83.3% of the index cases. Symptomatic seropositives index cases tended to have higher (1/320) brucella antibody titres (91.2 %). Of the 99 family members, 9 (9.1 %) manifested various symptoms, 90 (90.9 %) were asymptomatic, with an overall seroprevalence rate of 18 (18.2 %). The rate of seropositivity among the symptomatic family members was 9 (100 %) and for the asymptomatic was 9 (10 %) ($P < 0.001$). Acute brucellosis was diagnosed and treated in 18 (18.2 %) of the symptomatic / asymptomatic seropositive family members and in the asymptomatic seropositive family members with an acute brucellosis prevalence rate of 9 (10 %).

Conclusion: Clinical and serological analyses of Brucella patients' household members may help to detect early diagnosis.

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PROBIOTIC AND ZINK TREATMENT SHORTENED THE COURSE OF ACUTE VIRUS DIARRHEA IN INFANTS AND CHILDREN

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Aim: To evaluate the efficacy of the probiotic & zink use in shortening the duration of acute virus diarrhea in hospitalized children under 3 years old.

Methods: A single-center, randomized, controlled trial was conducted to collect 356

patients aged 3 mon. - 3 y. and hospitalized in Lviv Infection Diseases Hospital with virus gastroenteritis between October 2010 and 2012. Included were all previously healthy children with acute diarrhea and / or vomiting. Stool samples were tested for rotavirus & norovirus by enzyme immunoassay (ELISA) and stool samples were also cultured to exclude the presence of enteropathogenic bacteria. Patients were randomized to receive conventional treatment or add-on treatment of probiotic + zink to the conventional treatment.

Results: As a total, 310 children eligible for the study were evaluated (155 receive conventional treatment and 155 with add-on treatment of the probiotics + zink to the conventional treatmen given). Rotavirus antigen was detected in 61,4%, the rate of norovirus detection was 36,6% The virus-virus coinfection were found in 14,3%. The mean age of the children was 17,5±2,18 months. The mean duration of diarrhea was 3,7±0,29 days in a subgroup not received the probiotic + zink therapy and 2,4±0,33 days in a subgroup received it ($p < 0,05$). The administration of antimicrobials did not make any differences in diarrhea duration.

Conclusions: 5 days conventional treatment add-on treatment of the probiotics + zink were highly efficacious and safe in infants and in children for treating severe virus gastroenteritis.

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INVASIVE GROUP A STREPTOCOCCAL INFECTIONS IN PAEDIATRIC INTENSIVE CARE - AN AUDIT OF CLINICAL PRACTICE

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Aims: Describe the epidemiology, clinical features and management of children with invasive Group A Streptococcal infections requiring admission to the PICU.

Methods:

Patient population / Setting: Children aged 0-16 years of age requiring admission to the RHSC PICU over a 6 year period with invasive Group A streptococcal infections.

Case definitions / Inclusions: Patients undergoing therapy for invasive Group A Streptococcal (GAS) infections within the PICU. Invasive GAS infections were defined as one of three clinical syndromes: streptococcal toxic shock; necrotising fasciitis; or other invasive disease.

Data extraction: Data was extracted from the PICU Computerised Information System (CIS).

Study design and Patient identification: The study was a retrospective case note review.

Results: 24 patients were identified. 15 patients were boys. The median age was 3.1years. 2 patients died. The median PICU Length of stay was 7.1 days. 21/24 patients underwent invasive ventilation. The median duration of ventilation was 120 hours. 14/24 patients (58%) required inotropic support. 7/24 patients (29%) received iv steroids for primary blood pressure support. 3/24 patients (12%) received IvIG. 15/24 patients (62%) required surgical interventions. 5/24 patients (21%) had hospital acquired GAS infections (HAI), 19/24 (79%) were community-acquired infections (CAI).

Laboratory characteristics: All samples were reported as fully sensitive to all antibiotics tested. M-types reported were as follows: M1; M3.1; M12; M18; M89. The 2 patients who died had M-types M12 and M18.

Conclusion: GAS retains the ability to kill otherwise healthy children in resource rich settings and cause serious morbidity to others.

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POLIO RISKS IN ADOLESCENTS AND ADULTS IN THE XXI CENTURY

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Background and aims: In 2012, only 218 cases of paralysis caused by wild poliovirus were confirmed worldwide; however, non-immune people of all ages remain at risk if exposed to imported wild virus or to vaccine derivated poliovirus (VDPV). This study is a review of poliomyelitis, focusing polio risks in adolescents and adults.

Methods: Articles were retrieved from PUBMED and SCIELO databases issued from Jan/2000 to Dec/2012, and WHO, CDC, ECDC, PAHO sites were visited to assess polio epidemiologic information and recommended vaccination schedules.

Results: Polio sequelae and case fatality rates are higher in non-immune adolescents and adults as compared to children. The proportion of people with potential susceptibility to polio increases with age; in different countries, many people > 15 years of age, do not carry neutralizing antibodies against one or more PV, especially PV3. Imports of the wild virus and exposure to VDPV can be a risk to non-immune people even in countries that have adopted an IPV full schedule. The risks are higher for people who travel to areas which are endemic to polio, and who are in contact with immunocompromised individuals, like healthcare professionals, and parents of children recently immunized with OPV.

Conclusions: Improvement in polio surveillance and serosurveys to evaluate gaps of immunity could help public decision-makers establish the best vaccination strategies. It is clear that before global polio eradication, previous vaccination and herd immunity may be insufficient to avoid poliomyelitis in non immune individuals.

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CEREBRAL INFARCTION AND OTHER CEREBRAL COMPLICATIONS OF PNEUMOCOCCAL MENINGITIS IN AUSTRIAN CHILDREN

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Background: Pneumococcal meningitis, most common in young children, is associated with high mortality, substantial morbidity, and severe neurologic sequelae. The present study evaluates the outcome at hospital discharge and at follow-up investigations after pneumococcal meningitis in Austrian children.

Methods: All cases of pneumococcal meningitis aged below 5 years included in a prospective surveillance study on invasive pneumococcal infections in Austria between 2001 and 2008 were retrospectively analysed.

Results: Analysis of outcome at hospital discharge was possible in 57 children with pneumococcal meningitis (mean age 14.5 ± 13.3 months). 5 death cases (8.8%), 20 children (35.1%) with one or more neurologic sequelae and 32 (56.1%) without any sequelae were observed. Neurologic sequelae included hemiparesis, central motor disorder, facial nerve palsy, recurrent seizures and hypacusis or deafness. Related to neurological deficits, neuroimaging identified cerebral infarction in 3 children, cerebral venous sinus thrombosis in 1 child, ischemic-inflammatory brain lesions in 2 children and cerebral abscess in 1 child.

Analysis of outcome at follow-ups was possible in 41 children between 1 and 48 months (12.9 ± 13.5 months) after hospital discharge. At the last recorded follow-up 12 children (29.3%) showed one or two neurologic sequelae including mild or minimal residual hemiparesis (7.3%), deafness (9.8%), hypacusis (14.6%), and/or developmental delay (9.8%).

Conclusions: Our study confirms that pneumococcal meningitis causes substantial morbidity and severe neurologic sequelae in young children. Hemiparesis after ischemic or ischemic-inflammatory brain lesions and hypacusis or deafness were the most severe sequelae. Thus, prevention via vaccination is of highly importance.

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VACCINATION OF THE LIVER TRANSPLANT RECIPIENTS IN HUNGARY HOW WE DO IT

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Strategies to win the war against transplant rejection will always be a priority, but battles against vaccine preventable infections must also be fought and won.

Hungarian Special Immunization Service increasingly emphasizes immunization of patients with special conditions, especially before and after solid organ transplant (SOT). According to vaccination guidelines for SOT candidates and recipients we apply our own experiences.

We report 85 liver transplant patients (77 children, 8 adults) between March 2004 and September 2012. Most patients have already been transplanted (55) at the first visit to our service and 80% of them were incompletely or not immunized at all. After screening their serostatus, immunstatus and vaccination records, patients received catch up immunization according to the national immunization calendar. The vaccinations were given by GP's except the live attenuated varicella and MMR vaccines. Patients with stable graft function and well documented immunfunction 2 years after the transplantation have been vaccinated at our department with Varilrix and received preparedness acyclovir prescription. After two-dose Varilrix schedule we tested VZV IgG (ELISA) and after successful seroconversion patients received MMR vaccine. 73% of all patients seroconverted. We did not detect vaccine disease, and breakthrough infections (in 6 cases) were mitigate varicella. 82% of our patients are followed up yearly and receive a booster dose if needed.

We know the patients are not fully protected but at the worst case they expected to have mitigated infection. Our goal is to continue the immunization procedure of SOT patients and maintain their protection with booster vaccination.

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RISK FOR APNEAS IN PEDIATRIC ACUTE RESPIRATORY TRACT INFECTIONS

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Background: Apneas in young children are seen in association with respiratory syncytial virus (RSV) infections. Based on these observations, it is recommended to hospitalize young children (< 3 months) with an acute respiratory tract infection (ARI) caused by RSV. However, apneas also occur in children infected with other viruses than RSV. We hypothesize that apneas are not related to the microorganism itself, but reflect pathophysiological changes related to infectious status. Within a prospective cohort-study, we analyzed frequency of apneas in previously healthy young children with symptoms of ARI. We correlated apneas with the isolated micro-organisms, clinical findings, disease severity and outcome.

Methods: In a cohort of 582 previously healthy children with ARI, real-time polymerase chain reaction (RT-PCR) was performed on nasal washing specimens for fifteen respiratory viruses and three bacteria. In a subgroup of 241 children < 3 months of age, we compared the clinical data of children with and without apneas.

Results: Nineteen of 241 (7.8%) children had a history of apnea. RT-PCR results were RSV 9/19 (47.4%), non-RSV 5/19 (26.3%) and negative PCR in 7/19 (36.8%). The disease severity score was significantly higher in the apnea group. They also required extra oxygen for a longer period.

Conclusions: Apneas in ARI are not restricted to RSV as causative pathogen. The disease severity score is a better predictor for risk of apneas in young children with ARI than a positive RSV test. Guidelines that recommend to hospitalize young children with RSV based on the risk of apnea, should be revised.

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TEN YEARS´ EXPERIENCE OF VARICELLA REQUIRING PAEDIATRIC INTENSIVE CARE AT STARSHIP HOSPITAL, NEW ZEALAND

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Background and aims: Varicella is now a vaccine preventable disease but is generally considered benign, making it a low priority for a funded universal immunisation scheme. We aimed to increase knowledge of the severity, morbidity and mortality caused by varicella, by a review of cases requiring paediatric intensive care in New Zealand where vaccine is available but not funded.

Methods: Retrospective chart review of children admitted to PICU over a ten year period (July 2001 - July 2011) identified from the PICU database with a primary or secondary code for varicella.

Results: Thirty-four cases were identified and twenty-six cases were included. Of the 26 cases, 84.6% were Maori or Pacific Island ethnicity, 54% had no preceding medical condition and 23% were immunocompromised. Main PICU admission reasons were neurological (38.5%), secondary bacterial sepsis or shock (26.9%), respiratory (15.4%) disseminated varicella (11.5%), or other causes (7.7%). Fifty percent of children required inotropic support and 81% invasive ventilation. Four children died (15%), three of whom were immunocompromised. A further eight children (31%) had ongoing disability at hospital discharge of whom 6 had no pre-existing disease.

Conclusion: Varicella, or its secondary complications, requiring paediatric intensive care carries high mortality, particularly for immune compromised patients, and long-term morbidities mostly affecting previously healthy children.

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TETANUS IN NEW ZEALAND CHILDREN: REVIEW OF CASE MANAGEMENT, OUTCOME AND IMMUNISATION STATUS

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Background and aims: Almost all recent cases of tetanus in New Zealand, adults and children, have occurred in individuals without a documented history of a primary course of tetanus immunisation.It is known that disease does not confer immunity, so immunisation is an essential part of case management. We review the presentation and management of children with tetanus at our institution, including follow up of their immunisation status.

Methods: A retrospective chart review of all patients aged 0-15 years who were admitted to Starship Children's Hospital with tetanus since 2000.

Follow up of immunisation status via National Immunisation Register and contact with primary health care.

Results: Four cases were identified, all previously unimmunised. All required paediatric intensive care (length of unit stay 2.5-7 weeks) for ventilatory support, and 3 children required tracheostomy.Specific tetanus treatment included use of metronidazole, neutralisation of toxins with tetanus immunoglobulin, spasm management with magnesium and benzodiazepine; but active immunisation was only commenced in hospital in the two more recent patients. All 4 patients made a good recovery. Only the most recent family has committed to full catch-up immunisation, the others remain partially or un-immunised.

Conclusion: Tetanus in children is a life-threatening disease with significant morbidity. All survived due to modern intensive care management, at substantial cost. Immunisation is cheap and effective in preventing tetanus but none of these children is yet known to have achieved full immunisation after their disease.

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MACROLIDE RESISTANCE OF BORDETELLA PERTUSSIS STRAINS ISOLATED FROM IRANIAN CHILDREN

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Resistant isolates of Bordetella pertussis to macrolides in some countries have been published recently. Antibiotic treatment and prophylaxis play an important role in controlling the spread of pertussis. We studied susceptibility of the B. pertussis isolated to 3 macrolides. Relatedness of the strains recovered in this research was also examined.

A total of 779 nasopharyngeal swabs were collected from pertussis suspected patients during May 2009 to December 2010. The activity of 3 macrolides including erythromycin, azithromycine and clarythromycin against the recovered isolates was examined using agar dilution method. Strains relationship was characterized by PFGE.

Of total specimens, we recovered 10 strains of B. pertussis which all isolated from children up to 4 years old. Among these isolates, only two cases had high MIC values for erythromycin and clarythromycin. PEGE analysis of the isolates revealed 6 PFGE profiles (A-F) among which 3 and 2 isolates have the same patterns in profile A and B, respectively.

Azithromycin can be a good choice of drugs to treat patients infected by B. pertussis in our country. Clonal relationship of the isolates showed that the same B. pertussis strains were isolated from different patients in Iran. Screening for antimicrobial resistance of this causative agent of respiratory tract infection may be warranted in order to control spread of these bacteria.

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COMPARISON OF TUBERCULIN SKIN TEST AND QUANTIFERON®-TB GOLD IN-TUBE FOR THE DIAGNOSIS OF CHILDHOOD TUBERCULOSIS INFECTION

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Aim: Tuberculosis (TB) is an important worldwide ongoing health issue. Our aim in this study is to compare a century-old tuberculin skin test (TST) and QuantiFERON-TB Gold In-Tube (QFT-GIT) test.

Materials and methods: Three hundred fifty three children with the suspicion of TB infection or disease between 5 months and 17.5 years old and TST negative 92 healthy children from the same age group were recruited into the study. All children were performed TST and QFT-GIT test and their demographic, clinic and laboratory data were recorded.

Results: A positive QFT-GIT result was obtained in 85 (24%) of the 353 patients and in 2 among the control group. TST was only positive in 231 (%65) of 353 patients. TST was more positive with the increasing number of BCG scars. QFT-GIT test positivity was higher (p= 0.003) significantly in cases without scars compared with cases who have at least one scar. When all the cases were considered, agreement between the two tests were poor (=0.174) and concordance was 58%. There was a significant discordance between the two tests which arise from the high number of TDT (+)/QFT-GIT (-) results, especially in children with latent TB infection. The sensitivity and specifity of QFT-GIT test were 63% and 98% respectively. The sensitivity of TST was 79% and the specifity was 74.3%.

Conclusion: Although QFT-GIT test is highly specific, it is not sensitive enough to detect TB infection and the disease. Using TST and QFT-GIT test together may provide more efficient results.

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CUTANEOUS COMMUNITY ASSOCIATED METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS IN CHILDREN IN NICE, FRANCE. PROSPECTIVE STUDY IN A PEDIATRIC EMERGENCY DEPARTMENT

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Background: Community-associated Méthicillin resistant Staphylococcus aureus (CA-MRSA) are common in North America and Greece (up to 60%). In north Italia, forty kilometres from Nice, some USA300 stains were also isolated. This clone has a wide resistant profile and spread rapidly through the community. It seems important to know our local ecology to determine the well adjusted probabilistic antibiotic therapy.

Methods: Prospective study from March 1st , 2011 to February 29th, 2012, in the pediatric emergency department of Nice Pediatric University Hospital. Cutaneous lesions which were clinically suspected to be of an infectious bacterial origin were taken for bacteriological analysis. Patients who had been hospitalised or had surgery in the month before the infection were excluded. Samples which were positive for CA-MRSA were tested by the National Staphylococcus Reference Center for typing and to look for the gene encoding for PVL. Data regarding antibiotic prescriptions and hospital admissions were collected.

Results: 126 cutaneous lesions were sampled. 60.3% Impetigo, 15.9% Whitlow, 11.1% abscesses, 1.6% boils/Furuncles. 82.5% of samples were positive for S. aureus, 28.7% for Streptococcus Pyogenes. 8.7% of the children were hospitalized, 6.7% were treated with intravenous antibiotics and 1.6% by dual intravenous antibiotics. 93.9% of the S. aureus were penicillin resistant, 3.7% were strains of C-MRSA. All C-MRSA stains were from the ST80 clone and produced PVL.

Conclusion: Prevalence of C-MRSA is low in cutaneous infections in children in Nice. Nationals' recommendations should not be modified. But it is advisable that careful and regular monitoring should continue in France.

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LYMPHOCYTIC MENINGITIS OF THE CHILD WITH THE CHU OF BATNA

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Introduction: Acute lymphocytic meningitises are most frequent in the child, generally of viral etiology,Their evolution is generally benign with cure without after-effects.

Objective: To evaluate the frequency of lymphocytic meningitises at the department of paediatrics. To study their profile epidemiologic, clinical, biological and evolutionary.

Materials and methods: Retrospective study made on the files of the children hospitalized for a lymphocytic meningitis at the department of paediatrics of the CHU of Batna during one 03 years (01/01/2009 at the 31/12/2011).

Results: We compiled 191 cases of lymphocytic meningitis with a hospital incidence of 1.98.

Lymphocytic meningitis accounts for 55 .5% of the whole of meningitides of the child

The 28 day old older child to 10 years is most concerned by far of which 53.9% of the cases are older children < 05 years.

The boys are touched by lymphocytic meningitis in our series (67.5%) with a sex-ratio of 2.08.

A high incidence of the new cases during the summer period (in connection with the frequency of viral meningitises).

The child touched by lymphocytic meningitis presented a pleiocytose of 10-500 elements/mm3 in 71.7%, a normal albuminorrachie in 66.7%, a normal glycorrachie in 91 .2 %.

CRP positive in 41.5% of the cases, a VS accelerated at 65% of the patients.

Only 17% of our patients received a antibiothérapie according to our national consensus.

Conclusion: This study confirmed the frequency of lymphocytic meningitis in pediatry. Preponderance of the viral cause what corresponds to the literature.

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PREVALENCE OF MENINGOCOCCAL CARRIAGE AMONG ADOLESCENTS IN CAMPINAS, BRAZIL

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Background and aims: Meningococcal disease is a rare consequence of N. meningitidis infection, with the highest incidence rates in young children. In contrast, meningococcal carriage is common, especially in teenagers. Taking in account the very limited published data currently available describing meningococcal carriage in Brazil, we performed a study to evaluate the prevalence of N. meningitidis carriage among adolescent students.

Methods: Cross-sectional study, including a representative sample of 1,208 adolescents attending 73 public and private schools in Campinas city. Oropharyngeal swabs were collected and phenotypic and genotypic characterization of carriage strains isolated among adolescents from 3 defined age subgroups: A(11-13y); B(14-16y) and C(17-19y) was performed. The effect of social behavior and previous vaccination against serogroup C were also analyzed.

Results: The overall carriage prevalence was 120 carriers per 1,208 subjects (9.9%), with the highest prevalence (12%) in older adolescents (17-19 years). The proportion of carriers was also higher among students attending public schools, sharing the dormitory with ≥ 2 people, or reporting passive smoking. Carriage of serogroup C dominated (1.3%), followed by serogroups B (0.99%), Y (0.49%), and W135 (0.16%). The most frequent strain isolated was C:23:P1.14-6. Previous vaccination did not interfere in the carriage rates.

Conclusions: The evidence gathered during this study in a representative Brazilian student cohort showed that the highest rates of carriage were observed in older adolescents, with an unusually high dominance of serogroup C. Social behavior was associated with increased risk of carriage. These results will have important implications in future vaccination strategies in Brazil.

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EPIDEMIOLOGICAL AND CLINICAL DATA OF RSV INFECTION IN HOSPITALISED CHILDREN UNDER 5 YEARS OLD IN SPAIN: FIVE MULTICENTER STUDY

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Aims: To assess the percentage of patients with underlying diseasses out of the total children hospitalized due to RSV infection and to compare clinical characteristics and outcome for both groups

Methods: Prospective, observational, multicenter, national study performed in 26 Spanish hospitals (December 2011-March 2012). Investigational cases were defined as children with underlying chronic diseases and control cases were healthy children (proportion 1/2). Clinical data were compared between the both groups.

Results: A total of 1763 children with RSV infection were admitted and 264 of them had underlying diseases (14.9%). 225 cases and 460 controls were analyzed. Underlying diseases were respiratory (64%), cardiovascular (25%), neurologic diseases (12%), chromosomal abnormalities (7,5%), immunodeficiencies (6,7%) and inborn errors of metabolism (3,5%). Clinical data are shown in table 1.

	CASES (n=225)	CONTROLS (n=460)	p value
Age (months)	16.2 (13)	5.5 (7)	<0.001
Prematurity	67/155 (43.2%)	63/386 (16.3%)	<0.001
Fever (>38ºC)	143/224 (63.8%)	245/448 (54.7%)	0.029
Oxygen therapy	184/225 (81.8%)	334/458 (72.9%)	0.014
Days of oxygen therapy	3.77 (4)	2.28 (2.4)	<0.001
Antibiotic therapy	111/225 (49.3%)	136/452 (30.1%)	<0.001
Mean length of stay in hospital	8.03 (9.9)	5.35 (3.2)	<0.001
Admitted to PICU	42/225	52/454	0.014
Invasive ventilation	14/225 (6.2%)	8/460 (1.7%)	0.0038

[Main clinical characteristics and outcome of cases]

Conclusions: A significant percentage of children with RSV infection have underlying diseases and the serverity of the illness is higher than in healthy children.

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ASSESMENT OF IMMUNE RESPONSES TO HEPATITIS A VACCINATION IN CHILDREN AGED ONE AND TWO YEARS

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Aim: Hepatitis A can be prevented with vaccination. The aim of this study is to determine seropositivity of hepatitis A before vaccination in healthy children 12 and 24 months of age and compare seroconversion rates after vaccination between these two groups.

Materials and methods: Fourty-nine children aged 1 years old (Group 1) and 51 children aged 2 years old (Group 2) were included in the study. Inactive hepatitis A vaccine (avaxim, 80 antigenic subtypes, 0.5 ml) were administered to every child in two doses, six months apart. Anti-HAV IgG and IgM antibodies were detected by Achitect HAVAb-IgG and HAVAb-IgM (Abbott, Wiesbaden, Germany) test kits.

Results: Nine percent of children (9%) were seropositive for anti-HAV IgG before vaccination. Seroconversion rate at 2 weeks was 34% and 44% in G1 and in G2; respectively. At four weeks seroconversion rate was 87.7% and 90.1% in G1 and in G2; respectively. All of the children who completed vaccination program were seropositive at 28 weeks (after the second dose). No serious adverse reaction was observed in any of the children.

Conclusions: In this study, it was determined that avaxim, including 80 antigen units, is safe and immunogenic in healthy children 12 and 24 months of age.

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REVIEW OF A NEW DTAP-IPV-HEP B-PRP-T VACCINE (HEXAXIM®) COMPARED TO A LICENSED HEXAVALENT VACCINE POST-PRIMARY SERIES ADMINISTRATION AT 2-4-6 MONTHS

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Background and aims: The development of new combination vaccines is a public health priority. The immunogenicity and safety of a new fully liquid DTaP-IPV-Hep B-PRP-T hexavalent vaccine, Hexaxim®, are compared to a control, re-constituted vaccine (Infanrix® hexa).

Methods: Immunogenicity 1 month post-primary series (Hexaxim or Infanrix hexa) at 2-4-6 months of age was investigated in four randomized clinical trials (Mexico, Thailand, Peru, Colombia/Costa Rica). Prevnar (PCV7) was co-administered at 2-4-6 months in Thailand and Colombia/Costa Rica, and Rotarix was co-administered at 2-4 months in Colombia/Costa Rica. Hepatitis B vaccine was given within 1 month of life in Thailand and Colombia/Costa Rica. Non-inferiority statistical analysis (of Hexaxim to Infanrix hexa) was done in Mexico (anti-D), Thailand (anti-Hep B, anti-PRP), Peru (anti-Hep B), and Colombia/Costa Rica (all antigens). Safety was assessed descriptively in each trial.

Results: Seroprotection (SP) (anti-Hep B, anti-D, anti-T, anti-polio, anti-PRP) or seroconversion (SC) (anti-PT, anti-FHA) rates (% subjects) (per protocol population):

	Mexico		Thailand		Peru		Colombia/Costa Rica	
Hexaxim (H) or Infanrix hexa (I-h)	H	I-h	H	I-h	H	I-h	H	I-h
Number of participants	N=695	N=119	N=189	N=190	N=132	N=130	N=1002	N=338
Anti-Hep B ≥10 mIU/mL	98.3	100	99.5	99.5	99.2	100	99.7	100
Anti-Diphtheria ≥0.01 IU/mL	96.4	99.2	97.4	100	95.5	100	100	100
Anti-Tetanus ≥0.01 IU/mL	100	100	100	100	NA	NA	100	100
Anti-Polio 1 ≥8 (1/dil)	99.9	100	100	100	NA	NA	100	100
Anti-Polio 2 ≥8 (1/dil)	100	100	100	100	NA	NA	100	100
Anti-Polio 3 ≥8 (1/dil)	99.9	100	100	99.5	NA	NA	100	99.7
Anti-PRP ≥0.15 µg/mL	98.8	99.2	97.9	96.3	100	99.2	94.6	95.9
Anti-PT titer ≥4-fold increase	97.4	95.8	93.7	93.7	NA	NA	97.5	98.4
Anti-FHA titer ≥4-fold increase	98.4	96.5	94.7	95.2	NA	NA	99.8	99.4

NA=not assayed

[SP/SC rates:]

For each antibody and country (when tested) SP/SC rates were high and similar for Hexaxim and the control. Non-inferiority of Hexaxim was demonstrated whenever assessed. The anti-Hep B response was similar irrespective of whether a dose of hepatitis B vaccine was given in the first month of life. Both vaccines had a similar safety profile.

Conclusions: The new fully liquid hexavalent vaccine, Hexaxim, induced high and similar immunogenicity for each antigen to the control vaccine, and there were no safety concerns.

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PERTUSSIS IS ASSOCIATED WITH HIGH MORBIDITY AND CASE FATALITY RATE IN INFANTS SÃO PAULO, BRAZIL

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Background and aims: In São Paulo since 2010 it was observed a great number of pertussis cases (1,889) and deaths (52); 73% of cases (1374) and 100% of deaths were confirmed in children < 6 months of age. The aim of this study is to analyze the clinical presentation of pertussis in children < 7 months, the group of higher risk for pertussis complications and deaths.

Methods: This is prospective study, including a convenience sample of children attended in pertussis reference centers from Nov/2011 to May/2012. In São Paulo state there are 33 pertussis reference centers and pertussis diagnosis were confirmed by culture, RT-PCR or epidemiologic linkage with a confirmed case in a household contact.

Results: 97 babies were included (55% residents in São Paulo capital). In 67 (69%) the diagnosis was confirmed by RT-PCR; in 27, by culture and RT-PCR (28%); one, only by culture and 2 by epidemiologic linkage. 77 babies (19.4%) were < 4 months. The most frequent symptoms were: cough (96%); cyanosis (81%); paroxysm (64%), whooping (43%), vomiting (46%) and apnea (23%). A total of 82 babies (85%) were hospitalized, and 19% had pneumonia. There were 4 deaths (CFR = 4.1%).

Conclusions: More then 50% of pertussis cases were diagnosed in children < 2 month. Pertussis morbidity was substantial, and even in children attended in reference centers, CFR was high. It is necessary to implement new strategies to prevent pertussis in children very young to receive the first 2 doses of vaccines.

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MANAGEMENT OF GROUP A STREPTOCOCCAL PHARYNGITIS FOLLOWING ACUTE ADMISSION TO THE ALEXANDRA HOSPITAL REDDITCH, WORCESTERSHIRE

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Background and aims: The most common bacterial cause for pharyngitis is a Group A Streptococcus (GAS), which accounts for 20-30% of pharyngitis cases seen in children. Although usually a self-limiting illness, it is recommended that we treat GAS pharyngitis with antibiotics. This is for several reasons, for example to prevent complications such as development of acute rheumatic fever, improve clinical symptoms and to reduce its transmission. The aim of this audit is to determine whether the management of GAS pharyngitis complies with recommendations as set by the Infectious Diseases Society of America (IDSA) 2012 guidelines.

Method: All case notes of patients with GAS cultured from throat swabs between May 2009 and May 2012 were reviewed (n = 15). Data collected included indication for throat swabs and subsequent management provided. Standards were based on the IDSA guidelines.

Results: The mean age was 4 years 7 months. All 15 cases were diagnosed with throat swabs and 73% of patients were suitable for testing. 93% were given antibiotics, and in all of these the antibiotic choice was appropriate. 11 of 15 (73%) children were given Penicillins. Of patients given antibiotics, 79% were given an incomplete course.

Conclusion: Patients with clinical features were diagnosed appropriately with a throat swab as recommended by the IDSA guidelines. The majority of patients had indications for diagnostic studies except those under 3 years who were swabbed against recommendations. Within the sample the vast majority were treated appropriately. However most were treated for less than the recommended duration.

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BELL'S PALSY: A RARE COMPLICATION OF INFECTIOUS MONONUCLEOSIS IN CHILDREN

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Background and aims: Bell's palsy rarely may be caused by Epstein-Barr virus(EBV) infection as either an isolated manifestation or as part of systemic infectious mononucleosis(IM).We describe a boy 5.5 years old who developed Bell's palsy during an EBV infection.

Methods: The patient was admitted to the Paediatric Department with a 48h history of high temperature(max 41^0C), malaise, and difficulty breathing. Clinically, he had adenoid facies, large tonsils with severe tonsillopharyngitis, purulent exudates, bilateral cervical lymphadenopathy, hepatomegaly and splenomegaly confirmed by ultrasound. He was initially treated with clarithromycin.On day five, he developed a right-sided(R) facial palsy with flattening of the forehead and nasolabial folds, eyebrow sagging, inability to close the eye; mouth drawn to the non-affected side.Otoscopy was normal bilaterally.Ibuprofen, acyclovir and methylprednisolone were added to his treatment.The patient progressively improved and recovered completely three months after initial presentation.

Results: WCC was elevated(17.06K/μL(3.8-10.5), Neutrophils 41%(45-75), Lymphocytes 47%(20-51), Monocytes 12%(2-11), AST 45U/L(0-38).IM was confirmed by elevated EBV IgM and IgG viral capsid antibody(VCA) titers.Excitability test(the House-Brackman six-point grading scale) was performed to assess the severity of the paralysis showed reduced electrical response at the (R) upper branch of the facial nerve and absence at the lower branch respectively.Tympanogram and otoacoustic emissions were normal; cerebral magnetic resonance imaging excluded any pathology.

Conclusion: EBV has been associated with Bell's palsy.The pathogenesis of these complications has not been clarified.The later may be due either to direct viral infection, or to autoimmune mechanisms. However, prognosis is good and most patients recover within 4 months.

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NEISSERIA MENINGITIDIS AND STREPTOCOCCUS PNEUMONIAE SEROTYPE 19A AS LEADING AND EMERGING CAUSES OF BACTERIAL MENINGITIS IN NORTHERN MEXICAN CHILDREN

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Background: We have previously published that meningococcal meningitis has a high incidence rate on the US-Mexico border (the most transited in the planet). Nevertheless, little information based on active surveillance is available on bacterial meningitis (BM) in Mexico and Latin America.

Aims:

1. To describe clinical and microbiological characteristics of BM.

2. To recognize emergent BM pathogens.

Methods: Based on 7 years of active surveillance (Oct/2005 - Sept/2012) all children < 16 years old with culture-confirmed (from CSF and/or blood) BM were admitted at the General Hospital of Tijuana, Mexico. Following isolation, and either meningococcal serogroup or pneumococcal serotype identification, both clinical and demographic analysis were performed.

Results: A total of 56 culture-confirmed BM were admitted, from which 35 (62.5%) were caused by N. meningitidis, 12 (21.4%) by S. pneumoniae, followed by S. pyogenes and S. agalactiae (2 cases each), and others (on case each). For both meningococcal meningitis (MM) and pneumococcal meningitis (PM), half of children were < 2 years of age, with a mortality of 25%. In MM, serogroup C was the most frequent (54.3%). For pneumococcal meningitis (PM), heptavalent pneumococcal vaccine (PCV-7) associated serotypes accounted for 75% of all cases before its introduction, with a decrease to 9.1% following PCV-7 implementation, and emergence of serotype 19A in 71% of cases.

Conclusions:

1. MM still remains very high, with rates in children < 1 year old of 12/100,000.

2. There is emergence of PM by serotype 19A in children following PCV-7 implementation.

3. New vaccination strategies are needed.

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SEPTIC ILLNESS CAUSED BY STREPTOCOCCAL INFECTION AFTER LYMPH NODE RESECTION DUE TO INFECTION WITH BARTONELLA HENSELAE

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Introduction: Cat scratch disease is caused by Bartonella henselae, a gram negative bacteria. The course is often self-limited. Streptococci group A can cause a toxic-shock-syndrome due to the production of toxic-shock-syndrome-toxin (TSST), an exotoxin. In a toxic-shock-syndrome (TSS) sepsis like courses of illness are seen.

Patient: 15-year old girl presented with swelling of the left inguinal side. An inflammatory changed lymph node was surgically excised. Few hours postoperatively an erythema developed quickly at the operation side and the patient deteriorated despite immediate treatment with ampicillin/ sulbactam and clindamycin. She was transfered to our PICU and mechanical ventilation was initiated due to the development of ARDS (minimal oxygenation index 150). Circulatory failure was treated with catecholamines. The erythema was already in regression. Wound swap showed twice beta-haemolytic TSST producing streptococci group A and the patient fulfilled the CDC criteria for TSS. Positive serology for Bartonella henselae was found with increasing IgM (initially 1:20, after 7 d 1:320, IgG > 200). Lymph node histology was seen in accordance with cat scratch disease, cocci were seen within the lymph node, but no growth could be initiated. Treatment consisted of supportive intensive care and cefuroxime, clindamycin, and erythromycin (maximum CrP 254 mg/l). One surgical wound revision was done followed by satisfactory wound healing. She was weaned from ventilation after 7 days, and discharged at day 16 after transfer.

Conclusion: The complication would possible have been avoidable without initial extirpation of the lymph node, since cat scratch disease is often self-limited.

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DIAGNOSTIC PERFORMANCE CHARACTERISTICS OF IMMATURE GRANULOCYTES AND IMMATURE MYELOID INFORMATION IN NEONATAL SEPSIS

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Background and aims: Timely and accurate diagnosis of neonatal sepsis remains a central effort in neonatal intensive care. Besides the development of promising new inflammatory laboratory parameters, notice is attracted to traditionally used markers of infection as the number of immature granulocytes (IG#) thanks to new precise techniques of automated determination. In our study we examined diagnostic performance parameters of IG# (myelocytes, metamyelocytes, and promyelocytes) and the number of as immature classified cells including IGs, bands and blasts - the so called immature myeloid information (IMI#).

Methods: 133 blood samples were analyzed using the Sysmex XE-2100, a multiparameter automated hematology analyzer. 21 neonates were diagnosed with sepsis whereas the control group consisted of 112 neonates with a negative infectious state. Besides routine determination of white blood cell differential, we performed automated measurement of IG# and IMI#.

Results: We found that IG# and IMI# were significantly elevated in patients with sepsis compared to the control group. Determined by ROC analysis IMI# seemed to be superior to IG# in regard to the PPV.

Conclusions: Our data suggest that additional automated determination of IG# and IMI# by performing an automated routine white blood cell differential could be a useful adjunctive tool in the diagnosis of neonatal sepsis without the need for further sample volume, personal or economic costs. Evaluating diagnostic accuracy of various cut-off values dependent on the time point of blood sampling and the gestational age represents an important question for future trials.

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SAFETY/IMMUNOGENICITY OF A TWO-DOSE SCHEDULE (12 MONTHS AND 18 MONTHS OF AGE) OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE IN QUEBEC

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Background: Monovalent serogroup C meningococcal conjugate vaccine (MCC) has been provided through Quebec programs since 2001. A 2-dose schedule of a quadrivalent meningococcal conjugate vaccine (MenACWY-D) at 12 and 18 months of age would fit current programs.

Methods: All participants received MMRV and PCV13 at 12 months and MMR and DTaP-IPV-Hib at 18 months in a 2-armed, open-label, parallel descriptive study. Randomized participants received either a 2-dose schedule of MenACWY-D at 12 and 18 months of age (MenACWY-D Arm) or a single dose of MCC at 12 months of age (MCC Arm). Blood samples were collected pre-Dose 2 at 18 months and 1 month post-Dose 2 in the MenACWY-D Arm and at 1 and 7 months post-MCC in the MCC Arm to measure immunogenicity via baby rabbit serum bactericidal assay.

Results: Participants in the MenACWY-D Arm (n=61) achieved robust immune responses 1 month after the second vaccination as measured by the % achieving ≥1:8 1/dil: A (100%), C (96%), Y (100%), W-135 (98%). In the MCC arm (only serogroup C response was expected; n=62), 67% of participants achieved this threshold 1 month postvaccination declining to 26% 7 months postvaccination. Both vaccines were well tolerated. Three SAEs were reported; none related to vaccination.

Conclusion: A MenACWY-D 2-dose series given concomitantly with a booster dose of DTaP-IPV-Hib at 18 months of age demonstrated a good immunogenicity and safety profile and suggests MenACWY-D could be considered as an alternative for MCC in Canadian vaccination programs. (NCT01359449)

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WHAT DUTCH SCHOOLCHILDREN KNOW, THINK AND FEEL ABOUT TICKS AND LYME DISEASE?

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Background and aims: Lyme disease (LD) can be contracted by children through a tick bite. Although relatively innocent when detected and treated in the early stage, LD can be associated with serious morbidity if treated incorrectly. Fortunately, LD is preventable, preferably through body checks and timely removal of attached ticks. The aim of this study was to examine knowledge, attitude and behavioral responses of schoolchildren in relation to tick bites and LD in the Netherlands, a high-incidence country for LD.

Methods: In total 1447 9 to 13 year old children from 40 voluntarily participating primary schools across the country completed a written questionnaire in April 2012.

Results: Overall knowledge scores were remarkably good (70% at least 6/7 knowledge questions correct). However, only 36% knew that ticks do not drop from trees. On average, 69% of children thought that they could contract LD. Although the majority of children (93%) think that tick checks are important, 18% indicated that they were checked regularly, 52% were occasionally checked and 30% had never been checked after visiting a nature area. Knowledge level and knowing somebody who contracted LD are important predictors for attitude towards- and frequency of tick checks.

Conclusions: Most of children's tick and LD knowledge is good and they consider tick checks important. It is striking that only 18% indicated that they were checked regularly. Future information for children should include a LD case story, show clearly where ticks reside. And motivate children to ask their parents for a timely tick check.

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USE OF GUIDELINES FOR TETANUS POST EXPOSURE PROPHYLAXIS BY GENERAL PRACTITIONERS AND EMERGENCY DEPARTMENTS IN THE NETHERLANDS

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Background and aims: The Dutch National Immunisation Programme includes six tetanus toxoid (TT) containing vaccinations. In 2003, the Dutch Health Council (HC) reviewed the use of tetanus post exposure prophylaxis(T-PEP). In fully vaccinated persons, T-PEP with TT is advised if the last vaccination is ≥ 10 years ago.

We aimed to evaluate whether the recommendations on T-PEP were in place and followed, and to assess possible differences in the use of guidelines for T-PEP between general practitioners(GPs) and emergency departments(EDs).

Methodology: 178 GP offices and 60 EDs in the Netherlands were asked to participate in this cross-sectional questionnaire study. Additionally, participants were asked to send in their guidelines.

Results: The response rates for GPs and EDs were 37.6% and 70.0%, respectively. 98.1% (n=107) of the participants stated they used a guideline for T-PEP. Only 28.4% (n=23) of the guidelines was fully consistent with the HC-recommendations, more among EDs (41.4%) than among GPs (21.2%). Another 35.8% (n=29) adhered to the guideline of the College of GPs (CGP) which is consistent with the HC-recommendations, except that in the GP-guideline 'type of wound' is used as a criterion.

Conclusion: 98.1% of all EDs and GPs use a guideline on T-PEP. Only 28.4% of the guidelines are fully consistent with the HC-recommendations. This discrepancy is mostly because many GPs consider ´type of wound´ as a criterion for T-PEP, which is in line with the guideline of the CGP. Whether this aspect should be considered in T-PEP should be studied further.

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PERSISTENCE OF BACTERICIDAL ANTIBODIES TO 5 YEARS OF AGE FOLLOWING A 'PRE-SCHOOL' BOOSTER DOSE OF SEROGROUP B MENINGOCOCCAL VACCINE

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Background and aims: A booster dose of an investigational serogroup B meningococcal vaccine (4CMenB, recently recommended for European licensure by CHMP) administered to 40 month-old children resulted in human complement serum bactericidal activity (hSBA) ≥1:4 in 100% of participants for strains H44/76 and 5/99, and 93% for strains NZ98/254 and M10713. Persistence of these bactericidal antibodies to age 5 years is unknown.

Methods: Sera were obtained from 5 year-old children previously immunised at 6, 8, 12 and 40 months with 4CMenB or an investigational formulation (rMenB) lacking the outer membrane vesicle component of 4CMenB. MenB vaccine-naïve participants recruited as controls had blood samples obtained before and 1 month after 2 doses of 4CMenB at 60 and 62 months of age.

Results: At 5 years of age 8/12 (67%) 4CMenB recipients had hSBA ≥1:4 for strain 44/76, compared with 100% for strain 5/99, 17% for NZ98/254 and 45% for M10713. These proportions were similar for rMenB recipients (n = 13) with the exception of NZ98/254 (0%). In control participants (n=46) proportions were 4% (H44/76 and 5/99), 0% (NZ98/254) and 67% (M10713), which increased after immunisation with 2 doses of 4CMenB to 100% (H44/76 and 5/99), 89% (NZ98/254) and 97% (M10713) (n = 35).

Conclusions: In this small study, waning of hSBA titres following four doses of 4CMenB varied between strains. Whether this will influence the breadth of persisting protection afforded by 4CMenB immunisation is uncertain. Two doses in 5 year-old children were immunogenic and may be used for catch-up immunisation.

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COMPARATIVE EVALUATION OF BIONEXIA® INFLUENZA A+B TO QUICKVUE® INFLUENZA A+B TEST FOR THE DETECTION OF INFLUENZA IN PEDIATRIC SAMPLES

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Background and aims: Influenza is an infectious viral disease, responsible for epidemics involving paediatric populations. Rapid diagnostic tests (RDT) for influenza are easy-to-use tools for doctors. The aim of this study was to compare the performance of a new rapid test bioNexia® Influenza A+B (bioMérieux SA) to QuickVue® Influenza A+B test (Quidel Corporation).

Material and methods: In France, surveillance of influenza in the general population is organized through the GROG* network. Diagnosis of respiratory viruses is performed using MDCK culture and PCR. Nasopharyngeal swabs from children less than 17 years old sent to the laboratory were selected during the winter 2011-2012 influenza A H3N2 outbreak for this study.

Results: 108 clinical samples were included. Compared to viral culture and PCR, the sensitivity of bioNexia® for influenza A was higher than QuickVue® (63.27% and 57.14% vs. 57.14% and 51.79%, respectively) contrary to specificity (96.61% and 98.08% vs. 98.31% and 100%, respectively), representing a statistically non-significant difference of $p< 0.05$). One false positive result for Influenza A was observed for bioNexia® in a patient associated with RSV infection. When the sample was tested again, the result was not confirmed.

Conclusion: In this paediatric study, bioNexia® RDT showed similar or slightly higher sensitivity for influenza A H3N2 compared to QuickVue®. The specificity of bioNexia® was found to be highly satisfactory for an easy-to-use rapid test. Further studies on paediatric populations should be performed to extend the number of samples to other influenza virus subtypes.

*GROG = Groupes Régionaux d'Observation de la Grippe.

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KNOWLEDGE AND ATTITUDES OF TURKISH FEMALE HIGH SCHOOL STUDENTS ABOUT GENITOURINARY SYSTEM INFECTIONS

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Background and aims: Adolescent girls are particularly under risk for genitourinary system infections due to various reasons like their anatomic characteristics, start of menstruation and lack of knowledge. The aim of this study was to determine the female student's knowledge and attitudes about genitourinary system infection.

Methods: The study was conducted with 415 female high school students who accepted to participate in the study between October - December 2012. A questionnaire, prepared by the researchers, was used to collect data. Percentage distributions and Chi-square test were used to evaluate data.

Results: Mean age of the participant students was 15.71±1.16. It was detected that 8.4% of students had burning urination right now, 28.9% had complains about burning urination in the past and 20.5% had diagnosis of vaginal infection. 48.9% of the students used cotton underwear, 61.7% changed underwear twice or three times a day, 22.9% ironed their underwear after washing and 21% had bath once a week.

As the result of the statistical analysis, it was discovered that there was a statistically significant difference between mothers' educational status of the students and frequency of having bath, between social security coverage and living place and frequency of changing underwear and between hand-washing frequency and diagnosis of urinary tract infection ($p < 0.05$).

Conclusions: The results of our study indicated that adolescent girls did not care about genital hygiene enough. Exploring inadequate hygiene practices and training adolescents about genital hygiene and infections are very important in terms of providing them with positive health behaviors.

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KNOWLEDGE AND PRACTICES OF TURKISH MOTHERS ABOUT CHILDHOOD VACCINATION

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Background and aims: Vaccinations save lives of millions of children and adults, improve health and increase quality of life. High knowledge level of childhood vaccination of parents and appreciation of the importance of this issue augment the rate of vaccination. This study was descriptively conducted in order to determine knowledge and practices of Turkish mothers about childhood vaccination.

Methods: The study was composed of 130 mothers who came to 7th Family Health Center located in Yozgat city center between September-December 2012, had children aged 6-60 months. A questionnaire was used to collect data. Percentage distributions and Chi-square test were used to evaluate data.

Results: It was found out that mean age of the participant women was 29.17±6.88, 37.0% of them had lower educational level, 81.5% did not work. It was noted that nearly all of the women considered vaccination necessary and 94.1% of them had their children vaccinated in accordance with vaccination cards. Only 29.6% of the mothers knew about self-paid vaccines apart from routine free vaccines and 44.4% of these mothers had their children vaccinated against chickenpox. Nearly half of the mothers (46.4%) didn't know about the side effects of vaccines.

In this study there was a statistically significant difference between the status of income and education of mothers, and vaccination and having knowledge about vaccination ($p< 0.05$).

Conclusions: In light of the study, it was explored that rate of childhood vaccination was not at the desired level and mothers lacked knowledge about vaccines.

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DISSEMINATED CUTANEOUS MYCOBACTERIUM CHELONAE INFECTION IN A 9.5-YEAR-OLD DIABETIC GIRL

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Background: Mycobacterium chelonae is a fast growing mycobacteria that mainly causes localized cutaneous infections. Disseminated cutaneous infections are quite exclusively seen in immunosuppressed individuals. We present a case of disseminated cutaneous infection in a young diabetic patient.

Case report: A 9.5-year-old girl followed for well controlled type 1 diabetes (diabetes duration: 3 years, mean HbA1c over the last 12 months: 7.9%, last HbA1c 7.1%, insulin requirements: 0.76U/kg/day) presented with an inflammatory nodule of her right buttock at the site of a previous insulin injection. The lesion did grow significantly over a week and evolved as an abscess needing incision and drainage. Classical bacterial cultures remained negative. Despite antibiotic therapy (co-amoxicillin, clindamycin), the infection recurred and similar lesions appeared bilaterally on both calves over the next weeks, with some of them discharging spontaneously. New bacterial and fungal cultures remained negative. Mycobacterial cultures revealed positive for M. chelonae. Laboratory assessment of immunity (immunoglobulins and complement) was normal. An oral clarithromycine treatment to which the mycobacteria appeared sensitive was introduced.

Discussion: Infection with M. chelonae primarily occurs by direct inoculation of the skin with contaminated medical equipment. We couldn't cultivate the injection material as all the equipment batches was changed early in the course of the disease. M. chelonae is usually sensitive to clarithromycine and needs a long course of treatment to obtain a sustainable cure.

Conclusions: This case underscores the need to consider atypical mycobacterial infections in any patient with culture-negative cutaneous infections resistant to conventional antibiotic treatment.

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S.PNEUMONIAE NASOPHARYNGEAL CARRIAGE AND ACUTE OTITIS MEDIA

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Introduction: The role of S.pneumoniae (SP) nasopharyngeal carriage in development of acute otitis media (AOM) is not well described.

Methods: Children below 6 years of age with acute respiratory disease participated in the clinical study evaluating distribution of serotypes of SP in naso-pharynx. The sub-cohort of children with the final diagnosis of AOM was analysed.

Results: AOM was diagnosed in 41 out of 590 enrolled into the study.

Positive samples for SP nasopharyngeal carriage during the first days of illness had 24 children. (58.5%). There was no difference according children age, gander, day-care centres attendance, siblings, previous antibiotic use in SP positive and negative groups. Children with AOM and SP carriage had longer history of illness, 20% of them were treated with two different antibiotics, whilst none was given antibiotics in SP negative group. Clinical symptoms (body temperature, redness of mucosa, nose secretion) during the first days of illness did not let us now about diagnosis. Children with positive SP more often had signs of bronchitis. Eleven different SP serotypes were found (3, 6A, 6B. 6C, 11, 14, 15, 18F, 19F, 23F, G+) and most of them are present in pneumococcal conjugated vaccines.

Conclusions: SP carriage in naso-pharynx may be related to the prolonged course of AOM and more complicated antibacterial treatment. Clinical signs during the first days of illness do not indicate the future severity of AOM. Conjugated pneumococcal vaccines can be highly effective in preventing of AOM.

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OBSERVATIONAL STUDY OF ROUTINE ENDOTRACHEAL TIP CULTURING IN NEONATAL INTENSIVE CARE UNIT

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Background and aims: Endotracheal(ET) tubes are routinely used for intubation in Neonatal Intensive Care Units(NICU). These tubes may become colonised or act as foci for respiratory infection / sepsis. At removal it is a common practice in many NICUs to send tips routinely for culture and sensitivity.

We examined the bacteriology associated with ET tube tips after removal.

Methods: Retrospective observational study in UK tertiary NICU of all ET tube tips from April 2012 to Sept 2012. All ET tube tips sent for culture during the 6 month period were analysed.

Results: 110 ET tube tips were sent during study period. 28(25%) had a positive culture. There were multiple tips from same patient, which grew the same bacterial growth because of colonisation.

Patient	A	B	C	D	E	F
Number of ET tips sent	6	4	3	2	2	2
Bacterial growth	Enterobacter	Coagulase Negative Staphylococcus (CONS)	CONS + E.Coli	Enterobacter	CONS + Acetobacter	CONS + Enterobacter

[ET tip culture in each patient]

In rest of the 9 patients only a single tip was sent which grew respiratory commensals and CONS.

None of the positive cultures led to antibiotic prescription.

Type of bacterial growth	CONS	Enterobacter	E.Coli	Enterococcus	Group B Streptococcus	Staph. aureus	H.influenza	Acetobacter	Candida
Number ET tips	10	7	7	1	1	1	1	1	1

[Type of bacterial growth]

30 bacterial growth from 28 tips.

Conclusions: Most of the positive ET tube tips were due to colonisation. None of them warranted antibiotic prescription.

Sending routine ET tube tips for culture is not beneficial.

ET secretions for culture may be more useful if clinical concern of respiratory infection in ventilated neonates.

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CHICKEN POX: NOT YET SPOT ON?

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We present two cases of complicated varicella zoster infection and discuss the wider implications that these cases illustrate.

Case 1: A 3.5 year-old female developed pyrexia, vesicles and bilateral periorbital swelling. After 48 hours, she was unable to open her eyes. The vesicles spread to cover her face and torso. She refused all oral intake. Raised inflammatory markers, hyponatraemic dehydration and deranged clotting were seen. IV Aciclovir, Co-Amoxiclav and Clindamycin were commenced. Over 5 days, a lesion on her ear developed extensive necrotic cavitation exposing cartilage. A submandibular ultrasound revealed extensive subcutaneous inflammation. She required 15 days of IV antibiotics and a protracted inpatient stay.

Case 2: A 2 year-old male with 8 days of cough, coryza and pyrexia developed marked truncal ataxia. He was unable to sit unsupported or walk, exhibiting overall paucity of movement and difficulties feeding. No clear cause necessitated MRI under sedation. After 5 further days, varicella lesions emerged on his trunk. Prior to emergence of vesicles, he was on the ward with an immunosuppressed child. This child required successive blood tests, further inpatient stay and VZIG.

Median hospitalisation stays are 7 days for complicated infections. With the USA reducing its rates of varicella by 80% through vaccination, should the UK follow suit? The vaccine's favourable safety and seroconversion profiles, and ease of administration support this suggestion. Cost-benefit analysis has not been recently addressed. We argue that this should be repeated in light of reports of significant morbidity as illustrated here.

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PERSISTENT OUTBREAKS OF HAND, FOOT, AND MOUTH DISEASE CAUSED BY EV71 IN SHANGHAI SINCE 2007

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Background and aims: Since 2008 Hand-foot-mouth disease (HFMD) has become a major infectious disease in China. Understanding of the local epidemiology of HFMD is helpful to formulate the strategy of preventing the outbreak of HFMD.

Methods: This study analyzed the demographic data, seasonal pattern, pathogen of HFMD in children in Shanghai between 2007 and 2011.

Results: A total of 39807 outpatients were diagnosed as HFMD, 1169 (2.9%) were confirmed to have neurological complications and 15 (0.04%) developed pulmonary edema/hemorrhage and 12 (0.03%) died. HFMD peaked from April to July in Shanghai. Since 2008, the major population affected has shifted from local preschool-attending children to migrant and home-care younger children. Between 2009 and 2011, 3254 stool samples taken from inpatients were tested for EV-A71 and Cox-A16, which were detected in 1906 (58.57%) and 407 (12.51%) samples, respectively. Besides, EV-A71 and Cox-A16 were detected in 871 (88.97%) and 15 (1.53%) of 979 specimens from severe cases, and in 1035 (45.49%) and 392 (17.23%) of 2275 specimens from uncomplicated cases. All 16 cases with pulmonary edema or hemorrhage were attributable to EV-A71 infection.

Conclusion: HFMD is a top health priority problem in Shanghai. Home-care, migrant young children are the predominantly susceptible population. The dominant circulation of EV71 is associated with the outbreak of HFMD and the occurrence of severe and fatal cases.

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IDENTIFICATION AND CHARACTERIZATION OF A NON-SIALIC ACID-BASED DRUG AS AN INHIBITOR OF HPIV-3'S HEMAGGLUTININ-NEURAMINIDASE WITH ANTIVIRAL ACTIVITY IN VITRO

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Background and aims: The human parainfluenza type-3 virus (hPIV-3) is one of the principal etiological agents of acute respiratory infections (ARIs) in less than 2-years old worldwide. Although a few molecules have shown antiviral potency in vitro, they remain poorly efficient. This study aims to discover non-sialic acid-based inhibitors of hPIV-3 hemagglutinin-neuraminidase (HN) that could help better understand the mechanism of sialidases, and potentially give rise to combinatorial therapies.

Methods: A library of 1280 approved-drugs was screened by neuraminidase-inhibition assay. The hit compounds were then characterized for their ability to inhibit both functions of HN, as well as infection in vitro. Their inhibitory mechanism towards HN was then investigated by enzyme kinetics, and confirmed by competition STD-NMR experiments.

Results: The drug E02 was found to efficiently inhibit both the neuraminidase and hemagglutinin activities of HN with IC_{50}s of respectively 12.67 µM and 30 µM. In addition, the drug inhibits viral propagation at binding stage in vitro with an IC_{50} of 3 µM. The enzyme kinetics data suggest that the drug inhibits the sialidase via a non-competitive mechanism (Ki=4.9 µM), which was confirmed by competition STD-NMR experiments in presence of a competitive inhibitor of HN.

Conclusion: We successfully identified E02 as a non-competitive inhibitor of hPIV-3 HN. Together with further investigations into the localization of the drug binding site as well as combinatorial drug tests, these findings will greatly help understand how to better impair the mechanism of HN for the development of new anti-parainfluenza therapies.

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COMMUNITY BASED ACTIVE SURVEILLANCE OF RESPIRATORY INFECTIONS IN CHILDREN 0 - 5 YEARS OF AGE IN PAKISTAN

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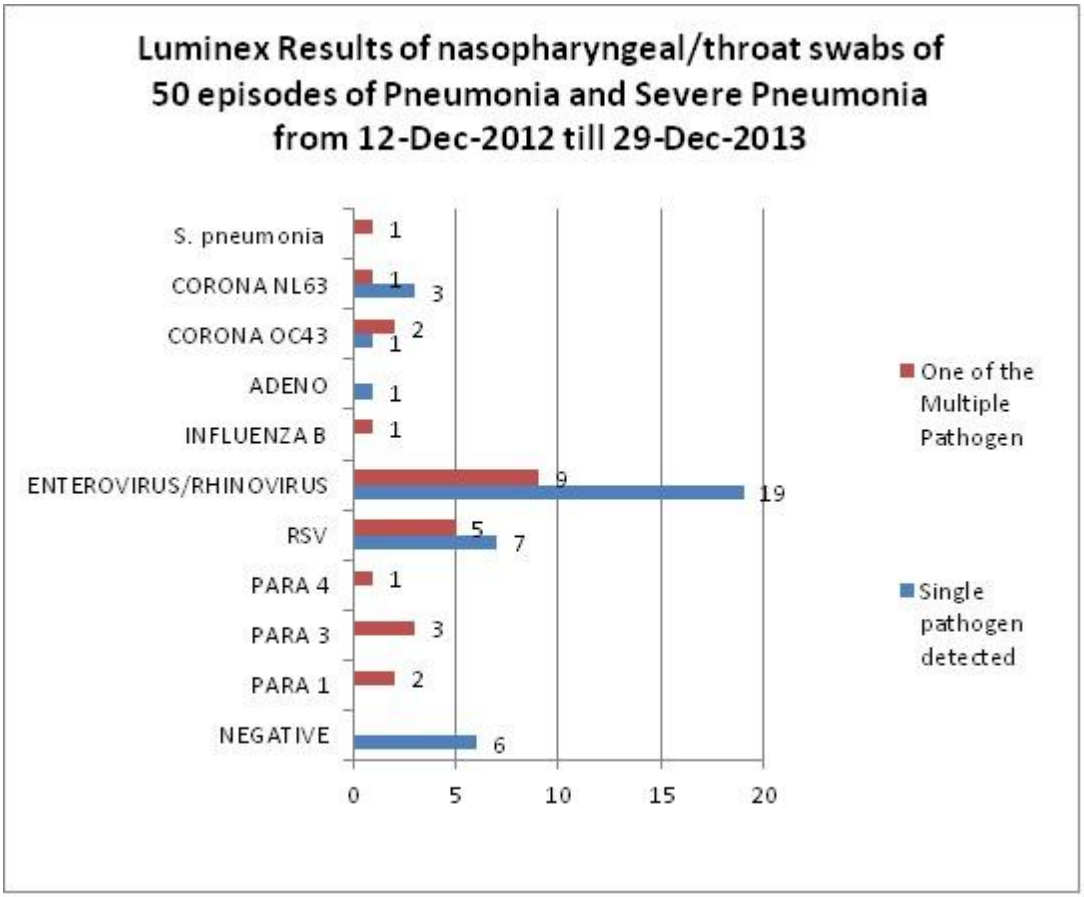
Background: In Pakistan more than 500,000 children < 5 years of age die annually and pneumonia is responsible for 21 % of these deaths. Respiratory viruses are considered as important etiological agents for pneumonia, either by themselves or as precursors for bacterial pneumonia. Before widespread use of preventive and therapeutic interventions (e.g., vaccines, antivirals) against respiratory viruses is recommended, it is important to determine the incidence of respiratory viral infections in children in community settings.

Methods: We conducted a longitudinal observational study at Ali Akber Shah, semi urban area of Karachi, from Dec 2012 to Dec 2013 where we followed a cohort of 350 children 0 to 5 year old. We added 20 newborns every month to the cohort. The children were actively followed for episodes of pneumonia or severe pneumonia through once weekly home visits. Each episode of pneumonia or severe pneumonia using the WHO guidelines was eligible for a nasopharyngeal/throat swab test for viral diagnosis.

Results: 585 children were enrolled and 50 eligible episodes of pneumonia (13) and severe pneumonia (37) have been captured. The nasopharyngeal/throat swabs were tested using Luminex platform and showed infection with single viruses in 31 specimens and with multiple viruses in 12 specimen. 6 specimens were negative and one had no result.



[Fig]

Conclusions: Respiratory viruses are associated with majority of pneumonia and severe pneumonia cases in children in community settings in Pakistan.

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COMPARISON OF PERFORMANCE OF THREE IMMUNOASSAY TESTS: VIDAS MEASLES IGG, ENZYGNOST ANTI-MEASLES IGG AND CAPTURE EIA MEASLES IGG

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Background and aims: The recent measles epidemic in France has reinforced the interest of immunoassay tests for monitoring the serological status in order to administer vaccination. Specific anti-measles IgG screening is generally used for this purpose. In this context, we evaluated 3 automated immunoassay methods: VIDAS® Measles IgG (bioMerieux), Enzygnost® Anti-Measles IgG (Siemens) and CAPTURE® EIA Measles IgG (Microimmune).

Methods: 321 samples were collected. 76 samples were collected from patients with a typical clinical presentation of measles and the diagnosis was confirmed by the presence of specific anti-measles IgM and IgG (group A). 125 samples were from patients vaccinated or with a clinical presentation of measles but with no specific IgM (group B). 120 samples were obtained from healthy blood donors (group C) . The international standard (NIBSC code : 97/648) was used to determine the detection limit of the tests.

Results: Data analysis showed more than 97 % global concordance between VIDAS and the other two methods. Relative sensitivity and concordance of VIDAS vs Enzygnost were respectively 100%, 97.5%, and 99%, 97.1% between VIDAS and CAPTURE® EIA Measles IgG . The detection limit of the VIDAS test was equivalent to the other methods (< 100 mUI/ml).

Conclusions: VIDAS Measles IgG shows equivalent performance to other automated immunoassay tests and fits the needs of small volume testing laboratories through its single-dose format.

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IMMUNOGENICITY AND SAFETY OF 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE CO-ADMINISTERED WITH DTPA IN JAPANESE CHILDREN

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Background and aims: This phase III, randomised, open-label, multi-centre study (NCT01027845) assessed immunogenicity, safety and reactogenicity of primary and booster vaccination with 10-valent pneumococcal non-typeable Haemophilus influenzae protein D conjugate vaccine (PHiD-CV, GlaxoSmithKline Vaccines, intramuscular) co-administered with DTPa vaccine (Kaketsuken, subcutaneous).

Methods: 360 Japanese infants were randomised (2:1) to receive either PHiD-CV and DTPa (Co-ad-group) or DTPa alone (DTPa-group) as 3-dose primary (at age 3-4-5 months) and booster (at 17-19 months) vaccination. Blood samples were taken before and 1 month post-primary/booster vaccination. Immune responses were measured using 22F-inhibition ELISA and opsonophagocytic activity (OPA) assays (pneumococcal serotypes) and ELISA (protein D). Solicited/unsolicited symptoms recorded for 4/31 days post-vaccination, respectively, and serious adverse events (SAEs) recorded throughout the study are presented.

Results: For each PHiD-CV serotype, high percentages of children had pneumococcal antibody concentrations ≥0.2 µg/mL and OPA titres ≥8 post-primary/booster vaccination (Table). Geometric mean antibody concentrations and OPA titres were higher post-booster than post-priming for each serotype (except OPA for 6B). All PHiD-CV-vaccinated children had anti-protein D antibody concentrations ≥100 EL.U/mL 1 month after both primary and booster vaccination. Redness and irritability were the most common solicited symptoms in both groups. Incidences of unsolicited symptoms were comparable between groups. SAEs were reported for 47 children (Co-ad-group: 28; DTPa-group: 19), none were assessed as vaccine-related.

Table. Percentages of children with serotype-specific pneumococcal antibody concentrations ≥0.2 µg/mL and OPA titres ≥8 at 1 month after 3-dose priming and after booster vaccination (Booster ATP cohort for immunogenicity)

Serotype	% of children with antibody concentrations ≥0.2 µg/mL		% of children with OPA titres ≥8	
	Post-priming (N=214–216)	Post-booster (N=213–214)	Post-priming (N=193–211)	Post-booster (N=212–214)
Vaccine serotypes				
1	100	100	99.0	100
4	100	100	99.5	100
5	100	100	99.5	100
6B	92.6	97.7	96.2	98.1
7F	100	100	100	100
9V	99.5	100	100	100
14	100	100	100	100
18C	100	100	96.6	100
19F	99.5	100	98.5	99.5
23F	94.4	99.1	96.1	99.1
Cross-reactive serotypes				
6A	69.8	95.3	85.5	92.9
19A	76.9	95.8	61.5	89.6

OPA, opsonophagocytic activity; ATP, according-to-protocol; N, minimum–maximum number of subjects with available results

[Table]

Conclusion: PHiD-CV induced robust immune responses and was well-tolerated when co-administered with DTPa as 3-dose priming and booster vaccination in Japanese children.

Funding: GlaxoSmithKline Biologicals SA.

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SEROTYPE 19A AND THE 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE (PHID-CV): LESSONS LEARNED TO DATE

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Background and aims: After introduction of the 7-valent pneumococcal conjugate vaccine (7vCRM, Pfizer Inc.), significant reductions in invasive pneumococcal disease (IPD) incidence were observed. In some settings, this was followed by a rise in IPD caused by non-vaccine serotypes, mainly serotype 19A, suggesting that potential cross-protection against 19A disease by the 19F-containing 7vCRM may be limited. For PHiD-CV (GlaxoSmithKline Vaccines), a different method was used for 19F conjugation which positively affects its immunogenicity and immunological cross-reactivity against 19A. As it is unknown whether the heightened immune response is sufficient to provide any cross-protection against 19A IPD, we examined the data available to date from PHiD-CV post-marketing studies.

Methods: We summarized the occurrence of 19A IPD cases in the first 1-2 years after PHiD-CV introduction in infant immunization programs in Canada, Brazil and Finland in cohorts targeted for vaccination.

Results: Results from recent post-licensure epidemiological studies after introduction of PHiD-CV showed trends for reduced 19A IPD in children eligible for PHiD-CV vaccination, while increases in 19A IPD were observed over the same periods of time in non-vaccine-eligible individuals (Table). Results from double-blind randomized clinical trials assessing 19A nasopharyngeal carriage after PHiD-CV vaccination will also be presented.

Region	Age	Period assessed		Number of 19A IPD cases	
Vaccine-eligible cohorts					
		Pre-PHiD-CV implementation	Post-PHiD-CV implementation	Pre-PHiD-CV implementation	Post-PHiD-CV implementation
Quebec, Canada[1]	6-18m	Sep 2007-Dec 2008[a]	Sep 2009-Dec 2010[b]	15	9
	13-28m	Sep 2008-Dec 2009[b]	Sep 2009-Dec 2010[c]	12	8
Quebec, Canada[2]	6-11m	2008-2009[d]	2010[e]	12*	2
	12-23m	2008-2009[b]	2010[c]	24.5*	26
Ontario, Canada[3]	5-11m	Jan 2009-Jun 2009[d§]	Jan 2010-Jun 2010[e§]	1	1
	16-22m	Feb 2008-Aug 2008[b§]	Feb 2009-Aug 2009[c§]	1	1
Brazil (UH-USP)[4]	<2y	Jan 2006-Jun 2010[f]	Jul 2010-Jul 2012[g]	0.9*	0*
Brazil (SIREVAII)[5]	<2y	2008-2009[f]	2011[g]	8.5*	6
Finland[6]	0-11m	2004-2009[f]	2011[e]	2.7*	0
Non-vaccine-eligible cohorts					
Quebec, Canada[2]	0-6m	2008-2009	2010	4*	6
	2-5y	2008-2009	2010	19*	22
Brazil (SIREVAII)[5]	≥2y	2008-2009	2011	15.5*	30
Finland[6]	≥12m	2004-2009	2011	27.1*	31

*Average number of cases per year; §Birth cohort; observation period truncated for age to observe either priming or booster effect; [a]7vCRM priming + booster; [b]PHiD-CV priming + booster; [c]7vCRM priming + PHiD-CV booster; [d]7vCRM priming; [e]PHiD-CV priming; [f]no PCV in national immunization schedule; [g]PHiD-CV priming (+ booster) or catch-up; m, months; y, years; UH-USP, University Hospital of the University of Sao Paolo

References: [1]De Wals et al. *Vaccine* 2012; [2]Pneumococcal Surveillance Program Quebec, 2010 report, Laboratoire de santé publique du Québec; [3]Wong et al. *IDWeek* 2012, abstract 503; [4]Santos et al. *ICAAC* 2012, poster G-861; [5]SIREVAII annual reports 2008-2011; [6]Jokinen et al. *ISPPD* 2012, poster 165

[Table]

Conclusions: These findings may be consistent with the hypothesis that cross-reactive anti-19A antibodies elicited by PHiD-CV provide some protection against 19A IPD. However, the limited duration of surveillance and low numbers of cases warrant caution interpreting these results.

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A QUALITATIVE ASSESSMENT OF FACTORS INFLUENCING CHILDHOOD VACCINATION DECISION-MAKING AMONG PARENTS OF DIFFERENT ETHNIC BACKGROUNDS IN THE NETHERLANDS

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Background and aims: In the Netherlands there are disparate results with regard to participation in childhood vaccination among groups of non-Western descent. Therefore, our aim was to explore factors that influence childhood vaccination decision-making among parents with different ethnic backgrounds.

Methods: Six focus groups with 33 mothers of Moroccan, Turkish and other ethnic backgrounds who had at least one child aged 0-4 years were conducted. Additionally, two interviews with nurses from Child Welfare Centers (CWCs) working with Moroccan and Turkish parents were conducted. A thematic analysis was used.

Results: Most mothers had a positive attitude towards childhood vaccination. None of their children missed vaccinations due to transition to the Netherlands. They perceived no problems in receiving vaccination invitations or responding to calls. They were not always satisfied with the CWC services (i.e., limited time and little attention). The mothers perceived vaccination as self-evident and important. They perceived low social norms, while the nurses believed that their social environment is very important. Cultural aspects or religious beliefs did not seem to play a role. The mothers perceived a language barrier in understanding provided information about the National Immunization Program (NIP) and wanted more information.

Conclusions: Mothers wanted to be educated by the childhood vaccine providers about the targeted diseases and advantageous and disadvantageous of vaccination. Investigation of the utility of information provision in Turkish, Arabic and Berber language is recommended. Providing information tailored to these parents' needs is important to sustain vaccination participation and to ensure acceptation of future vaccinations.

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BURDEN OF RESPIRATORY SYNCITIAL VIRUS IN CHILDREN IN PAKISTAN

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Background and aims: Respiratory syncytial virus (RSV) accounts for up to 25% of cases and 12% of deaths in childhood pneumonia. The aim of our study is to define the burden and seasonality of RSV infection in children in Pakistan, so that important interventions for its prevention and treatment can be implemented.

Methods: Our study was conducted at Aga Khan University Hospital (AKUH) in Karachi, Pakistan, between August 2009 and June 2012. Children under 5 years admitted with an acute respiratory illness(ARI) were enrolled and questionnaires regarding the subjects' socio-demographic and clinical condition were administered. Throat swabs were collected and tested for RSV via real time RT-PCR. After discharge, another questionnaire was completed to document the child's clinical course and outcome.

Results: The study included 1151 children with ARI. 223(19%) were found to be positive for RSV. The highest incidence was in the 3-13 months age group. RSV was found to be highly seasonal, being most prevalent from July to October. The major distinctive clinical features associated with RSV were nasal congestion (75%,p=0.01) and shortness of breath (75%,p=0.05). During their stay, 3.6% children required intubation, 4% required ICU admission/transfer and 0.9% died during hospitalization.

Conclusion: There was a high incidence of RSV associated pneumonia in children admitted to the hospital for ARI, especially in the rainy season. Timely interventions to prevent and manage RSV infection are needed to reduce the incidence of ARIs and hence the unnecessary antibiotic usage, morbidity and mortality related to it.

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IMPACT OF TWO INFORMATION INTERVENTIONS IN MATERNITY HOSPITALS ON THE PERTUSSIS VACCINATION COVERAGE OF PARENTS

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Objective: The objective was to evaluate the impact of information interventions in maternity hospitals on pertussis vaccination coverage of young parents and their children, using standardised information.

Methods: A prospective, multicentre study was conducted between September 2011 and February 2012. The study was offered consecutively to all parents over the age of majority. After an observational phase (OP), an interventional phase (IP) was performed. Parent couples who were not up-to-date with vaccination were randomly enrolled in 1 of 2 groups, either with or without an added information letter to their general practitioner. Primary endpoint was parents' vaccination status, obtained by a follow-up telephone interview 3 months later.

Results: Enrolment included 453 subjects, 414 (91.4%) of whom were contacted. In maternity hospital, 18.8% of mothers and 19.7% of fathers, but only 7% of couples, were up-to-date with pertussis vaccination. For couples previously not up-to-date, 19.4% and 35.2%, respectively, achieved update 3 months following OP and IP, p=0.003. Added information to medical practitioners was not statistically significant, p=0.40. Parents were vaccinated earlier after IP and parental vaccination status significantly improved initiation of vaccination in infants (p=0.002).Vaccination was initiated in 92.5% of infants (median 65 days), predominantly with a hexavalent vaccine (83.8% of cases).

Conclusion: Providing standardised information on the importance of pertussis vaccination to an infant's immediate circle during maternity hospital stay has a considerable impact on the vaccination coverage of parents and their children.

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CHRONIC MUCOCUTANEOUS CANDIDIASIS IN PATIENTS HARBOURING MUTATIONS IN THE DNA-BINDING SITE DOMAIN OF STAT1

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Chronic mucocutaneous candidiasis (CMC) encompasses a group of syndromes with variable clinical phenotype, characterized by recurrent fungal infections of the skin, nails and mucous layers. During recent years, several genetically determined CMC syndromes have been described, resulting in impairment of the Th17-mediated immunity against Candida albicans. Typically, the clinical onset of these diseases is during childhood or early adolescence, with a considerable rate of patients not being diagnosed in-time.

The herein presented index case, from a group of patients, is a girl presenting with persistent aphthous lesions in the oral cavity and several episodes of bronchitis starting at the age of 3 months. When presented at our department at the age of 8 months, the patient suffered from an extended diaper rash and refractory fungal esophagitis in addition to recurrent bronchitis and chronic enteritis concomitant with sustained IgG2/4 subclass deficiency. No mycobacterial or viral infections were observed. A candidate-gene approach revealed deleterious mutations in the DNA-binding site domain of the signal transducer and activator of transcription 1 (STAT1) in all individuals of the group of patients.

STAT1 is a crucial component of the downstream signaling of cytokine receptors and possesses functional capability in all lymphoid lineages. Analysis of the index patient`s leucocytes revealed multiple defects in the differentiation and function of T-, B-, and NK-cells, as well as in granulocytes. Both Th17 cell function, memory B cell differentiation and IgG2 production, and release of neutrophil extracellular traps (NETs) were significantly reduced, resembling a pathophysiological framework for proneness to fungal infections.

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NASOPHARYNGEAL CARRIAGE OF STREPTOCOCCUS PNEUMONIAE IN HEALTHY CHILDREN AND ADULTS AFTER IMPLEMENTATION OF CONJUGATE-PNEUMOCOCCAL VACCINE IN NATIONAL IMMUNIZATION PROGRAMME

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This study was performed to determine the carriage rate of nasopharyngeal (NP) S. pneumoniae after implementation of the pneumococcal conjugate vaccine (PCV) in the national immunization program (NIP) of Turkey. Between may 2012 and August 2012, 1000 nasopharyngeal swabs were obtained from 500 children aged 1 month to 15 years and 500 adults aged 20 to 90 years without evidence of acute infection. The pneumococcal carriage rate was 10.2% in children and 1.6% in adults. S. pneumoniae NP colonization rates were similiar in all age groups of children (0-23 months [10.8% colonization rate], 24-60 months [12.7%] and > 60 months [8.8%]). Of the children included in the study, 19.4% had received PCV7 and 10.4% had received PCV13. Among all children 350 (70%) were not vaccinated with PCV. In children, only having 3 or more siblings under age 8 in the family and history of sinusitis were found to be risk factors for carriage ($p< 0.05$). The most common isolated serotypes were 23F (21%), 6A/B (16.3%), 19F (9.3%), 22F/22A (9.3%). Serotype covarege rates of PCV7, PCV10 and PCV13 were 62.7%, 67.4 and 72%, respectively. Serotypes 22F (9.3%), 15A/15F (6.9%) and 35A/35C (6.9%) were the most common isolated serotypes that was not existing in PCV13. This study provides data about the carriage rate and serotype distribution of S. pneumoniae strains in Turkish children and adults after introduction of PCV into the NIP.

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BURDEN OF HUMAN METAPNEUMOVIRUS IN CHILDREN IN PAKISTAN

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Background and aims: Human Metapneumovirus(hMPV) is a newly recognized cause of pediatric respiratory tract infections worldwide. Role of hMPV in causing severe pneumonia in children in Pakistan is not known. Our objective is to determine the prevalence, seasonality and clinical features associated with hMPV at the Aga khan University Hospital(AKUH), Karachi, Pakistan.

Methods: Children under 5 years of age, admitted between August 2009 and June 2012 with an acute respiratory illness (ARI), were enrolled and questionnaires regarding their socio-demographic and clinical condition were administered. Throat swabs were collected and tested for hMPV via real time RT-PCR. After the child's discharge, another questionnaire was completed to document the child's clinical course and outcome.

Results: 1151 children with ARIs were enrolled in the study. 84(7%) were found to be positive for hMPV. The highest incidence was in the 4-17 months age group. hMPV had a bimodal seasonal distribution. The peak incidence was found in January-February, followed by another peak in August-September. The major distinctive clinical features associated with hMPV were sore throat(69%,$p< 0.01$) and post-tussive emesis(44%,$p=0.03$). In the course of their stay, 3.6% children required intubation, 4% required ICU admission/transfer and 0.9% died during hospitalization.

Conclusion: hMPV is an important cause of ARI in Pakistan, and may have a significant clinical impact on infants and children.

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INTRATHECAL ANTIBODY RESPONSES IN MYCOPLASMA PNEUMONIAE ENCEPHALITIS

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Background and aims: We aimed to test for the presence of the rarely analyzed specific intrathecal antibody responses in patients with Mycoplasma pneumoniae encephalitis (MPE) as they may be diagnostic and have an impact on course severity.

Methods: Two patients fulfilling the etiological case definition for confirmed MPE [Epidemiol Infect 2010;138:783-800] were enrolled between November 2010 and November 2012. Investigations are detailed below.

Results:

Case	15-year-old girl	9-year-old boy
Diagnosis	**Meningoencephalitis**	**Bickerstaff brainstem encephalitis**
Clinical findings (on admission and over the course)	Glasgow coma scale (GCS) score 15; neck pain, headache, and diplopic images	GCS score 5; meningism, ataxia, ophthalmoplegia, and hemiplegia
Magnetic resonance imaging	Normal	Brainstem encephalitis
Cerebrospinal fluid (CSF)	39 cells/µL (95% mononuclear), normal protein and glucose levels	11 cells/µL, normal protein and glucose levels
M. pneumoniae real-time PCR	Pharyngeal swab: negative **CSF: positive**	**Pharyngeal swab: positive** CSF: negative
M. pneumoniae ELISA (serum) [≤11 U/ml]	IgM 31.7, IgG 15.5, IgA 40.7 U/ml	IgM 67.0, IgG 48.7, IgA 34.3 U/ml
Intrathecal antibody synthesis [Reiber index: cutoff 1.5]	No	**Yes: IgM 15.5, IgG 7.2, IgA 5.4**
Treatment	Azithromycin PO (5 days)	Doxycycline IV (1 week) Intravenous immunoglobulin (1 g/kg once) Prednisolone IV (5 days)
Sequelae	No	Yes

[Confirmed MPE cases]

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Conclusion: Our observations show that intrathecal specific antibody responses may help ascertaining etiological diagnosis of MPE. Furthermore, they may contribute to a more severe course, and in their absence, MPE can be self-limiting despite microbial invasion of the CNS.

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BEHAVIOUR OF PERTUSSIS IN CHILDREN LESS THAN 2 MONTHS IN ARGENTINA

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Incidence of pertussis increased during the recent years in Argentina. Clinical features in younger infants are atypical and the mortality risk high. Mothers are the most frequent source of infection.

Objectives: Identify epidemiology, clinical, and outcome of children less than 2 months old with Bordetella pertussis (B. pertussis) infection.

Material and methods: Prospective observational study. We included patients (p) ≤ 60 days admitted in the neonatal unit with B. pertussis infection confirmed by polymerase chain reaction from 2005 to 2012.

Results: We included 29 patients. Most of them, 28p (97%) diagnosed out of the winter season, more than half during summer. Twenty four (83%) were healthy term born. Mean age at diagnosis was 34 days (r:18-60d) and the most common chief complaints were paroxysmal cough and breathing difficulty (76% and 34%). Ten p (34%) were also febrile at admission. Eight p (28%) required mechanical ventilation, 2p (7%) ECMO. Twenty one (72%) had epidemiologic contact, 86% was the mother. Chest radiographs demonstrate pulmonary interstitial infiltrates in 17p (60%). White blood cell counts (WBC) mean 29.867 mm/3 (r: 8.700 - 102.000/mm3) and 75% lymphocyte count > 9.400 mm/3.

Coinfection was present in 5p (17%): adenovirus 2p, RSV 1p, pneumococus 1p and Chlamydia 1p. Four (90%) of them required Intensive Care Unit and mechanicalventilation. Three p (10, 3%) died. Mean WBC for those were 75.000mm/3 2p coinfected.

Conclusion: B. pertussis has a seasonal distribution. The mother is the main source of infection. Coinfection and leucocitosis were related with desfavorable outcome.

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LEUCONOSTOC AND VANCOMYCIN-RESISTANT INFECTIONS

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Leuconostoc species are catalase-negative Gram-positive lactobacillus resistant to vancomycin and generally susceptible to penicillin, which are now recognized as emerging opportunistic pathogens. Infections due to these microorganisms are rare and mostly seen in children with immunodeficiency disorders and chronic underlying conditions. Disrupted integrity of the gastrointestinal mucosa and enteral and parenteral nutrition are thought to predispose to Leuconostoc bacteremia in susceptible patients.

We describe the cases of two immunocompromised children under parenteral nutrition with unexplained persistent fever despite an antimicrobial regimen that included a glycopeptide.Vancomycin-resistant Gram-positive coccobacillary bacteria were isolated from blood cultures and identified as Leuconostoc spp.Bacteremia resolved in both patients following a course of i.v β-lactam antibiotic and after the central venous catheter was removed in one patient.

This report highlights the importance to consider Leuconostoc infections when vancomycin-resistant Gram-positive are identified in cultures of patients at risk.

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CLINICAL AND LABORATORY CHARACTERISTICS AND GENETIC ANALYSIS OF AN ECHOVIRUS 30-ASSOCIATED OUTBREAK WITH A HIGH MENINGITIS ATTACK RATE

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Background and aims: Echovirus 30 (E30) has been linked with outbreaks of aseptic meningitis. We describe the clinical characteristics and genetic analysis of an E30-associated outbreak in young children residing in two cities of Thrace, Greece.

Methods: Between late May and July 2012, 105 children (62 boys, 43 girls) were examined because of fever, headache, abdominal pain, nausea, and vomiting. Thirty-three of them (median age 5.8 years, 20 boys, 13 girls) with symptoms and/or signs of meningitis or who had fever and inadequate oral intake were hospitalized. RNA from fecal and CSF samples was isolated and analyzed for enterovirus presence by real-time RT-PCR. Positive stool samples were then inoculated into RD cells. Cell culture enteroviral isolates were typed by seroneutralization, while genotypic identification was performed by seminested RT-PCR amplification and direct sequencing of the VP1 region.

Results: Hospitalized children had normal hemograms, and mild to moderate CSF pleocytosis. Fecal and CSF samples were tested for enteroviruses from 29 and 18 children, respectively. Twenty-four positive fecal samples were typed using antisera and/or sequencing, and 9 out of 12 positive CSF samples were typed using sequencing. In all positive cases except one, E30 was detected. All patients recovered without complications. Phylogenetic analysis revealed a nucleotide identity of 98.6% to 100% and an amino acid identity of 97.4% to 100% between the identified E30 strains.

Conclusions: Substantial resources were saved by the rapid dissemination of information and protective guidance about this summer outbreak of E30 in the communities affected.

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SEVERE ADENOVIRUS INFECTION IN THE PAEDIATRIC POPULATION OF SOUTH EAST SCOTLAND

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Background and aims: Adenovirus infection is known to have high morbidity and mortality in paediatric severely immunocompromised patients. However, there are limited reports for patients without immunocompromise. Our aim was to characterise severe adenoviral infection in the paediatric population in South East Scotland.

Methods: Patients with systemic adenoviral infection were identified from positive blood PCR results between Sep 2011 and August 2012. Further information was gathered from clinical and laboratory records.

Results: 16 patients with positive blood adenovirus (Adv) PCR were identified. The adenovirus types were Adv2 (1 case), Adv3 (13 cases), and Adv14 (2 cases). 9 (56%) were male, 7 (44%) female, with median age 16 months (range 6 months to 15yrs 5 months). Two patients had significant immunocompromise, 6 had other underlying conditions and 8 were otherwise well.

Symptoms observed at presentation were fever, respiratory symptoms, sepsis/septic shock, gastrointestinal symptoms, petechial rash, stridor, prolonged febrile convulsion and intussusception.

Mean CRP at presentation was 86, mean white cell count was 11.6, mean neutrophil count 6.9 with 58% having normal cell counts.

Of the 16 patients identified, 5 required intubation and ventilation. 1 required inotropic support. 4 patients were treated with the antiviral cidofovir according to local protocol. There were no fatalities.

Conclusion: Severe adenoviral infection is emerging as a cause of severe disease in immunocompetent children as well as significant morbidity in children with underlying conditions. It is not restricted to one adenovirus type. Inflammatory markers are often normal. Cidofovir has been used successfully in severe cases.

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ASSESSMENT OF MF59-ADJUVANTED A/H1N1 INFLUENZA VACCINE

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Background and aims: Pandemic influenza causes clinical illness and hospitalization in all age groups; however, conventional inactivated vaccines have only limited efficacy in children. Vaccines against pandemic A/H1N1 influenza are required to protect all ages including children. We aimed to assess immunogenicity and safety of MF59-adjuvanted A/H1N1 influenza. vaccine in children.

Methods: We conducted a systematic review of the literature. Databases used were MedLine, Embase, Cochrane Library, CRD, Lilacs, ECRI, clinical trial register, and manual search in specialties journals. As MeSH terms we used “influenza A virus H1N1 subtype”, “influenza vaccines”, “efficacy”, and “safety”, and free terms “adjuvant vaccine” “influenza A-H1N1”, and “MF59”. Inclusion criteria were clinical trials with children vaccinated with MF59-adjuvanted influenza A/H1N1 vaccine, compared with other doses vaccines with/without MF59-adjuvanted. We registered results of immunogenicity and safety of the vaccine. The quality of included studies was assessed by CASP checklist.

Results: We found 142 references, and after title/abstract review, four clinical trials were selected, with moderate quality. The local and systemic adverse effects were rare and mild, without differences between groups. Seroconvertion and seroprotection levels were higher with MF59-adjuvanted vaccines. Antibody titers were higher too with the adjuvant vaccines.

Conclusions: The adjuvant vaccine has a good efficacy and safety profile. The adverse effects that may result are common and appear in similar way in both groups of vaccination.

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HEARING IMPAIRMENT AS A COMPLICATION OF ACUTE MENINGITIS

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Background and aim: Meningitis continues to result in substantial morbidity and mortality despite the availability of effective antimicrobial therapy. In survivors, neurologic complications can develop at any time during the course of meningitis and may be sudden or gradual in onset. Although many neurologic complications are severe and readily apparent, others, such as hearing loss, may be subtle or inapparent during the early phases of infection. The aim of the study was to determine the incidence of hearing loss in a pediatric population affected by meningitis.

Methods: We retrospectively reviewed the medical records of children 0-18 years old hospitalized at Infectious Diseases Unit, Bambino Gesù Hospital, Rome, Italy, for a laboratory confirmed meningitis between 1st January 2001 and 1st January 2013.

Results: We reviewed 214 cases of meningitis. The mean age was of 4,5 years (range 5 days-17.3 years). Neurologic sequelae occured in about 16,8% of children with meningitis; the distribution was as follows: hearing loss (22patients), cranial nerve palsy (3patients), paresis (3patients), visual field defects (3patients), ataxia (3patients) and aphasia (2patients). In two cases, a cochlear implantation was required.

Conclusions: The most common sequelae was hearing loss. In details, in this series, 22 (10,2%) children experienced hearing loss, consistent with previously reported rates of 5% to 35% within the pediatric population. In all but one children affected by hearing loss, no hearing impairment was clinically detached during hospitalization. Early prediction of an adverse outcome may help to determine which children require prompt surgical intervention or longer follow-up.

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CLINICAL MANIFESTATION OF TETANUS IN AN UNVACCINATED CHILDREN OF GEORGIA

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Background: The current systematic vaccination program of the population has been successful drastically reducing the incidence of tetanus. Tetanus infection remains a rare disease in Georgia. Our research aimed to identify epidemiological and clinical aspects of tetanus and their correlations with the date of hospitalization and outcome.

Methods: We retrospectively studied the cases of tetanus (age ≤18 years) admitted at the Infectious Diseases, AIDS and Clinical Immunology Scientific Practical Center of Georgia through the years 2008-2012.

Results: Totally 4 patients were registered. 2008- 1(2.5y , male); 2009-2010 - 0 patient, 2011 - 1 (6y, female); 2012 - 2 (2.7y, male and 13y, female).The cause in all cases included head laceration after a fall. All patients manifest dysphagia, trismus, neck stiffness and muscle rigidity on a admission of our hospital. Average date of admission in our hospital after first clinical symptoms - 7 th day. The reason of late hospitalisation were absent of classical symptoms at the beginning : in two cases - facial edema , other- paralysis of lower branch of right facial nerve and jaw and cheek edema. Clinical findings included : mild fever - 100%; pneumonia - 75%; respiratory insufficiency - 75%; sinus tachycardia - 75%; anemia - 25%. Recovery was achieved in 100%.

Conclusions: Tetanus is rare, but potentially life-threat disease. Tetanus should always considered in non-immunized patients with atypical symptoms, that can be manifest after trauma/injury. There is high correlation between late hospitalization and complications and outcome ($p< 0.05$).

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REFERENCE VALUES FOR INTERLEUKIN-6 AND INTERLEUKIN-8 IN CORD BLOOD OF HEALTHY TERM NEONATES AND THEIR ASSOCIATION WITH STRESS-RELATED PERINATAL FACTORS

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Background and aims: Clinical signs of early-onset neonatal sepsis (EONS) are unspecific and the diagnostic procedure for the detection of EONS (measuring the concentration of C-reactive protein (CRP) in neonatal blood and the culture of blood) has severe restrictions and is therefore not ideal in the acute setting of EONS. As EONS is associated with serious morbidity and even mortality, prompt diagnosis and treatment is crucial. There is much interest in new markers that are able to rapidly detect EONS, such as interleukin-6 (IL-6) and -8 (IL-8). The goal of this study was to determine IL-6 and IL-8 values in cord blood of healthy term neonates, because reference values for automated assays are incompletely known.

Methods: Women were recruited from April 2012 to August 2012. 114 healthy term neonates were included in the study. Immediately after birth, venous cord blood (with a maximum of 7 ml) was collected.

Results: A mean value for IL-8 of 8.1 ± 3.0 pg/ml was found in cord blood of healthy term neonates, which apply to both vaginal delivery and caesarean section. Regarding IL-6, two values apply. For vaginal delivery, a median value of 3.3 pg/ml (range, < 2 to 9.53 pg/ml) was found, while for caesarean section, a median value of < 2 pg/ml (range, < 2 to 12.8 pg/ml) applies.

Conclusions: We propose a reference value of < 15 pg/ml for IL-8. For IL-6 we propose reference values of < 10 and < 13 pg/ml for vaginal delivery and caesarean section, respectively.

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SEQUENCE ANALYSES OF HUMAN ROTAVIRUS STRAINS: COMPARISON OF VP7 AND VP8* ANTIGENIC EPITOPES BETWEEN TUNISIAN AND VACCINES STRAINS

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Background and aims: Group A rotaviruses (RVA) are the leading cause of severe gastroenteritis in infants and young children worldwide. Due to the epidemiologic complexity of RVA, it is important to compare genetic characteristics of the vaccine strains with the RVA strains circulating before the introduction of the vaccine in the national immunization program. In the present study, we determined sequences of the VP7 and VP8* proteins, which are the main targets for neutralizing antibodies.

Methods: We compared the antigenic epitopes of representative G1P[8], G2P[4], G3P[8], G4P[8], G6P[9] and G12P[8] RVA strains circulating in Tunisia from 2006 to 2011 with the RVA strains in both vaccines Rotarix and RotaTeq.

Results: The analyses showed that multiple amino acid differences existed in or near putative neutralizing domains of VP7 and VP4. Interestingly, we characterized two G1P[8] strains that clustered very closely to the sequence of Rotarix sharing high amino acid identities (95.8%-96.3%). In particular, the Tunisian G3 RVA strains were found to possess a potential extra N-linked glycosylation site compared to the G3 RVA vaccine strain of RotaTeq. Concerning the Tunisian G4 RVA strains, they were closely related to the G4 vaccine strain in RotaTeq, but the alignment of their VP7 amino acids revealed an insertion of an asparagine residue at position 76 which is close to the glycosylation motif, a conserved site in most human G4 strains.

Conclusions: Despite several differences detected between Tunisian and vaccines strains, our results can suggest good perspective and efficiency with the future RVA vaccine program.

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COINFECTION IN ACUTE GASTROENTERITIS PREDICTS A MORE SEVERE CLINICAL COURSE IN CHILDREN

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The objectives of this study were to determine the incidence of enteric pathogens causing acute gastroenteritis among hospitalized children in a Italian hospital, to measure the incidence of coinfections with viral or bacterial agents, and to compare the clinical characteristics of those infected with one versus multiple agents. A prospective study was conducted from March 2010 to April 2011 at the Bambino Gesù Pediatric Hospital in Rome. All patients between 1 month and 16 years of age admitted to the Pediatric Department with a diagnosis of AGE. Two stool samples for each patient were tested for gastrointestinal pathogens. We summarized the clinical severity of episodes describing duration of diarrhea, duration and frequency of vomiting, fever and severity of dehydration. All the patients underwent medical evaluation with estimation of dehydration (Gorelick score). One or more etiological agents were detected in 151 out of 232 patients (65.1%), while we did not detect any etiological agent in 81 (34.9%). Rotavirus was detected in 96 (63.6%), Adenovirus in 17 (11.2%), Norovirus in 7 (4.6%), toxin producing C. difficile in 23 (15.2%), Salmonella spp. in 15 (9.9%, B group in 12/15 and D group in 3/15); C. perfringens in 12 (7.9%), Campylobacter spp. in 6 (4%) and VTEC in 2 (1.3%). In 27 children out of 151 (17.9%), we found evidence of coinfection. Coinfection with Rotavirus and toxin producing C. difficile was the most common (63%). Children with coinfection had a more severe clinical presentation and had a higher probability to be severely dehydrated.

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RELAPSING CAMPYLOBACTER JEJUNI SYSTEMIC INFECTIONS IN A CHILD WITH X-LINKED AGAMMAGLOBULINEMIA

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Background and aim: X-linked Agammaglobulinemia (XLA) is a Primary Immunodeficiency of the humoral compartment, due to a mutation in the Bruton Tyrosine Kinase (BTK)-gene, characterized by a severe defect of circulating B-cells and serum immunoglobulins. Recurrent infections are the main clinical manifestations; although they are especially due to common bacteria, a specific association with infrequent species has been reported.

Methods: We report the case of a boy with XLA who presented relapsing Campylobacter jejuni systemic infections.

Results: A 11 years old boy affected by XLA was admitted to our unit with sepsis and acute enteritis. White blood cells count and C-reactive protein were increased. Cultures performed on blood and stool revealed the presence of Campylobacter jejuni susceptible to macrolides. One year later the boy was admitted again with a picture of bilateral cellulitis of ankles and legs and persistent fever. C. jejuni spp jejuni grew in three consecutive blood cultures. Therapy with meropenem and clarithromycin was started with resolution of the clinical picture.

Conclusions: C. jejuni should always be suspected in XLA patients with signs and symptoms of systemic infection and treatment should be based on antibiogram to assure the eradication of the pathogen.

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EVOLUTION OF BKV INFECTION IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Background and aims: Active infection by BK virus (BKV) can cause progressive impairment of renal function and ultimate graft loss in renal transplanted children. Viral load quantification can detect this condition and a reduction of immunosupression permits to resolve the infection. The aim of this study was to describe the evolution of BKV infection in paediatric renal transplant recipients.

Material and methods: 1316 whole blood and 410 urines were collected during a period of two years posttransplation in 70 patients. In order to determine the presence of BKV, a quantitative Real Time PCR (Artus) was carried out.

Results: We detected active BKV infection in 36 patients (51%). Intermitent replication was found in 21 cases (10 in urine and 11 in blood), persistent replication only in urine in 9 cases, and in both samples in 6 cases. Polyomavirus-associated nephropaty (PVAN) was developed in two of this patiens, with loss of graft in one of them.

Conclusions: Measuremenr of BKV loads in urine and blood of renal transplant recipients is a powerful tool for identifying patients at risk of PVAN allowing for preemptive management through modification of immunosupression.

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INVESTIGATING ATTRIBUTES OF VACCINE ACCEPTANCE IN CONTACTS OF NEWBORNS USING DISCRETE CHOICE EXPERIMENT: A NEW APPROACH TO COCOONING IN PERTUSSIS

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Background and aims: Inadequate vaccination coverage, loss of immunity over time and lack of booster dose in adolescents and adults are the main causes making newborns at higher risk for pertussis. Vaccinating parents and contacts (i.e. cocoon strategy) reduces the risk; however cocooning programs face barriers to implementation and generally sub-optimal adherence from families. We aim to identify what influences newborn contacts' preferences for cocooning, and elicit the trade-offs they make. The question is: what is needed for newborn contacts to accept cocooning and thereby reduce the risk for pertussis in newborns?

Methods: First, focus groups in Italy and Spain will determine key attributes and levels to identify the decision-making pattern of contacts of newborns when evaluating the cocooning proposal. Then, a questionnaire will be administered to 300 subjects in each country. This will help quantify the “trade-offs” enrolled subjects make between the attributes selected by the focus groups. Non-compensatory respondent behaviors will be accounted using an adaptive approach to conjoint analysis. Attribute level's utilities and elasticities will be estimated using hierarchical Bayes model.

Results: This study design allows quantifying the relative importance of attributes and levels presented to contacts of newborns in a series of choice sets. Information regarding the sub-populations (e.g. age, gender and country) and the relevance of health care systems on acceptance rate of pertussis immunisation will be collected.

Conclusion: Deeper understanding of the decision-making process may contribute to increase the uptake of dTap booster vaccination, leading to better control of pertussis in infants.

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CARBAPENEMASE-PRODUCING KLEBSIELLA PNEUMONIAE: AN EMERGING PROBLEM IN CHILDREN

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Background and aims: Over the last decade, carbapenemases-producing Klebsiella pneumoniae (CPKP) have become a significant problem; literature regarding outbreak and treatment in the pediatric population is scarce. We describe our two-year-experience in a children hospital.

Methods: Isolate identification and susceptibility test were performed by Vitek-2 and E-test (Bio-Merieux). Carbapenemases production was confirmed by modified Hodge test and carbapenemase inhibition tests. Combined disc tests containing Meropenem + Boronic Acid or Dipicolinic Acid or Cloxacillin were used to classify carbapenemases. Molecular analysis (Diversilab) was performed to identify epidemic clusters.

Results: 256 K.pneumoniae specimens were isolated within 20 months. Twenty-nine were CPKP: 21 colonizations, 8 infections. All isolates presented multidrug resistance (rate of colistin-resistance: 28%). Disc test was performed in 21, showing metallo-betalactamases production in 5, KPC-A in 14 and OXA-48 in 2.

Molecular identification detected two clonal types in neonatal surgery, the former in February 2012 (5 patients) and the latter between March and May 2012 (5 children).

In colonized patients, only isolation measures were adopted.

In 8 cases CPKP was treated, 6 because of severe bacterial infection (4 bacteremia, 1 urinary tract infections, 1 peritonitis) and 2 colonized patients because of immune-compromised status. Most patients received a colistin-containing combination treatment with favorable outcome; one died of septic shock.

EPIDEMIOLOGICAL DATA	Age range (months):24
	Sex (M:F) 21:8
DEPARTMENT OF ADMISSION	Surgery 41.3% (12)
	Onco-haematology 27,6% (8)
	Medicine 17,2% (5)
	PICU and NICU 13,7% (4)
SITE OF BACTERIA IDENTIFICATION	Stool 18/40
	Blood 4/40
	Urine 8/40
	Other 10/40

[Table-1]

Conclusions: CPKP spreading is an emerging concern also in pediatrics and active surveillance is essential.

The treatment of these infections in children is challenging because the available drugs are mostly “off-label” and clinical evidence is poor.

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A 4 YEARS PROSPECTIVE STUDY OF NOSOCOMIAL BLOODSTREAM INFECTION IN A TEACHING PEDIATRIC HOSPITAL IN TEHRAN, IRAN

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Background and aims: NBI in pediatric age group are an important cause of morbidity & mortality. We conducted this study to identify pathogens causing NBI, associated risk factors for implementation of preventive measures.

Methods: We conducted this prospective study from march 2007 to march 2011 at Alliasghar pediatric hospital as 140 beds educational & referral center in Tehran, Iran.

All admitted patient from 1 day of life to 16 years of age were checked daily for NNIS criteria of bloodstream infection and those who met the above criteria were included. The results of blood culture and their sensitivity patterns (according to CLSI methods) were tracked year by year. Demographic & their problem as well as risk factors were also evaluated.

Result: We identified 108 NBI during above period (0.86/1000patient-day). High rates were detected in NICU(2/1000patient-day) and PICU(1.97/1000patient-day).

The highest rate of mortality was observed in PICU & NICU, 34% &32% respectively.

The most frequent risk factors in PICU &NICU were duration of admition more than14 days, intubation & TPN.

Contribution of CONS in our confirmed NBI have been increased in late years.

Gram negative isolated were identified less than previous years.

Conclusion: NBI in our center had a very high mortality specially in ICU setting.

Long stay in that setting as well as avoidance from unnecessary procedures like prolong intubation & TPN are our targets from preventive of their infection.

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CHARACTERISTICS AND RISK FACTORS IN VENTILATOR ASSOCIATED PNEUMONIA IN LEVEL III NEONATAL INTENSIVE CARE UNIT IN NEW DELHI

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Background and aims: Ventilator-associated pneumonia (VAP) is a serious problem in neonatal intensive care units (NICU). The objective was to find the incidence of VAP and identify factors associated with its development.

Methods: Medical records of newborns ventilated in the period between 1st October 2011 and 31st March 2012 were reviewed. Data on patient demographics, underlying diseases, medications, central catheters, nutrition, ventilator use etc. was retrieved. For patients with VAP, risk factors were evaluated from the time of admission until the onset of VAP and then throughout their NICU stay. For patients who did not develop VAP, risk factors were evaluated for their entire NICU stay. Data analysis was performed using SPSS Version 20.0. Risk factors were evaluated using Univariate and Multivariate Logistic regression Analysis.

Results: A total of 49 patients (9.7%) were ventilated during the study period. VAP incidence was 39 per 100 ventilated babies or 117 per 1000 ventilation days. Birth weight, Gestation, Duration of ventilation, Asphyxia, Surfactant administration, Antenatal Steroids, Central catheters, Total parenteral nutrition, or Blood transfusion had no influence on occurrence of VAP.

Table-1

Univariate Analysis

Variable	O.R.	Confidence Interval		p value
Gestation	1.053	0.858	1.292	0.622
Birth Weight	1.000	1.000	1.001	0.264
Duration of Ventilation	1.009	1.000	1.018	0.06
SGA	1.111	0.216	5.727	0.900
Apgar < 5 @ 5 min	2.222	0.462	10.682	0.319
Surfactant	3.667	0.636	21.147	0.146
Steroids	1.833	0.299	11.259	0.513
Central Catheter	0.500	0.117	2.132	0.349
TPN	0.686	0.158	2.985	0.615
Blood Transfusion	2.167	0.521	9.017	0.288
Breast Milk	0.149	0.026	0.852	**0.032**

[Table-1]

Multivariate logistic analysis revealed that Breast milk was protective.

Table-2

Logistic Regression Analysis

Factors	Odds Ratio	Confidence Interval		p value
Breast Milk	0.069	0.007	0.680	0.022

[Table-2]

Babies with VAP were significantly more likely to die (O.R. 6.6 , C.I. 1.3-34.1 $p< 0.05$).

Conclusions: VAP occurred at high rates in sick neonates in the NICU. Breast milk had protective effect. Patients with VAP were more likely to die.

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GRAM-NEGATIVE SEPSIS DIAGNOSIS IN A TERTIARY-CARE PAEDIATRIC HOSPITAL: THE ADVANTAGE IN COMBINING MARKERS

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Background and aims: Gram-negative sepsis represents a significant cause of morbidity and mortality. Early management is a critical issue. Blood culture (BC) is the current gold standard to detect pathogens, even though affected by limitations. Polymerase chain reaction (PCR) allow for rapid detection of target pathogens within 6 hours, bypassing effect of antibiotics. We aimed to evaluate the concordance between BC and multiplex PCR in children affected by gram-negative sepsis, and to compare PCR sensitivity alone and combined with C-Reactive Protein (CRP).

Methods: BC positive for Enterobacteriacae or non-fermentative bacteria collected during 2011 were included. Those with a multiplex PCR contextually performed were selected. We calculated the sensitivity of PCR (LightCycler® SeptiFast) and CRP in diagnosis of gram-negative sepsis. We also calculated sensitivity of SeptiFast combined AND/OR associated with CRP (cut-off >= 1.5 mg/dl).

Results: Eighty positive BC were also tested with SeptiFast. Fifty-three confirmed the same BC isolates and were classified as concordant whereas 23 showed a negative result (3 positive for strains not detected by SeptiFast). Four discrepant SeptiFast isolates were considered contaminant. Sensitivity of SeptiFast resulted 66.2% whereas sensitivity of CRP 80.0%. Combined, positive PCR AND CRP showed a sensitivity of 56.2%. When considered alternative (PCR OR CRP), sensitivity resulted 92%.

Conclusion: Results are affected by the lack of negative BC and consequently specificity assessment. Nevertheless, they suggest that test based on PCR OR CRP can achieve a sensitivity of 92% in the diagnosis of gram-negative sepsis within 6 hours, being a useful tool in early management.

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VANCOMYCIN-INTERMEDIATE STAPHYLOCOCCUS AUREUS (VISA) HARBORING THE PVL GENES ISOLATED FROM A NEWBORN: THE FIRST CASE IN A BRAZILIAN HOSPITAL

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Methicillin-resistant Staphylococcus aureus (MRSA) can cause superficial and invasive infections. In newborns, the immunologic system and skin barriers are not well formed and infections by MRSA are of great concern in intensive care units. The Panton-Valentine Leukocidin (PVL) is a virulence factor associated to MRSA SCCmec IV, V and VI. The agr operon regulates the expression of virulence genes, and can be associated to reduced sensibility to vancomycin. The aim of this study was to analyze a MRSA SCCmec IV pvl+, collected from a sepsis of a male newborn, weighing 0.53 pounds. The isolate was included in the USA1100/ST30/CC30 lineage. The antimicrobial susceptibility was assessed by disc-diffusion test and E®test for vancomycin. The isolate was resistant only to the cefoxitin disk, and presented a MIC=4µg/mL for vancomycin. A population analysis (PA) test was assessed to compare the MRSA isolate to known isolates with intermediate resistance for vancomycin/VISA (MU50 and MU3). The graphic shows that the curve of PA was between MU3 and MU50 curves. To determine if the agr operon could be involved in this reduced susceptibility, we detect the production of delta-haemolysin in sheep blood agar before and after stimulation in subinhibitory vancomycin concentrations of 0,5µg/mL. The isolate did not presented delta-haemolysin activity only when stimulated. The isolate showed agr type III polymorphism, determine by nested-PCR, usually related to community-acquired isolates belonging to the USA1100/ST30/CC30 lineage. This is the first report in Brazil of a VISA pvl+ isolate.

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DISCITIS IN CHILDREN: AN EVOLUTION IN DIAGNOSTIC SUCCESS WITH THE USE OF 16S RDNA PCR

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Discitis in children is uncommon and it is difficult to secure a microbiological diagnosis. Fever and elevated inflammatory markers are uncommon. Effective treatment comprises prolonged antibiotic therapy, so establishing the causative pathogen is important.

In the past 3 years, 7 children with discitis aged under 36 months have been managed at a London tertiary children's hospital by a multi-disciplinary team including Paediatric Infectious Disease, Spinal, Interventional Radiology and Microbiology specialists .

Chronologically, the first patient had had 2 months of back and loin pain without fever, normal inflammatory markers before xray and MR imaging demonstrated T12/L1 discitis. Logistic difficulties precluded timely biopsy so antibiotics were started empirically without tissue for microbiology.

The subsequent 6 children presented with refusal to weight bear or sit; in all 6, a pre-antibiotics biopsy was secured at the time of diagnostic MRI under GA. All 6 biopsies (sites L4/5, L2/3, L2/3, L4/5, L5/S1 and L3/4 respectively) were culture-negative. Four of these samples were subsequently sent for 16S rDNA PCR, and in three of the four Kingella kingae was identified. The result for the fourth sample is currently pending. The first 5 children have made a full recovery following long course antibiotic therapy.

Kingella kingae is an increasingly recognized pathogen in discitis of young children due to increased availability of molecular diagnostics, specifically 16S rDNA PCR. An accurate microbiological diagnosis of bacterial infection leads to appropriate patient management, informs prognosis, allows use of narrow-spectrum antibiotics, determines treatment duration and may slow the spread of antibiotic resistance.

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HOSPITAL ACQUIRED GRAM-NEGATIVE BACTEREMIAS IN A UNIVERSITY HOSPITAL, ISTANBUL

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Background and methods: Hospital acquired Gram-negative bacteremia is a significant cause of mortality in pediatric medical centers. The clinical and laboratory features, risk factors and prognosis of patients who were hospitalized for a minimum duration of 48 hours and had hospital acquired Gram-negative bacteremia were analysed in a 12 month period with the aim of choosing appropriate antibiotics for empiric therapy.

Results: 312 bacteremia/fungemia attacks were detected in 284 patients. Most of these attacks were caused by Gram-positive cocci, 71 (22.7%) caused by Gram-negative bacteria. The annual nosocomial bacteremia rate was found as 10.7% .

Pediatric Intensive Care Unit (PICU) had the highest Gram-negative bacteremia rate. The most encountered Gram-negative bacteria were Klebsiella pneumoniae (n=22,29.3%), E.coli (n=14,18.7%), Acinetobacter species (n=13,17.3%) and Pseudomonas species (n=8,10.7%). Extended spectrum beta-lactamase (ESBL) activitiy was positive for 1/3 of Gram-negative bacterias cultured.

More than 50% of ESBL producing K.pneumonia strains cultured were resistant to 3rd generation cephalosporins. For E.coli,no resistance was observed to carbapenems;resistance to aminoglycosides and quinolones were 14.3% respectively. For A.baumannii, resistance to 3rd generation cephalosporins,carbapenems,quinolones, and amikacin were 70%,50%,62.5%,62.5% respectively. All of the A.baumannii strains were sensitive to colistine.

Conclusions: According to our results, it is reasonable to consider carbapenems or cephepime combined with aminoglycosides as the therapy of choice in empiric treatment of possible Gram-negative bacteremias.

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PEDIATRIC TUBERCULOSIS AT A CHILDREN´S HOSPITAL IN TURKEY: 2005-2012

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Background and aim: Tuberculosis (TB) among children is significant public health problem because it is an indicator of the recent transmission of TB in the community. The aim of this study was to describe the patient characteristics, demographical, clinical profile and treatment outcome of childhood TB at a referral center in Turkey.

Methods: We retrospectively reviewed records of patients < 18 years of age diagnosed as having TB at the Pediatric Infectious Disease Unit of the Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Center between January 2005 and September 2012.

Results: A total of 237 cases of TB were identified [54 (22.8%) definite TB, 183 (77.2%) probable TB]. The mean age of the patients was 80.62± 57.24 months (range: 1-207 months). Ninety-three (39.2%) of the patients had a history of contact with a TB patient. Pulmonary involvement was the most common form of TB (83.5%). The most common extrapulmonary manifestations were lymphadenopathy, central nervous system and abdominal TB. Other manifestations were muscle/skeletal, renal, ocular, miliar TB and pericarditis. TST was negative in 71 (31.6%) children. TST sensitivity was 68.5%. The diagnosis of TB was microbiologically confirmed in 54 (22.8%) cases. TB was successfully treated in all of the patients.

Conclusions: Household contact of an adult patient with TB and TST positivity were valuable clues for the diagnosis of pediatric TB and microbiological confirmation level was low. Pulmonary TB was the most common form. TB cases in childhood could be successfully treated in this setting.

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CLINICAL SPECTRUM OF DENGUE FEVER AND DENGUE HEMORRHAGIC FEVER IN CHILDREN'S HOSPITAL, LAHORE DURING DENGUE EPIDEMIC OF 2011

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Aim: To find out the clinical spectrum in children suffering from dengue fever age 1 to 14 year admitted from September 2011 to November 2011 in Children Hospital and ICH Dengue ward.

Material and methods: A descriptive study. During this period, 10250 patients visited the triage area of dengue. Patients were divided into three groups on basis of their ages. Data was recorded on a pre-designed pro forma. Relevant investigations were done. Children having enteric fever, hematological and oncological problems were excluded. Informed consent was taken for all patients.

Result: 450 children were included in study. 54.44% patients were seen in group-III. (n=245) and then in group II: 32.66%. High grade fever was present in 86.66% in group II & III. Common clinical features were bone pains and myalgias (28%), pain abdomen (25.7%) and vomiting (24.8%). Systemic findings were: Hepatomegaly (49.7 %), Lymphadenopathy (33.7%), Tachypnea (22.8%), ascites (14.8%), pleural effusion (11.3%) and rapid pulse (12.6%). Signs of circulatory failure; cold clammy skin (32.8%) and low grade fever with weak pulse (27.5%). Investigations showed Low TLC (47.3%), low platelets count (47.3%) and raised hematocrit in 35.1% of patients. Anti-Dengue IgM antibodies were present in 327 cases. Out of these, 63.7% were diagnosed as Dengue fever and 8.8% were labeled as Dengue Hemorrhagic Fever on the basis of clinical criteria and investigations.

Conclusion: More cases of Dengue fever were present in children from age 10 to 14 year of age. DHF was less common in children of any age.

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1-YEAR FOLLOW-UP AFTER NEONATES WITH URINARY TRACT INFECTION (UTI): EPIDEMIOLOGIC AND MICROBIOLOGIC CHARACTERISTICS, IMAGING FINDINGS, PROPHYLAXIS EFFICACY AND DISEASE RECURRENCE

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Background and aims: To analyze the epidemiologic/microbiological characteristics of 1st and recurrent UTI (R-UTI) episode in neonates < 2 months and antibiotic prophylaxis efficacy in prevention of further UTI.

Methods: A retrospective study including all neonates with UTI admitted between 2005-2009.

Results: 151 neonates were enrolled (2.7% of all 5617 neonates < 2 months of age, 2.1 cases/1000 live births); 56.3% were males and 5.9% had renal pathologies. One pathogen was isolated in 133 (88.1%) episodes. E. coli, Klebsiella spp., Enterococcus spp., M. morganii, Proteus spp. and Enterobacter spp. represented the most common pathogens (57.9%, 12.2%, 7.9%, 6.7%, 6.1% and 5% of all pathogens, respectively). Trimethoprim/sulfamethoxazole (TMP/SMX), ampicillin and cefuroxime-axetil were the most commonly used prophylactic antibiotics (45%, 13.2% and 8% of all enrolled patients). Ultrasound and VCUG examinations were abnormal in 18.1% and 21.2% patients, respectively. Twenty-three R-UTI episodes were recorded in 20 (13.2%) patients; 6/23 (26%) were diagnosed within 1 month following 1st episode. E. coli was the most frequent UTI pathogen recovered in R-UTI (12/23, 52.2%). No differences were recorded in E. coli distribution among the pathogens of first UTI vs. R-UTI. Seventeen (74%) of the 23 R-UTI episodes were caused by pathogens different (phenotypically) from those isolated in the 1st episode. R-UTI episodes occurred in 25.0%, 8.3% and 0 patients receiving TMP/SMX, cefuroxime-axetil or amoxicillin prophylaxis, respectively.

Conclusions: E. coli was responsible for the majority of 1st and R-UTI episodes. R-UTI was caused mostly by pathogens different than the pathogen isolated at the initial episode.

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BONE TURNOVER ALTERATIONS IN HCV INFECTED CHILDREN AND ADOLESCENTS

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Background: Although several studies have demonstrated a higher incidence of bone disorders in HCV-infected adults, the bone turnover alterations occurring in children and adolescents with chronic hepatitis C has not been thoroughly focused yet.

We performed a study on a cohort of 30 HCV infected caucasian children and adolescents to assess the prevalence of osteodistrophy and evaluate a possible prophylactic and therapeutic approach.

Methods: Data regarding biochemical markers of bone metabolism were collected. Moreover, results of ultrasonographic bone densitometry yearly performed were evaluated in comparison with data obtained from more than 500 healthy children and adolescents.

Results: Osteocalcin and telopeptide of the collagen molecule type-1, CTX, appeared higher than normal in 8/30 and in 7/30 respectively; the 25OH vitamin D values were normal in 25/28 cases. By densitometry osteoporosis was detected in 2 patients and osteopenia in other 5.

After stratification of cases by age groups, the incidence of osteopenia/osteoporosis appeared higher among children than among adolescents. Osteocalcin levels tended to be higher in cases where hepatic fibrosis were not detected.

Conclusions: The higher number of cases of osteopenia/osteoporosis in children than in adolescents is worthy of note, although not statistically significant. Ultrasound densitometry confirmed its important early diagnostic role in asymptomatic HCV infected children; moreover, also the increase in serum levels of osteocalcin may be considered as early marker of osteodystrophy of complementary value.

Larger studies will be needed to confirm the efficacy and safety of antiviral and supportive care in these patients.

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CARING FOR INTERNATIONALLY ADOPTED CHILDREN: IMMUNIZATION AND INFECTIOUS DISEASE SCREENING

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Background: During the last years the number of international adoptions has more and more increased in Italy: during the period 2006 - 2009 more than 4000 foreign born children were adopted from Italian families. Children involved in international adoption are at high risk of infectious diseases because of their previous life conditions; moreover they were not always adequately immunized against vaccine-preventable diseases.

Methods: From June 2007 to June 2010, 65 adopted children and adolescents (37 males, 28 females, aged from 6 month to 17 years) have been evaluated with a complete sanitary screening.

Results: In our cohort most subjects were coming from Latin America (about 33%) and East Europe (26.6%). We detect fifteen cases not fully immunized against poliomyelitis. Just 40% of the screened patients resulted vaccinated against hepatitis B, while in two Asiatic children hepatitis B surface antigen (HBsAg) was detected with impaired hepatic function. Although adequate immunity against tetanus and diphtheria resulted in more than 80% of cases, only 48% of them were fully protected against measles, mumps and rubella.

Finally, multiple intestinal parasites were found in 40% of screened subjects with Giardia lamblia and non-pathogenic amoebae the most frequently identified protozoa; among the worms Hymenolepis nana was mostly detected.

Conclusions: To test internationally adopted children for infectious diseases even uncommonly encountered in industrialized countries and to assess their immunization status is mandatory in order not only to promote their integration into a new social environment but also to protect the adoptive families.

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CARESS: THE CANADIAN REGISTRY OF PALIVIZUMAB (SYNAGIS) 2005-2012

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Background and aims: To evaluate the utilization, compliance and health outcomes of children at high-risk of respiratory syncytial virus (RSV) infection who received palivizumab prophylaxis in hospitals and community settings using a Canadian Registry Database.

Design and methods: A prospective, observational, registry of infants who received ≥1 dose of palivizumab during the 2005-2012 RSV seasons across 32 sites. Monthly follow-ups were conducted for respiratory illness (RI) events and hospitalization. Data was analyzed using standard descriptive methods, comparative statistics and regression analysis.

Results: 13,310 infants were enrolled. Participants were typically male (56.7%), Caucasian (70.8%), with an average gestational age 32.1±5.5 completed weeks. 8751 (65.7%) infants received palivizumab for prematurity (≤35 weeks) only, 1414 (10.6%) for congenital heart disease, 1048 (7.9%) for chronic lung disease and 2097 (15.8%) for other risk factors (e.g., CNS disorders, airway anomalies and cystic fibrosis). Patients received 98±32% of expected injections, with 55,523 doses given overall. 3% of patients withdrew from the study. 874 infants had a total of 1042 hospitalizations for RI resulting in a hospitalization rate of 6.6%.The overall RSV positive hospitalization (RSVH) rate was 1.56% with 3 deaths unrelated to prophylaxis. Living with siblings, daycare, household smokers and crowding was significantly correlated with a shorter time to first RSVH (Hazard Ratio [range 1.6-2.0]; all $p < 0.05$).

Conclusions: The RSVH rate observed in the 2005-2012 RSV seasons was similar to published reports of infants receiving prophylaxis (range 1.3%-8.1%) despite the largest number of assembled patients with complex underlying disease.

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EXPERIENCE OF A PERTUSSIS NATIONAL REFERENCE LABORATORY IN BRAZIL, IN THE ANALYSIS OF 7,553 SAMPLES USING CULTURE AND RT-PCR TESTS

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Background and aims: In Brazil, pertussis laboratory diagnosis is based on detection of B. pertussis using culture, a highly specific method, but with variable sensitivity. In 2010, the real-time PCR (RT-PCR), a more sensitive technique, was introduced. This study aims to describe the results of the culture and RT-PCR tests for pertussis diagnosis in samples analyzed in the Adolfo Lutz Institute - National Reference Laboratory for Pertussis.

Methods: 7,553 samples of nasopharyngeal secretions collected from patients with suspected pertussis (age range, eight days to 85 years) were tested from January/2010 to December/2012. The samples were cultured on charcoal agar with 10% sterile defibrinated sheep blood and cephalexin, and incubated at 35-37°C for ten days. RT-PCR was performed in the thermocycler LightCycler ®480 Software release 1.5.0 SP3 - Roche®, using specific primers and probes for the detection of the toxin gene ptxS1 and the insertion element IS481, and results were obtained within 24/48 hours.

Results: 19% of the samples (1,448) were positive on RT-PCR and/or culture tests, and the number of positive tests in the last three years were 151, 750, 547 in 2010, 2011 and 2012, respectively. 376 (5.0%) samples were positive using both growth culture and RT-PCR; 1,051 (14.0%) were only RT-PCR positive and 21 (0.3%), only culture positive. In 61 (0.8%) samples, RT-PCR results were not conclusive.

Conclusion: RT-PCR introduction has improved pertussis diagnosis in all age groups, including children < 6 months of age, but it should be performed simultaneously with growth culture to monitor strain variations.

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MICROBIOLOGY OF BLOODSTREAM INFECTIONS IN INFANTS WITH AND WITHOUT INTESTINAL INJURY

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Background and aims: Some bloodstream infections (BSIs) in infants with mucosal barrier injury (MBI) may be due to translocation from the intestinal lumen. The microbiology of these BSIs may differ from BSIs caused by other mechanisms. We assessed the microbiology of BSI in neonatal intensive care unit (NICU) patients with and without intestinal insufficiency (II).

Methods: A multicenter, retrospective cohort study of all primary and secondary BSIs in NICU patients with central lines was conducted using CDC definitions and existing infection control surveillance data. A focus group of pediatric gastroenterologists and neonatologists derived an a priori list of intestinal conditions that could be associated with MBI and a definition of II: MBI condition plus parenteral nutrition (PN) within 7 days before BSI. Chart review was performed to identify underlying intestinal conditions and receipt of PN within 7 days of BSI.

Results: There were 443 patients with BSIs from 11 NICUs. Most (85%, n=377) received PN within 7 days of infection and 44% (n=194) had one or more MBI conditions: active/prior necrotizing enterocolitis (n=127), bowel obstruction/resection (n=100), gastroschisis/omphalocele (n=40), intestinal atresias (n=29), other (n=6). II was present in 40% of patients (n=178). Enteric organisms tended to be more prevalent in patients with, than without, II (Table, p=0.054).

	Intestinal Insufficiency	
	Present (n=219)	**Absent (n=225)**
Enteric organisms		
Enterococcus spp.	27	28
Enterobacteriaceae spp.	38	49
Candida spp.	17	9
Bacillus spp.	1	1
Polymicrobial – enterics	17	9
SUBTOTAL	**100**	**96**
Other organisms		
Staph epidermidis/Staph aureus	107	111
Other gram positive organisms	3	2
Other gram negative organisms^	7	12
Polymicrobial – no enterics	2	4
SUBTOTAL	**119**	**129**

^includes *Pseudomonas, Stenotrophomonas, Acinetobacter*

[Table]

Conclusions: BSIs due to enteric organisms may be somewhat more common in NICU patients with than without II. Additional research is needed to examine the mechanism(s) of BSI in patients with II.

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EPIDEMIOLOGY OF BORDETELLA PERTUSSIS (BP) INFECTION IN CHILDREN ATTENDING A TERTIARY PAEDIATRIC REFERRAL HOSPITAL IN PORTUGAL, 2005-2012

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Background and aims: Despite very high vaccine coverage for Bp in Portugal (infant schedule and pre-school booster), an increase in disease notifications has been observed in the last years. The aim of this study is to analyse trends and clinical and demographic characteristics of cases.

Methods: Retrospective analysis of all patients < 18Y with Bp infection confirmed by PCR, observed in a paediatric emergency service that receives ~60.000 children/year, from January 2005 to December 2012.

Results: 78 cases of Bp infection were identified. There were two peaks: 31 cases in 2005 and 29 in 2012. 64% of the cases occurred in children < 4M, 22% between 4M-5Y, 4% between 6-11Y and 10% in children >11Y. A probable epidemiological contact was identified in 56%, mainly adolescent or adult relatives. 60% required hospitalization. The most frequent indications for admission were: severe paroxysmal cough (27%), age < 4M (22%) and apneas (9%). The median duration of hospitalization was 6 days (1-47). 22% had complications: respiratory failure (mainly low SpO2) (17%), apneas (9%), pneumonia (6%) and seizures (4%). 10% were admitted for intensive care and 5% needed ventilatory support. There was 1 case of leukemoid reaction (WCC=76300/uL). The outcome was favourable in all.

Conclusions: Despite high vaccine coverage, pertussis was a common disease, affecting predominantly children too young to have completed the vaccine schedule. There were 2 peaks in activity, 7 years apart. Family adolescents/adults seemed to be the main contagious source. As done in other countries, new vaccination strategies should be considered.

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CAN MINOCYCLINE BE INDICATED FOR THE TREATMENT OF MACROLIDE-RESISTANT MYCOPLASMA PNEUMONIAE INFECTION IN CHILDREN UNDER 8 YEARS OF AGE?

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Background: The characteristics of hospitalized children with respiratory tract infection due to macrolide-resistant Mycoplasma pneumoniae (M. pneumoniae) remain unclear. The treatment with minocycline for macrolide-resistant M. pneumoniae infection in children is controversial. The aim of this study was to clarify retrospectively the characteristics of children hospitalized for respiratory tract infection caused by macrolide-resistant M. pneumoniae.

Methods: Children who were hospitalized for respiratory tract infection due to M. pneumoniae were enrolled in this study. The diagnosis of M. pneumoniae infection was made based on the results of PCR assay. To identify macrolide-resistant M. pneumoniae infection, we analyzed the nucleotide sequence of the 23S rRNA gene of M. pneumoniae.

Results: Thirty-three children were hospitalized due to M. pneumoniae infection. Of the 33 children, 31 (median age 5 years) were identified as being infected with macrolide-resistant M. pneumoniae (A2063G:30, A2064G:1) by sequence analysis. Of the 31 children, 21 (68%) had received 14- or 15-membered macrolide antibiotics and 4 (13%) had received minocycline before hospitalization. During hospitalization, minocycline was administered in 16 (52%) of the 31 children infected with macrolide-resistant M. pneumonia. Of the 20 children infected with macrolide-resistant M. pneumonia under 8 years of age, 7 (35%) were treated with minocycline during hospitalization. The difference in total febrile days between children receiving minocycline treatment before hospitalization and children not receiving minocycline treatment was 3 days.

Conclusions: The administration of minocycline as a second-line antibiotic in children under 8 years of age cannot be avoided when clinical symptoms are not improved by macrolide antibiotics.

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ANTIBIOTICS IS NOT INDICATED IN ASYMPTOMATIC INFANTS BORN WITH PROLONGED RUPTURE OF MEMBRANES OVER 24 HOURS

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Background: Routine septic work up and empirical antibiotics are recommended in infants born to mothers with prolonged rupture of membranes (PROM) for more than 24 hours' duration, but very few infants among these infants had evidence of bacterial infection. We conducted a retrospective charts review to evaluate the need of the septic intervention.

Methods: This retrospective cohort study included neonates ≥ 35 weeks' gestation and with birth body weights ≥2,000 g who were born to mothers with PROM for more than 24 hours' duration and without confirmed maternal chorioamnionitis. Confirmed infection of the infant was defined as the presence of a positive blood culture. Possible infection was defined as having one or more of these laboratory findings:

1) absolute neutrophil count(ANC) ≤1750 /mm^3;

2) immature-to-total neutrophil ratio (I/T) ≥ 0.2 and

3) a C-reactive protein (CRP) value > 1.0 mg/dL.

Results: There were 12,270 infants born at the Changhua Christian Hospital during January 2005 to July 2010. Septic work up and empirical antibiotics were given in 131 enrolled infants that met the selected criteria, none had confirmed infection with pathogen growth from the blood culture. Twenty-one of the 131(16.0%) infants had respiratory symptoms because of TTNB and MAS and short term oxygen support. Laboratory findings of possible infection were noticed in 8 infants (8/131, 6.1%).

Conclusion: Neonates ≥ 35 weeks' gestation age that born to mothers with PROM for more than 24 hours' duration may not need routine empirical antibiotics if without symptoms of respiratory distress after birth.

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COMMUNICATION THROUGH NEW MEDIA: IS THERE A PLACE FOR PRO-VACCINE MESSAGES? EXPERIENCE OF VACCINEWSNET

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Background and aims: One-third of consumers now use the Internet to obtain health-related information, including information about vaccines. Vaccines, often seen as one of the greatest public health interventions, are recently losing a certain degree of public confidence. The internet and social media (e.g. Facebook, Twitter) have not only allowed for rapid sharing of information and misinformation, but also as forums for antivaccination groups.

Methods and results: VacciNewsNet (VNN) is a platform to provide up-to-date information to the public, media, health professionals and policy makers to help them understand the facts about vaccines. VNN uses the power of social media: the website www.vaccinews.net had more than 55,000 page views in 2012; the twitter account @VacciNewsNet is the most successful pro-vaccination account and reached more than 65,000 active followers in 2012. The Facebook page of VNN (www.facebook.com/VacciNewsNet) started on June 4th 2012 and has a weekly total reach going from 3,000 to more than 20,000 people. The Facebook page provides correct information on immunization and is used intensively by parents, health professionals and public health advocates to discuss news and views on vaccines.

Conclusions: Pro-vaccine initiatives can successfully make use of the online social media and can make evidence-based pro-vaccine messages 'go viral'. Social media can contribute to inform and educate the public about vaccinations.

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SALMONELLA BONE AND JOINT INFECTIONS IN PREVIOUSLY HEALTHY CHILDREN: REPORT OF 5 CASES AND REVIEW OF THE LITERATURE

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Background and aims: Salmonella bone and joint infections in children are an uncommon condition, typically associated with hemoglobinopathies or other underlying disorders. Only few cases have been sporadically reported in children without predisposing factors. We report a series of five previously healthy children with salmonella bone and joint infections that were admitted to our hospital during a 10-year period. This series represents the largest single-hospital experience of salmonella osteoarticular infections in children without predisposing factors.

Methods: Retrospective review and analysis of the medical records of previously healthy children with salmonella bone and joint infections, admitted at a tertiary Children's Hospital in Athens, Greece, between January 2002 and December 2011.

Results: Four out of five children (80%) presented with osteomyelitis and one with septic arthritis. Of the four children with osteomyelitis, two presented with tibial, one with femoral and one with humeral involvement. Age distribution ranged from 3.5 months to 13 years. In all children, treatment was a combination of surgical debridement and administration of antimicrobials. Salmonella enteritidis was isolated in three out of five children. Treatment duration ranged from 4 weeks to 6 months. All patients had complete recovery and no recurrences occurred.

Conclusion: Osteoarticular infections from Salmonella spp, although rare, can occur even in healthy children. There is no consensus regarding treatment, as no randomized or case-controlled studies have been performed. Although successful treatment with antimicrobials alone has been reported, it appears that a combination of surgical debridement and administration of antimicrobials is associated with a favorable outcome.

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THE HIDDEN BURDEN OF VTEC INFECTION: AN AUDIT OF DAYCARE EXCLUSION PRACTICES OF UNDER 6-YEAR OLD CHILDREN

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Background and aims: Exclusion of children Verotoxogenic Escherichia coli (VTEC) infection from daycare is an established communicable disease control measure. We aimed to audit exclusion practices against national Health Protection Agency (HPA) guidance requiring two negative stool samples taken at least 24 hours apart before return of young children to daycare with confirmed VTEC infection.

Methods: Retrospective data collection of children under 6 years with confirmed VTEC infection between January and November 2012 in North West England from the national electronic HPA database.

Results: VTEC 0157:H7 was isolated from all 32 children identified, of whom 26 attended daycare. All cases were primary, there was no evidence of secondary transmission. Faecal shedding occurred mostly whilst children were asymptomatic and the median (range) duration was 28 (11-72) days. Duration of daycare exclusion and achievement of microbiological clearance matched HPA guidance in 92% of cases. Two children with prolonged asymptomatic faecal shedding returned to school early under HPA supervision.

Conclusions: Exclusion practices of young children with VTEC infection in this cohort followed national guidance, apart from early supervised return of 2 children with prolonged asymptomatic faecal shedding with no evidence of secondary transmission. Median duration of faecal shedding was amongst the longest observed in published reports. Apart from associated educational consequences of prolonged daycare exclusion, parents may suffer financial loss from missed work. Future work should aim to decrease this 'hidden burden' of VTEC and further investigate the role of early supervised return to daycare of asymptomatic children with prolonged faecal shedding.

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WHAT HAPPENED AFTER THE INFLUENZA A (H1N1) PDM09 PANDEMIC? A SPANISH PAEDIATRIC TERTIARY HOSPITAL EXPERIENCE

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Introduction: Along 2009, the new influenza A(H1N1)pdm09 virus spreads worldwide. The WHO advised to be aware about changes in epidemiology and clinical expression of the disease during the first postpandemic season.

Methods: To compare epidemiological and clinical data between infected patients during the pandemic (7/2009-7/2010) and those of the first post-pandemic season (8/2010-7/2011), we included prospectively all the patients < 18-year with influenza infection requiring hospitalization in a tertiary paediatric hospital (Hospital Sant Joan de Déu(Barcelona)) from 7/2009-7/2011. Diagnosis of infection was made using a real-time-PCR in nasopharyngeal aspirate.

Results: 127 children of 2009-2010 season were included and 28 of 2010-2011. Patients tended to be younger during the second season (4.1 years (IQR:1.1-8.5) vs 1.9(IQR:0.1-6.7);p=0.1). The ratios of patients with comorbidities were similar (55/127 vs 14/28;p=0.5). Respiratory symptoms were the main clinical manifestation for both seasons, but extrapulmonary symptoms were more frequent during the pandemic (53/127 vs 6/28;p=0.04). The rate of patients requiring for intensive care was similar (24/127 vs 7/28;p=0.4). There were no differences regarding to pneumococcal coinfections (13/127 vs 3/28;p=0.9). The ratios of patients who did not receive antivirals were similar, but oseltamivir was started with more delay during the post-pandemic season (2 days from onset of symptoms (IQR:1-5) vs 6.5(IQR:4-8);p< 0.01). Median hospital stay was longer during the second season (4 days (IQR:2-6) vs 6 (IQR:4-11);p< 0.01).

Conclusions: During the post-pandemic outbreak**,** hospitalized children tended to be younger, there was more delay in the initiation of oseltamivir and hospital stay was longer. Main clinical manifestations were similar.

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BRAZIL PERTUSSIS HISTORICAL SERIES DATA REVIEW, 2001-2012

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Background: Since 2009, pertussis has reemerged in many countries. In Brazil, pertussis incidence rates remained very low, but in 2011 and 2012 the number of pertussis hospital admissions and deaths grew substantially. This study's aim is to describe the pertussis burden in Brazil in the last 12 years, by age group and state.

Methods: review of pertussis hospitalization and death cases historical series, based on National Information System (SINAN) and SIH/SUS data, from 2001 to 2012.

Results: A total of 15,340 pertussis confirmed cases, 11,411 hospital admissions and 302 deaths (CFR = 1.9%) have been recorded in SINAN from Jan/2001 to Oct/2012. During this period, 88% of all hospitalizations and almost all deaths (96%) affected children < 1 year of age, with 3.3% of CFR.The number of hospitalizations and deaths was observed in many States, independently of the introduction of RT-PCR test, used only in São Paulo state since 2010.

In 2012, the number of cases, hospitalizations and deaths were 3,408, 2,268 and 72, respectively, the highest number ever entered in SINAN since 2001.

Conclusions: The incidence of pertussis in Brazil is low in comparison with countries that use RT-PCR, serology and culture diagnostic methods. Almost all cases have been confirmed in very young children (inpatients < 12 months of age). Since pertussis occurs in all age groups, it is likely that the burden of the disease is underreported. The above information indicates the need to implement new pertussis diagnosis lab tests and new vaccination strategies to protect infants.

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CHRONIC CUTANEOUS ULCER AS THE FIRST MANIFESTATION OF SYSTEMIC TUBERCULOSIS

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Tuberculosis (TB) is still a worldwide disease despite advances in diagnosis and treatment. It is important to diagnose TB in an early disease stage in order to break the transmission chain.

Portugal has one of the most significant TB prevalence's in Europe. Despite the clinical effort in prevention, diagnosis and treatment there is still a delay in seeking medical care.

A sixteen years old girl, previously healthy, presented to the Pediatric Emergency Department with a leg ulcer which lasted for two months. She denied cough, fever, nocturnal chills and weight lost. Systemic evaluation showed bilateral pulmonary disease and the direct sputum sample was positive for Mycobacterium tuberculosis. The ulcer exudate was also positive for Mycobacterium tuberculosis. She was started on a four dose regimen of antituberculosis drugs. At day two, she initiated a 26^{th} day period of daily fever despite the progressive amelioration of her clinical state. The analysis denied systemic complications and HIV infection. She maintains ambulatory appointments, with a good compliance. In her past history we discovered an old contact with a friend with TB.

This case illustrates an unusual presentation of systemic TB disease with a leg ulcer after hematogenous spread.

The treatment may predispose to secondary manifestations like fever related to immunologic reconstitution syndrome. Nevertheless it's important to exclude other complications like disease spread to other systems.

After the diagnosis, the search for an index case is the best way to prevent the continuous spread of TB.

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NEW, RAPID METHODS FOR DIAGNOSING BORDETELLA PERTUSSIS. BORDETELLA PERTUSSIS PCR ADDED TO CURRENT VIRAL PCR SCREENING OF NASOPHARYNGEAL SAMPLES

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Currently, clinical symptoms of pertussis guide testing protocols, but symptoms may be atypical, particularly in young or partially vaccinated children. Broad screening protocols by molecular methods are now possible which can include viruses, Mycoplasma and Bordetella pertussis.

Aims:

1. To determine if a broad screening strategy using molecular methods identified more cases of pertussis in children under 1 year of age than clinically suspected.

2. To describe clinical outcomes of children with pertussis.

Methods: Nasopharyngeal samples (NPS) submitted for respiratory PCR testing in a 3 month period in 2012 were tested by broad respiratory PCR.

PCR to diagnosis pertussis was performed on clinical suspicion from Jan 2012 and these cases were reviewed.

Results: 280 patients under 1 year had a NPS, 112 had pertussis PCR requested (40%). Of these 112 samples, 5 (4.4%) were B. pertussis positive by PCR. A further 21 cases (12%) were identified from testing 168 samples where pertussis had not been initially requested. Viral co-infections were observed in 18/26 pertussis cases.

23 cases were diagnosed from clinical suspicion. 19/23 were < 3 months. 16/19 (84%) were admitted and 2 required ITU admission. Both ITU cases required high levels of support including prolonged ventilation and inotropic support.

None of the 4 cases older than 3 months were admitted.

Conclusions: Pertussis will be missed if only tested for when classical symptoms are present. B.pertussis is often found with other pathogens. Screening strategies using molecular methods should target all possible pathogens including pertussis as classic features often absent.

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CLINICAL PICTURE OF ROTAVIRUS INFECTION IN THE PATIENTS HOSPITALIZED THE DEPARTMENT OF PAEDIATRICS IN KATOWICE, IN THE YEARS 2008-2009

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Rotavirus infections are the most common causes of acute diarrhoea in infants and children under 4 years of age.

Aim: The aim of the study, was to analyse the clinical picture of rotavirus infections in children hospitalized in the Department of Paediatrics in Katowice, in the years 2008-2009.

Patients and methods: The study involved 226 children: 115 girls (51%) and 111 boys (49%), aged 0-18 years, who were hospitalized in the Department of Paediatrics, in Katowice, in the years 2008-2009 due to acute rotavirus infections. Rotavirus infections were diagnosed on the basis of the clinical picture and positive results of immunoenzymatic feces assays for RV infection. The analysis included: age, sex, clinical symptoms, results of laboratory tests and comorbidities. The obtained results were statistically analysed.

Results: Rotavirus infections mainly occurred in infants and young children (under 3 years of age), i.e. in 185/226 patients (82%). The highest incidence rate was observed from December to March. In infants, the clinical picture was dominated by abundant, watery diarrhoea and vomiting. Abnormalities in laboratory tests were accompanied by hypertransaminasemia (84%) and elevated levels of inflammatory markers (62%). Water, electrolyte and acid-base imbalance was observed more frequently in infants than in older children.In 28/226 (12.4%) children RV infection coexisted with a bacterial infection of the gastrointestinal tract (mostly enteropathogenic Escherichia coli, Campylobacter jejuni and Salmonella d-enteritidis).

Conclusion: RV infections mainly affect children under 3 years of age. The course of disease is varied and, to a large extent, depends on patient´s age and comorbidities.

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CHILDHOOD TUBERCULOSIS IN EAST UKRAINIAN REGION: RECENT CLINICAL FEATURES AND SOCIAL TRENDS

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Background: Childhood tuberculosis (TB) morbidity rates have been widespread increasing in recent years.

Objective: To study clinical features and social trends of TB in children and adolescents of East Ukrainian region.

Material and methods: 80 children and adolescents with different clinical forms of primary and secondary TB, from different social-class and age groups (aged 0-12 years (group A, n=68) and 13-18 years (group B, n=12)) were studied.

Results: The largest group was of patients infected with Mycobacterium tuberculosis (IMT) - 33 (41.3%), 21(26.2%) patients were with tuberculin skin test conversion (TSTC), 14(17.5%) - with diagnosed TB of intrathoracic lymph nodes (TB-ILN). Secondary pulmonary TB (SPTB) - focal and infiltrative form (FPTB, IPTB), occurred in 5(6.3%) and 5(6.3%) patients with 5.9% and 4.4% of group A patients correspondingly. Active tuberculosis (ATB) was diagnosed in 16(20%) patients, half of which had SPTB, 81.3% of ATB patients were from socially disadvantaged families with 37.5% and 43.8% from asocial and low-income families correspondingly. In total TB in the latest was diagnosed in 20% and 23.8% correspondingly.

Patients of group A more commonly had IMT (47%), TB-ILN (16.2%), TSTC (29.4%); of group B - IPTB (25%), FPTB (16.7%).

Conclusions:

1. The most commonly diagnosed form of TB was IMT.

2. SPTB forms (focal and infiltrative) occurred in young children.

3. Most common SPTB form in adolescents was IPTB.

4. 4/5 of patients with ATB were from socially disadvantaged families.

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BACTERIAL BLOOD PATHOGENS IN CHILDREN IN GOMBE NORTH- EAST NIGERIA - A FIVE YEAR REVIEW

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Background and aims: Childhood sepsis is life threatening. It is a significant contributor to infectious disease morbidity and mortality especially in developing countries. The risk is inversely proportional to age and mortality ranges from 30-45%.MDG4 aims at reducing childhood deaths. This study reviews pathogens in sepsis in children.

Methods: Federal Medical Centre Gombe is a tertiary health facility in Gombe, Gombe state. North-East, Nigeria.Records of all children managed for suspected septicaemia from Jan 2008 - December 2012, were retrieved and information including age, sex and bacterial isolates were obtained and analyzed.

Results: 5549 blood cultures were obtained from children and adults. 95.1% (5276/5549) were in children 0-< 18 years, 4.1%(273/5549) adults. 56.9%(2984/5276) were males and 43.1% (2260/5276) females. 40% (2115/5276) of cultures were from neonates. Children aged 1month-1year constituted 18.3% (970/5276). 22.2% (1169/5276) and 17.6% (928/5276) were constituted by children 1-5years and 5-< 18years respectively. 9.76% (515/5276) of cultures were positive.

Gram-negatives accounted for 55%(283/515) and gram positives 32.6% (168/515). 11.7% were contaminants. Klebsiella, Escherichia coli and Proteus constituted 45.2% (128/283), 16.3% (46/283) and 6.0% (17/283) of gram negative isolates respectively. Staphyloccocus aureus constituted 67.9%(114/168) and Enterococci 12.5% (21/168) of the gram positive isolates. The culture yield in neonates was 13.3%(282/2114) and Klebsiella 36.9%(104/282), Staph aureus 19.1%(282) and E.coli 9.6%(27/282) were the dominant pathogens.

Conclusion: The newborn period is associated with the highest risk of bacterial sepsis. Urgent improvements in perinatal care, early diagnosis and institution of empiric antibiotic therapy are key to improving outcomes.

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CONNECTIVE TISSUE DISORDERS AS MARKER OF SEVERITY OF CHILDHOOD TUBERCULOSIS

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Childhood tuberculosis(TB) morbidity in Ukraine remains high with changed clinical symptoms of TB and high prevalence of connective tissue disorders(CTD) in population.

Aim: To study TB clinical features in children and adolescents with CTD.

Material and methods: 80 children and adolescents aged 0-18 years with TB were studied. Unclassified CTD phenotype(UP-CTD) was detected in 41(51.2%) of them, increased CTD stigmatization(IS-CTD) - in 16(20%), Ehlers-Danlos-like CTD phenotype(EDP-CTD) - in 15(18.8%), Marfan-like(MP-CTD) - in 6(7.5%), no CTD manifestations - in 2(2.5%) patients.

Results: 33(41.3%) patients were infected with Mycobacterium tuberculosis (IMT), 21(26.2%) - with tuberculin skin test conversion (TSTC), 14(17.5%) - with diagnosed TB of intrathoracic lymph nodes (TB-ILN). Secondary TB was diagnosed in 5(6.3%) patients as focal form(FTB) and in 5(6.3%) as infiltrative form(ITB).

Patients with UP-CTD had IMT in 56.1%, TSTC in 13%, TB-ILN in 9.8%, FTB in 2.4%; with IS-CTD - IMT in 50%, TSTC in 37.5%, TB-ILN in 12.5%; with EDP-CTD - TB-ILN in 53.4%, IMT in 20%, FTB and IMT in 13.8% and 13.3% respectively; with MP-CTD - IMT in 66.7%, FTB in 33.3%. Children without CTD had TSTC. Active TB was detected in 20%(16) of the studied patients and in 83.3%, 60%, 7.3% of patients with MP-CTD, EDP-CTD and UP-CTD respectively.

Conclusions:

1. Close relationship between TB and CTD was revealed.

2. Highest level of TB activity was observed in patients with MP-CTD, 1.4 times less - with EDP-CTD, significantly less - with UP-CTD.

3. CTD phenotypes can be used in predicting course of TB.

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A RETROSPECTIVE STUDY OF CHILDREN WITH ACUTE ENCEPHALITIS

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Background and Aims: Encephalitis is a relatively rare but potentially devastating condition[1]. Our study investigated the presentation and management of children with encephalitis at a tertiary UK hospital.

Methods: Cases of encephalitis between 2001 - 2009 were identified using clinical coding records. Inclusion criteria were children between the ages of 3 months to 16 years presenting with an acute encephalopathy. A retrospective case notes review was then performed.

Results: 71 cases were identified and the notes found in 58 cases. 29 cases met the inclusion criteria.

Microbiological and metabolic workup was inconsistent in relation to local guidelines, with metabolic causes of encephalopathy excluded in only 28% of cases. Confirmed or probable infectious aetiologies were identified in 72% of children, with HSV (17%), VZV (10%) and EBV (7%) being the most commonly identified pathogens.

With regards to treatment, 97% were started empirically on aciclovir although 43% were prescribed half or less of the recommended dose for encephalitis. Anti-microbial use was inconsistent: ceftriaxone was started in 76%, azithromycin in 34% and amoxicillin in 12%.

Conclusion: The most important finding of this study is the high incidence of inadequate aciclovir dosing in children with suspected encephalitis. Recently published guidance highlights the importance of a full microbiological and metabolic work up and emphasises the correct aciclovir dose[1]. Although encephalitis is uncommon, correct management is vital to prevent the high disease associated morbidity.

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NONTYPHOIDAL SALMONELLA INFECTIONS IN CHILDREN WITH ACUTE GASTROENTERITIS: PREVALENCE, SEROTYPES AND ANTIMICROBIAL RESISTANCE IN SHANGHAI, CHINA

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Background and aims: Nontyphoidal Salmonella (NTS) infection is a leading cause of foodborne gastroenteritis. Information about Nontyphoidal salmonella (NTS) infection in children is limited in mainland China. The objective of this study was to investigate the prevalence, serotypes and resistance patterns of NTS infection in children in Shanghai.

Methods: All cases with a clinical diagnosis of bacterial gastroenteritis were enrolled from the enteric clinic of a tertiary pediatric hospital between July 2010 and December 2011. Salmonella isolation, serotyping and antimicrobial susceptibility testing were conducted by the microbiological laboratory.

Results: NTS isolates were recovered from 316 (17.2%) of 1833 cases. NTS infection was prevalent year-round with a seasonal peak during summer and autumn. The median age of children with NTS gastroenteritis was 18 months with 92.7% of cases occurring in children < 5 years. Fever and blood-in-stool were reported in 52.5% and 42.7% of cases, respectively. S. enteritidis and S. typhimurium were the most common serotypes. Antimicrobial susceptibility showed 60.5% resistant to ≥1 clinically important antibiotics. Resistance to ciprofloxacin and the third-generation cephalosporins was detected in 5.5% and 7.1%-11.7% of isolates, respectively.

Conclusions: NTS is a major enteropathogen responsible for bacterial gastroenteritis in Chinese children. Resistance to the current first-line antibiotics is of concern. Ongoing surveillance for NTS and control measures for drug resistance is needed to control this pathogen in Shanghai.

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OUTBREAK OF SCARLET FEVER ASSOCIATED WITH EMM12 TYPE GROUP A STREPTOCOCCUS IN 2011 IN SHANGHAI, CHINA

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Background and aims: An unprecedented large outbreak of scarlet fever among children occurred in Shanghai in 2011. The objective of this study is to investigate the 2011 scarlet fever outbreak in Shanghai and molecular epidemiological markers of circulating GAS isolates, as well as to monitor current antibiotic resistance of GAS.

Methods: We analyzed the demographic and seasonal characteristics of children with scarlet fever and outcome. During the peak month of the 2011 outbreak, 45 GAS isolates recovered from 114 pediatric patients and 13 (43.3%) GAS isolates recovered from 30 asymptomatic contacts were characterized by emm typing, superantigen profiles, PFGE genotypes and MLST and antimicrobial susceptibility.

Results: 1282 culture-proven scarlet fever cases were reported from our Hospital between Janurary and August 2011. Boys outnumbered girls (65.1% versus 34.9%). Preschool and primary school children accounted for 96% of cases. No severe outcome was found. The 2011 outbreak of scarlet fever started in April and peaked in May and June. emm1, emm12 and emm75 were identified among 58 GAS isolates and 53 (91.4%) isolates belonged to emm12, st36. Ten PFGE genotypes were identified among emm12 GAS isolates, 43 (81.1%) shared SPYS16.001 genotype and the remaining seven genotypes detected were related to SPYS16.001 closely or possibly. No speA and speM were detected in 58 isolates. All emm12 GAS isolates were resistant to azithromycin and clindamycin.

Conclusions: emm12 GAS strain caused the 2011 large outbreak of scarlet fever in Shanghai. The antibiotic resistance to macrolides and clindamycin in GAS was serious currently in Shanghai.

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IMMUNE-MODULATORS (CORTICOSTEROIDS AND INTRAVENOUS IMMUNOGLOBULIN) TREATMENT FOR SEVERE PNEUMONIA DUE TO MYCOPLASMA PNEUMONIAE IN CHILDREN

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Background and aims: Many studies have suggested that the pathogenesis of Mycoplasma pneumoniae (MP) pneumonia is associated with excessive host immune reaction. We investigated the efficacy of immune-modulators (corticosteroid and/or intravenous immunoglobulin, IVIG) treatment for severe MP pneumonia patients.

Methods: We retrospectively analyzed the medical records of 183 MP pneumonia patients admitted during recent epidemic (from June to December, 2011) in Korea. Among them, 90 patients those who had persistent fever for >48 h after admission or those who initially showed severe symptoms and signs received additional prednisolone (82 patients, 1 mg/kg/d, 2-3 days, tapering within a week) or intravenous methyprednisolone (8 patients, initially 5-10 mg/kg/day, tapering within a week) with various antibiotics. Four patients with aggravated clinical symptoms and chest radiographic findings after corticosteroid use, received IVIG (1 g/kg/day for 1- 2 days).

Results: Mean age of 187 patients was 5.5±3.2 y (6 months~ 15 y), and the male: female ratio was 1.1:1 (96:87). Fifty-seven patients (31%) were seroconverters and 126 seropositive patients showed increased diagnostic antibody titers (Serodia II and cold agglutinin) during admission. The majority of the patients who received corticosteroids (86/90 cases), showed rapid defervescence within 48 h with improved clinical symptoms, regardless of the used antibiotics including non-macrolides. Also, 4 patients who received additional IVIG improved both clinically and radiographically within 2-3 days without adverse reaction.

Conclusions: In the era of macrolid-resistant MP pneumonia, early immune-modulator therapy showed rapid clinical and chest radiographic improvement without side effects in this series.

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INCIDENCE AND RISK FACTORS OF VENTRICULOPERITONEAL SHUNT INFECTIONS IN CHILDREN

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Objective: The major aims of this study were to estimate the incidence and risk factor for ventriculoperitoneal shunt infections in children.

Methods: This study is a retrospective cohort analysis of 333 VP shunts that were consecutively placed into 224 pediatric patients at Seoul National University Children's Hospital in Korea over 6 years from January 2005 to February 2011. The isolation of a bacterial pathogen from reservoir cerebrospinal fluid (CSF) or ventricular fluid or blood was defined as documented infection, whereas CSF pleocytosis with signs of infection and a negative culture was classified as probable infection.

Results: The median age at shunt placement was 11 months (range, 0-193 months). Overall, 35 shunts (10.5%) were infected, which represented an infection rate of 0.075 infection cases per shunt per year. VP shunt infection occurred at a median of 1 month (range, 6 days to 8 months) after insertion. An independent risk factor for shunt infection was undergoing an operation before the first year of life (relative risk 2.31; 95% confidence interval, 1.19-4.48). The most common causative microorganism was coagulase-negative staphylococci in 16 (45.7%) followed by Staphylococcus aureus in 8 (22.9%), and Klebsiella pneumoniae in 2 (5.7%). Methicillin resistance rate was 83.3% among coagulase-negative staphylococci and Staphylococcus aureus.

Conclusions: In this study, CSF shunt infection rate was 10.5%, and VP shunt insertion before the first year of life Infection was a major risk factor. The infection was most often caused by methicillin-resistant coagulase-negative staphylococci and Staphylococcus aureus within two months after shunt surgery.

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RAPID DIAGNOSTIC TEST FOR GROUP A STREPTOCOCCAL ANTIGEN USING QUIKREAD GO® INSTRUMENT

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Background: Streptococcus pyogenes (Strep A) is a major cause of upper respiratory tract infection and rapid and accurate diagnostics guides its correct antimicrobial treatment.

Material and methods: Orion Diagnostica´s QuikRead go® Strep A is an immunoturbimetric test based on nanoparticles coated with anti-Strep A antibodies. A pharyngeal swab is extracted in a separate tube, and bacterial extract is moved into the reagent cuvette and closed with a cap containing reagents. Once inserted into the instrument mixing and adding of reagents proceeds automatically. After 1-3 minutes reaction the result (negative/positive) appears on the display. The test was compared to culture method (Streptocult®) with 279 pharyngeal swabs obtained from patients with pharyngitis, and four commercial lateral flow type tests using suspensions of eight different strains of Streptococcus pyogenes

group A bacteria.

Results: The sensitivity of the QuikRead go® Strep A was calculated on the basis of the densitivity of Strep A colonies on the culture slide: 95,5 % (≥100 CFU/slide), 91,0 % (≥51 CFU/slide), 83,1 % (≥10 CFU/slide) and 12,5 % (if the number of colonies is < 10 CFU/slide). The specificity was 97 % and no cross-reactivity was found with other organisms typically detected in the pharynx.

QuikRead go® Strep A test detected bacteria in amounts corresponding to $7x10^4$ CFU/swab, while lateral flow type tests detected 4-10 $x10^4$ CFU/swab.

Conclusion: QuikRead go® Strep A performs comparable to other rapid Strep A tests evaluated and provides an easy-to use, rapid and reliable method for diagnosis of pharyngitis.

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HIGH PREVALENCE OF ß-LACTAMASE NONPRODUCING AMPICILLIN RESISTANT HAEMOPHILUS INFLUENZAE IN CONJUNCTIVITIS-OTITIS MEDIA SYNDROME

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Introduction: Acute conjunctivitis is the most common ocular disorders among children and frequently concomitant with acute otitis media (AOM) as conjunctivitis-otitis media syndrome(COMS). Nontypeable Haemophilus influenzae (NTHi) together with Streptococcus pneumoniae are predominant pathogens responsible for COMS. In this study we attempted to document the current proportion of antimicrobial resistant NTHi and S. pneumoniae in COMS and further evaluated correlation between conjunctiva and middle ear isolates with nasopharyngeal isolates.

Methods: The 110 patients with COMS were enrolled. The antibiotic susceptibilities and PCR-based genotype of S. pneumoniae and NTHi isolated from the specimens were examined. When the pairs of bacteria isolated from nasal discharge and MEFs or conjunctival lavage were thought to be identical, the genomic polymorphism were further analyzed by pulsed-field gel electrophoresis (PFGE).

Results: NTHi is identified most often at 61.8% in conjunctiva exudates followed by S. pneumoniae at 28.2%. Genetic ß-lactamase nonproducing ampicillin resistant (gBLNAR) strains of NTHi and genetic penicillin resistant S. pneumoniae (gPRSP) were identified at 72.1% and at 74.2% among conjunctiva isolates, respectively. The restriction fragment of patterns of 89.7% pairs of NTHi isolates and 100% pairs of pneumococcal isolates from conjunctiva exudates, MEFs and nasopharyngeal swabs were identical.

Conclusion: It is noteworthy that gBLNAR strains is the most prevalent strains from COMS . The causative pathogen responsible for acute conjunctivitis will be originated from the nasopharynx. Bacteria in nasopharynx will cause COMS by ascending infections via Eustachian tube to middle ear cavity resulting otitis media and via nasolacrimal duct to conjunctiva resulting conjunctivitis.

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COMPARISON OF CURRENT PREHOSPITAL MANAGEMENT OF PNEUMONIA AND ARI TO WHO RECOMMENDATIONS

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The aim of the study was to determine the principles of pneumonia and ARI classification and treatment in outpatient clinics of Georgia and it´s comparison with WHO recommendations.

Methods: The retrospective analyses of medical records was conducted in 10 outpatient clinics (6 regional), addressing the management of children under 5 years with Pneumonia and ARI.

Results: A total of 320 medical records were revised, 30,9% (n=99) with pneumonia, 69,1% (n=221) with ARI, from those in 18,5 % (n= 41) were revealed bronchoobstruction. In 56.8% (n=182) of records children were checked for the presence of general danger signs (inability to drink, vomiting everything after each feeding, lethargy and convulsions) to detect cases with a very severe disease requiring urgent referral. All patients with severe pneumonia 2,8% (n=9) and 12,1 % (n=39) patients with pneumonia were referred for hospitalization. All cases of severe pneumonia were assessed correctly. Respiration rate was counted in 86,8 % (n=278) of cases. In all children (n=51) with pneumonia who were treated at home oral antibiotics were prescribed. In 66,6 % (n=34) were prescribed recommended first line antibiotics, while in 44,4 % the treatment was started with cephalosporin´s. 64,8 % (n=143) of children not needing antibiotics were not prescribed antibiotics, but in other cases (35,2 %) antibiotics were prescribed unnecessarily. The most common reason for giving antibiotics was bronchoobstruction and in some cases the data of blood test.

Conclusions: The results of the study emphasized that the basic principles of WHO recommendations in outpatient clinics are followed.

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OSTEOMYELITIS IN INFANTS AND CHILDREN: A REVIEW OF OUR SERIES

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Introduction: Although bone infections are rare in infancy, it is important to recognize its signs and symptoms promptly. The aim of the study is to describe the cases of osteomyelitis diagnosed in our hospital.

Methods: Descriptive, retrospective study of patients diagnosed of osteomyelitis from April 2004 to December 2012; analyzing epidemiological features, clinical and laboratory findings, diagnostic tests and treatments.

Results: 24 patients between 8 months and 15 years. 79.2% males. Incidence: 2 cases/year, with a peak in 2012 (33.3%).

Most frequent location: lower limbs (91.7%). 20.8% associated piomyositis and 8,3% arthritis. 100% had fever, 91.7% pain, 70.8% functional impotence.

Blood cultures were collected from all patients (S.aureus most common pathogen). 75% showed leukocytosis. The maximum CRP value was reached in the first 48 hours whilst the highest ESR level was between the 6^{th} and 7^{th} day of hospital admission.

Imaging tests used: radiography (87.5%), ultrasound (70.8%), scintigraphy (67.7%) and MRI (66.7%); conclusive in 14.3%, 29.4%, 87.5% and 93.8% respectively.

Intravenous antibiotics prescribed were: cloxacillin (33.3%), cefuroxime (20.8%) and cloxacillin associated with 3rd generation cephalosporin (8.3%) with mean duration of 14 days. Six patients required surgical drainage. Four patients suffered complications. All patients continued multidisciplinary follow-up.

Conclusions: Suspect this pathology on any child with fever, local pain and elevated acute phase reactants.

Profitability of microbiologic tests increase according to the number of samples collected.

Scintigraphy and MRI are the optimal diagnostic techniques.

Empiric antibiotic therapy was initiated on the basis of age, with an overall average duration of 6 weeks.

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TRANSIENT CEREBRAL ARTERIOPATHY IN YOUNG CHILDHOOD ASSOCIATED WITH CYTOMEGALOVIRUS INFECTION

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Background: Transient cerebral arteriopathy (TCA) is a recently described entity that is increasingly recognized as an important cause of arterial ischaemic stroke in children. Infectious agents associated with TCA include varicella-zoster virus, enterovirus, HIV and Borrelia burgdorferi. We report a patient with cytomegalovirus (CMV)-associated TCA.

Methods: A previously healthy 30-month-old girl presented with acute onset of left hemiplegia. Brain CT, magnetic resonance imaging (MRI) and angiography (MRA) were arranged. A testing for viral infection was performed and included detection of viral material in the cerebrospinal fluid (CSF) using polymerase chain reaction (PCR) techniques and detection of antibodies (IgG and IgM) in early and late sera.

Results: Cranial MRI and MRA showed proximal stenosis of the right medial cerebral artery and ischemic lesions in the territory of this artery. Intriguingly, "puff-of smoke" network of vessels in the right basal ganglion are also depicted on MRA. Analysis of the CSF showed pleocytosis but normal chemistry profiles and negative bacterial culture. Positive CMV IgG and IgM and detection of CMV-DNA in CSF specimens by PCR suggested active CMV infection. Treatment with ganciclovir and anti-CMV immunoglobulin in addition to prednisolone mediation for 4 months resulted in gradual improvement of clinical symptoms. Intriguingly, the subsequent MRA revealed reversible vascular changes in the previously occluded cerebral artery after 6 months.

Conclusions: To our knowledge, this is the first report of a CMV infection associated with TCA in an immunocompetent child. Our report demonstrates the propensity for CMV to be involved in pediatric cerebral vascular disease.

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THE CLINICAL COURSE OF THE SEVERE MENINGOCOCCAL INFECTION IN THE PEDIATRIC POPULATION

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Introduction: The incidence of the severe meningococcal infection is stabile in Georgian unvaccinated population and is not declining. This condition is frequently related to the development of shock and is characterized by a high mortality rate.

Methods: We retrospectively studied the cases of the meningococcal infection admitted at the Infectious Diseases Hospital of Georgia in 2005-2012y.

Results: Totally 130 patients were registered with the diagnose of the meningococcal infection. 109 patients < 18 y. (Totally 20 lethal outcome among which 14 cases were < 18 y). The condition was clinically recognized at the admission with the haemorrhagic skin rush. Shock was diagnosed in 68 cases among which 56 patients (82,3%) were under 14 years old. 16 patients were less than 1 year old (5 lethal cases - 38,5%) and 40 patients were 1-14 years old (9 lethal cases - 22,5%). Among children < 18 years old meningitis developed in 84 cases.

In all cases the meningitis developed at first or second day of the disease, was recognized with nuchal rigidity and other meningeal signs and was confirmed with the lumbal puncture. Isolated N.mengitidis serotypes C and B.The highest incidence was detected during 2009(24); The lowest -2012y (8).

Concussion: In a unvaccinated population the incidence of the meningococcaemia is stable and is not declining. The peak incidence was detected in 2009 respectively with a highest mortality rate in Georgia. The lowest incidence was detected in 2012. A permanent research is important for a better understanding of the disease pathogenesis.

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INVASIVE CANDIDA INFECTIONS IN PAEDIATRIC INTENSIVE CARE - RISK FACTORS, MANAGEMENT AND OUTCOMES

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Aims: To describe the incidence, epidemiology, microbiology, risk factors and outcomes of invasive candida infection amongst a cohort of paediatric intensive care patients.

Methods: Retrospective computerised case note review. Setting: Single tertiary paediatric intensive care unit (PICU). Definitions: Presence of a positive blood culture for Candida spp Patients: Patients 0-18 years requiring intensive care in the PICU between 2005 and 2011.

Results: Patients: 15 patients were identified. Median age 1.4 years. Median weight 9.5kg. Candida isolates: 61 positive blood cultures. 56% Candida albicans; 6.5% Candida glabrata; 31% Candida parapsilosis; 6.5% Candida lusitaniae. Susceptibility testing: All Candida albicans, Candida parapsilosis and Candida lusitaniae isolates were fully susceptible. The isolate of candida glabrata demonstrated intermediate resistance to fluconazole. Host Factors: All patients had underlying co-morbidity. Environmental risk factors at time of first positive culture: 11/15 patients were intubated and ventilated; 12/15 had a central venous line; 10/15 had an arterial line; 10/15 had a urinary catheter. 13/15 were receiving intravenous antibiotics (median 3 antibiotics). 2 patients were undergoing renal replacement therapy and 2 on ECMO. Prior antifungal prophylaxis: 10/15 had antifungal prophylaxis prior to the development of invasive fungal infection. **Outcomes:** Median PICU length of stay 23.1 days. 13/15 patients required inotropic infusions. 14/15 required invasive ventilation. 4/15 underwent renal replacement therapy. 3 patients died (20%).

Conclusions: Candida infections result in significant morbidity and mortality. All patients had significant host risk factors. Potentially modifiable environmental risk factors were identified. Non-albicans infections are increasing. This is temporarily associated with increased anti-fungal prophylaxis.

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UNDER- 5 BACTERIAL BLOOD ISOLATES IN A NORTH EAST NIGERIAN HEALTH FACILITY: A 5 YEAR REVIEW

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Introduction: Sepsis is the leading cause of death in children under 5years of age. Under-5 in Sub-saharan Africa are 16.5 times more likely to die from sepsis than in developed countries. Early and accurate identification of pathogens is imperative in improving outcome of sepsis.

This study reviews the pathogens in sepsis in under-5.

Method/aims: Federal Medical Centre Gombe is a 400 bed capacity tertiary hospital in Gombe State, North East Nigeria.

Gombe state has an estimated population of 2.3Million people.

Average yearly paediatrics admission is 1200, distributed among paediatric medical ward, special care baby unit, and emergency paediatric units.

Records of blood cultures (JAN 2008- DEC 2012) of under-5 children were retrieved and analysed.

Result: 5276 childhood blood culture reports were obtained. 81%(4253/5276) were under-5.

56.7% (2414/4253) were males, 43.1% (1835/4253) were females. 10.5% (448/4253) of cultures were positive, 89.5% (3805/4253) were negative. 55.8%(250/448) of positive cultures were in males, 43.1%(190/448) in females.

Gram negative pathogens constituted 43.8%(196/448) and Gram positive pathogens constituted 25.4%(114/448).

Klebsiella, 27%(121/448) was the commonest gram negative isolate in children under 5.Other Gram negative isolates were: E.coli, 8.3%(37/448), Proteus 3.1% (14/448). Pseudomonas and Salmonella each constituted 2.7%(12/448).

Staphylococcus aureus 22.1%(99/448) was the commonest gram positive isolate

Enterobacter 3.3%(15/448) was the next common gram positive isolate.

Conclusion: The leading pathogens in sepsis of under-5 children in our study were Klebsiella, Staph aureus, and E.coli.

Empiric antibiotic therapy in the tropics could be informed by this study.

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COMMUNITY ACQUIRED URINARY TRACT INFECTION IN HOSPITALIZED CHILDREN: ETIOLOGY AND ANTIMICROBIAL RESISTANCE. A COMPARISON BETWEEN FIRST EPISODE WITH RECURRENT INFECTION

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Background and aims: Urinary tract infection is a common infection in children. E.Coli is the leading pathogen and sensitive to aminoglycosides, cephalosporins, amoxicillin/clavulanate and trimethoprim-sulfamethoxazole. Emergence of resistance of uropathogens requires knowledge of the susceptibility to antibiotics. The study aims is to show the organisms that cause UTI, sensitivity, presence of ESBL and compare the sensitivity to previous study during 1999-2000.

Methods: A two part retrospective study on children hospitalized with UTI between 2003-2010. The first included first episode, and the second recurrent infection.

Results: First UTI 456 children, E.Coli was the leading pathogen(80.5%), klebsiella pneumonia(5.9%), proteus mirabilis(3.5%) and pseudomonas aeruginosa(1.5%). E.Coli was sensitive to gentamicin in 96.4% and to cefuroxime in 95.7%; with low sensitivity to amoxicillin/clavulanate and cefamezine 67.7% and 58.3%. Recurrent infection included 106 children. E.Coli was the leading pathogen, pseudomonas aeruginosa was found in 7.5% compared to 1.5% in the first episode (p=0.017). 6.6% of the isolates were ESBL compared to 1.1% in the first group p=0.002. Only 82.5% 0f the pathogens were sensitive to cefuroxime compared with 94.5% in the first group p=0.002.

Conclusions: E.Coli is the leading pathogen in first episode of UTI and in recurrent infection. Gentamicin is still efficient as an empirical mono-therapy. There is reduced sensitivity in first episodes to cefamezine and amoxicillin/clavulanate, when compared to previous study. Pseudomonas aeruginosa and ESBL uropathogens are more common in recurrent episodes. Each center has to re-evaluate the common pathogens and antibiotics sensitivity in order to give efficient empirical therapy for children with UTI.

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NEONATE SKIN LACERATION AS IATROGENIC RISK FACTOR OF MOTHER-TO-CHILD HCV INFECTION DURING DELIVERY

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Background and aims: HCV mother-to-child transmission occurs mainly in the peripartum period. There is no information about association between neonate laceration during delivery and HCV infection.

The aim of the study was to establish the rate of neonate injury during delivery and the influence of this complication over the risk of HCV transmission.

Methods: We collected data of type and course of delivery in 392 children born to anti-HCV(+) mothers: 34 HCV infected children and 358 without HCV infection.

Results: 235/392(60%) were delivered vaginally, 157/392(40%) by cesarean section. Skin laceration was observed in 9(2,3%): 4/235 (1,7%) delivered vaginally, 5/157(3,2%) by cesarean section. In the group of HCV infected children 25/34(74%) were delivered vaginally, 9/34 (26%) by cesarean section. The rate of HCV infection in children delivered vaginally was 25/235(10,6%), by cesarean section 9/157(5,7%). Among children with skin laceration 5/9(55%) were HCV infected, without skin laceration HCV infection was recognized in 29/383(7,5%). Elective cesarean section as a standard procedure has lower risk of laceration than emergency. There were 43 children delivered by elective cesarean section in 38Hbd and none of them was injured, none of them was HCV infected.

Conclusions:

1. Iatrogenic exposure to HCV during delivery may increase the risk of HCV mother-to-child infection.

2. There is a higher risk of skin laceration during emergency cesarean section than during vaginal delivery or elective cesarean section.

3. Children born by elective cesarean section without skin laceration were not infected with HCV.

VENTILATOR ASSOCIATED PNEUMONIA AN IMPORTANT PREDICTOR OF MORTALITY IN VENTILATED BABIES IN LEVEL III NEONATAL INTENSIVE CARE UNIT DELHI

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Background and aim: Ventilator-associated pneumonia (VAP) is a serious problem in neonatal intensive care units (NICU). The objective was to identify its contribution to the mortality in ventilated babies.

Methods: Medical records of newborns ventilated in the period between 1st October 2011 and 31st March 2012 were reviewed. Data on patient demographics, underlying diseases, medications, central catheters, nutrition, ventilator use etc. was retrieved. Diagnosis of VAP was made by the guidelines given by National Nosocomial Infection Surveillance System. Data analysis was performed using SPSS Version 20.0. Risk factors were evaluated using Univariate and Multivariate Logistic Regression Analysis.

Results: A total of 49 patients (9.7%) were ventilated during the study period. Twenty three babies out of 33 babies (69%) requiring ventilation for more than 48 hrs died. VAP incidence was 39 per 100 ventilated babies. Being small for gestational age, Asphyxia, Surfactant administration, Central catheters, Total parenteral nutrition, or Antenatal Steroids, had no influence on mortality. Factors with significantly high risk of mortality were Low birth weight, Prematurity, Blood transfusion and VAP.

Table-1

Univariate Analysis

Variable	O.R	Confidence Interval		p
Gestation	.758	.579	.992	**0.043**
Birth Weight	.999	.998	1.000	**0.031**
SGA	.708	.116	4.318	0.708
Apgar <5@ 5 min	.804	.162	3.987	0.789
Surfactant	.469	.080	2.755	0.469
Central Catheter	.667	.136	3.272	0.617
TPN	.389	.067	2.263	0.293
Steroids	.315	.033	3.035	0.317
Blood Transfusion	.188	.037	.946	**0.043**
VAP	6.611	1.280	34.142	**0.024**
Duration of Ventilation	1.006	.995	1.017	0.265

[Table-1]

Multivariate logistic analysis revealed that Prematurity (O.R. 0.667, C.I. 0.446-0.999 p< 0.05) and VAP (O.R. 11.306 C.I. 1.332-95.941.1 p< 0.05) were independent risk factors for mortality in ventilated babies.

Table-2

Logistic Regression Analysis

Factors	Odds Ratio	Confidence Interval		p value
Gestation	.667	.446	.999	.049
VAP	11.306	1.332	95.941	.026

[Table-2]

Conclusions: VAP occurred at high rates in sick neonates in the NICU. Prematurity and VAP are associated with high risk of mortality in ventilated babies.

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RISK FACTORS FOR SEPSIS IN INFANTS IN NEONATAL INTENSIVE CARE UNIT

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Bacterial infection continues to be the major cause of morbidity and mortality in the newborn. Infection, particularly of nosocomial or late onset, is very common in preterm infants.

Objective: To determine risk factors for late onset sepsis among infants in NICU.

Study design: We studied cases with sepsis in a 3rd level NICU.

Case patients had sepsis diagnosed more than 72 hours after hospitalization. Control patients (3 per case) were matched by birth weight, gestational age and date of enrollment. Potential risk factors included use of medical devices (büllau), total parenteral nutrition, gastrointestinal pathology (difficulty in feeding, abdominal distention, dysmotility, necrotizing enterocolitis), central venous catheter use and duration of mechanical ventilation.

Results: One hundred fifty two cases of sepsis occurred during the study period. The main causative pathogen organisms of infections were staphylococcus epidermidis (36%) and enterobacter aerogenes (15%). Multivariate analysis revealed that central venous catheter use (odds ratio [OR] = 1.09 per day of use; 95% CI = 1.02 to 1.23), duration of total parenteral nutrition (OR = 3.12; 95% CI = 1.96 to 4.72), duration of mechanical ventilation (OR = 2.13; 95% CI = 1.09 to 3.3), use of medical divices (OR = 4.02; 95% CI = 2.76 to 13.2), and GI pathology (OR = 3.17; 95% CI = 1.4 to 5.3) were significantly associated with sepsis.

Conclusions: We confirmed previous risk factors (use of medical divices, duration of mechanical ventilation) and identified novel risk factors (GI pathology) for sepsis in hospitalized infants.

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ANTIBIOGRAM OF BLOOD BACTERIAL ISOLATES IN CHILDREN IN A TERTIARY HOSPITAL IN NORTH EAST NIGERIA: A FIVE YEAR REVIEW

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Background/aims: Sepsis is a major cause of morbidity and mortality in children in developing countries. Inappropriate antibiotic use encourages the emergence of drug resistance. Sensitivity patterns guide empiric therapy. This study examines sensitivity and resistance patterns of isolates in our center.

Methods: The Federal Medical Centre in Gombe, Gombe state, is one of the leading tertiary health facilities in the sub-region. Bacterial isolates from children with suspected sepsis from January 2008 - December 2010 and antibiogram was analyzed.

Results: 5,276 blood culture results were obtained. 9.7% (515/5276) were culture positive. Klebsiella, Ecoli, Proteus and Pseudomonas were the predominant gram negative isolates constituting 30% (128/515), 9% (46/515) and 3%(17/515) and 3%(14/515) respectively. Staph aureus 22%(114/515) and Enterococci 4% (21/515) were the leading gram positive isolates.

37% of Klebsiella isolates were sensitive to Gentamicin; 28% to choramphenicol . 98% of klebsiella isolates were resistant to ampicilin; 93% to amoxicillin, 85% to amoxicillin - Clavulanate and 84% to Ceftadizime.

54% of E.coli were sensitive to choramphenicol; 39% to Gentamicin. 85.7% of salmonella isolates were sensitive to Gentamicin; 36% sensitive to choramphenicol and 71% to amoxicillin- clavulanate.76% of Proteus spp and 92% of Pseudomonas were sensitive to gentamicin. 67% of Shigella isolates were sensitive to amoxicillin-clavulanate, gentamicin and chloramphenicol.

67% of Staph aureus were sensitive to cloxacillin;58.8% to Gentamicin; 56% to choramphenicol; 54% to ceftazidime; 40% to amoxilicin- clavulanate, and 30% to Cefuroxime. 93% were resistant to ampicillin.

Conclusion: Regular surveillance is essential to inform and guide antibiotic use.

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COMPLICATIONS OF CHICKENPOX INFECTED CHILDREN HOSPITALIZED IN INFECTIOUS DISSEASE CLINIC

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Background and aims: Varicella, commonly known as chickenpox, is caused by the varicella-zoster virus (VZV).The diseaseis is high contagious, generally mild, self limited illness. Rash and fever are the typical findings. Prolonged fever is suspect on complication: neurology, respiratory, bacterial. Most frequent complications are pneumonia and cerebellitis. The maximum incidence in unvaccinated populations is in children aged from 1-6 years.

Methods: We analyzed complications among children 3-16 years old hospitalized in Infectious disease Clinic in Podgorica from January 2011 year with chickenpox infection. The diagnosis was confirmed by clinical examination, presents of typical rash.

Results: In Infectious disease Clinic from January 2011 year were hospitalized 44 children with complicated chickenpox infection, all had symptoms of rash and fever. Most common complications occurred pneumonia 16 patients: viral 10 and bacterial 6 patients. Streptococcal throat infection occurs in 10 patients, cerebellitis in 3, osteomiellitis in one, hepatitis in 3, mild thrombocytopenia in 3, otitis media in 3, iritis occurs in one patient. Toxic shock syndrome occurs in one due to streptococcus and one due to staphylococcus, verified by positive haemoculturas, these patients were treated in intensive care unit. Skin lesion infection occurs in 2 patients: one with impetigo and second with neck abscesses, and needed chirurgical intervention. We treat all patients with acyclovir and antibacterial therapy when needed.

Conclusions: In our country threes not mandatory vaccination against VZV and infection occurs frequent. The disease is generally mild, self-limiting with occasional complications. All patients recovered to normal range 2-3 week after admission.

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FREQUENCIES AND CHARACTERISTICS OF BRONCHOOBSTRUCTIVE SYNDROME IN CHILDREN - THEN AND NOW

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Background and aims: Upper and lower respiratory tract obstruction is often found in children. The aim of this study was to compare the frequency and characteristics of bronchoobstructive syndrome (BOS; obstructive bronchitis - OB and subglottic laryngitis - SL) in primary pediatric care during the period from 1987. - 1989. (period I) and the period from 2007. - 2009. (period II).

Methods: During those periods the same number of children (N=1717) aged from 0 to 6 years was used to edit data: number of children with BOS, number of attacks, characteristics of BOS during attacks (frequency of acute respiratory infection symptoms - ARIS, children treated with antibiotics, frequency of pneumonia, number of hospitalized children).

Results: In period II, statistically significant higher frequency of BOS was found (9.1% versus 25.3%; P< 0.001), particularly the frequency of OB (5.6% versus 15.7%; P=0.018), as well as the higher consumption of antibiotics during OB attacks (17.6% versus 40.2%; P=0.015). The frequency of pneumonia was higher during OB attacks (4.3% versus 11.6%; P=0.937). There was no difference in the frequency of ARIS during OB attacks (80.0% versus 81.4%; P=0.787) or SL attacks (60.8% versus 45.4%; P=0.085). The children hospitalized because of BOS attacks was lower during period II (4.2% versus 3.8%; P=0.419).

Conclusion: Despite the current antibiotic treatments during OB attacks, that has not significantly decreased the percentage of hospitalizated children. ARIS are commonly found in the clinical presentation of OB; therefore considering their virus etiology the consumption of antibiotics should be more rational.

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ARE POST-TRAUMATIC SPINAL CORD INJURIES IN PEDIATRIC AGE A RISK FACTOR FOR URINARY TRACT INFECTIONS BY MULTI-DRUG RESISTANT PATHOGENS?

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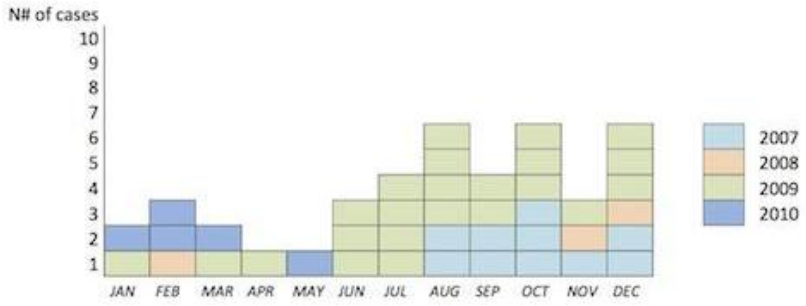
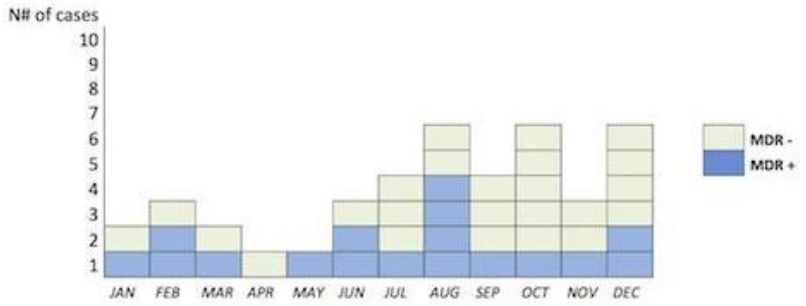
Background and aims: Despite the increasing global prevalence of Urinary Tract Infections sustained by multidrug-resistant pathogens (MDR) in adults with Post-Traumatic Spinal Cord Injuries (PT-SCI), very few studied evaluated such a topic in children and young adults. Here we present our experience.

Methods: A retrospective analysis about all patients admitted to G.Verdi Hospital in Villanova sull'Arda (Piacenza-Italy) between January 2007 and December 2010 was performed focusing on patients < 20 years old at the time of the hospital admission.

Results: 545 patients with SCI were identified (462 urinary isolates from 222 patients; infection rate of 17.1/1,000 hospital-days and 22.6/1,000 person-days). Twenty-four of them were ≤ 20 years old at the hospital admission (10.8%; mean age 17.4±3.0 y), with 41 urinary isolates from 8 patients (IR of 12.8/1,000 hospital-days and 4.39/1,000 person-days), who were slightly older (19.0±1.4 y vs 16.6±3.4 y; p< 0.046) and more frequently of male sex (6 vs 2). All isolates were Gram negative (8 E coli, 3 P mirabilis, 1 K pneumoniae). Relapses were more frequent in paediatric patients than in adults (Relative Risk = 1.395 95%CI:1.049-1.852), with a higher risk for MDR infections (RR 1.678 95%CI:1.111 2.533).



(1) Seasonal incidence of urinary isolates in paediatric patients.



(2) Seasonal incidence of urinary isolates in paediatric patients focusing on antimicrobial resistance status.

[Table 1. Incidence of UTI in PT-SCI patients.]

Discussion: Our knowledge of UTIs in paediatric PT-SCI remains unsatisfactory. Our study, despite the small number of cases, suggests the paediatric patient as less susceptible to UTI, but that in patients developing UTIs, MDR infections and relapses become more frequent. Eventually, paediatric PT-SCI patients should be treated even more accurately in terms of UTI prevention and antibiotic therapy.

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UNCOMMON ETIOLOGY FOR UNCOMMON DISEASE: STREPTOCOCCUS SALIVARIUS BRAIN ABSCESS

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Brain abscess is a rare disease in children, most of the cases occurring between 4 and 8 years and neonates. The aetiology comprises bacteria like streptococci, anaerobic organisms, gram-negative aerobic bacilli and fungi. The pathogenesis is undetermined in 10-15% of cases.

Streptococcus salivarius is a commensal bacterium of the oral cavity in humans and a normal inhabitant of the upper respiratory tract. It may infrequently enter by accident the blood stream and generate disease.

We report the case of a 7year-old female patient, without significant medical background, who was brought by her parents in PED for acute onset of headache. Clinical exam was normal, including the neurological signs. She was given symptomatics and parents were advised to address themselves to a paediatric neurologist if the child's headache persisted, which they did the next day. EEG and CT exam were indicated and performed 3 days later. Contrast CT exam revealed a left temporal abscess of almost 4cm diameter with mild mass effect. At this point the patient´s only symptoms were headache and mild lethargy and the lab tests were in normal ranges. The child was admitted to neurosurgery, broad spectrum antibiotic was prescribed and classical surgery was performed in order to take out the abscess. Microbiological cultures from the pus revealed Streptococcus salvarius sensitive to beta-lactamine. After surgery the child's recovery was complete, without complications, and she was discharged within two weeks, with neurological follow-up.

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ACUTE MENINGITIS CAUSED BY STREPTOCOCCUS PNEUMONIAE IN CHILDREN

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Introduction: Streptococcus pneumoniae infections present various clinical forms such as: pharyngitis, otitis, sinusitis, conjunctivitis, epiglottitis, pneumonia, meningitis and sepsis.

Objectives: This paper's objective is to analyze the clinical evolution of acute meningitis caused by Streptococcus pneumoniae in children.

Material and methods: We have conducted a retrospective study over a period of 5 years (2008-2012) on cases of acute purulent meningitis caused by Streptococcus pneumoniae, which were admitted in the ICU of the National Institute of Infectious Diseases “Prof. Dr. Matei Bals”. In all patients we have monitored: sex, age, background, clinical onset, workup, imaging studies, treatment, evolution and complications. The positive diagnosis was established through usual and specific workups: 8 positive blood cultures, 6 positive pharyngeal cultures, 11 positive latex-agglutination tests, 9 positive CSF cultures and 4 cases - Plex ID (modern method of diagnostic).

Results: Streptococcus pneumoniae was identified as the cause for 22 cases out of all 123 cases of acute purulent meningitis that were admitted in our clinic. The most frequent serotype was 19 F (22.7%), followed by serotype 6A (18.8%).

Most cases were registered in the 0-3 year's age group, 63.6% being male patients originating from rural areas (72.7%). The evolution was fatal in 6 cases, representing 27.2%. In 10 cases (45.5%), the evolution was severe, with neurological sequels. The most frequent complications were: seizures, psychomotor retardation, hydrocephalus, deafness, blindness.

Conclusions: Pneumococcal meningitis represents one of the most severe bacterial meningitis that in many cases can lead to death and high frequency of neurological complications.

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CONSERVATIVE MANAGEMENT OF LIVER ABSCESSES IN A CHILD WITH CHRONIC GRANULOMATOUS DISEASE (CGD)

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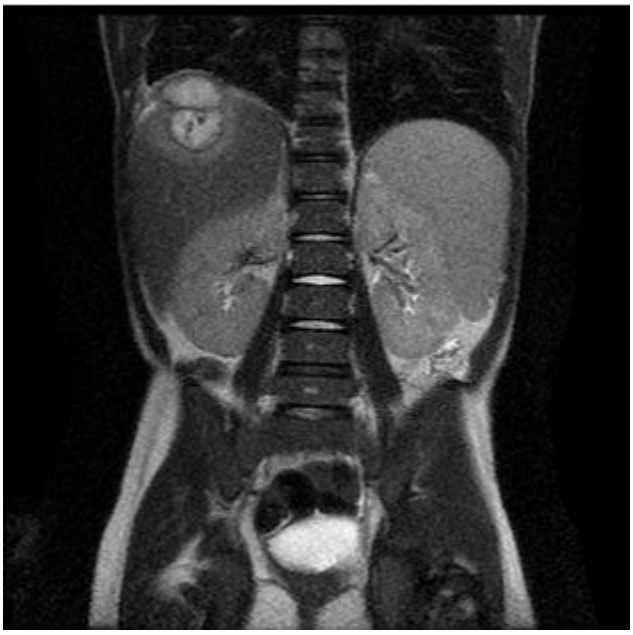
In pediatric patients with primary liver abscess it is important to keep in mind the possibility of CGD.Treatment is controversial as antibiotics may not have good penetration and surgery may have severe complications.

We report the case of an 8-year-old boy with a history of 15days of fever,abdominal pain and arthromyalgia.Our patient presented for the first time at 2years of age with fever and was subsequently diagnosed with Actinomycetal intra-abdominal abscesses treated with antibiotics and surgery.During the current admission the lesions have been detected by abdominal-ultrasound and confirmed by computed tomography(CT)in the VII-VIII liver segments(hypodense and round-shaped lesions 57x63and27x30mm).



[Liver abscesses]

The abscesses were aspirated and initially treated with meropenem+metronidazole.In retrospect they were known to grow S.aureus so the treatment was changed to cloxacillin+rifampicin+co-trimoxazole,according to sensitivities. X-linked CGD was confirmed.Interferon-gamma was associated.Drainage by interventional radiology was not successful and was complicated by pleural empyema.After two months of antibiotics and Interferon-gamma withdrawal he became afebrile and well-appearing.However,acute phase reactants remained elevated. Ten newsmall abscesses were identified on the CT-scan. After discharge he completed six months of oral cefalexine along with routine prophylaxis and has remained asymptomatic for the last three years.

CGD should initially be ruled out in cases of primary hepatic abscess.Prompt diagnosis and treatment may improve the outcome.Conservative management should be considered in patients with adequate antimicrobial coverage and high-risk for surgery.Interferon-gamma withdrawal may help resolution of inflamatory parameters following good antimicrobial coverage in conservative management of liver abscesses in CGD patients.

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CHARACTERISTICS AND OUTCOME OF NEWBORNS WITH METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS SEPSIS IN A LEVEL III NEONATAL INTENSIVE CARE UNIT DELHI

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Background and aim: Staphylococcus aureus (SA) is an important cause of neonatal sepsis. However limited data is available regarding effect of Methicillin resistance on morbidity and mortality in neonates with SA blood stream infection (BSI). The aim of this study was to identify risk factors for methicillin-resistant Staphylococcus aureus (MRSA) BSI and its contribution to length of stay and mortality.

Methods: A retrospective cohort of thirty newborns with SA BSI between 1 January 2012 and December 31, 2012 was analysed. Data on patient demographics, type of delivery, onset of sepsis, respiratory support, previous antibiotic exposure, central catheters, duration of stay and outcome was retrieved. Univariate analysis was used to compare variables for the outcome groups of interest. The $\chi 2$ statistic was used to compare categorical variables. Continuous variables were compared using Student's t test.

Results: Out of total 30 babies with Staph BSI, MRSA was seen in 19 (63%). Babies with MRSA and Methicillin Sensitive Staph aureus (MSSA) BSI were comparable as far as demographic and clinical characteristics were concerned. Twenty four SA (MRSA 15, MSSA 9) BSI were of late onset. MRSA BSI did not increase the duration of hospital stay. Mortality was similar in the two groups.

Table-1

Clinical Characteristics of Newborns with Staph Sepsis

Variable	MRSA (N=19)	MSSA (N=11)	OR	C.I.		p value
Birth Weight <1500	14	7	1.600	.324	7.905	.564
SGA	3	5	4.444	.803	24.609	.088
Male	10	6	.926	.209	4.108	.919
LSCS	7	4	1.021	.218	4.772	.979
EOS	4	2	1.406	.250	7.896	.699
Antibiotic exposure	6	3	.813	.157	4.197	.804
Respiratory Support	11	9	.429	.090	2.051	.289
Central Line	11	7	1.273	.276	5.873	.757
Death	1	1	1.800	.101	31.988	.689
Duration of Stay	16,58 ±5.9	15.36 ± 6.08		-3.409	5.849	.549*

All the proportions were analyzed using Chi square test except marked * where student t-test was used

[Table-1]

Conclusions: Newborns with MRSA and MSSA BSI have equivalent morbidity and mortality. Practices should provide equal focus on prevention and management of both MRSA and MSSA infections among septicemic neonates.

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MODERATE TO SEVERE BRONCHIOLITIS TREATMENT WITH HIGH FLOW THERAPY VS NEBULIZED 3% SALINE SOLUTION IN INFANTS LESS THAN 6 MONTHS

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Introduction: There are new therapeutic options in the treatment of bronchiolitis. The objective of this study is to compare the effectiveness of high flow therapy (HFT) against nebulized 3% saline solution (3%SS) in the treatment of moderate bronchiolitis in infants less than 6 months.

Methods: Clinical trial phase III, randomized, open, and controlled with parallel groups, developed by two secondary hospitals of the Community of Madrid. 75 children less than 6 months diagnosed of moderate bronchiolitis were randomly assigned to one of the treatment groups: HFT and 3%SS. Both groups received adrenaline. Two scales were used to assess treatment response. Respiratory distress was tested with RDAI scale and respiratory rate (RR) and combining both parameters, we obtained a measure of the size of the effect (RACS). Punctuations in rest, feeding, alertness and facial expression were used to evaluate comfort. We compared the results obtained with both treatments at defined moments.

Results: Groups were homogeneous for epidemiological and clinical variables analyzed. 39 patients were assigned to 3%SS group and 32 patients to HFT. 8 patients of 3%SS group were switched to HFT group during follow-up because of clinical worsening. Intention to treat analysis was performed. No significant differences were observed between groups in mean punctuation of RACS or comfort scale at defined moments considered, in length of hospital stay, or number of patients transferred to ICU.

Conclusions: High-flow therapy offers no benefit over nebulized 3% saline solution in the treatment of moderate-severe bronchiolitis in children less than 6 months.

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RHINOETHMOIDITIS IN A NEWBORN: CASE REPORT AND REVIEW OF LITERATURE

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Background: Rhinoethmoiditis complicating subperiorbital abcess is rarely encountered in newborns. Etiology is due to S.aureus, GBS, E.coli and Pseudomonas spp. Vision loss and cavernous sinus thrombosis represent potential complications of the condition.

Patient and method: Observational case report of a case of complicated subperiorbital abcess.

Results: An 18 days-old female was admitted for fever, edema and hyperemia of left eye. The disease started 3 days prior to admission with moderate fever and progressive development of left eye symptomatology. At admission she was febrile (40.9º C) and impressive eye edema and hyperemia were present, together with eye discharge. The WBC count was 8500/mm^3 (neutrophils 5850/mm^3) and CRP was 12.19 mg/dl. Blood and conjunctival cultures grew methicillin sensitive S. aureus (MSSA). CT-scan showed a suborbital and lateral periorbital fluid collection extended towards ethmoidal and maxillar sinuses, consistent with the diagnosis of periorbital abcess complicated with rhinoethmoiditis. Initial treatment was with cefuroxime (100mg/kg/day) and gentamicin (5mg/kg/day). On 3rd day WBC count increased to 29.300/mm^3 (neutrophils 20.450/mm^3) and edema worsened. A 10 mm incission beyond the fluctuent area of the abcess was was performed, with growth of MSSA from the drained pus. The treatment was changed to meropenem and teicoplanin for 14 days, with general and local improvement. We review 10 cases published in the literature describing periorbital abscesses occurring in neonates.

Conclusion: A case of complicated subperiorbital abcess associated with rhinoethmoiditis occurring in a neonate is described. This condition should be considered in the differential diagnosis of orbital pathologies in this age group.

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THE EPIDEMIOLOGY OF VARICELLA-RELATED HOSPITALIZATIONS IN TURKEY FROM 2008 TO 2012: A NATIONWIDE SURVEY DURING THE PRE-VACCINE ERA (VARICOMP STUDY)

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Background: Although it is usually self-limiting, varicella can cause complications that are potentially serious and require hospitalization. The aim of VARICOMP study was to evaluate pediatric varicella-related hospitalizations in children before vaccine introduction.

Methods: Medical records of children requiring hospitalization due to varicella from 28 health care centers in 14 cities (representing 50% of the childhood population in Turkey) from 2008-2012, have been evaluated.

Results: 1936 children (69.2% previously healthy) were hospitalized for varicella over the 4-year period. Most cases occurred in January-March and May-July. The median age was 3 years, and boys outnumbered girls. Most cases were in children under 5 years of age, and 28.1% were < 1 year of age. Among the 1936 children, most common complication is neurological (18.6%). Secondary bacterial infections are reported in 17.8%, respiratory complications in 15.6%, hematological complications in 4.9%. 17.6% out of children have been hospitalized due to underlying disease, 9.6% due to severe varicella, 6.7% due to fever, 8.5% due to feeding difficulties. The median length of the hospital stay was 6 days and the mortality rate was 0.36%.

Conclusion: This study confirms that varicella-related hospitalizations are common, especially in previously healthy children. The incidence of this disease was higher in children < 1 year of age. Varicella vaccine was introduced to the National Immunization Program in January 2013 and we plan to evaluate vaccine effectiveness in the next 4 year period in same geographical area and to evaluate potential need for the second dose at preschool period.

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PORTUGUESE MULTICENTER PAEDIATRIC STUDY OF HOSPITALISED PERTUSSIS FROM 2007 TO 2012

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Background: Portuguese vaccination schedule includes three DTaP doses (2, 4 and 6 months) and two boosters (18 months and 5-6 years).

Aims: Describe the epidemiological, clinical and outcome features of hospitalised paediatric patients with pertussis.

Methods: Portuguese multicenter retrospective observational chart-review study was conducted in hospitalised paediatric patients with laboratory-confirmed pertussis from 2007 to 2012.

Results: Pertussis was diagnosed in 428 patients, with incidence peaks in 2008 (18.7%) and 2012 (48.1%), predominantly in hot months (64.5%) and in the North of Portugal (58.2%). Probable source of transmission was identified in 188 (52.2%) patients, 81.3% being adolescents/adults.

Patients had a mean age of two (IQR: 1-3) months; 51.4% were female, 55.9% non-vaccinated and 11.9% premature. Among 45 patients aged 6 months-17 years, 82.1% had vaccination up-to-date.

Days of illness on admission was significantly lower in infants compared to children/adolescents (median: 7.0 vs.14.5; $p< 0.01$). The incidence of cyanosis and respiratory distress was significantly higher in infants ($p< 0.01$). Chronic cough was associated with aged ≥ 12 months ($p< 0.01$).

Complications occurred in 134 (31.4%) patients; 40 (9.4%) of them had severe pertussis. Six (1.4%) infants developed sequelae and six (1.4%) died. Young age (< 3 months) and prematurity were associated with severe pertussis ($p< 0.05$).

Conclusions: In Portugal a pertussis outbreak occurred in 2012 with an increase of morbidity. As adolescents and adults seem to be the main reservoirs of the disease, immunization strategies in these groups must be reviewed in order to obtain higher protection of the vulnerable population.

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ROLE OF INFLAMMATORY MARKERS IN SEVERITY ASSESSMENT OF PNEUMONIA AT CHILDREN

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Background: Pneumonia remains one of the leading causes of hospitalization at children.

Aim of the study: To correlate the severity of the pneumonia, using the chest X ray classification of WHO, with the C- reactive protein (CRP), leucocytes and hospitalization days.

Patients and methods: Retrospective study over a 5 years period between 1st January 2007-31st December 2011 that included patients that have fulfilled the WHO criteria of chest X ray for alveolar pneumonia.

Results: We have included 1288 cases of alveolar pneumonia over the study period. The patient from rural area were 58% and there were 52.8% boys. The median age was 3 years and 9 months. The mean hospitalization duration was 8.93 days, mean leucocyte value was of 16608,20/mm^3 and mean CRP value of 7.26mg/dl. There was a strong corelation between CRP leucoctyes and mean hospitalization days. There was also a strong corelation between the chest X ray reading of alveolar pneumonia with the inflammatory markers of CRP and leucocyte values.

Conclusion: It is useful to use the inflammatory markers CRP, leucocytes and chest X rays in evaluating the severity of pneumonia.

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BACTERIAL FLORA AND INCREASING RESISTANCE TO ANTIBIOTICS OF CLINICAL ISOLATES FROM THE NEONATAL UNIT IN POLAND

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Infections are leading cause of morbidity and mortality in neonatal units. The bacterial pathogens and their susceptibility patterns should be monitored in hospital settings.

The aim of the study was to describe micro-flora and its susceptibility to antibiotics in newborns hospitalised in the Special Neonatal Care Unit.

A retrospective analysis of results of cultures of clinical samples (blood, cerebrospinal fluid, urine, stool, eye, ear, naso-pharyngeal and skin swabs) taken from newborns hospitalized in one unit in Warsaw. The analysed period was 1st Juli-31st December 2010.

A total of 832 samples were collected with 398 (43%) positive results. The vast majority of the cultured microorganisms were Gram-negative bacteria (73,8%). The most common were Escherichia coli (28.6%) and Klebsiella pneumoniae (13.6%). Gram-positive bacteria were the main etiological agents of neonatal sepsis.

57.9% of Escherichia coli isolates were resistant to amoxicillin/ampicillin and 98.2%-100% were resistant to cefuroxym, ceftazidim, amikacin and netylmycin. 100% of Klebsiella pneumoniae was resistant to amikacin and netylmycin. Methicillin resistant Staphylococcus aureus (MRSA) strains were cultured in 2.7% of cases. There were single isolates of ESBL(+) Enterobacteriaceae (2 E. coli and 2 Kl. pneumoniae). They all came from rectal swabs and were classified as colonization. No VRE, VISA or KPC (+) (Klebsiella pneumoniae carbapenemase) producing strains were isolated.

Conclusion: gram-negative bacteria continue to predominate as neonatal colonizing microflora and important causative agents of neonatal infections. Increasing resistance to aminoglycosides, cephalosporins and commonly used ampicillin is a cause for concern.

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A CASE OF TUBERCULOUS MENINGOENCEFALITIS IN A ROMANIAN GIRL

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Background and aims: Tuberculosis incidence is higher in Romania compared to other EU countries. Tuberculous meningoencephalitis(TBME) is one of the most severe forms of extrapulmonary tuberculosis with a fatal outcome in the absence of the etiological treatment.

Methods: We present the case of C.C,8 years old girl,from urban area,with tuberculosis contact (her grandmother) that had fever and frontal headache for 3 weeks before her admittion to Pediatric Hospital.Although the patient received antibiotherapy (Ceftriaxone,Gentamicin),her general state deteriorated progressively:she accused somnolence,fatigue,loss of appetite,vomiting and photophobia.She was transfered to Pneumophtisiology Clinic.

Clinical examination:fever, sleepiness, with photophobia, a positive tuberculin skin test (firm bump of 20mm) and no other changes.

Biological tests revealed leukocytosis (15890/mm3) with neutrophilia (73.5%), inflammatory syndrome, a positive QuantiFERON.

Glucose (mg/dL):	32,58 mg/dL
Protein (mg/dL)	45 mg/dL
WBCs (cells/µL)	196 cells/µL
Cell differential:	Predominance of Lymphocytes(80%)
Culture:	Positive for bacillus Koch
Direct smear	negative bacillus Koch
Opening Pressure	high

[Cerebrospinal fluid]

No pathological changes on chest radiography and skull MRI.

Results: Based on the epidemiological context, clinical and paraclinical examination and CSF aspect, the patient was diagnosed with TBME.

Emergency tuberculostatic therapy with Isoniazid,Rifampin,Pyrazinamide, and Streptomycin was initiated with favorable evolution. As a side effect a hepatocytolisis syndrome was developed after 2weeks.

Conclusions: TBME diagnosis should be taken in consideration in any case of prolonged febrile syndrome accompanied by neurological manifestations in a patient with tuberculosis contact,even if CRS aspect it´s not tipical for it.

The disease may progress to cure if treatment is early instituted.

Although tuberculostatic therapy has many side effects,the benefits are greater than its risks.

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HENOCH-SCHÖNLEIN PURPURA COMPLICATED WITH VARICELLA - A CASE REPORT

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Background: The Henoch-Schönlein (H-S) purpura is the most frequent vasculitis of childhood. The relationship between this type of purpura and the varicella zoster virus (VZV) is not well understood. Moreover, the most cases reported in the literature outline the varicella zoster infection as a trigger of the purpura and not as a complication. We are presenting a case of Henoch-Schönlein purpura where ten days after the beginning of the vasculitis, the varicella outbreaks.

Case report: A 5 year old asthmatic girl was admitted at the hospital for purpuric skin rash of the legs and buttocks, inflammation and limited mobility of the tibio-tarsal joints and abdominal pain. The diagnosis of the Henoch-Schönlein purpura was established based on the clinical findings in the presence of normal haematological, renal, bacteriological and immunological tests. As a result of the articular and abdominal involvement, a steroid therapy was introduced. Ten days later, while the articular and abdominal pain was under control and the steroid dose was decreased, the child presented high fever, muscle pain and the characteristic vesicular rash of varicella which complicated the vasculitic skin rash. Acyclovir was introduced while the steroid treatment was stopped with a favourable therapeutical response.

Conclusion: In rare cases varicella can complicate a Henoch - Schönlein purpura and have an atypical evolution caused by the steroid treatment as well as the worsening of the VZV - induced vasculitis.

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TULAREMIA: DIFFERENTIAL DIAGNOSIS OF GRANULOMATOUS ADENITIS

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Background: Tularemia is a complex zoonosis disease transmitted by arthropods and caused by Franciscella tularensis, a gram-negative aerobic bacillus. It is endemic in many parts of the world, although outbreaks in non-endemic zones have been reported. It causes a wide range of clinical manifestations, including glandular syndromes. The management is usually conservative and the recovery may be protracted, although rarely fatal.

Method: Case report of an illustrative case of glandular tularaemia.

Results: A previously healthy 11 years old boy was referred because of a history of 2 ½ months of neck swelling and weight loss. At the beginning he presented high fever and rigors with a painful swelling on the neck and flu like symptoms. His fever persisted in spite of oral antibiotics but the swelling decreased in size and pain eventually. However, once apyrexial, the neck swelling increased in size, showing inflammatory signs. Two weeks prior to the onset of his symptoms, he was bitten by an insect but was not unwell. He lived in a small village with countryside in Lithuania and had cats and dogs at home.

The fine needle aspirate showed a necrotising granulomatous inflammation and was positive for 16s for Francisella tularensis.

He was treated medically with a 10 days course of iv amikacin and ciprofloxacin and 7 days of oral ciprofloxacine. He recovered completely without any surgical drainage.

Conclusions: Tularemia must be included in the differential diagnosis of any patient presenting with granulomatous linfadenitis coming from an endemic area.

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THE OLD MAN OF THE SEA: A CASE OF NEONATAL PROTEUS MENINGITIS AND REVIEW OF THE LITERATURE

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Background and aim: Proteus mirabilis is a gram-negative rod-shaped bacterium, first discovered by Hauser, a German pathologist. He named it after a character in the Odyssey by Homer, “the old man of the sea”, highlighting the gift of Proteus for endless transformation. Proteus mirabilis is an important and often forgotten causative agent of neonatal meningitis, with potentially devastating consequences. We highlight the importance of clinical suspicion of Proteus meningitis in neonates with umbilical infection and suspected sepsis.

Methods: Following the review of records and bacteriological confirmation of our index case, a literature review was performed of peer reviewed journals.

Results: We report a full term male neonate with CSF confirmed Proteus meningitis secondary to omphalitis and no perinatal risk factors. Proteus mirabilis has a particular association with cerebral abscesses, often with poor neuro-developmental outcomes and mortality. No evidence of brain abscess was noted on MRI and follow up neuro-developmental assessment at six months of age was normal in our case. Incidence of Proteus meningitis in neonates varies, with the highest rates seen in Eastern Europe. Our literature review revealed 26 reported cases from 4 countries over a 23 year period.

Conclusions: Neonatal meningitis secondary to Proteus mirabilis is often associated with poor outcomes. Perhaps the early bacteriological confirmation, use of sensitive antibiotics with good CSF penetration and institution of the principles of 'save sepsis campaign' resulted in a satisfactory outcome for our patient. Recent studies also report some success of prevention of omphalitis with umbilical chlorhexidine application.

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ORAL PENICILLIN PRESCRIPTIONS FOR CHILDREN IN THE UK: EVIDENCE OF WIDE DOSING VARIATION IN PRIMARY CARE

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Background and aims: The British National Formulary for Children (BNFC) recommends dosing oral penicillins according to age-bands, weight-bands, and weight-based calculations. This study evaluated how UK GP prescribing follows current age-band recommendations, which could lead to sub-therapeutic dosing because of rising childhood obesity.

Methods: Detailed oral penicillin prescriptions for 0-18 year-olds were analysed from the 2010 IMS Disease-Analyzer database, comprising computerised medical records from 125 general practices (approximately 2% of the UK population).

Results: For 2010, 388,926 patients aged 0-18 years received 65,737 prescriptions for oral penicillins in total: amoxicillin (63%), phenoxymethylpenicillin (17%) and flucloxacillin (20%).

The amoxicillin results (for example) showed:

(1) In the age-band under 1 year, no child was prescribed the recommended unit-dose (62.5mg); the majority received double the unit-dose (125mg);

(2) In the age-band of 1-5 years, 96% were prescribed the recommended unit-dose (125mg);

(3) 40% of 6-12 year-olds and 70% of 12-18 year-olds were prescribed unit-doses below the BNFC recommendations.

Otitis media prescriptions were analysed separately. The dose in mg/kg/day was calculated using average weights from the 2010 Health Survey of England, as patient weight was not available. From these data, only children under 1 year received the recommended dose (40-90mg/kg/day). For children aged 4-15 years, the prescriptions equated to 10-20mg/kg/day, approximately 33% of the recommended dose.

Conclusions: These results show extensive variation in the dosing of penicillins for children in primary care. There is an urgent need to review and simplify dosing guidelines, in relation to the weights of children today.

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CLINICAL AND LABORATORY ASPECTS OF COMMUNITY-ACQUIRED CLOSTRIDIUM DIFFICILE ASSOCIATED DIARRHOEA (CDAD) IN CHILDREN IN NORTH-EASTERN PART OF POLAND

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Background and aims: C.difficile is important etiologic factor in hospital and community-acquired diarrhoea not only in adults, but in children.

Methods: Prospective analysis of 491 children with community-acquired diarrhoea. All patients were tested for C.difficile and its toxins.

Results: In 166/491 (33.8%) children C.difficile was found in stool samples and in 100/491 (20.4%) patients C.difficile associated diarrhoea according to European CDAD definition was diagnosed. History of prior antibiotic use was found only in 33% of children. Most common clinical presentation were watery stools (58%) with mucus (33%) or blood (10%) contamination, vomitting (69%), apetite loss (57%). Fever (42%) and stomachache (33%) were less frequent. 23 presented with elevated CRP (>2 mg/dl) and 50/100 had WBC >10 $x10^3$/µL. 31 children had abnormal fluid-electrolite balance and 20- acid-base imbalance. After dividing our group according to age (≤5 y.o., n=66 and >5 y.o., n= 34), stomachache was more prevalent in older children (85.3% vs. 6.1; p< 0.00001) and mucus was found more frequently in younger patients (42.4% vs. 14.7%; p=0.0052). Leukocytosis >10 $x10^3$/µL was found in 44/66 (60.6%) of younger children and only in 6/34 (17.6%) of older patients (p< 0.00001). In multivariate regression models risk factors for CDAD were stomachache (OR 1.839 [95%Cl 1.154;2.931]) and apetite loss (OR 1.658 [95%Cl 1.085;2.534]). Female gender (OR 0.613 [95%Cl 0.396;0.949]) and >5 loose stools per day (OR 0.324 [95%Cl 0.210;0.498]) were factors indicative of diagnosis other than CDAD.

Conclusions: Further studies are neccesarry to evaluate role of C.difficile in community-acquired diarrhoea in children.

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CHILDREN HOSPITALIZED WITH CLINICALLY DIAGNOSED COMMUNITY-ACQUIRED-PNEUMONIA WITH AND WITHOUT RADIOLOGICAL CONFIRMATION

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Background and aim: Significant proportion of clinically diagnosed pneumonia cases does not have radiographic confirmation. We assessed the differences in evolution between children hospitalized with community-acquired-pneumonia diagnosed on clinical grounds, treated with aqueous penicillin G, with and without chest x-ray confirmed pneumonia on admission.

Methods: This study was a retrospective cohort. Data on demographics and clinical status on admission, daily evolution during the first 7 days of treatment and outcome were collected from the medical charts.

Results: The study group comprised 148 (46.1%) children with radiologically confirmed pneumonia and 173 (53.9%) children without radiological diagnosis of pneumonia. On admission, the latter group was younger (median [25th-75th percentile]: 14 [8-28] vs. 24 [12-49] months;P< 0.001) and presented more frequently breathlessness (71.1% vs. 56.1%;P=0.005), crackles (57.2% vs. 32.4%;P< 0.001), wheezing (57.2% vs. 25.7%;P< 0.001), chest indrawing (38.7% vs. 27.7%;P=0.04), severity (31.8% vs. 19.6%;P=0.01) and received more often bronchodilator (89% vs. 62.8%;P< 0.001) and systemic corticosteroid (64.2% vs. 25.0%;P< 0.001). The group with radiologically confirmed pneumonia received antipyretic (63.5% vs. 52.6%;P=0.049) more frequently on admission, stayed hospitalized longer (8 [5-11] vs. 7 [5-8.5] days;P=0.03), and presented fever more frequently on D1 (38.5% vs. 19.1%;P=0.001), D2 (38.1% vs. 15%;P< 0.001), D3 (16.5% vs. 7.3%;P=0.03) and D4 (22.1% vs. 8.4%;P=0.01). The subgroup without radiological pneumonia had chest indrawing on D1 (22% vs.12.8%;P=0.03) and D6 (14.3% vs. 0%;P=0.007), besides cough on D5 (47.6% vs. 27.0%; P=0.02), detected more often.

Conclusion: The compared subgroups evolved differently. Resolution of disease was slower in patients with radiologically confirmed pneumonia.

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DIFFERENCES ON ADMISSION AND EVOLUTION AMONG CHILDREN WITH RADIOLOGICALLY DIAGNOSED PNEUMONIA TREATED WITH DISTINCT EMPIRIC ANTIBIOTIC SCHEMES

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Background and aim: Pneumonia remains a significant cause of child mortality, and empiric antibiotic therapy is a valuable strategy in its management. We compared the evolution of patients with radiologically diagnosed pneumonia when different antibiotics were given.

Methods: This was a retrospective cohort of 192 children aged≥02 months. Data collected from the medical charts included: demographics, clinical history and physical examination on admission, given therapeutic items and daily evolution during the first 7 days of treatment.

Results: Aqueous penicillin G, erythromycin and others were given to 151(78.6%), 8(4.2%) and 33(17.2%) patients, respectively. On admission, age< 1 year(p=0.03), wheezing(p=0.03), severe pneumonia(p=0.002) and absence of fever(p=0.02) were more frequent in the “erythromycin” subgroup than in the “penicillin” subgroup; whereas very severe pneumonia(p< 0.001), oxygen support(p< 0.001) and electrolyte therapy(p< 0.001) were more frequent in the “other antibiotic” subgroup than in the “penicillin” subgroup. The “other antibiotic” subgroup also stayed hospitalized (days) longer (median[25th-75thpercentile]:12[7.5-15]vs.8[5-11];p=0.002) than the “penicillin” subgroup. Compared to the evolution of the “penicillin” subgroup, children using erythromycin presented more respiratory abnormalities up to the fifth day of evolution (chest indrawing on D1, cyanosis on D3, and tachypnea on D4 and D5) and children using other antibiotics presented more respiratory findings up to the third day of evolution (nasal flaring on D1 and chest indrawing on D2 and D3).

Conclusions: Children hospitalized with pneumonia who received either penicillin or other empiric antibiotic schemes were different on admission and evolved differently. The subgroups might have distinct respiratory diseases related to different causative agents.

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ANTIBIOTIC SUSCEPTIBILITY OF STAPHYLOCOCCUS STRAINS ISOLATED FROM BLOOD IN CHILDREN

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Staphylococcus is one of the major causes of blood infections in all age groups. The spread of antibiotic resistance among staphylococci is the great concern in the treatment of staphylococcal infections.

The aim of this study was to investigate antibiotics susceptibility of Staphylococcus spp. isolated from blood samples in children.

A total of 191 Staphylococcus strains were isolated during 2011 from blood samples collected from different departments of Institute for children diseases in Podgorica. Staphylococci were identified by the following tests: catalase, Slidex Staph Plus (bioMerieux, Germany), API Staph (bioMerieux, Germany) and VITEK2. Antimicrobial susceptibility testing was performed by standard disk diffusion method using penicillin, cefoxitin (for testing susceptibility to methicillin), erythromycin, clindamycin, trimethoprim/sulfamethoxasole, gentamycin and vancomycin and by VITEK2.

Out of 191 isolated Staphylococcus strains, 15 (7.9%) were identified as Staphylococcus aureus (SA). Out of 118 coagulase negative staphylococci (CoNS) identified to the species level, there were 64 (54.2%) Staphylococcus epidermidis. Three (20%) out of 15 SA and 64 (36.4%) out of 176 CoNS were resistant to methicillin. Sensitivity of SA and CoNS isolates was 0% and 10.3% to penicillin, 80% and 40.3% to erythromycin, 93.3% and 74.4% to clindamycin, 76.9% and 65.4% to trimethoprim/sulfamethoxasole, 53.8% and 47.4% to gentamycin, respectively. All strains were sensitive to vancomycin.

Our study shows that the resistance to all tested antibiotic except penicillin and vancomycin is more frequent in CoNS than in SA. According to our results the rate of MRSA corresponds to the rate recorded in the southern part of Europe.

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ASSESSMENT OF GERM CIRCULATION AND RESISTANCE TO ANTIBIOTICS IN A LEVEL III MATERNITY HOSPITAL

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As the ability to support the survival of premature newborns progresses, the spectrum of germs with the potential to cause opportunistic infections increases exponentially. These microorganisms include nowadays some germs not previously accepted as true potential pathogens - coagulase-negative staphylococcus (CoNS) are the most prevalent in late-onset infections, but also E.coli and multidrug-resistant Gram-negative organisms, such as P.aeruginosa, Klebsiella spp and fungi.

Aim: To evaluate germ circulation and the resistance to antibiotics of various organisms isolated in peripheral and blood cultures sampled from newborns admitted to Cuza-Voda Maternity Hospital, in Iasi, Romania, over three years.

Material and methods: A retrospective study over three years (2009-2011), based on the analysis of newborns´ and mothers´ charts and of the hospital's bacteriology registers, in order to assess the most prevalent germs in our hospital and to attempt a correlation between maternal colonization and neonatal colonization and/or infection.

Results: The most prevalent germs in neonates were: CoNS (29.55%), E.coli (15.17%), S.aureus (7.88%) and Enterobacter spp. (5.37%). In their mothers' cultures, the germs most isolated were: E.coli (8.78%), S.aureus (5.1%), Enterobacter spp. (3.89%), Candida (3.46%), Enterococcus spp. (3.05%). There was an increased resistance to antibiotics of the isolates in positive peripheral and blood cultures in 2011 (37.12%), compared to 2009 (21.45%).

Conclusions: Medical invasive procedures together with the extensive use of broad-spectrum antibiotics have contributed to this day to the selection of antimicrobial-resistant pathogens. Judicious use of antibiotics should increasingly be promoted as a means to limit antimicrobial resistance, and to prevent infectious complications.

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PNEUMOCOCCAL PNEUMONIA IN CHILDREN: A FRENCH PROSPECTIVE STUDY IN THE ERA OF 13 VALENT PNEUMOCOCCAL CONJUGATE VACCINES IMPLEMENTATION IN FRANCE

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Background and aims: Since the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7), serotype replacement has occurred, and non vaccine serotypes have increased particularly serotypes 1, 3 and 19A, which are major providers of empyema and pneumonia. In France the switch to PCV13, which includes additional serotypes 1, 3, 5, 6A, 7F, and 19A, occurred in june 2010. To analyze clinical and biological features of pneumococcal pneumonia before and after PCV13 implementation, the French Pediatric Infectious Diseases Group has set up an active surveillance network.

Methods: Observational prospective study performed in 7 French Pediatric Emergency Department, from July 2009 to December 2011. All children between 1 month and 15 years with radiographically confirmed pneumonia were included.

Results: 5174 patients were enrolled (median age 3.1 years). 342 pleural effusions were reported. 89.1% of children < 5 years were PCV7 vaccinated. 1610 patients had blood culture and 61 (3.8%) were positive. Pleural sample were obtained in 133 cases and 101 (75.9%) were positive. Pyogenic pneumonia was diagnosed in 147 cases (2.8 %): S. pneumoniae 123, S. aureus 16, and Group A S. pyogenes 8. Sp serotypes were available for 56 cases. Additional PCV13 serotypes were predominant (84%) and were: 1 (22 cases), 19A (13 cases), 7F (7 cases), 3 (5 cases).

Conclusion: Serotypes 1, 19A, 7F and 3 were the main serotypes of pneumococcal pneumonia in France before PCV13 implementation. Continuation of the study should assess the efficiency of PCV13 to prevent pneumonia in children and detect occurrence of serotype replacement.

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NARCOLEPSY TRIGGERED BY STREPTOCOCCAL INFECTION: CASE PRESENTATION AND LITERATURE REVIEW

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Background: Narcolepsy is a chronic disabling disease with a prevalence of 1/2000. It is characterised by excessive daytime somnolence, episodes of sudden loss of muscle tone triggered by emotions - cataplexy, sleep paralysis, hypnagogic hallucinations, automatic behaviour, and abnormal sleep-wake patterns. Onset is rare before the age of 10. Presentation may be variable and makes diagnosis difficult. Cerebrospinal fluid (CSF) level of hypocretin is reduced.

Susceptibility to narcolepsy is genetically determined, but studies have shown that streptococcal infections are a significant environmental trigger for narcolepsy.

Method: We report the case of a 7 year old boy who presented with excessive tiredness and sleepiness in keeping with narcolepsy.

Results: The previously fit and healthy child presented with symptoms of excessive daytime tiredness and sleepiness. He had some hypnagogic hallucinations but not a clear cut history of cataplexy or sleep paralysis except few episodes of facial sagging (facial cataplexy). His symptoms were preceded by behavioural difficulties (becoming clingy with clacking sounds of the throat). Investigations revealed positive HLA DRB1*15 and HLA DQB1*0602, as well as persistently elevated ASOT titers. Anti dsDNA and Helicobacter pylori antibodies were negative, and neuroimaging normal. MSLT was confirmatory. Parents declined CSF hypocretin studies. He was commenced on Penicillin V with rapid improvement of his symptoms followed by slow release methylphenidate with further benefit.

Conclusion: This case report presents one of many aspects of autoimmune neurological disorders triggered by Streptococcal infection. Early recognition and treatment are crucial as they can significantly improve the patients' quality of life.

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MANAGEMENT OF SUSPECTED CHILDHOOD BACTERIAL MENINGITIS IN A UK DISTRICT GENERAL HOSPITAL

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Background and aims: To compare the management of meningitis with published NICE guidelines (2010) - Guideline CG102.

Methods: Notes were requested for children aged >4 weeks to 16 years, coded as meningitis, within Sandwell and West Birmingham NHS Trust (2006-2011). Of 42 notes, 34 fitted criteria. 22 were male. Age range and presenting complaints are described (table 1).

Table 1: Presenting symptoms and signs

Symptoms and signs as per NICE guidelines	Age of patient (N 32, 2 excluded from initial sample)			
	< 3months (N = 6)	3 months to < 5yrs (N = 19)	5-8 years (N = 4)	8 - 16years (N = 3)
Top 3 Common non-specific symptoms/signs	fever, irritable/unsettled, refusing food/drink	fever, irritable/unsettled, ill appearance	fever, vomiting/nausea, headache	vomitng/nausea, headache, fever
Top 2 Less Common non-specific symptoms/signs	sore thrat/coryza, diarrhoea/abdo pain	sore thrat/coryza, diarrhoea/abdo pain	sore throat/coryza	diarrhoea/abdo pain
Top 3 More Specific symptoms/signs	unusual skin colour, bulging fontanelle, hypotension + cold	stiff neck, altered mental state, unusual skin colour	stiff neck, Kernig's sign positive, back rigidity + photophobia	Non-blanching rash, photophobia

[Table 1 Presenting symptoms and signs]

Results: 100% of patients were expected to have;

1) **Initial investigations** (table 2).

Table 2: Initial investigations completed at presentation (N=33, 1 exlcuded)

	% Investigation performed (N)	% Abnormal result (N)
FBC	100 (33)	54.5 (18: raised WCC)
Blood Culture	97.0 (32)	18.7 (6)
CRP	90.9 (30)	73.3 (22)
Blood gas	36.4 (12)	Not analysed
Coagulation screen	54.5 (18)	27.7 (5)
Blood glucose	66.7 (22)	4.5 (1)
Blood PCR (N=30, 4 exlcuded)	20.0 (6)	0 (6)

[Table 2: Initial investigations]

2) **Lumbar Puncture (LP) if no contraindications (N=23):** 100% (N=23) were attempted, 3 failed, 95% (N=19) were abnormal. 3 cases LP was contraindicated but performed.

3) **Laboratory blood glucose at time of LP (N=22).** 36.4% (N=8) had a laboratory glucose. Of remaining 14, 78.6% (N=11) had a capillary glucose level.

4) **Recommended empirical antibiotics.** Of those aged < 3 months (N=6), 4 received recommended antibiotics. All ≥3 months (N=28) received recommended antibiotics.

5) **Received antibiotics for recommended duration** (table 3). Out of 31 eligible patients 45.2% received recommended duration, increasing to 83.9% if trust guidelines followed.

Table 3: Duration of antibiotics received compared to NICE guidelines

Age	Disease Confirmed / Unconfirmed?	Duration on antibiotics	No. of patients
≥ 3 months (3 excluded)	Confirmed (positive blood/CSF culture and/or PCR)	Correct	3 meningococcal 3 pneumococcal
		Incorrect	2 pneumococcal 1 gram negative
	Unconfirmed (failed investigations or negative blood/CSF culture and/or PCR)	Correct	6
		Incorrect	10
< 3 months (0 excluded)	Confirmed (positive blood/CSF culture and/or PCR)	Correct	1 pneumococcal
		Incorrect	0
	Unconfirmed (failed investigations or negative blood/CSF culture and/or PCR)	Correct	1
		Incorrect	4

[Table 3: Duration of antibiotics received]

6) **Follow up:** 87.1% received audiological and 77.4% paediatric referral upon discharge. (N=31). There were no deaths from meningitis.

Conclusions: The NICE guidelines were followed in a majority of cases. We are going to review departmental guidelines, develop education on recommended practice and incorporate automated alerts to ensure recommended investigations are completed.

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ADHESION TO INFLUENZA VACCINATION AMONG MEDICAL STUDENTS DURING AND AFTER INFLUENZA A (H1N1) PANDEMIC

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Background and aims: Despite evidence that influenza vaccination reduces risk of infection and prevents transmission to patients, compliance to immunization guidelines is low among healthcare workers (HCW). We evaluate adherence to influenza vaccination among medical students in 2010 (during influenza pandemic) and in 2011 (post-influenza pandemic) and assessed their perception about influenza vaccination.

Methods: In a cross-sectional study just after the 2011 influenza season, medical students were asked if they had received influenza vaccine in 2010 and in 2011, and the reasons for vaccine acceptance or non-acceptance. First grade students in the year 2011 were excluded because they had not yet entered medical school when the pandemic occurred.

Results: 144 students were interviewed, varying from 39 from second grade to 25 in the fifth grade; 50% were male and median age was 23.3 years. In 2010, 131/144 (91.0%) medical students were vaccinated against influenza, while only 60/144 (41.7%) were vaccinated in 2011. This decay was observed in all grades. When inquired on the reasons for receiving influenza vaccine, the most frequently cited reason was “to be protected” in both years. The most cited reason for not receiving immunization was “because I forgot”. The knowledge about influenza vaccination being recommended for HCW increased from 59% for 2nd grade students to 96% among 6th grade students.

Conclusions: The adhesion to influenza vaccine was very high during the pandemic, but decreased significantly in the following season in all grades. Knowledge on immunization recommendations for HCW does not necessarily reflect higher adhesion to vaccination.

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PEDIATRIC GASTROENTERITIS IN THE EMERGENCY DEPARTMENT: PRACTICE EVALUATION IN BELGIUM, FRANCE, NETHERLANDS AND SWITZERLAND

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Background and aims: Based on European recommendations of ESPGHAN/ESPID from 2008, first line therapy for dehydration caused by acute gastroenteritis (AGE) is oral rehydration solutions (ORS). In case of oral route failure, nasogastric tube enteral rehydration is as efficient as intra-venous rehydration but seems to lead to fewer major adverse events. The primary objective was to describe the rehydration strategy in case of AGE in the emergency departments of hospitals in Belgium, France, The Netherlands, Switzerland.

Methods: Electronic survey sent to physicians working in pediatric emergency departments. The survey contained a scenario describing a toddler with moderate dehydration caused by AGE.

Results: We analyzed 68 answers: Belgium N=10, France N=37, The Netherlands N=7, Switzerland N=14. Oral ORS was the first intention treatment for 90% of the respondents. In case of failure, intravenous rehydration was used preferentially by 95% of respondents from France whereas the nasogastric route was used more likely by those of Belgium (80%), The Netherlands (100%) and Switzerland (86%). Serum electrolyte measure was more frequently prescribed in France (92%) and Belgium (80%) than in The Netherlands (43%) and Switzerland (29%). Racecadotril was more frequently used in France and ondansetron is more frequently used in Belgium, The Netherlands, Switzerland. No respondent suggest routine use of antibiotics.

Conclusion: We found variations in practices in terms of invasiveness and testing. Our study supports the need for further evaluation and implementation strategies of ESPGHAN/ESPID guidelines. We plan to extend the study through whole Europe with the support of the Young ESPID Group.

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HEPATITIS B VACCINATION DURING MAINTENANCE CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Children with leukemia are at high risk of hepatitis B virus (HBV) infection. The aim of this study was to asses the immunogenicity of an intensified immunization schedule during maintenance chemotherapy for acute lymphoblastic leukemia (ALL).

Methods: Immunization against HBV was carried out in HBsAg negative and unvaccinated children receiving maintenance chemotherapy (week 28 to 99) of the Boston 2005-01 protocol.

Four doses of recombinant DNA vaccine were delivered at 0,1,2, 6 months.

The vaccine dosage was 5 µg for children less than 10 years of age, and 10 µg in the older children.

Anti-hepatitis B antibody level was measured by ELISA method 4 to 6 weeks after the fourth dose.

Seroconversion with protective rate was defined by the presence of antibody titers ≥ 10 UI/l.

Non-responders received a booster dose after completion of chemotherapy and anti-HBSAg titer was measured 4 to 6 weeks after.

Results: Immunization was initiated on average at week 46 (SD: 19.7) in 25 children with a median age of 4 years (IQR 1-14) .

Among them, 32% (8/25) achieved protective titers (GMT: 101.9 UI/l, 95% CI: 91.9-111.9 UI/l).

Responders were more likely vaccinated after week 40 of the protocol (OR: 9.7, 95%CI: 1.4-68.8).

Among non-responders, 10 received a booster dose and only 4 of them achieved protective titers.

Conclusion: HBV vaccination during maintenance chemotherapy is sub-optimal in children with ALL: only one third of children responded to vaccination.

Hepatitis B immunization should be started preferentially during the second year of the chemotherapy.

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SEROTYPE COVERAGE OF PNEUMOCOCCAL CONJUGATE VACCINES AND ANTIMICROBIAL SUSCEPTIBILITY OF STREPTOCOCCUS PNEUMONIAE FROM INVASIVE DISEASES IN CENTRAL THAILAND, 2009-2012

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Background and aims: Evaluation of serotype coverage of current pneumococcal conjugate vaccines (PCV), and antimicrobial susceptibility of pneumococci causing invasive disease (IPD) are important to guide the strategies of prevention and treatment.

Methods: Pneumococci from normally sterile sites during March 2009-August 2012 isolated in the 4 large public and several private hospitals in Bangkok were tested. The serotyping was performed by Quellung test (State Serum Institute, Denmark). Antimicrobial susceptibility was evaluated by disk diffusion using CLSI 2012 criteria. Penicillin and cefotaxime susceptibilities and MICs were performed by E-test.

Results: There were 238 isolates studied; 88.7% from blood, 3.4% from cerebrospinal fluid. Eight (9.9%) of 81 patients with available data received prior conjugate pneumococcal vaccines according to age except one. Mortality rate was 13.0%. Serotype 19A was found in 18.3%, 10.6%, 3.6%, and 11.7% among patients age ≤5 years, 6-49 years, 50-64 years, and ≥ 65 years, respectively. High susceptibilities were observed to penicillin (90.2%), cefotaxime (95.7%), ofloxacin (97.9), and linezolid (97.9%)%), but low to erythromycin (53.3%), clindamycin (67.7%), tetracycline (41.4%), and co-trimoxazole (32.4%). All were susceptible to levofloxacin, and vancomycin. Serotype coverage (%) by 7-, 9-, 10-, 11-, 13- and 15-valent PCV in different age groups is shown in Table 1.

Serotype coverage	Age ≤ 5 years (N = 82)	Age 6-49 years (N = 66)	Age 50-64 years (N = 28)	Age ≥ 65 years (N = 60)
PCV7	46.4	25.8	39.3	31.7
PCV10	48.8	31.8	46.4	40.0
PCV13	73.2	45.5	53.6	58.3
PCV15	73.2	47.0	53.6	58.3

[Table 1]

Conclusions: PCV13 and PCV15 provide significantly better coverage for children ≤5 years and adults ≥ 50 years. Susceptibilities to penicillin, cefotaxime, and fluoroquinolones remained excellent, whereas macrolides and co-trimoxazole were poor.

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SOURCE OF IMMUNOGLOBULINS A IN THE COLOSTRUM AGAINST ANTIGENS OF VIRULENCE OF ORAL CARIOGENIC AND INITIAL COLONIZATORS OF ORAL CAVITY

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The oral cavity is a gateway of entry of several species of microorganisms. Some species can only cross the oral cavity but other colonize and can cause several diseases, such as dental caries. The ability of these species to cause disease is associated with several virulence antigens of these species may present. The investigation of immune response against those antigens can be important in the control of colonization. Newborn babies did not have a mucosal immune response mature to control the infectious challenge, so breastfeeding represent an important source of protection. However, little is known about the variability of antibodies against antigens of virulence of oral species. For this, the specificity of IgA of 100 samples of colostrum was analyzed by the western blot against extracts preparation of S. mutans, S. mits, S. gordonii and S. sanguinis. The results showed that the glycosyltransferases 153 kDa-S. gordonii and 170kDa-S. sanguinis were frequently detected in samples (83.7 and 85.7% respectively). Also, IgA against the antigen of 202 kDa of S. mitis (IgA1 protease) found 66% of samples. The three major antigens of virulence of S. mutans (glycosyltransferase, antigen I/II and glucan binding protein B) were detected respectively in 75, 75 and 58,2% of samples of colostrum. So, the breast milk presented significant levels of IgA specific against important virulence of antigens those oral streptococci, which can disrupt the installation and accumulation process of these microorganisms in the oral cavity.

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TOXIN PROFILES OF STAPHYLOCOCCUS AUREUS FROM CLINICAL ISOLATES IN CHILDREN IN JAPAN

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Background and aims: Staphylococcus aureus is a common pathogen for children both in community and hospital settings. The toxins are known for virulent factors, but little is known regarding to the prevalence in Japan. Our aim of study is to identify toxins profile from clinical strains of children.

Method: We evaluated toxins in S. aureus isolates at Tokyo Metropolitan Children´s Medical Center from March 2010 to August 2012. We investigated the strains with toxin assays for Staphylococcal Enterotoxins (SEs), Toxic Shock Syndrome Toxin-1 (TSST-1), Exfoliative Toxins (ETs) and Panton-Valentine Leukocidin (PVL).

Results: We identified 68 S. aureus isolates; 30 MSSA (44.1%) and 38 MRSA (55.9%). The specimens obtained from blood, skin, joint fluids, lympho nodes and sputum were 37, 26, 2, 2 and 1, respectively. Thirty two (47.1%) isolates with diverse infections were positive for SE. Seventeen (25%) isolates were positive for TSST-1; 3 strains caused Neonatal TSS-like exanthematous disease (NTED). Among those, 15 (88.2%) isolates were MRSA. Six (8.8%) isolates with Staphylococcal Skin Scalded Syndrome were positive for ETs. Among those, 5 (83.3%) were MRSA. Eight (11.8%) isolates were positive for PVL and all of them were MRSA with skin and soft tissue infections.

Conclusions: MRSA were predominantly identified in the strains with TSST-1, ETs and PVL. Among MRSA strains, 21% were positive for PVL. This is the first report of PVL prevalence in Japanese children. Although SEs and TSST-1 were not associated with specific infection, ETs and PVL were found more in skin and soft tissue infections.

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WOOF, WOOF; COUGH COUGH. BORDETELLA BRONCHISEPTICA IN A CHILD WITH SYSTIC FIBROSIS (CF); CASE REPORT AND REVIEW OF THE LITERATURE

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Background and aims: Bordetella bronchiseptica is a rare human pathogen associated with pulmonary disease. This organism is a zoonosis responsible for morbidity in domestic animals such as kennel cough in dogs. It has been reported in one adult with CF but this is the first case of a child.

Method: We report the case of a 4 year old boy with CF who developed whooping cough during a routine ward admission, and a review of the literature.

Results: The patient had a typical whooping cough, post-tussive vomiting and increased sputum production. He had a lymphocytosis and Bordetella bronchiseptica was grown in his sputum. His family had a pet dog that also had a cough which was treated by the vet, though a specimen was not obtained. There were other dogs belonging to CF families that were spending time together, leading to treatment of them also.

Conclusion: Patients with CF come into contact with organisms from many sources; the health of their pets should also be enquired about and promoted, through vaccination to reduce transmission.

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POST SURGICAL MEDIASTINITIS DUE TO ANAEROBIC BACTERIA: CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Post surgical mediastinitis is a rare but life-threatening condition, involving mediastinal space and sternum. The most frequently involved bacteria are Staphylococcus aureus, CoNS and enterobacteriaceae.On the contrary, anaerobic bacteria appear to be rarely present.

Methods: Case report and review of the literature.

Results: A three years old male child with congenital heart defect was admitted for palliative surgical procedure known as Fontan procedure. Eight day after-surgery mild fever appears, the wound was secreting and presented superficial dehiscence. Thus, the child underwent surgical debridement and placing of mediastinal tubes for continous irrigation. During the intervention deep tampons were taken and a blood culture was performed: Finegoldia Magna (previously known as Peptostreptococcus) susceptible to all the tested drugs and S. epidermidis oxacillin-resistant were isolated from surgical stitches and S. epidermidis from blood. The child was treated with vancomycine ev for 2 weeks then switched to linezolid per os for further 2 weeks. At three months follow up the child is doing fine.We perform a review of the literature on anaerobic postsurgical mediastinitis (fig1) and we found only 4 case reports in pediatric age.

Author	Age (years) and Gender	Type of Surgery	Direct samples	Blood Culture	Regimen	Outcome
Ceral G.[3] (1976)	65 M	Coronary bypass	Bacteroides fragilis	Bacteroides fragilis	Clindamycin	Favorable
Wills P.L[17]. (1981)	/	/	Bacteroides fragilis	/	Cefalotlin, Cephalexin, Clindamycin	Favorable
Smith P.S.[5] (1985)	65 M	Coronary bypass	B Bacteroides brevis/ S. Epidermidis	Bacteroides brevis	Clindamycin, ticarcillin, gentamicin	Favorable
	44 M	Coronary bypass	Bacteroides fragilis/ S. Epidermidis	Bacteroides fragilis	Clindamycin, nafcillin, gentamicin	Favorable
Czachor J.S.[6] (1988)	48 M	Coronary bypass	Bacteroides oralis/ S. Epidermidis/ a-hemolytic streptococci	Bacteroides fragilis	Clindamycin, vancomycin	Favorable
Brook I.[4] (1989)	Adults (15 patients)	various	10 Peptostreptococcus (of whom 4 F.Magna) 4 Bacteroides 2 Propionibacterium 3 Clostridium	not detailed	various	not detailed
Brook I.[7] (1996)	43 F	Coronary Bypass	Finegoldia magna/ S. Aureus	S. Aureus	Vancomycin, gentamicin	Favorable
	29 M	Cardiac assist device	Propionibacterium acnes/ S. Epidermidis	Propionibacterium acnes	Vancomycin, penicillin	Favorable
Brook I.[8] (2001)	7 F	Ventricular septal defect	Prevotella intermedia/ peptostreptococcus micros	Negative	Imipenem, amoxicillina/clavulanate	Favorable
	3 F	Ventricular septal defect	S.Aureus/ Bacteroides thetaiotaomicron/ Peptostreptococcus prevotii	S.Aureus	Clindamycin, vancomycin	Favorable
	5 F	Fallot's tetralogy	E.Coli/ Clostridium perfrigens	E.Coli	Clindamycin, vancomycin	Favorable
	2 M	Transposition of the great vessels	Prevotella melaninogenica/ Peptostreptococcus spp./ Propionibacterium acnes	Prevotella melaninogenica	Ticarcillin-clavulanate, amoxicilline-clavulanate	Favorable
Tammelin A.[9] (2002)	Adults (8)	Elective cardiac artery bypass grafting or heart valve replacement	8 Propionibacterium acnes	not detailed	not detailed	not detailed
Kenneis S.[10] (2009)	50 M	Finegoldia Magna	Finegoldia Magna	Negative	Metronidazole, amoxicillina	Favorable
This study	3 M	Fontan procedure	Finegoldia Magna/ S. Epidermidis	S. Epidermidis	Vancomicyn, linezolid	Favorable

[Literature Review]

Conclusions: Anaerobic agents can be responsible for postoperative mediastinitis in pediatric age. This should particularly be kept in mind when facing a patient with negative blood cultures and should encourage appropriate sampling, which would probably lead to increased isolation of anaerobic pathogens. This is crucial for therapeutic management, allowing the use of the most appropriate antimicrobial therapy.

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ADENOVIRUS RESPIRATORY INFECTION (ARI) AMONG IMMUNOCOMPETENT PATIENTS IN PEDIATRIC INTENSIVE CARE UNIT (PICU)

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Background and aims: Adenovirus is responsible for 7-8% of childhood viral respiratory infections, 5-11% of viral pneumonia and bronchiolitis; mostly self limited. Severe cases may occur among immunocompromised patients. Treatment with Cidofovir was offered for immunocompromised patients. Our aim is to describe ARI among immunocompetent children in PICU.

Methods: Between 2007 and 2012; children with ARI in our PICU were included. Data was retrospectively retrieved including background, clinical manifestation and treatment. Adenovirus was diagnosed by polymerase chain reaction (PCR), Immune fluorescence (IFA) or both.

Results: 412/3826 samples were positive for adenovirus. Twenty two were admitted to PICU. Six were referred from other hospitals. Age was 4 months-11.5 years; only one > 3 years. 17/22 (77%) had underlying conditions (heart, lung , neurological). 68% had fever and cough, 3 had conjunctivitis. 18% received antibiotics before admission.WBC ranged from 1900 to 27300 (mean-14622), and 36% had blood count above 15000. Chest x ray was consistent with viral infection in 77% of the patients and normal in 3 (13.6%), two patients had status epilepticus. Co-infection was found in 4 (3/ RSV and 1/ Parainfluenza). Four patients had bacterial infection (3 had pneumonia and 1 had mastoiditis). Mechanical ventilation was needed in 11 patients (50%); for 1-14 days (mean=4). None received Cidofovir, 17 (77%) received steroids, 86% antibiotics. all survived.

Conclusions: ARI can cause severe disease necessitating PICU admission and mechanical ventilation (mostly with underlying condition). Many patients receive steroids and antibiotics which may be unnecessary. The disease was self limited and all recovered.

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CURRENT CLINICAL PROTECTION OF POSTEXPOSURE PROPHYLAXIS AGAINST MEASLES WITH IMMUNE GLOBULIN INTRAVENOUS

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Background: Measles is highly contagious by airborne transmission. The illness may be transmitted in hospitals and physicians´ offices. Mortality rate is 4 to 10% in developing countries. Case fatality rates are increased in younger children and immunocompromised children. Immune globulin intravenous (IGIV) is given to prevent measles in healthy children below 6 months of age with maternal measles negative and in immunocompromised children within 6 days of exposure. However, to the best of our knowledge, any studies have not been reported previously about clinical protection of IGIV as postexposure prophylaxis against measles.

Aim: To assessed clinical protection of postexposure prophylaxis against measles with IGIV.

Methods: A number of imported measles cases in Istanbul reminds us that measles rates in Turkey have decreased significantly during the last five years, in parallel with the achievement of >95 % vaccination coverage in the country. Of the children exposed with 13 confirmed cases, 31 were healthy children below 6 months of age with maternal measles anti-IgG negative and 2 were immunocompromised children. These children were administered IGIV (0.4 g/kg) to prevent measles within 6 days of exposure and were followed up until 28 days after exposure.

Results: Any children administered IGIV did not develope measles. Clinical protection of IGIV against measles was %100.

Conclusions: Effectiveness of IGIV against measles as postexposure prophylaxis were found very highly. Future and large studies are warranted to determine the exact clinical protection of IGIV as postexposure prophylaxis in measles.

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EVALUATION OF THE INCIDENCE OF CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Clostridium difficile is an aerobic, gram-positive, endospore-forming bacterium, which pathogenicity is associated with the production of epsilon-toxin in the gastrointestinal tract. It has been proven that inflammatory bowel disease is a risk factor for C. difficile infection.

Aim: The aim of the study was the retrospective estimation of incidence of Clostridium difficile infection in children with non-specific inflammatory bowel diseases.

Method: The retrospective study consisted of 47 children, in age from 6 to 18 years, with newly diagnosed or worsening symptoms of inflammatory bowel disease, hospitalized during the period from 1 July 2011 to 31 September 2012. Ulcerative colitis occurred in 14 children and Crohn´s Disease in 29 examined cases.

The degree of disease activity was determined using the PCDAI and PUCAI. The presence of Clostridum difficile toxins A and B was detected by using the TechLab EIA.

Results: C. difficile toxins in feces were found in 4 patients (8.5%). Among patients with ulcerative colitis incidence of C. difficile infection was 14.3% and in patients with Crohn´s disease -6.9%.

Conclusions: The incidence of C. difficile infection was significantly higher in children with ulcerative colitis than with Crohn´s disease. Clostridium difficile infection occurred in children with moderate or severe form of disease, and inflammatory lesions involved their entire large intestine.

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CHARACTERIZATION OF HUMAN IMMUNODOMINANT B-CELL EPITOPES WITHIN VIRULENT SURFACE PNEUMOCOCCAL PROTEINS (SPNPS)

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Background: We have previously identified 10 immunodominant B-cell epitopes within antigenic fragments of SPnPs (CbpD, PhtD, PhtE, ZmpB, PspA and PavB) with a potential role in host-pathogen interaction, by screening sera from patients with invasive pneumococcal disease (IPD) against 20-mer synthetic peptides covering the whole amino-acid sequence of previously defined antigenic regions. This work aimed to further characterize the selected epitopes regarding their specificity in patients with IPD and their immunoreactivity within each corresponding protein.

Methods: ELISA using selected B-cell epitopes, synthesized in their free soluble form, as capture antigens was applied to validate their immunoreactivity in sera from 35 IPD patients aged 2-16 years and 140 age-matched children with no history of IPD. Specific antibodies (eluents) against antigenic peptides were purified using sepharose B immunoaffinity columns. Antibody purification was confirmed by ELISA using the homologous peptide as capture antigen. Eluents' immunoreactivity was assessed against pneumococcal whole protein extract by Immunoblotting.

Results: Pep #4 derived from CbpD, pep #19 from PhtD and pep #40 from PhtE were consistently and specifically recognized by IPD patients' sera compared to controls' ($p < 0.0001$). Each eluent reacted with the homologous peptide in the confirmatory ELISA and recognized a protein band with a molecular mass matching to the corresponding parent protein, in whole pneumococcal cell lysates.

Discussion: Three of 10 previously identified B-cell epitopes reacted consistently and specifically with IPD sera. Purified anti-peptide antibodies recognized each corresponding parent protein in pneumococcal whole cell lysates, encouraging further investigation of their surface accessibility and opsonophagocytic function.

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EVALUATION OF EFFICACY OF INTERFERON INDUCER IN TREATMENT OF ACUTE GASTROENTERITIS IN CHILDREN

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Background: In most cases acute gastroenteritis (AG) in children is caused by viruses. The opportunities of use of interferon inducer (IFN-inducer) in treatment of AG are unknown.

Aim: To evaluate the efficacy of IFN-inducer containing release active antibodies to interferon-γ (RAAB IFN-γ) in treatment of children with AG.

Methods: A comparative, randomized, double-blind placebo-controlled trial of RAAB IFN-γ (IFN-inducer "Anaferon for children") efficacy in treatment of acute viral diarrhea in a 86 children of 1 month - 3 years with AG. 46 patients of the 1-st group obtained RAAB IFN-γ and 42 patients of group 2 took placebo. Proportions of subjects with axillary temperature, frequency of stool normalized and vomiting absent for 2-5 days of treatment were evaluated. Fecal PCR was performed on days 1 and 5 of the treatment.

Results: Percent of children with normalized temperature was 48% of children in group 1 vs 14% of patients of group 2. Percentage of subjects with vomiting on day 2 of the treatment was 9% and 24% in groups 1 and 2, respectively. On day 4 of the treatment 74 % subjects of group 1 had stool frequency normalized vs. 48% in group 2. On the first day PCR revealed rotavirus in 85% and 83% in groups 1 and 2, respectively. After the treatment rotavirus isolation persisted in 39% subjects of group 1 and 74 % in group 2.

Conclusions: Administration of RAAB IFN-γ increases percentage of subjects with reduced clinical symptoms of AG and improved rotavirus elimination.

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THE HEALTH AND ECONOMIC VALUE OF ROTAVIRUS VACCINATION IN KAZAKHSTAN

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Background and aims: Rotavirus-gastroenteritis (RV-GE) is a leading cause of morbi-mortality in Kazakhstan generating significant economic burden, including direct and indirect costs. We aimed to assess the public health and societal cost-effectiveness of universal rotavirus vaccination with RIX4414 (GlaxoSmithKline), a 2-dose human rotavirus vaccine, compared to no vaccination.

Methods: A static, deterministic, decision-tree previously described model was used to estimate direct/indirect associated costs and Quality-Adjusted Life-Years (QALYs) based on the number of RV-GE cases (mild, moderate and severe) and deaths, over a one year period for children under five-years of age in Kazakhstan. Country-specific epidemiological data and related costs recently published were used. Vaccine efficacy as reported from clinical trials and utility data from literature were included. Payer and societal perspectives were considered at 3% discount rate. Incremental cost-effectiveness ratio (ICER) was calculated defining threshold as per WHO-guidelines (1 GDP-per-capita for highly-cost-effective=1,933,100KZT). Sensitivity analysis was conducted on main parameters including an alternative scenario with a 3-dose regime.

Results: Rotavirus vaccination is expected to reduce rotavirus disease burden by preventing 95,008 mild, 25,116 moderate, 3,909 severe RV-GE cases and 63 deaths. Vaccination would be a cost-effective intervention from payer perspective (ICER= $KZT440,700-per-QALY-gained discounted and $KZT219,314-per-QALY-gained undiscounted) and from societal perspective would be cost neutral but generating additional QALYs. Additionally, a 2-dose program would be cost-saving as compared to a 3-dose program.

Conclusions: Our analysis indicates that universal rotavirus vaccination program would be a cost-effective intervention and would generate more value for money respectively from payer and from societal perspectives in Kazakhstan.

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INCIDENCE OF ACUTE OTITIS MEDIA IN CHILDREN BELOW 6 YEARS OF AGE IN MEDICAL PRACTICES IN FIVE EAST EUROPEAN COUNTRIES

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Background and aims: Acute Otitis Media (AOM) is a frequent respiratory illness in children worldwide, with peak age of infection between 6-12 months. AOM is among the major reasons for outpatient antibiotic therapy; it also negatively impacts the quality of life of children and their caregivers. Previous studies have demonstrated the significant impact of pneumococcal conjugate vaccination on AOM incidence. Given the paucity of data on AOM incidence in Eastern Europe, this study estimated the AOM burden in the region.

Methods: We conducted a multi-center, observational cohort study (June2011-July2012) to determine the incidence, complications, and AOM symptoms among children aged < 6 years. Data on physician-diagnosed AOM episodes in the year preceding enrolment or since birth for children aged < 1 year was collected from retrospective review of medical records. AOM was defined as an inflammation of middle ear, manifested by localized signs/symptoms (ear pain, hearing loss, bulging, diffused/localized inflamed tympanic membranes/spontaneous ottorhea) accompanied by non-specific symptoms (fever, irritability, nausea, vomiting).

Results: 2257 children (median age=28 months [range: 0-71 months]) were included in the analysis; 50.1% were male. The overall physician-diagnosed AOM incidence was 181.8 cases (95% CI:163.5-201.5) per 1000 person-years; highest and lowest incidence was observed in Slovenia and Estonia, respectively (Table).

Table Incidence of AOM episodes as diagnosed by a primary care physician by country (Retrospective analysis [N=2257])

Country	Retrospective data P=1991.34			
	N	n	AOM Incidence (in 1000 person-years)	95% CI
Estonia	250	24	97.7	(62.6-145.4)
Lithuania	300	58	225.3	(171.0-291.2)
Poland	1106	121	130.5	(108.3-155.9)
Romania	301	34	118.7	(82.2-165.9)
Slovenia	300	125	455.4	(379.0-542.5)
Total	2257	362	181.8	(163.5-201.5)

AOM: acute otitis media; N: number of children included in the analysis from each country; n: number of AOM episodes; P: total number of person-years; 95% CI: Exact Poisson 95% confidence interval

[Table Incidence of AOM episodes as diagnosed by a]

Conclusions: This study provides useful information on the public health burden of AOM in Eastern Europe. AOM incidence in the region is high and differences observed between East European countries indicate possible differences in social structure and diagnostic behavior.

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PLEURAL EMPYEMA DUE TO STREPTOCOCCUS PNEUMONIA SEROTYPE 19F IN A PATIENT WITH ATAXIA-TELANGIECTASIA AND HYPER IGM SYNDROME

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Background: Ataxia-telangiectasia (AT) and Hyper IgM (HIGM) syndrome are both primary immunodeficiency diseases caused by different genetic defects. In this case report, we aimed to present a girl who was admitted with pleural empyema and was diagnosed both Ataxia-telangiectasia and Hyper IgM syndrome respectively.

Case: A six year old girl was hospitalized with fever, fatigue and cough. On physical examination, her weight was 11 kg (< 3 p), height was 102 cm (< 3p). She had 39 degree fever, with reduced breath sounds, hepatomegaly, telangiectatic lesions on the conjunctiva and ataxic gait. She had experienced recurrent respiratory infections and hepatosplenomegaly since the age of 6 months. Laboratory data revealed leukocytosis, elevated CRP (102 mg/dL), decreased serum IgG (97 mg/dL), raised IgM (1013 mg/dL). She was treated with teicoplanin and ceftriaxone for three weeks with adequate clinical and laboratory response. In pleural culture S.pneumoniae serotype 19F was isolated. In immunophenotype test CD40 was 0.09 (N: 14-33). Also she had elevated AFP. She was discharged with regular intravenous immunoglobulin infusions and antimicrobial prophylaxis.

Conclusions: While a small proportion of AT patients have increased serum IgM concentrations during the course of a disease, a high level of IgM at onset is rare. Hyper IgM syndrome is also be considered in the differential diagnosis.

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NOSOCOMIAL INFECTIONS IN THE INTENSIVE CARE UNIT OF A PAEDIATRIC GREEK HOSPITAL IN ATHENS

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Aim: To monitor the nosocomial infection rate in our PICU and the risk factors that are associated with.

Methods and materials: A prospective observational study was carried out from January 2011 to March 2012, applying the methodology of the INICC and the definitions of the NHSN-CDC.

Results: During this period from 264 children that were hospitalized for 326 days in our PICU, 14 manifested nosocomial infections. Mean duration of hospitalization stay was 22 days (SD=23). Our patient's median age was 2,5 years, 50% were males. Nine children (64%) suffered from a severe underling disease and five of them from cancer. Six children (43%) had multiple previous hospitalizations in paediatric and surgical wards. Nine patients (64%) had central vascular catheter with a mean duration of catheterization 24 days, five (36%) had arterial catheters, nine (64%) were intubated and all of them had urinary catheter. The mean day presence of nosocomial infection was the 8^{th} day of hospitalization. Twelve children (86%) developed septicemia with positive blood culture, one pneumonia and another one urinary track infection. The causative microbial agent was: Candida albicans 21%, Enterobacter 21%, Enterococcus 14%, Serratia 14%, Klebsiella 14%, Staph. epidermitis 14%, Pseudomonas aeroginosa 7%. The mortality rate was 7%.

Conclusions: The incidence of nosocomial infection in our PICU is 5,3%. The most important risk factors for nosocomial disease are severe underling disease, multiple previous hospitalizations and the length of hospital stay rather than central vascular catheter and intubation.

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QUANTITATIVE DETERMINATION OF HAEMOGLOBIN USING THE NEW QUIKREAD® GO CRP+HB POINT-OF-CARE TEST

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Background and aims: A new easy-to-use QuikRead go CRP+Hb POC test gives simultaneously two results (CRP and haemoglobin) from one whole blood sample. Whole blood sample is added to the cuvette, a cap is put on after which the analysis in instrument is automatic and the result is available in two minutes. In this study we evaluated the performance of the QuikRead go CRP+Hb test to the ICHS (cyanomethemoglobin) standard 1995 and two clinical chemistry analysers.

Methods and results: The haemoglobin determination of the QuikRead go system is based on measuring oxyhemoglobin photometrically. The measurement range for hemoglobin is 50-245 g/l and for CRP 5-200 mg/l.

The linear correlation of QuikRead go haemoglobin result to the ISCH 1995 method was y=1.07x-7.5, R=0.99 (n=59), and to Sysmex XE-5000 y=1.04x-1.0, R=0.99 (n=107). Correlation of QuikRead go CRP whole blood results to Cobas 8000 (Roche Diagnostics GmbH) plasma results was y=1.01x+1.5, R=0.99 (n=117).

Linearity of the test was studied by diluting venous whole blood samples with plasma and calculating the corresponding recoveries, which varied between 95-104 %.

Precision for haemoglobin was determined according to CLSI guideline EP5-A2. The between-day (d=20) precision (CV%) for whole blood samples of 96, 134, and 164 g/l were 1.2, 1.3 and 0.9 %, respectively. Precision of the control material (126 mg/l) was 2.1 %.

Conclusions: Performance of the QuikRead go CRP+Hb test corresponds well with the clinical laboratory methods. The QuikRead go CRP+Hb test is a fast, reliable and precise method for simultaneous analysis of Hb and CRP.

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NEUROBRUCELLOSIS: A REPORT OF SEVEN CHILDREN

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Neurobrucellosis is a severe and rare complication of brucellosis in children. We retrospectively reviewed 74 children with brucellosis, seven (9.4%) of them had neurobrucellosis. The clinical presentation included meningitis (five patients), encephalitis, neuropsychiatric disorder (one patient). Additional findings were cranial nerve palsies (sixth and eighth) and ataxia in three patients. Brucella serum agglutination test (SAT) titers of the blood were greater than or equal to 1:160 in four patients. SAT titer of the cerebrospinal fluid investigated in three patients and found greater than or equal to 1:20 in two patients. Serum ELISA for Brucella Ig M and/or Ig G was positive in four patients. Brucella spp. was isolated from the blood in two patients. CSF cultures showed no growth in all patients. Cranial computed tomography (CT) was performed in six patients and found normal in five patiens. The remaining had vasogenic edema on CT. Magnetic resonance imaging (MRI) was performed in all patients and found normal in five patients, the remaining had vasogenic edema and gliosis in the cerebral white matter. Patients were treated with a combination of doxycycline, rifampicin, gentamicin and ceftriaxone for 8-24 weeks based on their clinical and CSF findings. No relapses and mortality occured. Patient with eighth cranial nerve palsy had hearing loss as a sequelae.

In conclusion, neurobrucellosis was diagnosed on the basis of epidemiological risk factors in combination with clinical, laboratory and radiological findings. The increased rate of neurobrucellosis was attributed to the referral of most of brucellosis patients to our center.

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SAFETY AND IMMUNOGENICITY OF A QUADRIVALENT INACTIVATED INFLUENZA VACCINE CONTAINING TWO A AND TWO B STRAINS IN CHILDREN/ADOLESCENTS AND ADULTS

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Background: Trivalent influenza vaccines (TIV) contain two A strain; H1N1, H3N2, and one B strain. Recently, 2 distinct B lineages (Victoria and Yamagata) have circulated worldwide, with neither providing good cross-protection against the other. Prediction of which B lineage would dominate during successive influenza seasons has been problematic, resulting in frequent mismatches. Quadrivalent influenza vaccine (QIV) was designed to address this issue by incorporating both B lineages.

Methods: A Phase III randomized, controlled, multi-center study, 385 children/adolescents and 1705 adults were randomized to receive one IM dose of QIV containing the B/Brisbane strain (Victoria lineage) and the B/Florida strain (Yamagata lineage), or the licensed TIV for the 2011-2012 season containing the B/Brisbane strain. Both vaccines contained the same H1N1 (A/California/07/2009) and H3N2 (A/ Perth/16/2009) strains. Safety was monitored and blood specimens for the immunogenicity assay (hemagglutination inhibition) were collected before and 21 days after vaccination.

Results: Overall, the safety profiles between QIV and TIV were similar in both age groups tested. A strong immune response was induced in both age groups following a single injection of either influenza vaccine. In adults, the three EMA criteria were met (95% CI inclusive) for each strain in the QIV group. In general, higher immune responses after QIV injection were observed in the children/adolescents than in adults against all strains.

Conclusions: QIV is well tolerated by adult and child/adolescent subjects and induces a strong immune response in both age groups following a single injection.

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HIGH RATES OF STREPTOCOCCUS PNEUMONIAE CARRIAGE DETECTED IN SALIVA OF CHILDREN

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Background and aims: With the introduction of pneumococcal conjugate vaccines, in-depth carriage studies are required to monitor the effects of vaccination. Here, we investigated saliva as a means of detecting Streptococcus pneumoniae colonization for potential use in surveillance studies.

Methods: Saliva was collected from 49 students (age 5 to 10 years, median 8) of a rural school near Utrecht. Samples were transported to the lab on ice, cultured and the remaining volume stored frozen. Cultures were inspected for S. pneumoniae colonies, then all bacterial growth was harvested and frozen. DNA was extracted from thawed raw and culture-enriched samples using a modified Agowa protocol, tested by quantitative-PCR (qPCR) targeting S. pneumoniae specific genes lytA and piaA and considered positive when both genes detected.

Results: Two children (4%) were culture-positive for S. pneumoniae. Thirty (61%) children were qPCR-positive for S. pneumoniae in raw saliva whereas 41 (84%) were q-PCR positive in culture-enriched samples. There was a negative correlation between age and quantity of lytA detected in raw saliva samples (Spearman's r=0.3, p=0.03).

Conclusion: Conventional culture detection of S. pneumoniae in saliva is extremely difficult due to saliva's polymicrobial nature. These limitations were addressed by combining culture-enrichment and sensitive molecular methods. This resulted in more than ten-fold higher rates of pneumococcal carriage detected in schoolchildren compared to results of conventional culture. The simplicity of sample collection and the high sensitivity of pneumococci detection suggest that saliva could be considered as an alternative to nasopharyngeal swab sampling in surveillance on pneumococcal carriage in children.

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OPPORTUNITIES AND OBSTACLES TO THE ELIMINATION OF SCHISTOSOMIASIS FROM THE MIDDLE EAST: A CASE STUDY IN YEMEN

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Background and aims: Schistosomiasis, among the most prevalent neglected tropical diseases, is a life-threatening public health problem in Yemen especially in rural communities where schistosomiasis is still considered as the second cause of death, after malaria. This study aims to determine the current prevalence and distribution of schistosomiasis among rural communities under active schistosomiasis control and surveillances in Yemen.

Methods: A cross-sectional study was conducted among 399 children in 5 different governorates in Yemen namely, Taiz, Ibb, Thamar, Sana'a and Hodeidah. Urine and stool samples were collected and examined for the presence of Schistosoma haematobium and S. mansoni eggs. Demographic, socioeconomic and environmental information were collected by using a validated questionnaire.

Results: Out of 399 children (59.4% males and 40.6% females; aged ≤ 15 years) participated in this study, 127 (31.8%) participants were found positive for schistosomiasis. The overall prevalence of S. haematobium and S. mansoni infections were 23.6% and 9.5%, respectively. The highest prevalence of S. mansoni was reported in Ibb province while the highest prevalence of S. haematobium was in Taiz and Thamar. Among those infected, 38.4% and 14.6% were anaemic and had hepatosplenomegaly, respectively. Large populations of snails (both Bulinus and Biomphalaria species) were observed.

Conclusions: This study reveals an alarmingly high prevalence of schistosomiasis among rural communities in Yemen and this supports an urgent need to implement innovative and integrated control measures to save the lives and future of the most vulnerable children. A regional integration strategy is crucial to eliminate the disease from the region.

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SEROPREVALENCE OF IGG ANTIBODIES TO PERTUSSIS TOXIN IN CHILDREN AND ADOLESCENTS IN ESTONIA

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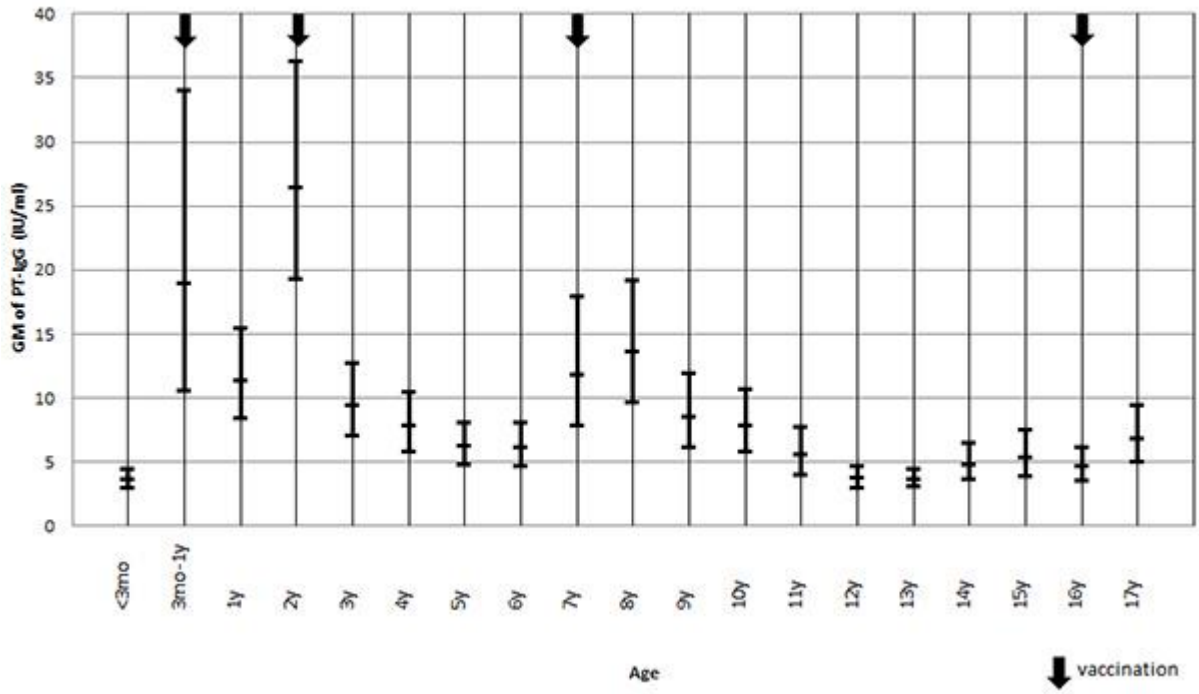
Background and aims: Estonia is characterised with 6 doses of acellular pertussis vaccine in immunisation programme and high immunisation rate (in 2011 at age of 2 years 93.3% and of 6-7 years 87.6%).We aimed to measure the concentration of IgG antibodies to pertussis toxin (anti-PT IgG) in children below 17 years in Estonia in 2012.

Methods: The leftover sera of 1053 children and adolescents (equally distributed across age groups) without known diagnosis of pertussis were collected by the laboratory of the Children´s Clinic of Tartu University Hospital. Anti-PT IgG concentration was measured by ELISA (Euroimmune). The antibody titres ≥125IU/ml were considered suggestive to pertussis in last 6 mo and those ≥62.5IU/ml in a last year.

Results: The highest, but rapidly declining GM of anti-PT IgG was observed at age when immunisations are given (Figure 1).

Figure 1: Age-specific distribution of anti-PT IgG GM and 95% CI



[Figure 1: Age-specific distribution of anti-PT IgG]

By excluding these age groups (< 3y, 7-8y and 15-17y) we observed that 1% (95% CI 0.4-2.3) of 3 to 6y and 9 to 14y old children had anti-PT IgG titres ≥125IU/ml and 2.1% (95% CI 0.7-4.8) and 3.6% (95% CI 1.9-6.2), respectively ≥62.5IU/ml. About half of sera in all age groups had antibody levels below 5IU/ml.

Conclusions: Despite 6 doses of acellular vaccine and high immunisation rates pertussis is still circulating in significant numbers in Estonia suggesting for the need of more efficacious vaccines than those currently available.

Acknowledgements: This study was founded by grant from the Estonian Science Foundation (9259).

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IMPACT OF CONJUGATE VACCINES ON INCIDENCE OF INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN < 2 YEARS IN CASTILLAYLEON (SPAIN), 2007-2012

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Background and aims: In Castilla y Leon (Spain) the pneumococcal conjugate vaccine (PCV) is not included in the Public Health Childhood Vaccination Program but it is recommended by pediatricians. The aim of this study is to assess the impact of new conjugate vaccines on the incidence of invasive pneumococcal disease (IPD) in children aged < 2 years in Castilla y Leon (2007-2012).

Methods: IPD is a notifiable disease in Castilla y Leon. The case definition includes the identification of pneumococcus in a normally sterile site. We analysed the incidence in two periods: pre-introduction of new PCV (10 and 13): 2007-2009; and post-introduction: 2010-2012. Annual incidence rates per 100.000 persons were calculated.

Results: 53 cases of IPD were registered: 24 (45,3%) in PCV7 vaccinated, 8 (15,1%) in PCV13 vaccinated and 1(1,9%) in PCV10 vaccinated. Septicaemia (30,2%) and meningitis (28,3%) were the most frequent diagnoses. IPD incidence rate was 23,66 (27 cases) in 2007-2009 and 21,64 (26 cases) in 2010-2012 (no statistical significance=ns). The rate of meningitis decreased in 2010-2012 in relation with the previous period (10,52 vs 2,50; p=0,02).

	2007-2009 Incidence	2010-2012 Incidence	CI (95%) p	% decrease
IPD by 1, 5, and 7F stp (common PCV10/ PCV13 but not in PCV7)	8,76	5,83	0,57-3,95 p=ns	33,4
IPD by 3, 6A and 19A stp (exclusively in PCV13)	5,26	4,18	0,32-5,23 p=ns	20,5
IPD by 1, 3, 5, 6A, 7F and 19A stp (in PCV13 but not in PCV7)	14,02	9,99	0,66-2,96 p=ns	28,7

[Table 1]

Conclusions: The incidence of IPD in young children slowly decreased after introduction of new PCV. We think that is early to observe the effect of PCV13. Active surveillance remains essential.

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SELECTION OF RESISTANT BACTERIAL STRAINS IN CHILDHOOD URINARY TRACT INFECTION

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Introduction: Urinary tract infections (UTI) are among the most common bacterial infections in children. Antibiotic therapy is mandatory but may lead to resistant bacteria.

Aim: To determine the bacterial specimens, resistance patterns and the risk of non E. coli (EC) or resistant EC UTI in children with and without urinary tract or kidney pathologies (UTKP).

Method: We evaluated positive urine cultures (≥ 100.000 CFU) during 2011- 2012 and compared bacterial specimens and resistance patterns of children with and without UTKP.

Results: A total of 470 positive urine cultures were analyzed (female 87%; mean age 7,4 years, range 1 month - 18 years). 103 patients (22%) had UTKP. 76% of the bacterial strains were EC, 5% Proteus ssp., 4,3% Pseudomonas ssp., 4% Klebsiella ssp., 3,5% Enterococcus ssp. and 7,2% others. Children with UTKP had more non EC infections (n=44, 43%) than children without UTKP (n=72; 20%), relative risk 2.2 (CI 95%; 1.6- 2.9, p< 0.0001). We found more EC resistant to ampicillin (AMP) and/or sulfamethoxazole/trimethoprim (SXT) in children with UTKP (37%) than in children without UTKP (27%). Multiresistant EC (≥ three resistances) were found in 12% of UTKP and in 4% without UTKP, relative risk 1.52 (CI 95%; 1.12- 2.07, p= 0.0071).

Conclusion: Children with UTKP are at increased risk for UTI caused by resistant EC strains or by non EC bacteria.

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CAN RSV- RAPID DIAGNOSTIC TEST REPLACE THE RTPCR METOD IN EVERYDAY RSV DIAGNOSIS IN CHILDREN

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Introduction: Lower respiratory tract infections among young children caused by the respiratory syncytial virus (RSV) belong to the most common infections. To determine the RSV etiology, rapid diagnostics tests can be very helpful. An explicit confirmation is the presence of the RSV genetic material in the rtPCR.

Aim: Comparison and compliance of the RSV rapid diagnostics test (RSVrdt) results with the rtPCR method.

Material and methods: The study included 49 children in the age from 0 to 3 years old (average $^{4}/_{12}$ months) who were admitted to the Bielanski Hospital because of a lower respiratory tract infections. An RSVrdt (Biomerieux) and a pharyngeal swab were performed simultaneously on each child, and were sent to the NIH laboratory in order to detect the RSV genetic material by the rtPCR method.

Results: In 41/49 (83.7%) patients the RSVrdt had a positive result, and in 8 (15.3%) negative. In the rtPCR, the RSV presence was confirmed in 46 cases (93.9%). In the three cases in which the RSVrdt was negative, the rtPCR results were also negative (6.1%). In five children (10.2%), despite the negative rapid diagnostics test, in the rtPCR the RSV etiology was confirmed. The specificity of the RSVrdt was estimated to be 33.3%, and the sensitivity - 84.8% .

Conclusions: The high sensitivity of the RSVrdt allowed to confirm the RSV etiology in the majority of children. The rapidity, simplicity and non-invasiveness of this diagnostics test are a remarkable advantage as a diagnostics test i children.

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CHANGES OF THE PNEUMOCOCCAL NASOPHARYNGEAL CARRIAGE FROM ERA OF PCV7 TO PCV10 OR PCV 13 IN KOREA

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Background and aims: S. pneumococcus (SP) is a known pathogen of invasive or non-invasive diseases in children. The introduction of protein-conjugated pneumococcal vaccine (PCV) since the year of 2000 reduced pneumococcal diseases. SP serotypes of nasopharyngeal colonization have been affected by PCV vaccination. We describe the change of SP serotypes colonized in Korean children.

Methods: Nasopharyngeal aspiration samples were obtained from children visited at Severance Children's Hospital from March 2009 to July 2012. We applied the multiplex PCR technique for the identification of pneumococci and determinations of their serotypes.

Results: Among the 2379 children enrolled, 84.2% were vaccinated with any type of PCVs and we checked vaccine type of 40.3% of them from Korean CDC databank. 19.0% of total samples were SP PCR positive and there was no difference by year (from 18.1% to 20.5%). Proportion of serotypes included PCV13 decreased from 58.9% in 2009 to 29.3% in 2012 (p-value = 0.002). Depending on the type of vaccination (PCV7, 10, and 13), SP positive rates were 22.2%, 23.5% and 17.0% respectively (PCV10 vs PCV13, p-value 0.258.). According to PCV vaccination types, 19A was present in 22.0% in PCV7, 12.5% in PCV10 and 24.0% in PCV 13 (PCV10 vs PCV13, p-value 0.365). The emerging of non-PCV13 serotypes since year of 2011 was remarkable.

Conclusion: In Korea, the overall pneumococcal carriage rate was 19.0% during recent 4 years and there was significant emerging in the serotypes not included in PCV13 after PCV10 or PCV13 implementation.

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LABORATORY DIAGNOSIS OF SEPSIS BY MULTIPLEX REAL-TIME PCR

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Bloodstream infections (BSI) are an important cause of prolonged hospitalization of infants admitted to neonatal intensive care units. Early diagnosis of sepsis and rapid and correct initial antimicrobial treatment reduces mortality. In the last decade was used multiplex Real-time PCR (Magicplex Sepsis Real-time PCR) that allows identification of 90 bacterial and fungal pathogens as well as 3 drug resistance markers (macA, vanA and vanB) directly from whole blood samples.

In this study, we aimed to assess the clinical utility of a newly available, commercial real-time PCR test in newborns with a clinical suspicion of sepsis. A total of 32 newborns were enrolled in this study. Peripheral venous blood was collected and sepsis was evaluated by bloodculture and the Magicplex Sepsis Real-time PCR assay, using 5 ml and 1 ml blood for each method, respectively. A BSI was detected in 6/32 (18.75 %) patients by blood culture or Magicplex Sepsis Real-time PCR. In six cases, both methods were in agreement. In six cases, only Magicplex Sepsis Real-time PCR identified the presence of pathogens in blood samples. In the remaining 18 cases (56.25 %), were obtained negative results by both methods. Although the Magicplex Sepsis Real-time PCR test does not provide information on antimicrobial susceptibility or microorganism viability, its results are available within 6 hours versus blood culture results obtained within72-96 hours. A more rapid obtaining of the results could reduce the inappropriate use of antimicrobial therapy, the risk of developing antibiotic resistance and hospital stay.

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THE IMPACT OF CHANGING DEMOGRAPHY ON THE HISTORY AND FUTURE OF VARICELLA-ZOSTER VIRUS EPIDEMIOLOGY IN ITALY

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Background and aims: Varicella-Zoster Virus (VZV) causes disease in two different forms: varicella (primarily in children), and herpes zoster (HZ, primarily in older adults). The epidemiology of the latter is strongly influenced by that of the former through the effect of immunological boosting, i.e. the reduction of HZ risk occurring in varicella-experienced individuals upon exposure to varicella-infectious hosts. Clearly, demographic processes play a key role in defining the population age structure and immunity profiles, and therefore in the overall epidemiology of VZV disease.

Methods: In this work, a disease transmission model informed with longitudinal demographic data on birth, death and immigration rates is used to reconstruct the changing age profile of HZ incidence in Italy in 1901-2009. The progressive immunity conferred to individuals by the exposure to varicella cases is taken into account, following Hope-Simpson's hypothesis. The model reproduces serological data of varicella and epidemiological data of HZ incidence and is used to predict the effect of different demographic scenarios on the future evolution of HZ incidence.

Results: We show that the demographic history of the population has determined changes in incidence and immunity profiles over time, with remarkable shifts in age distribution of susceptible individuals and age at infection.

Conclusions: This work supports the importance of accounting for the demographic history of populations as an important driver of epidemiological changes in infectious diseases. In particular, demography may play a key role in the assessment of the potential impact on HZ epidemiology of mass vaccination programs against varicella.

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THE ASSOCIATION OF GENETIC VARIANTS IN TOLL-LIKE RECEPTOR 2 SUBFAMILY WITH ALLERGY AND ASTHMA AFTER HOSPITALIZATION FOR BRONCHIOLITIS IN INFANCY

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Background and aims: Toll-like receptors (TLR´s) are a pivotal part of the innate immunity system. Despite of having a key role in pathogen defense, variations in TLR genes have also been connected to autoimmune conditions, such as allergy and asthma. TLR2 subfamily comprises TLR1, TLR2, TLR6 and TLR 10. We hypothesized that polymorphism of TLR2 subfamily may be associated with post-bronchiolitic asthma and/or atopy prevalence.

Methods: TLR1 rs5743618, TLR2 rs574308 and TLR6 rs5743810 SNP´s of 135 children who had been hospitalized for bronchiolitis at < 6months of age were analyzed. Present doctor-diagnosed asthma and allergic conditions were evaluated during a follow-up visit at preschool age, as well as asthma and atopy occurrence during first six years of life.

Results: Asthma was present in 17(12.6%), atopic dermatitis in 39(29%) and allergic rhinitis in 36(26.7%) children at the mean age of 6.3 years (SD). Children homozygous for the minor allele T at TLR6 rs5743810 were almost twice as likely to be present atopics (61% vs. 34% of allele C carriers, p=0.02). Further, those carrying the allele T at TLR2 rs574308 had asthma more often during first 6 years of life (41% vs. 24% of non-allele T carriers, p=0.05).

Conclusion: TLR6 rs5743810 and TLR2 rs574308 SNP´s were associated with asthma and atopy after severe bronchiolitis in infancy. Thus, TLR2 subfamily may be involved in childhood asthma.

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DEVELOPMENT OF A MENINGOCOCCAL SEROGROUP B VACCINE FOR USE FROM INFANCY THROUGH ADOLESCENCE

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Background: Availability of glycoconjugate vaccines against meningococcal serogroups A, C, W135 and Y, leaves serogroup B as the last major cause of childhood meningitis and septicaemia.

Methods and results: Novartis' investigational vaccine, 4CMenB, recently received a positive opinion from the CHMP following evaluation in 4,843 infants/toddlers and 1,584 adolescents/adults. Schedules studied include three (2,3,4 or 2,4,6) and two (6 to 11 months) dose infant series, all with booster in the 2nd year of life. Toddlers (12-23 months) received two doses 2 months apart, and adolescents (11 to 17 years) two doses 1 to 6 months apart. 4CMenB is highly immunogenic in these schedules, inducing protective antibody levels (serum bactericidal activity titres ≥ 4 with human complement, hSBA) against serogroup B strains expressing vaccine antigens in > 95% of vaccinated cohorts. Although antibody levels wane, a booster response has been demonstrated in all groups where studied. Estimated coverage against serogroup B strains in different European countries using the MATS technique, predicts protection against 78% of all Men B strains.

Generally well tolerated, 4CMenB has been shown to induce incremental increases in local and systemic reactions typical of paediatric vaccinations, notably fever, when administered concomitantly with routine vaccines. In clinical studies prophylactic paracetamol was found to significantly decrease reactions in infants, with no clinically significant impact on immunogenicity of 4CMenB or concomitant routine vaccines.

Conclusion: The innovative candidate vaccine, 4CMenB, offers a potential solution to the unmet medical need of protection against meningococcal serogroup B disease in all paediatric age groups.

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CAT SCRATCH DISEASE WITH BONE INVOLVEMENT IN PEDIATRIC CASES

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Background: Cat-scracht disease (CSD) caused by Bartonella henselae is usually a self-limited lymphadenitis among children. Rarely, a focal osteomyelitis is the first expression of disease.

Methods: During 2010 to 2012 four children were diagnosed with atypical CSD. Epidemiological, clinical and laboratory data are described.

Results: Four children from 2 to 15 years old are reported. Three children had contact with cats and one had contact with dogs. All of them had an indolent (>2 weeks) semiology of local pain, three children had fever and one had multiple cervical adenopathies and splenomegaly. MRI revealed osteomyelitis of dorsal vertebraes in two children, of clavicle in one and bilateral iliac osteomyelitis and right sacroiliac arthritis in other. Clinical diagnosis was confirmed in all of the patients by seroconversion demonstrated by the appearance or increasing levels of IgM and IgG antibodies against B. henselae. In one patient diagnosis was also confirmed by molecular detection of B. henselae in a bone biopsy. They all made different antibiotic schemes: cotrimoxazole and gentamicin in one case; rifampicin was added to ciprofloxacin or azitromycin or doxycicline in others. Duration of treatment varied between 4 and 10 weeks,with full clinical recovery.

Conclusion: Bone infection is rare but should be considered when bone pain and fever are present in patients with epidemiological context or nodal CSD. Laboratory diagnosis by serological or molecular methods are essential to confirm the diagnosis and differentiate from other serious disorders that CSD may mimic. Antibiotic treatment type and duration still a controversial issue.

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FEVER, RASH AND ARTHRALGIA: WHEN THE DIAGNOSIS IS NOT INFECTIOUS

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Background and aims: Serum sickness-like reactions (SSLR) in children after the administrations of antibiotics, although rare in clinical practice, has long been identified. The main purpose of this study was to assess the importance of considering diagnosis of SSLR in childhood.

Methods: Review of the cases of SSLR admitted to our unit between 2002 and 2012. The diagnosis was based on clinical findings, exclusion of infectious etiology and history of exposure to antibiotics (about two weeks before).

Results: Six children, aged from 15 months to 17 years (median age 3), were observed at emergency department with fever, pruritic rash and arthralgia/arthritis. None presented enanthem. Epstein-Barr virus, citomegalovirus, parvovirus B19, enterovirus, influenza, adenovirus, Mycoplasma, Chlamydia and Streptococcus pyogenes infections were excluded. All the patients had been exposed to an antibiotic within 7 to 21 days (median 12.5 days) before the admission: amoxicillin-clavulanate (2), amoxicillin (2), cefaclor (1) and minocycline (1). Mild proteinuria was present in one-third of the children, serum complement levels were abnormal in one of the cases and circulating immune complexes were negative. All were treated with antihistamines, 2 with a non-steroidal anti-inflammatory drug and 4 needed a short course of glucocorticoids.

Conclusions: Although there may be analytic alterations like hypocomplementemia or renal dysfunction, their absence does not exclude this diagnosis. In most cases, the diagnosis is clinical, with the characteristic pattern of rash, fever and arthralgia, and can be confirmed after the exclusion of infectious causes.

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PERSISTENCE OF ANTIBODIES 18-24 MONTHS AFTER ADOLESCENT IMMUNIZATION WITH 1-3 DOSES OF A MULTICOMPONENT MENINGOCOCCAL SEROGROUP B VACCINE

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Background: Having previously demonstrated the immunogenicity and tolerability of 1, 2 or 3 doses of the investigational, multicomponent serogroup B meningococcal vaccine, 4CMenB, in 11−17 year-olds, we examined antibody persistence two years later.

Methods: Participants in this extension study provided another blood sample 18−24 months after their last immunisation, to assess serum bactericidal activity with human complement (hSBA) against three serogroup B strains representative for individual vaccine antigens - factor H binding protein, Neisserial adhesin A and New Zealand strain outer membrane vesicles (NZOMV) - in comparison with age-matched 4CMenB-naïve controls.

Results: 666 adolescents from the original study (mean age 16 years), and 151 vaccine-naive subjects (mean age 15.6 years) provided blood samples. Originally, one month after one dose of 4CMenB 93−96% of subjects had seroprotective hSBA titres (≥ 4), and these proportions increased to ~100% in those who received two or three doses over 1−6 months. When assessed 18−24 months after their last dose of 4CMenB titres had waned such that 62−73% had seroprotective titres after one dose, while 77−94% maintained protective levels after two doses, compared with 86−97% after three doses; only proportions with titres against NZOMV were significantly different (77% vs. 90% for 2 vs. 3 doses, $p < 0.0001$). Proportions of vaccine-naive controls with hSBA ≥ 4 were 50%, 25% and 40%, respectively.

Conclusions: These results confirmed that two 4CMenB doses, 1-6 months apart, can provide a high level of protection against serogroup B that is sustained over two years in the majority of adolescents.

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DOSING OF FREQUENTLY USED ANTIBIOTICS IN EUROPEAN NICUS: POINT PREVALENCE STUDY OF EUROPEAN STUDY OF NEONATAL EXPOSURE TO EXCIPENTS (ESNEE)

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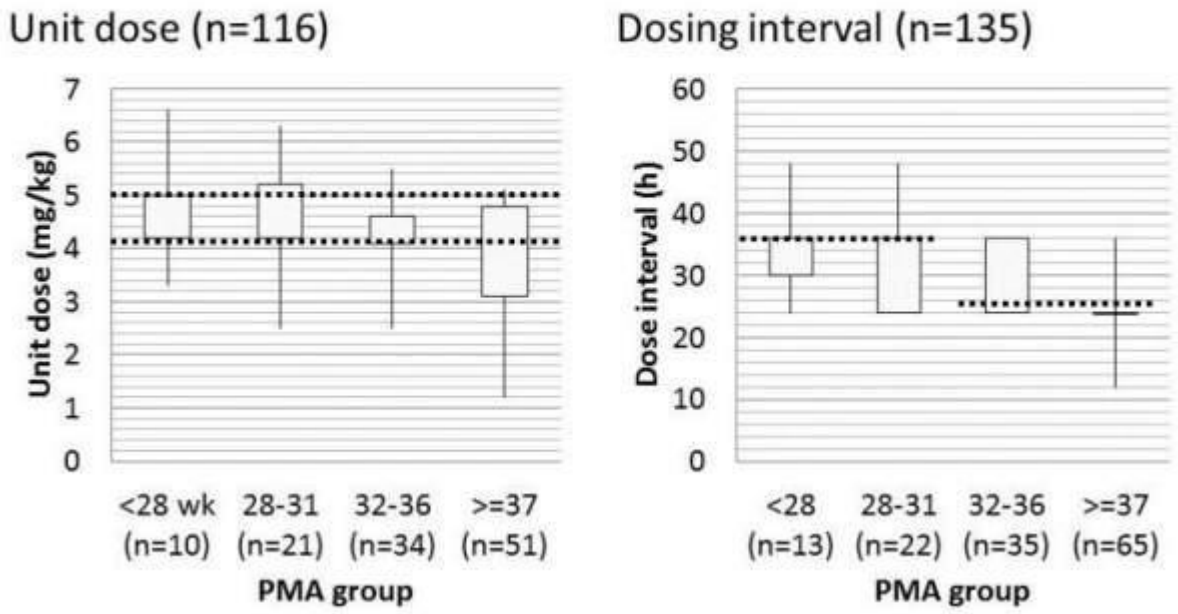
Background and aim: Little is known about dosing of the most frequently used drug class, antibiotics, in neonates. This analysis aimed to study dosing variations of frequently used antibiotics in European NICUs.

Methods: A point prevalence study reaching out to as many European NICUs as possible was performed. Demographic data of neonates receiving any drug on the study day morning chosen within one of three two-week study periods from January to June, 2012, and the dosing regimen and route of administration of each prescription was recorded.

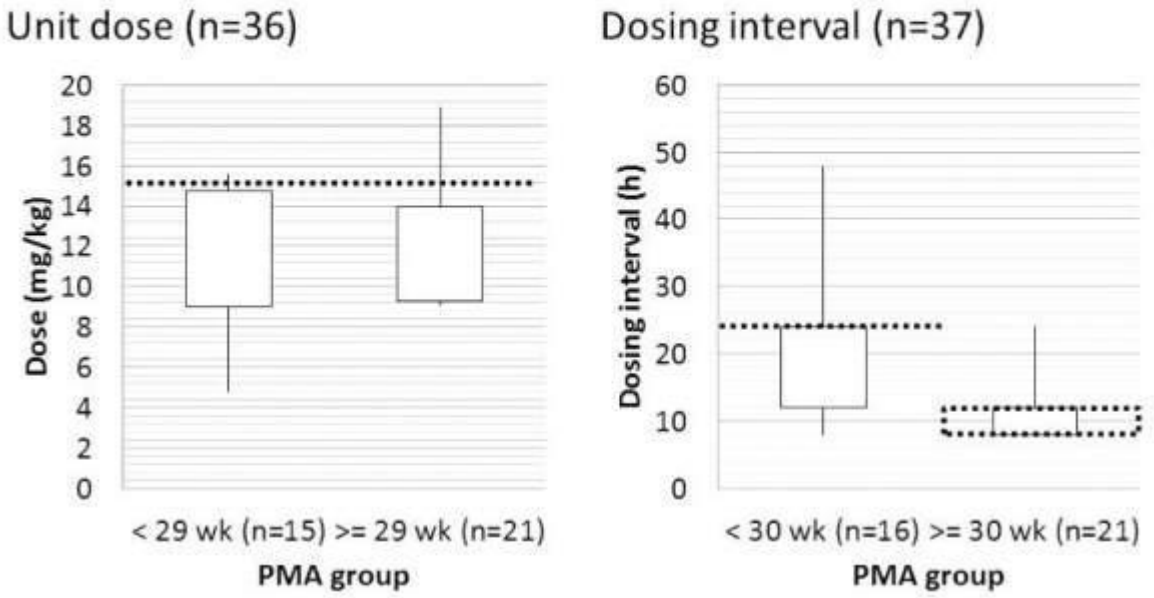
Results: In 21 countries 72 hospitals 824 neonates participated. Gentamicin, ampicillin, penicillin and vancomycin were used most frequently - in 138; 82; 73 and 36 neonates in 41; 31; 23 and 18 hospitals, respectively. Variability of gentamicin and vancomycin dosing by postmenstrual age is shown on Figures 1 and 2. Ampicillin was given in a median (IQR) dose of 52 (49;78); and penicillin 43 (30;51) mg/kg at median intervals of 12 (8;12) and 12 (12;12) h, respectively.

Figure 1. Gentamicin dosing in European NICUs. Data are presented as quartile range, min and max for dose and interval. BNFC recommended dose range and intervals are shown in dotted lines.



[Figure 1]

Figure 2. Vancomycin dosing in European NICUs. Data are presented as quartile range, min and max for dose and interval. BNFC recommended dose and intervals are shown in dotted lines.



[Figure 2]

Conclusion: While doses of gentamicin are within recommended ranges, the doses of penicillins are almost double of those in BNFC (30 and 25 mg, respectively). Vancomycin is given below recommended unit dose to ¾ of neonates. Variations in the dosing may rise from adjustments due to therapeutic drug monitoring of gentamicin and vancomycin but also from different recommendations in frequently used neonatal drug information sources.

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HIGH ANTI-RSV ANTIBODY LEVELS IN PATIENTS WITH SEVERE RSV MONOINFECTIONS

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Background: The clinical course of Respiratory Syncytial virus (RSV) infections varies from a mild cold to the necessity of mechanical ventilation. Although several risk factors are known, this does not fully explain why disease severity varies among young infants. We hypothesize that levels of anti-RSV antibodies present during primary infection and their neutralizing capacity play a role in the development of disease severity.

Methods: Blood and nasopharyngeal washings (NPW) were obtained from infants < 6 months of age with a RSV monoinfection. Based on the level of supportive care patients were allocated into a mild (none), moderate (supplemental oxygen and/or nasogastric feeding) or severe (mechanically ventilation) group. The levels of IgG directed against RSV were determined by ELISA in plasma and NPW. Subsequently, the neutralizing capacity of plasma on fluorescent rgRSV A2 infected HeLa cells was measured.

Results: Forty-one infants (54% male) were included. Mean age did not differ among the severity groups. Premature birth (n=4) or breastfeeding did not affect mean RSV specific IgG levels. The level of IgG correlated with postnatal age ($r=-0.5$, $p=0.001$). Plasma IgG levels were higher in the severe group compared to the mild and moderate group ($p< 0.05$). This difference was not seen in NPW samples. No difference was seen in neutralizing capacity of plasma between the severity groups.

Conclusion: In children with severe RSV mono-infections higher mean RSV specific IgG levels are found. This might indicate that the presence of high levels of (maternal) RSV specific antibodies positively influence severity of disease.

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HIGH PROPORTION OF MANNOSE BINDING LECTIN (MBL) DEFICIENCY IN CHILDREN LESS THAN 2 YEARS OLD WITH INVASIVE PNEUMOCOCCAL DISEASE

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Background and aims: MBL is a serum protein of the innate immune system whose deficiency is observed in 15-25% of all human populations. Our objective is to evaluate the association of MBL deficiency in patients with invasive pneumococcal disease (IPD) according to age group and clinical manifestations

Methods: Prospective study including all patients with IPD (children and adults) in two Catalan Hospitals (period February/2011-October/2012). Demographic and clinical variables were registered. Immunocompromised patients or those with anatomic anomalies that predispose to meningitis were excluded. IPD was defined as isolation of S.pneumoniae or DNA detection by RT-PCR in any sterile fluid. Genotypic study of the MBL2 gene was performed and patients were classified as sufficient or insufficient MBL levels.

Results: 127 patients had IPD, 6 refused to participate. 69(57%) were male. 26(21.5%) were < 2 years of age, 35(28.9%) between 2-5yr and 60(49.5%) >5yr. Most frequent serotypes were 1(21.5%), 3(14%) and 19A(9.1%). Overall MBL deficiency was observed in 15.7% (IC95%,8.8-22.5) of patients but significant differences were observed comparing children < 2yr. vs. other patients (30.8% vs. 11.6%,P=0.02). Most frequent IPD was pneumonia 82.6%(IC95%,75.4-89.8) but a significant higher proportion of meningitis was observed in children < 2yr. vs. others (23.1% vs. 6.3%; p=0.01). MBL deficiency was more frequent in patients with meningitis vs. others (21.1% vs. 7.8%; p=0.07).

Conclusions: MBL deficiency is highly prevalent in children younger than 2 years with IPD. Additional studies are needed to evaluate this fact.

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IMMUNOGENICITY AND REACTOGENICITY OF TWO-DOSE VACCINATION WITH INVESTIGATIONAL MENINGOCOCCAL B RECOMBINANT VACCINE AT 24 AND 26 MONTHS OF AGE

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Background: Previous studies of the investigational multicomponent serogroup B meningococcal vaccine, 4CMenB, demonstrated that three doses in infants from 2 months of age with a booster at 12−13 months, or two doses in 12−15 month-old toddlers, elicit protective antibody responses through 2 years of age. We report immunogenicity and reactogenicity of two doses of 4CMenB administered to vaccine-naive 2 year-olds (NCT01139021).

Methods: Participants received 4CMenB at 24 and 26 months of age, and were assessed for serum bactericidal activities with human complement (hSBA) against serogroup B strains representative of vaccine antigens - factor H binding protein (fHbp), Neisserial adhesin A (NadA), Neisseria heparin binding antigen (NHBA) and New Zealand strain outer membrane vesicles (NZOMV) before, 1 and 6 months after vaccination. Parents completed diary cards.

Results: Of 116 enrolled subjects (24.7 ± 1.4 months), 112 were vaccinated. Before vaccination 3%, 1%, 26% and 0% displayed seroprotective hSBA titres (≥ 5) against fHbp, NadA, NHBA and NZOMV, respectively. One month after the second dose, these proportions were 100%, 99%, 97% and 98%, respectively, and were 93%, 96%, 70% and 18% after 6 months. Although elevated, reactogenicity was transient and lower than seen in infants, and mainly local: 97% of subjects had injection site tenderness (25% cried when limb moved), 39% had temperature ≥38°C (one case ≥40°C). There were no vaccination-related SAEs.

Conclusions: Two 4CMenB doses administered two months apart to 2 year-olds induced immune responses against all antigens in the majority of subjects, with reactogenicity consisting mainly of injection-site reactions.

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IS THERE A LINK BETWEEN INFLUENZA-ASSOCIATED ENCEPHALOPATHY AND HUMAN HERPES VIRUS 7?

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Background and aims: The pathogenesis of influenza-associated encephalopathy is not clear. It is controversial whether the influenza virus invades the brain parenchyma. An association with human herpes virus 7 (HHV7) co-infection has been suggested previously.We describe a case of influenza-associated encephalopathy and HHV7.

Methods: We used data collected from our patient´s hospital file on December 2012, during epidemic seasonal influenza in Portugal (H3N2 virus).

Results: We report a 12-year-old male patient who presented severe acute behavioural disturbance, characterized by agitation, mental confusion, incoherent speech, sexual disinhibition and hetero-aggressiveness alternating with apathy, 3 days after fever, frontal headaches and vomiting. He had been vaccinated with Pandemrix® in 2010. Toxic screen was negative. CSF analysis showed 21 cells/µL, 100% lymphocytes with IgG oligoclonal bands. Brain MRI showed multifocal parenchymal lesions in cerebral cortex and subcortical white matter, thalami, brainstem and cerebellar peduncles The EEG revealed diffuse intermittent delta activity, more evident on frontal leads. Real time PCR in CSF was positive to HHV7 and negative to influenza virus but blood serologic tests for Influenza A ELISA IgG +, IgM+ were positive. Antipsychotics drugs and oseltamivir were administered. The outcome was excellent with no neurologic sequelae.

Conclusion: Influenza-induced inflammatory response and HHV7 co-infection may participate in the pathogenesis of meningoencephalitis. We can speculate that the encephalitis could result either from a dual infection of influenza virus and HHV-7 or a latent infection with HHV-7 in central nervous system could be reactivated by influenza virus infection.

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INVASIVE MENINGOCOCCAL DISEASE: THE USE OF POLYMERASE CHAIN REACTION TO INCREASE DIAGNOSTIC ACCURACY

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Background and aims: Invasive meningococcal disease (IMD) remains a serious public health problem. Bacteriological confirmation and serogroup determination is important for contact management, outbreak recognition and detailed epidemiological surveillance. Although culture is the gold standard, previous antibiotic therapy reduces its sensibility. The aim of this study is to assess the utility of polymerase chain reaction (PCR) to increase diagnostic accuracy of IMD.

Methods: Retrospective study of all children younger than 16 years with microbiologically (positive culture and/or PCR) confirmed IMD, admitted to our hospital between 2004-2012. PCR and culture were performed concomitantly in all cases.

Results: Seventy-five patients were included, median age was 3.1 years; 62.3% were male. Serogroup distribution was: B=86.7%; C=5.3% and Y=1.3% of cases. Almost 7% were caused by non serogroupable Neisseria meningitidis. Fifty-two percent of patients presented with sepsis, 30.7% with meningitis, and 17.3% with both of them. Forty-six patients had a positive culture and four of these had a negative PCR. Seventy-one patients had a positive PCR (29 with negative culture). Previously administered antibiotic was documented in 40 patients, 16 of these were confirmed by PCR only, but this was not significantly different from patients without previous antibiotic (p=0.11).

Conclusions: PCR was the only test providing evidence for IMD diagnosis and serogroup determination in 38.7% cases. Our study failed to show the association between previous antibiotic therapy and the usefulness of PCR, possibly due to the low number of patients included. The concomitant use of both techniques yields the best results in IMD diagnosis.

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BARTONELLA VERTEBRAL OSTEOMYELITIS

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A previously healthy ten-year-old boy is investigated for febrile back pain.

Five days after the back pain, fever appeared and he started to limp. Physical examination reveals Lasegue's sign (40°). C-Reactive-Protein is 36 mg/l, fibrinogen is 5.5g/l, white blood cells are 9500/mm3 with 67% of neutrophils. Bone scintigraphy shows hyperfixation on the fourth lumbar vertebra. Spinal MRI is performed at day 8 : it shows spondylitis of L4, intraspongious abscess of 7mm with possible cauda equina syndrome and inflammation of peri-lesional soft tissues. Medical treatment is initiated at day 5 by intravenous antibiotics (cloxacillin).

There is no surgical indication.

Fever is prolonged and biological results become worse (C-Reactive-Protein 73 mg/l, Fibrinogen 9,7 g/l). Blood cultures are sterile. At day 13, antibiotic therapy is changed to cefazolin and rifampicin. Pain resolves within 3 days, apyrexia is noted at day 18 and biological results improve gradually.

At day 25, serological analysis for Bartonella henselae is strongly positive. Treatment with ciprofloxacin and rifampicin is introduced for 6 weeks. Evolution is good.

Unusual but classic diagnosis of Bartonella henselae infection should be considered in children spondylitis.

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HETEROGENEOUS DIFFERENTIATION PATTERNS OF INDIVIDUAL CD8$^+$ T CELLS

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Upon infection antigen-specific CD8$^+$ T cell responses display a highly reproducible pattern of expansion and contraction that is generally assumed to reflect a uniform behavior of individual naïve T cells. To investigate this assumption we have tracked the progeny of individual CD8$^+$ T cells by in vivo lineage tracing and demonstrate that individual T cells follow highly heterogeneous differentiation patterns. First, even for T cells bearing identical T cell receptors, clonal expansion and differentiation vary considerably. Second, T cell diversification upon primary antigen encounter leads to stable clonal dominance during recall infections. The observation that the fate of individual naïve T cells is highly discordant suggests a division of labor between the progeny of individual naïve T cells and demonstrates that reproducibility of CD8$^+$ T cell responses is only achieved at the population level.These findings have important implications for the rational design of vaccines to infectious diseases.

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BLOOD CONCENTRATIONS OF METHYL AND PROPYL PARABENS IN NEONATES, TREATED WITH GENTAMICIN AS THE MOST COMMONLY USED ANTIBIOTIC

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Background: Methyl- and propylparaben as antimicrobial agents are widely used preservatives in medicines administered to neonates including some formulations of gentamicin. Hyperbilirubinaemia and hypersensitivity reactions following injection of paraben-containing preparations have been reported. Their acceptable daily intake has been established for adults but for neonates no data on safe concentrations exists.

Aims: To evaluate the blood levels of methyl- and propylparabens in neonates treated with gentamicin formulation.

Methods: Subanalysis of data from a multicentre study including neonates treated with gentamicin in an Estonian neonatal unit was performed. Paraben concentrations were measured by HPLC/MS in dried blood spots collected from each neonate at different time points aiming to cover the entire dosing interval. All participants were followed up for adverse drug reactions.

Results: A total of 46 samples from 13 neonates with mean (SD) gestational age of 35.2 (3.8) weeks and birth weight of 2317 (780) grams were studied. No additional sources of parabens were identified in the study population. Measurable methylparaben concentrations varied between 20 to 109 ng/ml (median 31 ng/ml, IQR 22,5-38) with 15 (33%) samples below the limit of quantification (LOQ) of 20 ng/ml. Only one sample had propylparaben concentration above the LOQ (20 ng/l) - 117 ng/ml. No adverse drug reactions occurred.

Conclusions: These exploratory data suggest that concentrations of methyl- and propylparabens in neonates treated with gentamicin are at low levels and likely to be safe. However, larger PK/PD studies are needed to establish accurate safety limits for neonates of various degree of maturity.

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Q FEVER OSTEOMYELITIS - CASE REPORT

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Introduction: Q fever is a worldwide zoonosis caused by Coxiella burnetii. It is a rare disease in children and the clinical presentation is variable. We present a rare case of chronic Q fever with osteoarticular involvement.

Case report: A six year-old-girl presented to the hospital with a three months history of pain and functional impairment in the right knee. She denied fever. The patient had contact with farm animals. At presentation she was apyrexial and showed only discrete inflammatory signs of the right knee. A magnetic resonance imaging revealed signs of osteomyelitis of the right distal femur and epiphysis. Histological analysis showed noncaseating granulomas. Cultures for bacteria and fungi, including atypical mycobacteria were negative. Results of Mantoux, granulomatosis study and serologic tests for Borrelia burgdorferi, Bartonella spp and Francisella tularensis were also negative. Chronic Q fever was suggested by the presence of antibody titters anti-C. burnetii phase I IgG of 6400 and IgA of 200, although PCR from femur biopsy and blood sample were negative. No C. burnetii growth was achieved by buffy-coat inoculation in cell cultures. Antimicrobial therapy with rifampicin and ciprofloxacin was started. The patient has now nine months of treatment with progressive clinical recovery and gradual decrease in antibody titers (with phase I IgG=1600 and IgA=50 in last IFA evaluation).

Comments: Q fever osteomyelitis is a rare diagnosis in children. The choice of antimicrobial treatment is difficult regarding limited data available. Duration of therapy must be guided by clinical and serologic responses.

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EPIDURAL ABSCESS CAUSED BY SCEDOSPORIUM APIOSPERMUM IN AN APPARENTLY IMMUNOCOMPETENT CHILD

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We report the case of a 7-year old boy without any known risk factors who presented with low grade fever, severe headache, back pain and stiffness 5 months after hurting his back on a tree stump. At the time of injury a superficial external wound in the lumbar area was stitched. Back pain and rachis stiffness appeared the week following the trauma. Both disappeared. The symptoms insidiously reoccurred. Five months post-trauma, the symptoms worsened with a lethargic state. An urgent spine MRI revealed an epidural abscess at L2-L3 level. He was managed with intravenous therapy including Ceftriaxone, Vancomycine and Metronidazole and referred to our centre for further management. Surgical debridement was performed with extraction of three pieces of wood in the muscular and epidural area at L2 level responsible for compression of the dural sac, drainage of the muscular mass abscess regarding to L3-L4, and debridement of the necrotic tissues. Scedosporium apiospermum grew on several specimens. Voriconazole was initiated and dosages were adapted according to serum level. The patient developed chronic meningitis and hydrocephalus requiring ventriculoperitoneal shunt. Immunologic study including complete phagocytic function was normal. After one year of antifungual treatment, despite a Voriconazole-induced photosensitivity, he is now asymptomatic and the control MRI shows reduction of meningeal enhancement. We decided to empirically stop the therapy and to follow clinically.

Central nerve system scedosporiosis remains rare and difficult to treat. To your knowledge this is the first case of a child described in the medical literature with such presentation.

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TRENDS IN THE EPIDEMIOLOGY OF BLOODSTREAM INFECTIONS AT A MAJOR EUROPEAN PEDIATRIC CANCER CENTER

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Background: Little data exist on the current epidemiology of bloodstream infections (BSI) in pediatric patients with cancer and/or hematopoietic stem cell transplantation (HSCT).

Methods: In a single-center, retrospective study, we analyzed all BSI in children and adolescents with cancer and/or allogeneic HSCT and compared the time periods 2000-2004 and 2006-2010. All pts. received MRSA-Screening, twice weekly TMP/SMX and non-absorbable polyenes. Quinolone prophylaxis was restricted to allo-HSCT pts., and systemic antifungal prophylaxis to pts. with AML, recurrent leukemia, and allo-HSCT.

Results: 446 BSI were observed in 289 pts. (55% male; median 8 yrs; 59.2% hem. malignancies, 35.6% solid tumors, 5.6% other; 24.9% s/p allo-HSCT; 23.6% recurrent cancer; 96.7% with indwelling permanent catheter). There was a significant increase in BSI over time from 32 to 46.7 /1000 discharges and from 5.6 to 8.4 /1000 inpatient days, respectively ($p< 0.001$) with a predominance of Gram-positive organisms (75.8%; Gram-negative, 22.3%; Candida spp., 1.9%; no trends). Coagulase-neg. staphylococci were most frequent (41.5%), followed by viridans streptococci (8.1%), Pseudomonas spp., E.coli (6.7% each). While MRSA and glycopeptide-resistant enterococci were not observed, ESBL producers and multiresistant E.coli and P.aeruginosa emerged in the second period (from 0% to 3.9, 1.4 and 1.4%, respectively ($p< 0.001$)). 31.5% of catheters were removed, and 5.5% of episodes resulted in ICU transfer. The 30-day overall mortality rate was 6% without trend.

Conclusions: This analysis documents a significant increase in the incidence of BSI and the emergence of resistant Gram-negative organisms in pediatric cancer/HSCT pts. receiving care at a major European treatment center.

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FREQUENCY OF DETECTION OF CLOSTRIDIUM DIFFICILE IN FECAL SAMPLES FROM CHILDREN WITH COMMUNITY-ACQUIRED DIARRHOEA IN NORTH-EASTERN PART OF POLAND

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Background and aims: C. difficile is emerging as a possible pathogen for community-acquired diarrhoea in children.

Methods: Prospective study was conducted in 491 children with community-acquired diarrhoea and in 137 patients without diarrhoea. Exclusion criterion was hospitalisation during 12 weeks prior to diagnosis.

Results: C.difficile was significantly more common in stool of children with diarrhoea (166/491; 33.8%) that without diarrhoea (33/137; 24.1%) (p=0.0306). Significant differences in C. difficile occurence were found in children divided according to age groups (in 1-2 y.o. 41/116 [35.5%] children with diarrhoea and 4/31 [12.9%] children without diarrhoea; p=0.0160; in 2-3 y.o. 22/57 [38.6%] children with diarrhoea and 4/26 [15.4%] children without diarrhoea; p=0.0345). Analysis of other age groups did not show significant differences in C. difficile occurence (p>0.05). C. difficile was found with similar frequency in children with diarrhoea who were and were not previously treated with antibiotics (106/298; 35.6% and 60/193; 31.1%; p=0.3051). Gender, place of residence and previous nursery/kindergartens/school attendance vs. staying only at home did not influence C. difficile infection. In 66/166 (39.8%) C. difficile was concomitant to other enterpathogens (in 26 cases other bacteria were found- Salmonella, EPEC, Klebsiella, S.aureus; in 33 patients viruses were present- Rotavirus, Adenovirus; and in 7 children both viruses and other bacterias were noted). In 100/166 (60.2%) Clostridium difficile associated diarrhoea diagnosis was made.

Conclusions: C.difficile could be important etiological agent of community-acquired diarrhoea in children and therefore routine screening for this pathogen should be conducted, despite previous antibiotics exposure or lack thereof.

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SPECTRUM OF RESISTANCE IN CONFIRMED PEDIATRIC BACTERIAL INFECTIONS

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Backgroud and aim: Bacterial infections are a constant threat to people's health in the era of antibiotic resistance. This impact seems to be more intense in poor-resource countries and in medical systems without national guidelines for infection treatment. The aim of this study was to evaluate the burden of resistance in confirmed bacterial infections in children.

Material and method: Retrospective analysis of data from centralized electronic files of our hospital, during one year [2011] was performed.

Results: During one year 32172 children were presented and 7783[24.19%] were admitted. Infection was suspected in 37.86%. 12180 cultures were performed. 35.53% were targeting potentially severe infections. 7753 samples of upper-respiratory tract [nasal and throat swabs] were excluded from this study.

15.9% documented positive results with 687 bacterial-proven episodes. 23%[158] were UTI's, 56.62%[389] enteritis, 12.22%[84] endotracheal samples and 2.48%[17] septicaemia.

Spectrum of pathogens identified: 68.27%[469] E.coli, 6.1%[42] Klebsiella, 13.68[94]% Pseudomonas, 7.28%[50] Salmonella spp, 2.76%[19] Proteus and 1.75%[12] other bacteria.

36.83%[253] of isolates were resistant. 32.81%[83] of resistant bacteria were ESBL bacilli. Klebsiella spp presented highest resistance patterns, 61.91%[26] being ESBL. There were 11[4.35%] XDR-isolates [4E.coli and 7Pseudomonas aeruginosa], only Colistin-sensitive.

Discussion: Bias can be generated by national regulations, because children with potentially-contagious diseases should be referred to PID-clinic.

Conclussions:

1. More than 1/3 of proven bacterial infections in our patients were generated by antibiotic-resistant strains.

2. Klebsiella is a multi-resistant pathogen with a worrisome pattern in recent years, 62% being ESBL-bacilli.

3. 4% of resistant isolates have extreme features, being only Colistin-sensitive.

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SIDEROPENIC ANAEMIA AS A SECONDARY DISEASE AT VARIOUS INFECTIONS IN CHILDREN

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The body needs iron to make hemoglobin. If there isn´t enough iron available, hemoglobin production is limited, which in turns affects the production of red blood cells (RBCs). A decreased amount of hemoglobin and RBCs in the bloodstream is known as anemia. Because RBCs are needed to carry oxygen throughout the body, anemia results in less oxygen reaching the cells and tissues, affecting their function.

Aim of the study: To present the patients with sideropenic anaemia associated with other diseases.

Material and methods: In our study we have included 200 children of different group-ages with sideropenic anaemia hospitalized in Hemato-Oncology Department of Pediatric Clinic. The diagnose is made based on history, physical examination and laboratory data.

Results: Anemia associated with any other disease was present in 117 cases (58.5%) while as the main disease was present in 83 cases (41.5%). Sideropenic anaemia as a main disease has showed significant difference (Chitesti = 5.78). In the total number of our patients with sideropenic anaemia the most frequent associated diseases were gastrointestinal diseases with 30 cases (25.6%), followed by respiratory diseases in 27 cases (23.1%), haematological disease with 21 cases (17.9%), with urogenital disease 13 cases (11.1%), cardiovascular diseases with 5 cases (4.3%) and malnutrition with 4 cases (3.4%).

Conclusion: The most common diseases that have followed sideropenic anaemia were respiratory infections, gastrointestinal and hematological diseases. Repeated infections has an impact on the appearance of sideropenic anaemia in children.

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POSTINFECTIOUS ENCEPHALITIS AFTER PEDIATRIC HERPETIC ENCEPHALITIS TREATED WITH INTERFERON. WHAT IS THE TRIGGERING FACTOR?

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Background: Postinfectious encephalitis (PIE) is an immune process caused by deregulation of the immune system following infection or immunization. Acute secondary neurological deterioration after herpes simplex encephalitis has been reported.

Methods: We discuss a case of PIE following herpetic encephalitis treated with interferon after respiratory infection and live vaccination.

Results: 12 month-old otherwise healthy child presented with vomiting, fever, tonic seizures, altered state of consciousness (Glasgow 8) and left hemiparesis. MRI showed multiple cortical lesions in temporal, parietal and occipital lobes. PCR HSV-1 in CSF was positive. Acyclovir was started on D2 (21 days) and per protocol interferon alfa-2b on D3 (10 days) without complications. She was discharged clinically asymptomatic with prophylactic acyclovir and antiepileptic drugs.

Two weeks later she had an upper respiratory infection. Also, live attenuated MMR vaccination was undertaken. Five weeks after herpetic encephalitis, she revealed irritability alternated with sleepiness, no interest on interacting, superior left limb and cervical choreiform movements, axial ataxia and stereotypies. Electroencephalography showed paroxysmal right predominant bifrontal activity. MRI showed deterioration of previous abnormalities with extensive white matter lesions, suggesting possible immune-mediated demyelization. PCR HSV-1 and measles in CSF were negative but oligoclonal bands in serum and CSF were found. She was treated with corticosteroids and human immunoglobulin with both clinical and imagiological improvement.

Discussion: An immune mediated process better explains the pathogenesis of this relapse. It may be due to the herpetic encephalitis itself or induced by interferon treatment, but viral infection or live vaccination cannot be overruled as triggering factors.

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LATE DIAGNOSIS OF CONGENITAL TOXOPLASMOSIS AFTER REACTIVATION OF INFECTION DURING PREGNANCY OF A HIV1-INFECTED WOMAN

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Background and aims: Congenital toxoplasmosis is a major public health problem. Serological testing reliably identifies transmission to infants from mothers infected in pregnancy. However, serology sometimes fails to detect reactivation of infection in immunocompromised women and therefore delays diagnosis in their offspring.

Methods and results (Case report): A late preterm developed a severe sepsis-like picture during the neonatal period without identification of any pathogen. Clinical response to broadspectrum antimicrobial therapy was poor, but symptoms finally resolved. Despite fever and high anti-T. gondii IgG in the HIV-positive mother, who needs haemodialysis for endstage HIV-nephropathy, no reactivation of toxoplasmosis was suspected, because of concomitant pneumonia and infection of her dialysis catheter. On a follow-up visit at three months of age to exclude HIV transmission in the infant, an afebrile seizure was reported. Now, anti-T. gondii-IgM was positive and although fundoscopy and EEG were normal, MRI showed pathological findings.

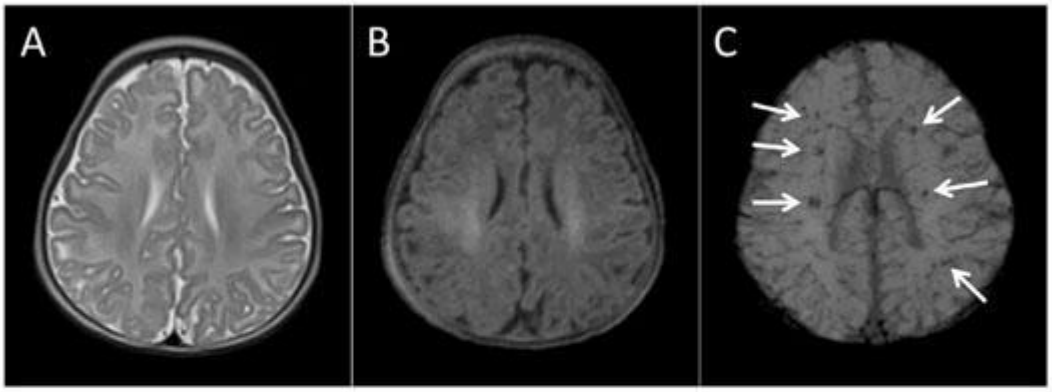

Figure X
T2- and T1-weighted images (**A**: T2, TR/TE: 7500/89 ms; **B**: T1 MPRAGE, TR/TE/TI: 2280/3.6/1000 ms) in transversal orientation at the level of the centrum semiovale show a normal myelination for a 3-months old infant, no focal lesions are detected. Susceptibility-weighted Imaging (**C**: SWI, TR/TE: 58/40 ms) reveals multiple focal hypointense lesions in the centrum semiovale consistent with microcalcifications (arrows; interpretation as calcification is confirmed by SWI phase images, data not shown).

[MRI]

Lumbal puncture revealed intrathecal anti-T. gondii antibody production and retrospectively, there was serological evidence for reactivation of infection in pregnancy in stored plasma samples with positive T. gondii-PCR in mother and child at time of delivery.

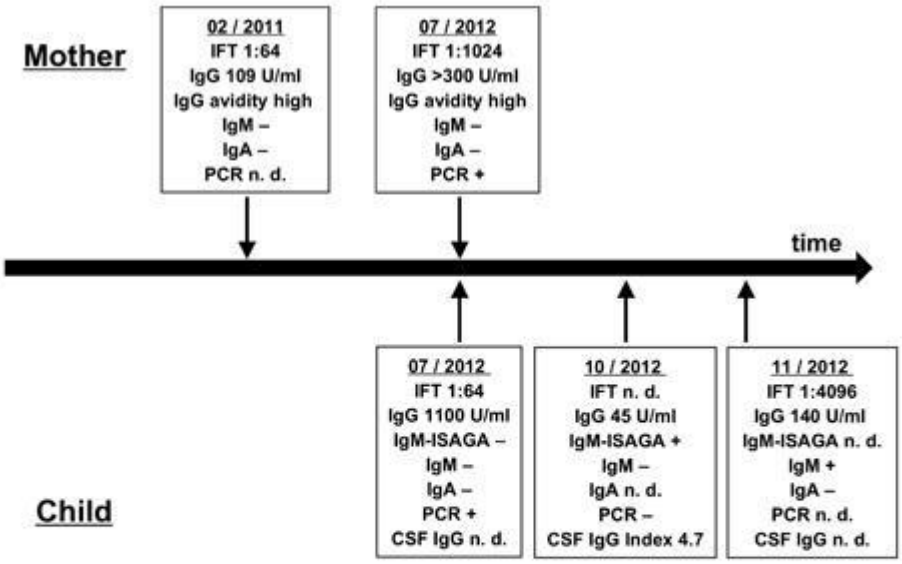

Fig. 2 Time courses in the antibody responses of mother and child.
Reactivation of toxoplasmosis in the mother at the date of birth (7 / 2012) was retrospectively diagnosed by significant increases in the IFT and IgG antibody titers and by positive PCR in the plasma. The child displayed a high maternal IgG-titer without reactivity for IgM or IgA at the date of birth. However, retrospectively, also serum of the child was revealed to be positive in the PCR at this time point. IgM antibodies of the child were first detected in 10 / 2012 by IgM-ISAGA, when the child had already developed signs of congenital neurotoxoplasmosis accompanied by a positive CSF IgG Index. Along with the appearance of IgM the filial IFT titers significantly increased between the date of birth and 11 / 2012. The IgG antibody response first decreased significantly (loss of maternal antibodies between 07 and 10 / 2012) and then stabilized at an intermediate level. (n. d.; not determined)

[time arrow]

Currently, the HIV-negative child receives pyrimethamine plus sulfadiazine and is clinically doing well.

Conclusion: High anti-T. gondii IgG without positive IgM or IgA in immunocompromised pregnant women should be taken serious and repetitive microbiological testing of the offspring should be mandatory.

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RHOMBOENCEPHALITIS BY LISTERIA IN AN IMMUNOCOMPETENT CHILD

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Introduction: Meningoencephalitis by Listeria monocytogenes is a rare infectious disease in immunocompetent children, and rhomboencephalitis is an unusual form of presentation.

Case report: A 21-months-old previously healthy girl was hospitalised due to 4-days-long fever, cough and headache, as well as lethargy during the last 8 hours. Physical examination revealed drowsiness and meningeal signs. Peripheral white blood cell count: 12,000 cells/mm3 (82% neutrophils), C-reactive protein 104 mg/L and procalcitonin 28 ng/mL. Cranial computed tomography (CT) was normal. Cerebrospinal fluid (CSF): 455 cells/mm3 (85% lymphocytes), proteins 0.89 g/L and glucose 71 mg/dL. Gram-staining and CSF culture were negative. She started acyclovir and cefotaxime, was admitted in the pediatric intensive care unit.

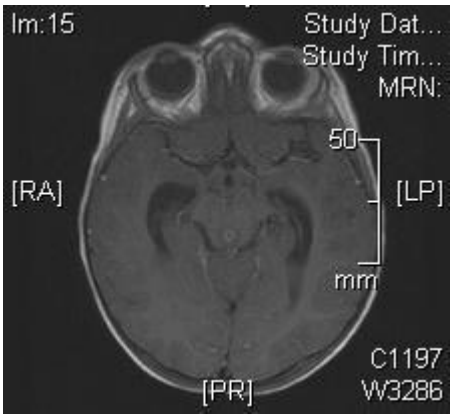
From the 5th day on she showed greater lethargy and abducens nerve palsy. New lumbar punction: 560 cells/mm3 (70% lymphocytes), glucose 7 mg/dL, protein 1.4 g/L, negative Gram-staining and adenosine deaminase (ADA) 29.8 UI/L. CT showed hydrocephalus. Anti-tuberculosis drugs were started. 24 hours later, CSF analysis revealed grampositive bacilli and growing of L. monocytogenes. Ampicillin and amikacin were started. External ventricular drain insertion was placed because of worsening hydrocephalus in MRI-scan. After 21 days of ampicillin, neurological exploration was normal. Permanent ventriculoperitoneal shunt was inserted.

Conclusions:

- L. monocytogenes has to be considered by lymphocytic meningitis and poor response to third generation cephalosporins.

- High ADA levels or negative Gram-staining in CSF do not exclude this infection.

- Repeated CSF studies and neuroimaging are essential for early detection of complications.



[MRI-scan: rhomboencephalitis]

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FIFTH YEAR POST-ROTAVIRUS VACCINATION IN BELGIUM: DECREASE OF ROTAVIRUS-POSITIVE STOOL SAMPLES IN HOSPITALISED CHILDREN

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Background and aims: Rotavirus vaccination has been reimbursed in Belgium since November 2006 and vaccine coverage is about 85%. We assess and compare here the impact of mass rotavirus vaccination on rotavirus-related hospitalisations in children ≤5y old pre-vaccination and up to 5 years post-introduction of the vaccine in 9 paediatric wards in Belgium.

Methods: All rotavirus detection tests were collected from ≤5y old children. The absolute numbers of rotavirus-positive tests pre-vaccine (01/06/2004-31/05/2006) were compared with data at launch (01/06/2006-31/05/2007), and post-launch (01/06/2007-31/05/2012). Data are presented as % reduction (95% CI) per year post-vaccination considering the annual average pre-vaccination period as reference.

Results: The number of rotavirus-positive stool tests in hospitalised children ≤5y old decreased from an average of 917 (Table 1) pre-vaccination to 619 during vaccine launch, 399 in the 1st year post-launch, 229 in the 2nd year, 209 in the 3rd year, 212 in the 4th year, and 158 during the 5th year. An overall decline (-53%, 95% CI:50%-55%) in all-cause acute-gastroenteritis (AGE) related hospital admissions is observed, from 1,793 per year pre-vaccination to 850 during the 5thyear post-launch. The number of bed-days due to AGE has fallen from 9,100 pre-vaccination to 4,016 (-56%, 95% CI:55%-57%) post-vaccination. A reduction from 6,026 to 3,656 (-39%, 95% CI:38%-41%) is also seen amongst the non rotavirus-positive cases.

Conclusions: Significant declines in number of rotavirus and all-cause AGE-related hospitalisations are seen in young children after 5 years of mass rotavirus vaccination in Belgium.

	Pre-vaccine	Vaccine launch	1st year post	2nd year post	3rd year post	4th year post	5th year post
	Jun 04-May 06	Jun 06-May 07	Jun 07-May 08	Jun 08-May 09	Jun 09-May 10	Jun 10-May 11	Jun 11-May 12
	Average # of tests /year	% decline compared with pre-vaccination period (95% CI)					
Total # of positive tests	917	32% (29%-36%)	56% (53%-60%)	75% (72%-78%)	77% (74%-80%)	77% (74%-80%)	83% (80%-85%)
Community aquired	767	33% (30%-36%)	59% (55%-62%)	75% (72%-79%)	75% (72%-79%)	76% (73%-79%)	82% (80%-85%)
Nosocomial	150	30% (23%-37%)	45% (37%-53%)	73% (66%-80%)	86% (80%-92%)	82% (76%-88%)	85% (80%-91%)
# of AGE admissions	1,793	4% (3%-5%)	29% (27%-31%)	33% (31%-35%)	42% (39%-44%)	37% (35%-39%)	53% (50%-55%)
# of AGE hospitalisation days	9,100	7% (7%-8%)	27% (26%-28%)	34% (33%-35%)	44% (43%-45%)	43% (42%-44%)	56% (55%-57%)

[Table1]

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OVERLAPING SEASONALITY OF PARANEUMONIC EMPYEMA AND BACTEREMIA DUE TO PNEUMOCOCCUS IN SOUTHERN CALIFORNIA CHILDREN: DOES INFLUENZA MATTER?

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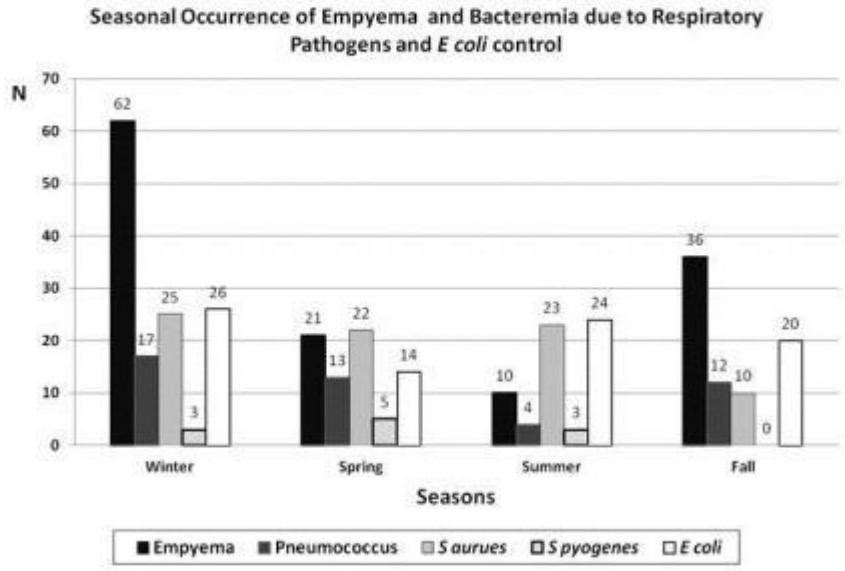
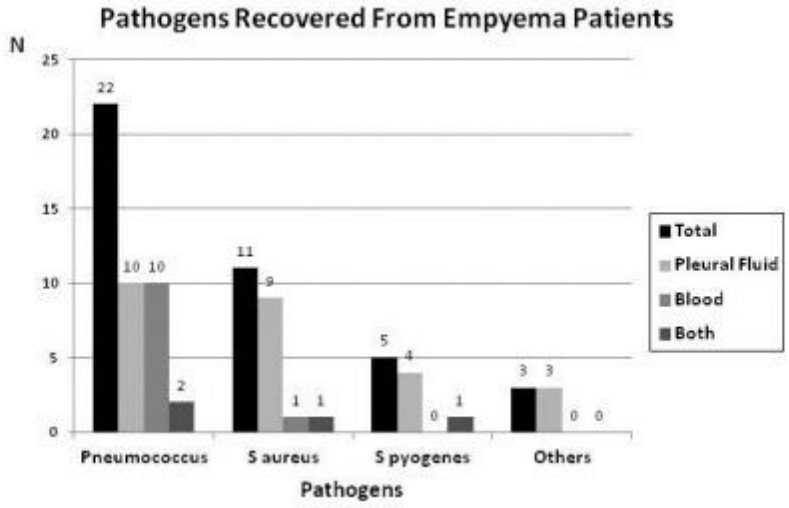
Background and aims: Parapneumonic empyema is common in children. Recent reports indicate increasing rates in contrast to decreasing rates of pneumonia. Although cultures are often negative pneumococcus and S aureus are common etiologies. Viral respiratory infections, particularly influenza, have been implicated preceding bacterial pneumonia. We hypothesized that the seasonality of empyema overlaps with pneumococcal bacteremia and both would be more prevalent during influenza season supporting etiologic role of pneumococcus and add information on treatment and prevention of empyema in children.

Methods: Retrospective chart review of patients discharged from our institution (July, 2005-December, 2012) with diagnosis of empyema, as well as those with bacteremia due to pneumococcus, S aureus and S pyogenes was performed using E coli bacteremia as control.

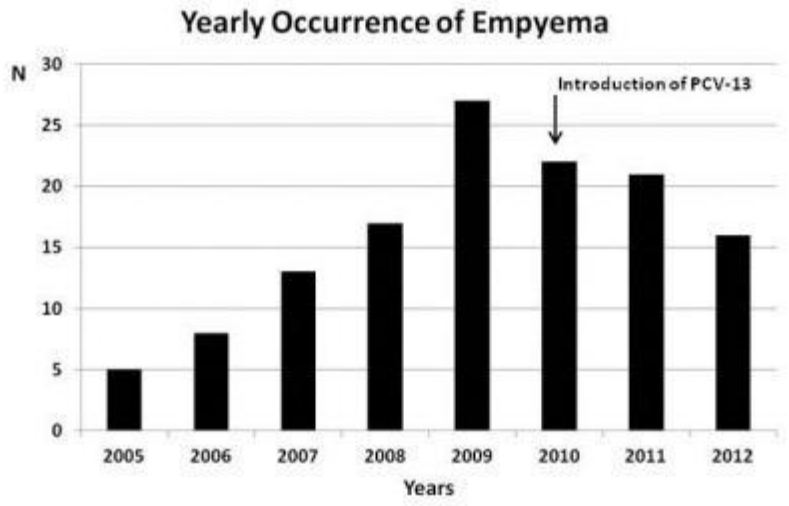
Results: Yearly cases of empyema increased until 2009. (Fig 1) Empyema (10/129) and pneumococcal bacteremia (4/46) decreased significantly during summer. (Fig 2) Blood and/or pleural fluid cultures were positive in 41 (31.8%) empyema patients, pneumococcus was most frequent (Fig 3); 19A(6 and 12) and 3(6 and 7) were most common serotypes from empyema and bacteremia respectively; 10/11 (empyema) and 17/70 (bacteremia) S aureus were MRSA.



[Fig 1]



[Fig 2]



[Fig 3]

Conclusions: Yearly cases of empyema increased during study until 2009. Seasonal occurrence of pneumococcal bacteremia closely overlaps with empyema supporting etiologic role. S aureus and S pyogenes were not seasonal. Influenza had no impact on empyema or pneumococcal bacteremia.

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INFECTIOUS ENDOCARDITIC IN CHILDREN

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Introduction: Infectious endocarditic is a very rare condition in children bout it has a high mortality rate and concerning its symptoms in primary health care is very important. The aim of this study is to evaluate the Infectious endocarditic in pediatric ward in Mashhad University of medical sciences.

Method: In this descriptive study all Infectious endocarditic cases aged lesser than 18 was evaluated in a 10 years period. 20 children with Infectious endocarditic were entered the study. SPSS was used to analyze the data.

Results: Average age of patients was 23/4 ±5/6year, their average weight was 64/0±94/2 Kg. the average of hospitalization was 8/6±25/19 days. Congenital heart diseases were the most common cause of Infectious endocarditic and the major organism was found in culture was staphiloccous arouse. ESR was more than 50 in 55 percent of cases. Heart vegetation incidence was 90%, heart murmur 70% and fever 40% and RF was positive in 25% of cases.

Conclusion: Regards to underlying causes of Infectious endocarditic it seems to determined the congenital heart patients as high risk ones. Rapid and correct diagnosis of Infectious endocarditic in children has an important role to reduce mortality.

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INFECTIVE ENDOCARDITIS IN A CASE OF BRUCELLOSIS

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Brucellosis is a zoonotic disease and it has been implicated in complications and focal disease in many human organ systems. Although the presence of brucella endocarditis is encountered rarely, it is the most fetal complication of brucellosis. Here, we report a 8-year-old case of brucellosis complicated with infective endocarditis as a rare but life-threatening complication.

The 8-year-old boy was admitted to our pediatric emergency department with the complaints of arthritis, fever, weight loss, abdominal and chest pain. Physical examination revealed a blood pressure of 110/75 mmHg, splenomegaly with six centimeters, abdominal defense-tenderness and $4/6^0$ pansystolic murmur at mesocardiac region. Laboratory investigations revealed hemoglobin 7.9 g/dl, white blood cell count 2900/µL, platelet count 140,000/µL, C-reactive protein 81 mg/dl. Serum electrolyte, liver enzymes, blood coagulation tests and urinalysis were within normal levels. The brucella agglutination test was ≥1/1280. Rose Bengal test was ++++. Abdominal ultrasonography showed hepatosplenomegaly and two-dimensional transthoracic echocardiography revealed vegetations attached to the right coronary cuspis of the aortic valve and on the bifurcation of pulmonary artery that caused stenosis in pulmonary artery. Blood culture for brucellosis was positive. The patient was hospitalized with the diagnosis of infective endocarditis due to brucellosis and ceftriaxone, rifampicin, streptomycin and trimethoprim sulfamethoxazole were initiated. After 4 weeks, the patient showed marked clinical improvement, became afebrile and the vegetations disappeared. In conclusion, this case may imply that brucellosis should be taken into consideration with its life-threatening complications such as infective endocarditis and it is vital to begin antibiotic treatment as soon as possible.

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IMMUNOGENICITY AND SAFETY OF MENACWY-CRM, A QUADRAVALENT MENINGOCOCCAL CONJUGATE VACCINE, IN INFANTS

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Background and aims: MenACWY-CRM (Menveo®) is a quadrivalent meningococcal conjugate vaccine against serogroups A, C, W-135 and Y currently licensed in Europe, the US and many other countries worldwide for 2 years of age and above. Integrated immunogenicity and safety data in infants from 2 months of age have not been presented.

Methods: Results of 2 phase III immunogenicity and safety studies and 1 phase III safety study were evaluated to provide a clinical picture of MenACWY-CRM and co-administration of MenACWY-CRM with routine infant vaccines (DTaP-HBV-IPV, +HIB or DTP-HIB-IPV+HBV, +Rotavirus, +PCV7 or PCV13) and routine toddler vaccines (PCV7 or PCV13, +DTaP, + Hib, +MMR/MMRV). Primary immunogenicity was assessed one month postvaccination via serum bactericidal assays using human serum as the exogenous complement source (hSBA).

Results: Overall, 12,818 subjects were enrolled in clinical trials and randomized to receive study vaccines at clinical centers in the United States, Australia, Canada, Taiwan, and Latin America (LA). One month after receiving a 4-dose infant/toddler series (LA: 2, 4, 6, 16 months; elsewhere: 2, 4, 6, 12 months), 89-95%, 95-98%, 97-100% and 96-100% of subjects had hSBA titers ≥8 against serogroups A, C, W, and Y, respectively. Safety profiles and immune responses to concomitant vaccine antigens were similar in groups that received MenACWY-CRM plus routine vaccines or routine vaccines alone.

Conclusion: In a database of 12,818 subjects from 2 months of age, MenACWY-CRM was well tolerated and induced robust immune responses without evidence of clinically relevant interference when co-administered with routine infant vaccines.

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ASSESSMENT OF HAND HYGIENE RESOURCES AND PRACTICES AT THE TWO CHILDREN`S HOSPITALS IN GREECE

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Background and aims: Hand hygiene (HH) is critical to prevent healthcare associated infections. We systematically assessed existing HH resources and practices.

Methods: Observational HH data and an inventory of HH resources were collected from 12 wards in 2 pediatric hospitals in Athens, including medical/surgical, oncology/transplant (BMTU), and intensive care units (ICUs), during 60, 1-hour observations periods. HH opportunities and attempts were designated as appropriate or inappropriate per WHO criteria.

Results: Overall HH compliance was 33.4% (396/1187). Of HH opportunities, 20.2% were appropriate. Compliance differed by role: nurses (52.8%), physicians (23.2%), students (22.2%) and others (19.2%) ($p=0.001$). HH compliance was greatest after body fluid exposure 66.1% (39/59) and 38.6% (34/88) before an aseptic procedure ($p< 0.001$). HH compliance was 30.3% (105/346) before patient contact, 33.1% (118/357) after patient contact, and 29.7% (100/337) after surroundings contact. Compliance was highest in ICUs and transplant unit: 63.1% in neonatal ICU, 60.9% in pediatric ICU, and 60% in BMTU; lower rate were observed in other units (13% - 18%). The median number of functional sinks per ward was 1 (IQR 1-1). HH resources at hand washing stations were soap (88%) and single use hand towels (60.4%). The median number of alcohol hand rub dispensers per examination and patient's rooms was 1 (IQR 1-1).

Conclusions: A low level of HH compliance was observed despite the availability of HH resources in most patient rooms. This report demonstrates a strategy to conduct an initial assessment and to gather baseline data that can be used to guide future improvement efforts.

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BARTONELLA HENSELAE IN IMMUNOCOMPETENT CHILDREN: REPORT OF TWO CASES

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Background and aims: Cat scratch disease (CSD) is a global endemic disease caused by Bartonella henselae which represent the most frequent etiologic agent in childhood. It causes various clinical syndroms in immunocompetent and immunocompromised hosts.

Methods: We described two cases of Bartonellosis in childhood.

Results: A 9-years old boy presented to our Unit with a clinical history of fever, vomiting and diarrhea and a localized tumefaction at right elbow. Previously he underwent oral antibiotic therapy for 2 weeks without resolution of the clinical picture. Microbiological tests for CMV, EBV, HIV, Toxoplasma were performed proving negative. Serology IgG (1:256) for Bartonella resulted positive whereas IgM were negative. Oral antibiotic therapy was started while surgical excision of the elbow abscess was performed with complete resolution.

The second case describes a 14-years old boy admitted to our Unit with persistent fever of unknown origin. Laboratory investigations showed elevation of inflammatory markers and an abdominal ultrasound scan revealed multiple hepatic abscesses. Serological tests revealed a high title of IgG for Bartonella henselae. A prolonged antibiotic therapy was undertaken with complete resolution of the clinical and radiological picture.

Conclusions: These two clinical cases underline the unusual presentations of Bartonellosis in childhood. Noteworthy, none of the patients had a history of contact with kittens. Bartonella Henselae infection is frequent in Italy and probably underdiagnosed. Thus clinical should be aware to consider Bartonellosis in differential diagnoses of any patient with a history of unknown persistent fever.

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RHEUMATIC HEART DISEASE IN A 9 YEARS OLD BOY

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Background and aims: Group A streptococcal infection is common in childhood and determine in susceptible people a picture of acute rheumatic fever , that can affect different organs and in which the most serious sequela is rheumatic carditis, almost disappeared from wealthy countries.

Methods: We present a case of a nine years old male child, who developed an acute heart failure as consequence of subclinical recurrent episodes of pharyngotonsillitis.

Results: The patient presented with abdominal pain, recurrent vomiting after meals, weight loss and fatigue. On admission, physical examination revealed a 2/6 systolic murmur. Investigations showed a mild increase of inflammatory markers (CRP 2,26 mg/dl, ESR 58 mm/h) and iron deficiency anemia (Hb 9,4 mg/dl). Inflammatory Bowel Disease and Celiac disease were ruled out by EGD and specific serological antibodies. Two weeks later an acute heart failure occurred (BNP 2160), documented by echocardiogram showing a severe multi-valve insufficiency. Further investigations demonstrated positivity of ASLO 1578 UI/ml and Streptozyme minor criteria while throat swab was negative and pointed toward rheumatic carditis. Antibiotics ,plastic mitral valve surgery and aortic valve replacement has been successfully performed.

Conclusions: The atypical presentation of this case with abdominal symptoms outline the need to consider cardiac rheumatic disease among the possible causes responsible for non innocent and new-onset murmurs, even in our latitudes.

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BACTERIURIA AND LEUKOCYTURIA AS INDICATORS OF URINARY TRACT INFECTION IN CHILDREN

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Background and aims: Paediatricians prescribe empirical antibiotics for urinary tract infections (UTI) taking in account the clinical presentation and urinalysis while waiting for the result of the urine culture. The aim of this study was to evaluate the diagnostic benefit of bacteria and leukocyte counts to urinalysis in comparison with urine culture as the reference method.

Methods: Urine samples were collected from children aged 6 weeks-6 years with suspected UTI from August - December 2011. A gold standard of a positive urine culture was used. Sensitivity and specificity were calculated for positive nitrite and leukocyte esterase (LE) and bacteria and leukocyte counts performed with the Sysmex UF-1000i.

Results: A total of 366 consecutive clean-void bag and catheter urine specimens were collected from children (median age 18 months) of both genders (56,0% females). A combination of more than 30 bacteria/microL and 40 leukocytes/microL had a sensitivity of 98,0% (higher when compared with LE, positive nitrite or a combination of both) and a specificity of 84,5%. 48 (13,1%) urine cultures were positive. Escherichia coli was the most common bacterial pathogen (66,6%) followed by Proteus mirabilis (22,9%). 18,7% of Escherichia coli were resistant to trimethoprim-sulfamethoxazole (n=32), 12,5% to amoxicillin/clavulanate (n=16) and 12,5% to cefuroxime (n=8). All Proteus mirabilis were resistant to amoxicillin/clavulanate.

Conclusions: The data support the use of bacteria and leukocyte counts as a reliable screening method, which can help the presumptive diagnosis and empiric treatment of UTI in children. Cefuroxime axetil as empiric antibiotic seems adequate in our region.

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A CASE OF SEPTIC ARTHRITIS IN IMMUNOCOMPETENT PREMATURE INFANT SECONDARY TO MATERNAL BREAST MILK, SHARING SAME GENOTYPE OF STAPHYLOCOCCUS AUREU

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Aim: Breast milk can occasionally transmit serious viral and bacterial infections to preterm infants. [9] We report a case of septic arthritis in immunocompetent premature infant secondary to maternal breast milk, sharing same genotype, signify unusual and potential source of culture proven sepsis/septic arthritis.

Methods: A case report on Septic arthritis in premature infant; staphylococcus aureus in maternal breast milk as a potential source and review cases.

Results: A premature baby girl born to primigravida mother at 28+2 weeks of gestation, by spontaneous vaginal delivery (SVD) with birth weight of 1.37Kg (50-75th centiles) and Apgar 9 at 1 and 10 at 5 minutes. Baby developed culture proven sepsis and septic arthritis on day 7. Maternal EBM sent for analysis, as a potential sourse of infection. At this point isolates of Staphylococcus aureus from both mother and neonate for genotyping. DNA fingerprinting using PFGE-Pattern A (Pulsed field Gel Electrophoresis) shows these 3 MSSAs display indistinguishable patterns suggesting person-to-person transmission may have occurred. Spa types t084 and t2119 are closely related and have been associated with strains belonging to MLST clonal complex 15.

Conclusions: In neonates (aged < 28 days), Staphylococcus aureus is the most common cause of septic arthritis. Time to diagnosis is the most important prognostic factor in septic arthritis. Early institution of therapy helps to prevent degenerative arthritis. Diagnosis may be delayed in young infants, which leads to a poorer outcome.

Breast milk can occasionally transmit serious viral and bacterial infections to preterm infants.

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KL-6, SP-A AND SP-D IN SERUM AND BRONCHOALVEOLAR LAVAGE FLUID IN CHILDREN WITH MYCOPLASMA PNEUMONIAE PNEUMONIA

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Background and aims: Study the Relationship of KL-6, SP-A and SP-D in serum and bronchoalveolar lavage (BALF) fluids in children with Mycoplasma pneumoniae pneumonia (MPP).

Methods: Self-control method has been used for the study on KL-6, SP-A and SP-D in serum and BALFs in 32 MMP children with only one side of lung infected.

Results: There were significant differences as KL-6, SP-A and SP-D in serum and non-infected lung BALF compared with that in infected BALF($P < 0.01$).There was no significant differences as SP-D and KL-6 in serum compared with that in non-infected lung BALF($P > 0.05$). There was close relationship as KL-6 in serum compared with that in infected lung BALF(correlation coefficient $P < 0.01$).

Conclusions: It implied serum KL-6 may be better than SP-D as convenient and accurate biomarker for pulmonary infection and injury in children with CAP.

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MOLECULAR GENOTYPING OF METHICILLIN- AND B-LACTAM-RESISTANT STAPHYLOCOCCUS AUREUS STRAINS FROM CHILDREN IN YUNNAN PROVINCE, CHINA

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Background: Elucidating the molecular mechanisms emerging of methicillin- and β-lactam resistant Staphylococcus aureus resistant pathogenic strains can provide new clues in prolonging these drugs lifespan, improving patient's management and containment of increasing antimicrobial resistance globally.We aimed at genotyping the molecular basis of methicillin- and β-lactam-resistant Staphylococcus aureus strains from children isolates in Yunnan, China.

Methods: We performed molecular genotyping of Staphylococcal cassette chromosome mec, pulsed-field gel electrophoresis and spa assays evaluated by multilocus sequence.

Results: A total of 407 MRSA isolates collected from 4 counties hospitals including TengChong and Dali-Puer, CDC during the period of February-October 2012. 70.1% of SCCmec type III was the most popular type and followed by 19.5% of SCCmec type II. Twenty-four PFGE types were obtained among 407 isolates collected, and 18 spa types and 52.0% spa type t030 corresponding to PFEG types A to E and 25.5% spa type t037 corresponding to PFGE types F and G. 16.0% were made up of the two spa genotypes. 15.95% spa type t002, which included isolates of PFGE types L to T, belonged to ST5 and SCCmec type II, and isolates of this type were distributed in 2 major counties and varied among the areas. spa type t002 was the most common in Dali (53.4%) and Tengchong (44.4%) towns; compared to spa type t037 predominant in Shanghai (74.8%). The prevalence of leukocidin gene was 2.6%.

Conclusion: Geographically establishing a network for molecular, in vitro monitoring and surveillance could prolong antibiotic usefulness and delaying the emergence of resistant strains.

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A RARE REASON OF ABDOMINAL LYMPHADENOPATHY: TULAREMIA; REPORT OF TWO PEDIATRIC CASES

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Tularemia caused by F.tularensis occurs worldwide in the northern hemisphere with great variation in geographic and temporal occurrence. It generally presents as an acute febrile diseases with the major clinical presentations including the six classic forms of tularemia: ulceroglandular, glandular, oculoglandular, oropharyngeal, typhoidal and pneumonic. In contrast to European countries where ulceroglandular form is more prominent, the oropharyngeal form is the most common presentation in Turkey. We present rare cases of oropharnygeal tularemia in a 16 year-old boy and 9 year-old girl to the best of our knowledge, firstly described as abdominal lymphadenopathy from Turkey. The second case was admitted with erythema nodosum and during investigation abdominal lymphadenopathy was detected. Excisional lymph node biopsy revealed abdominal tularemia. It is necessary to consider tularemia in the differential diagnosis of abdominal lymphadenopathy in tularemia regions. We also conclude that oropharyngeal tularemia could cause lymphadenopathy in any part of the gastrointestinal tract.

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CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS IN TWO GREEK CHILDREN`S HOSPITALS

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Background and aims: Central line associated bloodstream infections (CLABSIs) are the most common healthcare-associated infection in children and are associated with significant morbidity, mortality and hospitalization costs. There are no data available on the epidemiology of CLABSIs in hospitalized children in Greece. The study aim was to determine the rate of CLABSIs in the 2 largest children`s hospitals in Greece.

Methods: We conducted active surveillance for CLABSIs in pediatric and neonatal intensive care units (ICUs), oncology and transplant units between September-December 2012. CLABSIs were prospectively identified using the Centers for Disease Control and Prevention National Healthcare Safety Network definitions. Unit-specific rates of CLABSI (per 1000 catheter days) and device utilization ratios (catheter days per patient days) were calculated.

Results: During the 4 month surveillance period, 28 CLABSIs and 5907 catheter days were detected. Unit-specific CLABSI rates ranged from 17.2/1000 catheter days in the PICU to 2.4/1000 catheter days in the oncology unit. Device utilization ratios ranged from 0.21 (neonatal ICU) to 0.97 (transplant unit) (Table). Klebsiella was isolated most frequently (23%), followed by Enterobacter (19%), Candida (19%) and Escherichia coli (15%) from specimen cultures.

Conclusions: High rates of CLABSIs were identified in ICUs while rates were lower in transplant unit despite higher catheter utilization ratios. Infection control programs, including surveillance, evaluations of adherence to best practices of CLABSI prevention, and interventions to prevent CLABSIs, should be urgently implemented in children's hospitals in Greece.

UNITS	CLABSIs	Central Line Days	CLABSI Infection Rate	Patient Days	DU
NICUs	6	1197	3.92	6164	0.21
PICUs	10	560	17.15	957	0.63
Oncology	7	3137	2.44	4250	0.74
BMTU	5	1013	4.92	1039	0.97

[Distribution of CLABSI rates by type of location]

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MAIN FACTORS INFLUENCING INFANT'S VACCINE ADVICES GIVEN BY GENERAL PRACTITIONERS AND PEDIATRICIANS : A CONJOINT ANALYSIS STUDY

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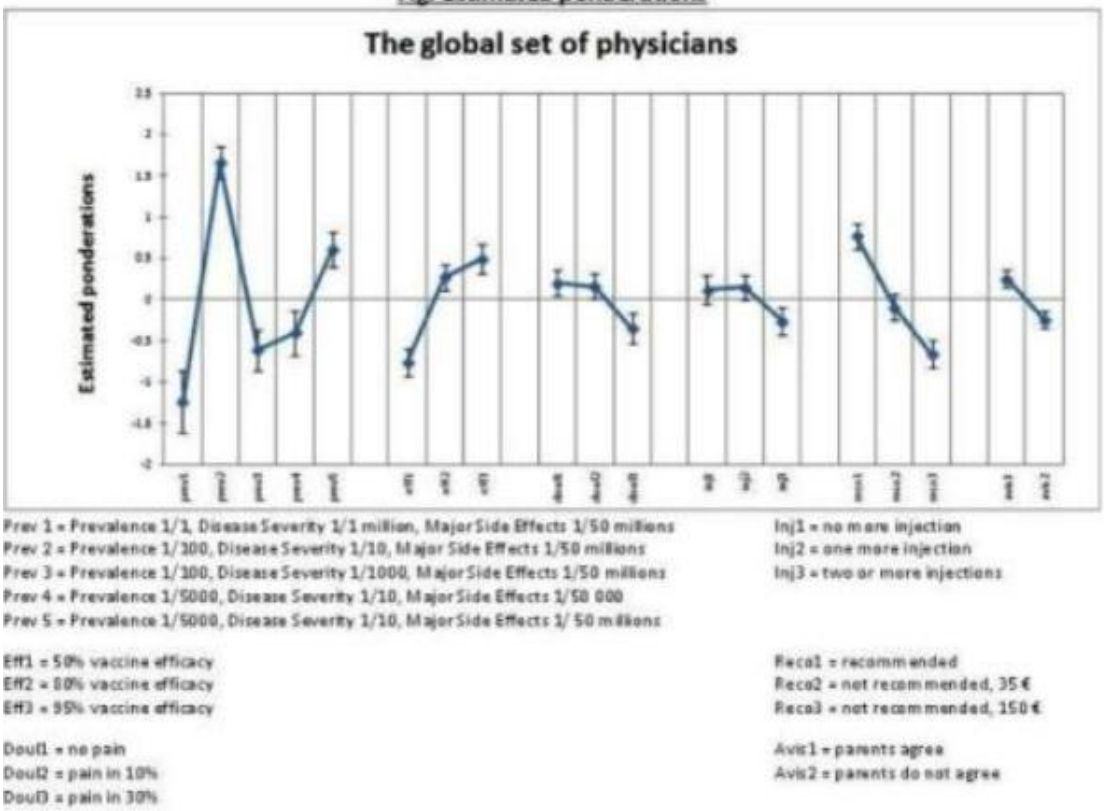
Objective: To estimate the importance of the vaccine's and illness' characteristics in the decision of physicians to propose or not a vaccine to parents of one year old infants.

Methods: A conjoint analysis method has been used. All general practitioners and pediatricians in Northern France have been invited to participate. A literature review and a focus group have been conducted to identify relevant attributes/levels. Then an electronic questionnaire has been developed. Choices have been presented by pairs to physicians (10 per physician). Selected attributes were: vaccine's characteristics (effectiveness, number of injections, major and minor side-effects, recommendations from the French Immunization Committee, price), illness' characteristics (prevalence, severity) and attitude of parents regarding vaccination. Design has been optimized. A conditional logit model was used for data analysis.

Results: 172 physicians have answered. 72.1% were “very favorable” to the vaccination, 26.2% “rather favorable” and 1.7% “rather not favorable”. Most important attributes were severity of disease and major side-effects. Less important attributes were the number of injections and minor side-effects (Figure). Physicians were influenced, but not much, by parental attitude.

Conclusion: This study provides coherent results to understand social behavior concerning vaccination. It also has shown the feasibility of this type of methodology that could be performed with more participants. Its understanding is essential to improve the vaccine coverage in France.

Fig. Estimated ponderations



[Estimated ponderations of vaccine characteristics]

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EPIDEMIOLOGY OF ANTIMICROBIAL RESISTANCE AND UTILIZATION IN CHILDREN WITH CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS (CLABSIS) IN GREECE.

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Background: Healthcare associated infections are associated with significant morbidity, mortality, and costs worldwide; many are caused by multi-drug resistant organisms (MDROs) which further results in worse outcomes. We examined the prevalence of MDRO pathogens causing CLABSIs and antibiotic utilization.

Methods: We conducted active surveillance for CLABSIs and antibiotic use in intensive care units, oncology and transplant units at 2 children's hospitals in Greece between September-December 2012. CLABSIs were prospectively identified using CDC definitions. An antibiotic day (AD) was defined as a calendar day in which at least one antimicrobial was given.

Results: 28 CLABSIs were identified from 22 children. Gram negative organisms were most commonly isolated (18, 64.2%): Klebsiella spp. (6, 33.3%), Enterobacter spp. (5, 27.7) and Escherichia coli (4, 22.2%). Resistance to third generation cephalosporins (likely ESBLs) were detected in 66.6% of Klebsiella spp. Carbapenem resistance was noted in 1 isolate of Klebsiella. CLABSIs were also caused by Candida spp (6, 21.4%) and gram-positive organisms 4 (14.2%), including 1 resistant isolate (vancomycin-resistant Enterococcus faecium).

On surveillance units there were 3423 antibiotic days during 6246 patient days (antibiotic utilization ratio 0.548). Meropenem (39%), amikacin (32%), and teicoplanin (28.5%) were the most frequently used antimicrobials.

Conclusions: The majority of pathogens causing CLABSIs in hospitalized children in Greece were MDROs requiring use of broad-spectrum antibiotics. These findings call for rapid and effective adoption of infection control and antimicrobial stewardship strategies to prevent further emergence and spread of MDROs.

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DETECTION OF STREPTOCOCCUS PNEUMONIAE IN DRIED SALIVA SPOTS: EXPLORATORY STUDY ON ALTERNATIVE DIAGNOSTIC APPROACHES IN SURVEYS ON PNEUMOCOCCAL CARRIAGE

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Background and aims: Saliva is an easily accessible body fluid and was historically the method to test pneumococcal carriage in surveillance studies. The aim of this study was to determine the feasibility of using dried saliva spots (DSS) as an alternative to raw saliva collected on dry ice for pneumococcal carriage studies.

Methods: Saliva was collected from healthy volunteers and spiked with clinical S. pneumoniae strains applied to Whatman 903 Protein Saver cards (cotton fibers), and allowed to air-dry for 2 hours in ambient conditions. Dried saliva spots (DSS) were stored sealed with a desiccant pack at 30ºC, room temperature (RT), 4ºC, or -20ºC for up to 35 days. DNA was isolated from spots with a modified Qiagen DNeasy kit and tested in quantitative-PCRs (qPCR) targeting pneumococcal genes lytA and piaA.

Results: DSS processed immediately after drying showed equal quantity of pneumococcal DNA compare to raw saliva samples. The lower limit of detection of DSS was 10^4 CFUs per spot. Pneumococcal DNA was stable for up to 10 days in DSS stored $\leq$ RT and for up to 7 days in DSS stored at 30ºC. Presence of pneumococcal DNA was still detected in DSS stored up to 35 days at any temperature. There were no differences between various clinical strains.

Conclusion: Pneumococcal DNA is stable in DSS stored for up to one week. DSS may be considered as an attractive alternative to nasopharyngeal samples in surveillance studies on pneumococcal carriage, particularly in studies conducted in remote settings.

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CRITICAL APPRAISAL OF WEB-BASED RESOURCES PROVIDING PROFESSIONAL EDUCATION ON ANTIBIOTIC PRESCRIBING IN CHILDREN: 10 MILLION HITS-ONLY 10 GOOD WEBSITES

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Background/aims: Web-based educational tools can provide easy-to-reach, regularly up-dated information to improve the knowledge about appropriate use of antimicrobials. We aimed to identify and appraise web-based educational resources for professionals on the optimal childhood use of antibiotics.

Methods: Websites of healthcare organizations and societies involved in infectious diseases and/or pediatrics and relevant international discussion forums were screened in May 2012 to identify online educational tools for childhood antibiotic prescribing. Two Google searches were conducted at the same time combining the following terms: “Antibiotics”, “Children”, “Education” and “Antibiotics”, “Children”, “Healthcare professionals”, “Website”. Identified resources were appraised using 6 criteria proposed for educational Internet resources (authority, objectivity/reliability, authenticity, timeliness, relevance for the targeted audience, accessibility/efficiency) with each criterion scored as met completely/met incompletely/not met.

Results: The two Google searches identified 9,700,000 and 2,790,000 results, respectively, with most of the websites excluded during title scanning leaving 10 and 12 websites, respectively, of potential interest. Targeted searching of institutional websites and discussion forums identified 31 further potentially relevant sites. On detailed review of the content only 10 websites addressed the relevant subject. Among these only APUA: Alliance for the Prudent Use of Antibiotics and Getsmart from the Centers for Disease Control and Prevention met all the quality criteria and provided relevant high-quality information.

Conclusion: Although a lot of material on improving childhood antibiotic prescribing targeting professionals is available online, only a very few websites provide high quality educational information. There is a need for improved evidence-based online educational material on this topic.

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SINGLE PRIMING DOSE OF NEISVAC-C IN INFANTS

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Several clinical studies with NeisVac-C have suggested that high seroprotective titers in infants can be induced with a single priming dose. This study assessed the feasibility of a single priming dose of NeisVac-C® given at 4 or 6 months of age.

956 subjects were randomly assigned to three treatment groups to receive a single dose at 4 or 6 months of age, or two doses at 2 and 4 months of age. All subjects received a booster at 12-13 months of age. Concomitant vaccinations with Infanrix®hexa and Prevenar13® were administered to all subjects at all timepoints.

Non-inferiority of seroprotection rates following a single dose was investigated as compared to a two-dose priming one month after primary vaccination (rSBA≥8), prior to the booster (rSBA≥8), and one month after the booster (rSBA≥128).

Rates of subjects with seroprotective titers (rSBA≥ 8) one month after priming was 99.6% in the 4 month group, 99.2% in the 6 month group, and 99.6% in the two-dose group. Prior to the booster, 78.0% and 90.7% of subjects had seroprotective antibody titers in the single dose groups (month 4 or month 6, respectively), compared to 67.8% in the two-dose group.

One month after the booster >98.5% of subjects in all three groups showed rSBA titers ≥128, with no differences between groups.

Thus, a single-dose priming at 4 or 6 months of age followed by a booster in the beginning of the second year of life can be considered a valuable alternative to the currently licensed two-dose priming schedule.

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PREVALENCE OF B.PERTUSSIS ,L, PNEUMOPHILA AND S. PNEUMONIA IN PATIENTS REFERRED TO SHAHID BEHESHTI HOSPITAL YASOUJ BY MULTIPLEX PCR

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Pneumonia is an acute infection of the lower respiratory tissues. It is usually caused by infection with viruses or bacteria and less commonly other microorganisems. Pneumonia is the leading cause of death in children worldwide. It kills an estimated 1.2 million children under the age of five years every year - more than AIDS, malaria and tuberculosis combined. S.pneumonia is the most common cause of bacterial pneumonia in children with high mortality and morbidity among adults and children. In addition L.pneumophila and B.pertussis are two agents that cause pneumonia. Accurate and timely diagnosis can lead to bacterial resistor and complication to unwanted side effects to patient. Among many laboratory tests PCR is a rapid test with high susceptibility to diagnosis of disease.

Material and method: After finding patients and completing the questionnaires, 126 samples of Sputum were collected from the patients. All the samples were exposed to PCR , culture and Gram Staining.

Results: Out of the 126 samples, 35.7 %were male, 64% were female, and the mean age was 44 years. the culture for B.pertussis and L.pneumophila were negative but the result for S.pneumonia was 71.4%. The result of PCR showed that 50% S.pneumonia, 10% L.pneumophila and 0.8% B.pertussis were detected respectively.

Discussion: The results of this study demonstrated that pneumonia is the important disease in the study area, it also show that PCR is one of the rapid method for the diagnosis of pneumonia.

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RESPIRATORY INFECTIONS WITH STREPTOCOCCUS PYOGENES AND THE ROLE OF THE PEDIATRICIAN IN THEIR DETECTION AND TREATMENT

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Aim: The aim of this work is to show the efforts of the primary health protection for early detection of streptococcus infections, their adequate treatment and by it prevention of Febris rheumatica and acute post-streptococcus glomerulonefritis as possible complications.

Material and Methods: Health records of pre-school and school children who are treated at the PHI D-r Angelovska and D-r Timovski for the period of 2 years (2011-2012) have been processed. Diagnoses have been set based on anamnesis, clinical picture, and smear from throat and lab analysis. Analytical methods have been used for comparisons.

Results: Out of 45878 examined children in the period of 2011 to 2012, smears have been taken from 4800 children. Positive findings have been obtained from 1600 samples (33,33%). Streptococcus pyogenes was isolated with 215(13,43%) from the sample. From the other agents the following have been isolated: Streptococcus pneumoniae with 420 (26,25%),Branchamella catarrhalis-Moraxella with 285 (17,81%),Haemophillus influenzae with 315(19,69%) . The other 365 (22,82%) are from different agents(reasons). Seasons for appearance of streptococcus infections are mostly autumn and winter. 45 children had elevated values of ASO. 151 children had leucocytes and elevated CRP. 17 children had scarlatina rash. All children were treated in the infirmary as follows: 194 children with Bensatine phenoximetil penicillin (90 % per os.) and 21 children with other antibiotics. Extended prevention with Bensatine phenoximetil penicillin had 34 children in a period of 1-3months.

Conclusion: Early detection and adequate treatment of streptococcus infections reduces the number of possible complications and number of hospitalized children.

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INFECTIONS BY EXTENDED-SPECTRUM B-LACTAMASE- AND CARBAPENEMASE-PRODUCING ENTEROBACTERIACEAE IN AN ITALIAN PAEDIATRIC HOSPITAL

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Background and aims: Paediatric morbidity and mortality rates can be severely affected by drug-resistant bacteria infections, especially in patients with prolonged hospitalization.

Methods: A prospective case-control study was conducted in the tertiary Regina Margherita Children's Hospital (Turin, Italy) between 1st May and 31st December 2012. Patients infected by extended-spectrum β-lactamase (ESBL) producing Enterobacteriaceae were recruited; each patient was randomly paired with a control growing the same but non-resistant pathogen in the same isolation site. P-values < 0.05 were considered statistical significant.

Results: Forty-six patients with ESBL-producing isolates (65% E.coli) were identified, predominantly in medical wards (66%). Sites of infection were mainly urinary tract (30) and bloodstream (9). Characteristics significantly associated with ESBL-producer infection were immunodeficiency (p=0.022), chronic co-morbidities (p=0.017), exposure to and treatment days with broad-spectrum penicillins (p=0.0464), aminoglycosides (p=0.0482), third and fourth-generation cephalosporins (p=0.00218) in the previous 3 months. Length of central venous catheter stay (p=0.009), urinary catheter stay (p=0.0322) and parenteral nutrition (p=0.0357) in the past 30 days were recognized as risk factors. Attributable mortality rate to ESBL-producer infection was 2% (20% among sepsis). Eight carbapenemase-producing Enterobacteriaceae were identified (75% K.pneumoniae, 25% E. coli), mainly in oncologic ward (75%); sepsis occurred in 4 cases, and 2 died. All patients had received carbapenems in the past 3 months.

Conclusions: Infections by resistant Enterobacteriaceae are relatively frequent in the paediatric setting and related mortality rate may be relevant. Active surveillance and implementation of infection control measures, along with antibiotic stewardship programs, are therefore crucial to limit drug-resistant bacteria spread.

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PREVALENCE OF CHAGAS DISEASE IN BOLIVIAN PREGNANT PATIENTS (JUNE 2008-SEPTEMBER 2011) IN LA PAZ UNIVERSITY HOSPITAL. RISKS OF VERTICAL TRANSMISSION

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Background and aims: Due to migration, our country hosts numerous persons with Chagas disease. The risk of transmission in Spain is not vectorial, but from pregnant to new born. The aims is estimate the prevalence of Trypanosoma Cruzi infection in bolivian pregnant patients which gave birth at La Paz University Hospital; as well as to compared two different periods of screening before and after protocol implementation for bolivian pregnant patients in our hospital.

Method: Retrospective study selecting the data of bolivian pregnant patients which have given birth between June 2008 and September 2011. Data was collected from positive serology (two positive indirect determinations through quick test, ELISA or IFI) and controls on the new borns of these mothers (microhematocrit and PCR at bird and seried serologies (IFI) until 9 months of age). A statistic report analysis was elaborated through the SPSS program and a comparison analysis (test Chi squared) between the periods of June 2008-May 2010 (period 1) and from June 2010-September 2011 (period 2)

Results: A total of 693 bolivian patients gave birth. Serology was requested in 229 (33%), more serologies were requested in period 2 after protocol implantation (85=44,3%) than in period 1 (144=28,5%) p< 0,001. 43 (19,9%) of patients analysed were diagnosis. New born follow up was only in 33 cases (76,7%). None of the children controlled has been infected .

Conclusions: Adequate control is not being made of the vertical transmission of Chagas disease in our environment, even after proven results after protocol implantation.

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PNEUMOCOCCAL MENINGITIS DUE TO SEROTYPE 35F: REPORT OF A CASE

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Introduction: Pneumococci are the most common cause of bacterial meningitis in children and unvaccinated children are more prone to invasive pneumococcal diseases.

Case report: An eleven-year-old boy presented with fever, headache, vomiting and sleepiness. His body temperature was 39.4°C, he had oropharyngeal hyperemia and meningeal irritation. He had not been vaccinated with pneumococcal vaccine previously. After the laboratory examination, meningitis due to penicillin sensitive Streptococcus pneumoniae was diagnosed and the patient was treated accordingly. Streptococcus pneumoniae serotype 35F was found out.

Conclusion: After mass infant vaccination has been introduced, while IPD due to the vaccine serotypes have tended to decrease both in vaccinated young children and among non-vaccinated groups due to herd immunity, unsurprisingly non-vaccine serotypes started to emerge. Streptococcus pneumoniae serotype 35F is a less known non-vaccine serotype that had been reported to cause meningitis. It has a mortality up to 37%. Pediatricians should always be aware of pneumococci even if the patient is vaccinated because of the serotype replacement.

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VARICELLA-ZOSTER VIRUS ENCEPHALITIS: A CASE REPORT

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Encephalitis is an acute inflammatory process of the brain. Varicella-zoster virus (VZV) is one of the agents most frequently identified in children. Clinical manifestations include headache, altered level of consciousness and signs of cerebral dysfunction.

We report the case of a 34-months-old girl who was presented in our pediatric outpatient clinic with acute ataxia associated with dysarthria and general irritability. Since three days she was presenting the classical rash of VZV infection and high fever.

There was no medical history and development was normal. Physical examination was remarkable for dysmetria and ataxic gait. Deep tendon reflexes were normal.

Diagnostic work-up included neuroimaging studies and analysis of blood and cerebrospinal fluid. The brain CT-scan showed no abnormalities, analysis of cerebrospinal fluid revealed pleocytosis (13 WBC/$mm^{3;}$ 60% lymphocytes) and polymerase chain reaction (PCR) for VZV virus was positive. Brain MRI showed small bilateral lesions of demyelination in the subcortical white matter suggestive of vasculitis in the context of meningoencephalitis. Intravenous aciclovir was given rapidly and there was important improvement. Cerebrospinal fluid analysis after 14 days of aciclovir treatment showed normocytosis and negative VZV-PCR analysis. On follow-up 6 months later we observed no neurological deficit.

VZV encephalitis is a medical emergency. No single clinical or CSF feature is sufficient to evoke the etiologic cause of the encephalitis. MRI is a more sensitive diagnostic imaging modality. Early empirical treatment is important in order to avoid neurologic sequelae or even fatal outcome.

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PERTUSSIS IN URUGUAY. ANALYSIS OF ADMISSIONS IN A PEDIATRIC HOSPITAL

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Objective: To analyze the clinical characteristics, evolution and epidemiological aspects of hospitalized children with Pertussis disease confirmed by PCR.

Methodology: Observational, descriptive, retrospective study. All children hospitalized between 0 and 14 years old with suspicion of pertussis from 1/8/2011 until 31/07/2012 were analyzed. Cases of apnea alone without associated respiratory symptoms were excluded. The data was collected from the clinical history. The considered variables were demography, clinical-evolution and laboratory. Investigation of Bordetella by PCR technique was made (kit Speed-oligo Bordetella Vircell®; detection limit: 15 copies). The detection of B. pertussis by means of the amplification of the sequences of insertion IS481 and the promoter of the gene ptxA-Pr. Data was analyzed by System EPIDAT 3.1 . A value of p was considered statistically significant if ≤ 0,05.

Results: Of 6771 children; 497 (7,3%) entered the Hospital as suspicious cases of Pertussis . 458 PCR studies were made. 172 were positive (37,5%). They were B.pertussis + 79%. Confirmed cases predominated in November (37%). They were associated with absence of respiratory difficulty, negative virology assays and high leukocyte counts. 9.3% required ITU, and 4 of 172 cases were lethal(2.3%).

Conclusions: Pertussis, was an important cause of hospitalization of young babies with many serious cases, with a highlight in November. Most were caused by B.pertussis, with a lethality of 2,3%.

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POSTINFECTIOUS ARTHRITIS IN PEDIATRIC PRACTICE: CASES REPORT

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Background: Postinfectious arthritis is a relatively common cause of presentation to pediatrician and also an diagnostic pitfall. Joint manifestations may occur simultaneously or after a free interval from an extraarticular infection (particularly gastrointestinal or genitourinary).

Objectives: In order to highlight the clinical and etiological diversity of these events, the authors present several cases with postinfectious arthritis, all of them as examples of diagnostic pitfalls.

Methods: In the year 2012, 76 children (aged 1 to 16 years) with articular manifestations were evaluated in the our Pediatric Department Among these, 4 cases considered representative for postinfectious arthritis were selected. Case 1: a 3 years old boy with right ankle arthritis in the 5th day of evolution of a gastroenteritis with Shigella flexnerii; case 2: a 12 years old girl with knee arthritis in the course of a digestive infection with Yersinia enterocolitica with pseudoapendicular onset; case 3: a 18 months old boy with bilateral ankle arthritis in the evolution of a rotavirus gastroentritis; case 4: a 6 years 11 months old girl developed right wrist arthritis associated with characteristic rash, as clinical manifestations of borreliosis.

Results: Postinfectious arthritis may occur in the evolution of digestive and / or genitourinary infections. Viral etiology is often involved.

Conclusion: Postinfectious arthritis occurred after rotavirus gastroenteritis is an exceptional event which suggests new aspects of this viral infection.

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CONTRIBUTION OF MULTIPLEX REAL TIME PCR IN DETECTION AND DIFFERENTIATION OF ENTEROCYTOZOON BIENEUSI AND ENCEPHALITOZOON INTESTINALIS AMONG IMMUNOCOMPROMISED PATIENTS

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Background: Intestinal microsporidiosis is among the most frequent opportunistic diseases in immunocompromised patients. Routine diagnosis is generally performed by light microscopy of stained fecal samples. While unequivocal non-molecular species identification, important for cases management, is achievable only through electron microscopy.

Objective: This study aimed to evaluate the contribution of multiplex real time PCR for simultaneous detection and differentiation of Enterocytozoon bieneusi and Encephalitozoon intestinalis in stool specimens of patients with immunosuppressive conditions.

Methodology: Stool samples were obtained from 78 immunocompromised patients suffering from diarrhea. The samples were screened for intestinal microsporidiosis by light microscopy using Weber´s modified trichrome stain. The samples were subjected to multiplex real time PCR using Enterocytozoon bieneusi (E. bieneusi) primers and a probe targeting the internal transcribed spacer (ITS) sequence. Encephalitozoon intestinalis (E. intestinalis) primers and probe were targeting the small ribosomal subunit RNA gene sequence.

Results: Of 78 samples, 20 (25.6%) were detected positive by multiplex real time PCR. E. intestinalis was identified in 8 cases (40%), E. bieneusi in 7 (35%), and both species in 5 (25%). Light microscopy detected a total of 22 samples (28.2%), 7 of which did not show the belt-like structure characteristic for microsporidial spores (empty-looking spores). Compared to real time PCR, light microscopy had 75% sensitivity, 87.9% specificity, 68.2% PPV, 91.1% NPV and 84.6% accuracy in detection of microsporidia.

Conclusion: Multiplex real time PCR proved to be more effective than classical trichrome stain for simultaneous identification and differentiation between E. bieneusi and E. intestinalis.

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EPIDURAL INTRACRANIAL ABSCESSES WITH SEVERE BRAIN EDEMA RESISTANT TO PHARMACOLOGICAL TREATMENT

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Background and aims: In the early stage of the formation of an intracranial abscess, brain edema is commonly found. Slowly there is necrosis and liquefaction. The edema tends to resolve. After 2 to 3 weeks, the lesion becomes surrounded by a fibrotic capsule. To treat the edema we add glucocorticoids to the antibiotic therapy. We aim to study the severe brain edema resistant to pharmacological treatment adjacent to 2 epidural abscesses.

Methods: In a retrospective case series of eighteen patients diagnosed with brain abscesses from 2000 to 2011, we found two patients that presented frontal epidural abscesses. Both developed severe brain edema.

Results: Two patients presented frontal epidural abscesses. The predisposing factor in both cases was an otogenic infection. MRI with gadolinium were performed. In the initial imaging in the first case, we visualized a frontal epidural abscess with no signs of parenchymal edema. The patient developed later on a severe brain edema. In the second case, the initial imaging already showed an intense brain edema. Both patients received antibiotic treatment and glucocorticoid therapy. The response to medical treatment was poor, having to submit the patients to surgery. The first patient underwent a craniectomy and the second patient a drainage. There were no sequelae.

Conclusions: Due to the location of the abscesses, the superficial cerebral venous system was affected, disrupting the blood-brain barrier. This probably caused the severe brain edema. An early diagnosis is important, to decide the best course of action.

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PRE-ERUPTIVE PTOSIS AS AN UNUSUAL MANIFESTATION OF VARICELLA

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Introduction: Varicella-related neurologic complications usually appear during or following the rash. Pre-eruptive neurologic complications of primary varicella zoster virus (VZV) infections are extremely rare. To the best of our knowledge, pre-eruptive ptosis as a manifestation of varicella has not been previously reported in literature.

Case report: A 5 -year-old and otherwise healthy boy admitted to our hospital with a 1-week history of ptosis of the right eye following 2 days of unsteady gait, diplopia. Five days after admission, he developed mild vesicular skin rash and VZV exposure was retrospectively confirmed to have occurred 10 days before. Cerebral spinal fluid (CSF) analysis revealed a lympho-monocytosis with positive VZV DNA PCR. Serum VZV Ig M and G antibodies were positive. Cranial magnetic resonance imaging (MRI) showed a hyperintense lesion on the T2-weighted sequences in the right mesencephalon. Four weeks after admission, his ptosis improved significantly without any treatment and the control MRI showed regressed hyperintense lesion in the right mesencephalon.

Conclusion: Physicians treating patients with neurological and ocular disorders should be aware of that VZV may cause neurologic complications at pre-eruptive period.

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CHARACTERISTICS OF NEISSERIA MENINGITIDIS GROUP B (NMB) CARRIED BY ADOLESCENTS IN MILAN, ITALY, AND THEORETICAL COVERAGE OF SPECIFIC PROTEIN VACCINES

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Background and aim: FHbp, NadA, NHBA and porA are conserved proteins of NmB that evoke protective antibodies against this pathogen and are currently used to prepare specific vaccines. Among the vaccines in development, one includes one variant of each of these proteins and a second is based on FHbp variants 1 and 2. However, protection offered by these vaccines could vary according to the type of variants of each preparation, and by distribution and genetic variability of the proteins in infecting strains. To evaluate theoretical coverage of vaccines, characteristics of Nmb carried by adolescents living in Milan, Italy, were studied.

Methods: In 29 detected NmB strains, protein expressions and genetic characteristics were evaluated after genomic DNA extraction with PCR, sequencing, sequence alignments and phylogenetic analysis. Characteristics of identified proteins were compared with those of NmB vaccines.

Results: NadA was ever found. FHbp was always identified as subvariants 1, 2 and 3 in 12, 14 and 3 cases, respectively with identity >80% with those included in the vaccines. NHBA was not present in 3 strains, in which FHbp subvariant 2 was found. When present, NHBA had identity of 64-100%, with 19/26 cases characterized by >80% identity. Identity of porA, always found, was between 81% and 100%

Conclusions: Both the NmB vaccines currently in development seem to permit very high theoretical coverage of actually circulating NmB strains in adolescents living in Milan, Italy. However, considering the large in time variability of NmB, periodical controls of the characteristics of conserved proteins are recommendable.

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A PROSPECTIVE ANALYSIS OF THE CLINICAL SPECTRUM OF DIFFERENT SUBTYPES ENTEROVIRUS AND HUMAN PARECHOVIRUS

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Background and aims: Enterovirus (EV) and Human Parechoviruses (HPeV) are a major cause of aseptic meningitis in children. There a 4 species (A-D) human EV and 2 species parechoviruses (HPeV and Ljungan virus). The aim of this study is to describe the clinical spectrum of different EV and HPeV subtypes.

Methods: This study is part of a multicenter prospective study, involving children 0-16 years visiting three major general hospitals in the Netherlands. Children with clinical suspicion of an EV or HPeV infection were included and those with other cause of illness are excluded.

Results: From 285 included patients, 140 (39%) and 44 (12%) had an EV and HPeV infection, respectively. There were no significant differences in baseline characteristics. 54% of the EV infected children had a meningitis and 15% a gastro-enteritis. EV subtype A (EV-A) was found in 9 children and EV-B in 109, in 22 the subtype was unknown. Children with EV-B infection had significant more often a meningitis than children with an EV-A infection (60% versus 33%, p=0.007). HPeV subtype 3 (HPeV-3) was most detected in 24 (55%) children, HPeV-1 in 6 (14%), HPeV-4 in 2 and HPeV-6 in 1, in 11 the subtype was unknown. Children with a HPeV-1 infection had more often a gastro-enteritis than children with a HPeV-3 infection (83% versus 4%, p< 0.01).

Conclusions: EV infection is more associated with meningitis than HPeV infection, especially EV-B. HPeV infection is more associated with a gastro-enteritis than EV infection, especially HPeV-1.

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UTIS IN HOSPITALISED CHILDREN: DIAGNOSIS, MANAGEMENT AND TREATMENT - GUIDELINES COMPLIANCE

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Urinary Tract Infections are common in Paediatrics. Upper UTIs may have serious complications such as renal scarring and hypertention. Undiagnosed UTIs or delay in therapy admission increases the risk for complications and end-stage renal disease. In a try to improve our health care practise, we conducted a retrospective analysis of children above 3 months of age, hospitalised with Utis in General Hospital of Lefkas, between June and December 2012. Using The Nice guidelines we investigated all the protocols followed in a district general hospital of Greece.

Basic apsects of our investigation were the decision for urine sample, the method of urine collection, the method of analysing urine in the laboratory- according to the age-,the antibiotic selection, the days of hospitalisation and treatment, the use of ultrasound and the recommendation of VCUG and DMSA.

We found that our practice did not match the standards in the urine collection method (Clean catch was not perfomed in no-toilet trained children), in urinalysis (Dipstick was not used in children over 3 years, Urgent microscopy and Culture were used in all patients) and in the usage of ultrasound during acute illness. Patient safety was preserved at all time. In conclusion, our deviations from the guidelines, were due to inadequate equipment. However, overuse of urgent microscopy should be assessed regarding cost effectiveness.

This study is an effort to identify the accordance of a DGH in European standards but also a try to compare our health care services in management of UTIs among hospitals worldwide.

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VARIATIONS IN MULTIDRUG-RESISTANT BACTERIAL PATHOGENS IN A PAEDIATRIC INTENSIVE CARE UNIT BEFORE AND AFTER TRANSITION TO A NEW HOSPITAL FACILITY

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Background and aims: Infections in Paediatric Intensive Care Units (PICU) caused by multidrug-resistant (MDR) bacterial organisms are increasing. We aim to establish whether a change in hospital facilities had an impact on the number of MDR organisms isolated in a PICU.

Methods: Retrospective study conducted in the PICU of a paediatric hospital that changed facilities in 2010. The PICU has an average of 380 admissions/year. All cultures performed in the PICU, in 2009 and 2011, were analysed and data on patients infected with MDR organisms compared.

Results: Two patients in 2009 and seven in 2011 had an infection by MDR organisms. Both patients in 2009 and 5/7 in 2011 had an underlying medical condition, with multiple hospital admissions. In 2009, methicillin-resistant Staphylococcus aureus (MRSA) was isolated in a child with catheter-related bloodstream infection (CRBSI); vancomycin-resistant Enterococcus spp was isolated in the peritoneal fluid of a child after complicated abdominal surgery. In 2011, three patients had MRSA infections: 2 CRBSI and one ventilator-associated pneumonia. Extended-spectrum β-lactamase (ESBL) producing Gram-negative organisms were the cause of infection in four patients, with appendicitis complicated with peritonitis, CRBSI, abdominal infection after liver transplantation and lower respiratory tract superinfection.

Conclusions: Albeit a small number of cases in both years, an increase in the number of emerging MDR organisms was noticed. However, most of these children are chronic patients, requiring multiple interventions, not only in the PICU but in other wards. Thus, an association with the change in hospital and PICU facilities cannot be conclusively established.

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CASE SERIES OF FATAL DISSEMINATED ENTEROVIRUS INFECTION IN THE NEONATAL PERIOD

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Background: Enteroviruses (EV) are members of the Picornaviridae Family. EV commonly cause a febrile illness but are important neonatal pathogens associated with high risk of disseminated infection and death.

Case presentations: We describe three cases of severe enterovirus infection in the early neonatal period, detected only at post-mortem. They presented at different hospitals in South-Eastern England over a period of two months in 2011 with non-specific symptoms, including lethargy and poor feeding. Rapid deterioration with significant thromobocytopaenia and coagulopathy, progressing to respiratory failure or meningo-encephalitis were some of the features seen.

Enterovirus RNA was detected by polymerase chain reaction (PCR) at post-mortem in cerebrospinal fluid, nasopharyngeal aspirate, and heart and lung tissue in all three cases. Typing was obtained by partial genome sequencing.

Coxsackie B2 and B4 subtypes were identified in the two cases with post-mortem findings of acute myocarditis and encephalitis. In the case with Coxsackie B4 infection cytomegalovirus (CMV) was also detected in different tissues, with a retrospective diagnosis of maternal primary cytomegalovirus. In the case with enterovirus 71 infection autopsy showed bronchopneumonia and myocarditis.

Discussion: Neonatal enterovirus infection can mimic bacterial sepsis and progress rapidly, with a high mortality seen in antenatal infection. It is important to consider disseminated viral infection in a sick neonate and investigate with cerebrospinal fluid, nasopharyngeal aspirate, stool and whole blood. Prompt detection of severe enterovirus can facilitate early supportive therapy and reduce overall mortality.

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EARLY-ONSET SEPSIS IN A PORTUGUESE NEONATAL INTENSIVE CARE UNIT: TRENDS IN INCIDENCE AND ANTIMICROBIAL RESISTANCE OVER A 5-YEAR PERIOD

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Background and aims: Early-onset sepsis (EOS) remains an important cause of morbidity and mortality amongst newborns, with group B Streptococcus (GBS) being the most frequent isolated pathogen.

Aim: To evaluate clinical data of newborns with EOS and trends in causative microorganisms and their antimicrobial susceptibility.

Methods: Retrospective analysis of medical records and microbiological data of all newborns with EOS, defined by signs/symptoms compatible with positive blood culture or laboratory studies suggestive of infection (WBC>30.000/µL or < 5.000/µL, platelet count< 100.000/µL, CRP>2mg/dL), within the first 72 hours of life. Study period: January 08 -December 12.

Results: Among a total of 14950 live births (LB), 64 newborns developed EOS (4,3 per 1000LBs). Twenty-one cases had positive blood cultures (1,4 per 1000 LBs): 43% were preterm newborns. Respiratory distress and grunting were the most frequent signs; CRP was >2mg/dL in 76%.

The most frequently isolated bacteria were GBS (12; 0.8 per 1000LBs) and E. coli (4; 0.2 per 1000LBs). Most newborns with GBS infection were term (83%) while those with E. coli were preterm (median 31weeks).

Ampicillin and gentamicin were the main antibiotics used. GBS showed no resistance to penicillin as well as E. coli to gentamicin. MRSA was isolated in 1 case. Lethality occurred in 2 preterm newborns with positive blood cultures.

Conclusions: In agreement with literature, GBS was the most frequent pathogen in term newborns and E. coli in preterm, with low levels of resistance to commonly used antibiotics. Continuous surveillance of antibiotic susceptibility is essential to rationalize antibiotic prescribing.

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CLINICAL SPECTRUM OF CONFIRMED PEDIATRIC SEVERE BACTERIAL INFECTIONS

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Backgroud and aim: High index of suspicion should be present when we evaluate a possible case of severe-bacterial infection in children. The aim of this study was to evaluate the clinical spectrum of invasive bacterial infections in children, in a tertiary referral hospital.

Material and method: Clinical spectrum of invasive and non-severe bacterial infections was compared in two groups admitted during 2011.

Retrospective analysis of data from centralized electronic files and source documents was performed.

Results: 17598 children were presented in ED and 4320[24.55%] were admitted. Infection was suspected in 38.24%[1652]. 6764 cultures were performed. 21[0.87%] children had dramatic features of invasive disease.

15.86%[381] samples documented bacterial-proven episodes. 23.1%[88] were UTI's, 64.57%[246] enteritis, 9.97%[38] endotracheal samples and 2.36%[9] septicaemia.

Children with invasive disease had more often an isolated pathogen [p=0.0278].

In invasive disease vs non-invasive they were younger [mean age 14.52 months vs 18.78], they had a longer length-of-stay [19.76 days vs 4.78%] and had more comorbid conditions [10/21 vs 41/381, p=0.001]. Other clinical features were similar excepting shock [tachycardia 131/min (SD 33.99) vs 92/min (SD 23.84), capillary refill-time 4.4 vs 2.1sec] and proportion of prolonged fever [8/21 vs 17/381, p< 0.01].

Outcome was worse [but not statistically significant, p=0.2004] in invasive disease with a case-fatality rate of 4.76% vs 0.79% in non-invasive.

Conclusions:

1. Etiology can be more often documented in invasive vs non-invasive disease.
2. Pronged fever and shock should initiate an aggressive approach.
3. Invasive disease generates a higher burden [longer LOS and higher case-fatality rate].

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IMPACT OF RESPIRATORY VIRUSES IN PULMONARY EXACERBATIONS IN CHILDREN AND ADOLESCENTS WITH CYSTIC FIBROSIS (CF)

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Background and aim: The impact of respiratory viruses in cystic fibrosis (CF) exacerbations remains unclear. The aims of this study were to evaluate the respiratory viruses associated with pulmonary exacerbations in CF and to determine the clinical severity due to exacerbations associated with viral infections.

Methods: A total of 54 CF patients (19 males; age range, 5-25 yrs) were enrolled. Among them, 33 had acute pulmonary exacerbations, whereas 21 were stable since more than 3 months. Nasopharyngeal swabs were obtained and evaluated for 17 respiratory viruses (influenza A/H1N2, A/H3N2, B; RSV-A and -B; parainfluenzavirus -1, -2, -3 and -4; adenovirus; metapneumovirus; coronavirus 229E, NL63, OC43 and HKU1; enterovirus/rinovirus; bocavirus) by means of Luminex xTAG Respiratory Virus Panel Fast assay. The samples that were positive for enterovirus/rhinovirus were retested in order to identify the rhinovirus. Nutritional status, pulmonary function tests, clinical conditions, severity scores, and sputum cultures were recorded.

Results: Nine patients (27.7%) with pulmonary exacerbations and 4 of those stable (19%; p=0.38) resulted positive for respiratory viruses. Among those with pulmonary exacerbations, rhinovirus alone was detected in 6 cases, metapneumovirus in one, influenza A in one and rhinovirus plus metapneumovirus in one. Viral-related exacerbations appeared similar in clinical severity to non-viral exacerbations. Rhinovirus was the only virus detected in the 4 stable cases.

Conclusions: Rhinovirus seems the respiratory virus with the major role in patients with CF regardless of the presence of pulmonary exacerbations. Its contribution in pulmonary inflammation and decline in lung function should be clarified.

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A CLINICAL EPIDEMIOLOGY STUDY OF THE CHARACTERISTIC OF NTHI ISOLATED FROM THE NASOPHARYNX OF YOUNG CHILDREN WITH AOM IN KOREA

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Objective and background: The increase of NTHi AOM in many countries after introduction of PCV is becoming a problem. Also, NTHi antibiotic resistant strains by PBP3 mutation is increasing. So the authors evaluated the colonization rate of NTHi in the nasopharynx of Korean children under five years of age with AOM, and also to evaluate the antibiotic resistance distribution and mechanism.

Method: This study was conducted from January 2011 to March 2012 in seven hospitals in Korea. Nasopharyngeal secretion was collected from children with AOM under five years of age, who had been just before antibiotic treatment. The sample was cultured and the colonization rate and the antibiotics resistance was evaluated. Tyepable and non-typeable strains were differentiated, and the distribution of beta-lactamase producing strains and PBP3 mutant strains were evaluated.

Result: Of the 419 subjects who participated in this study 136 Haemophilus influenzae were isolated so that the total colonization rate was 32.5%. All 136 isolates were NTHi, 56(41.2%) isolates produced beta-lactamase, of those beta-lactamase producing isolates, 53 showed resistance to beta-lactamase inhibitor antibiotic amoxicillin-clavulanate (BLPACR; 39.0%), 65 isolates were resistant to ampicillin without producing beta-lactamase (BLNAR; 47.8%). Most beta-lactam antibiotics revealed antibiotic resistant. Cefditoren-pivoxil showed the lowest MIC range.

Conclusion: The majority of Haemophilus influenza colonizing the nasopharynx of Korean children with AOM under five years was non-typeable. The rapid extension of antibiotic resistance due to PBP3 alterations is serious and further studies are needed. Cefditoren-pivoxil may be effective secondary antibiotic drug to control NTHi AOM in our country.

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STUDY OF INTESTINAL MICROSPORIDIOSIS AMONG KIDNEY TRANSPLANT PATIENTS IN HAMADAN, WEST OF IRAN

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Background and objective: Organ transplantation and using immunosuppressive drugs continuously are major risk factors for opportunistic infections that sometimes resulted severe conditions that must monitored constantly. Microsporidia is an obligate intracellular parasite and one of the important agents causing chronic diarrhea in immunocompromised patients. The laboratory diagnosis of organism is relatively difficult and chromotrope staining is a standard diagnostic method for detection of Microsporidia. The aim of present study was to determine the frequency of intestinal Microsporidia infection among kidney transplant patients.

Methods: A total of 180 stool specimens were taken from kidney transplant patients admitted to Beheshti teaching Hospital of Hamadan, Iran. The patients were using the immunosuppressive drugs continuously. Patients selected neither or not they had gastro-intestinal symptoms. The modified trichrome staining and with calcofluor white was used to identify Microsporidia in stool samples. Air dried, methanol fixed thin stool smears prepared and stained by modified trichrome staining and slides examined using light microscopy.

Results: Totally 86 patients (47.7%) of patients were female and others were male. The mean duration of kidney transplant and immunosuppressive drug using in the patients was 5.5 Years. Only one (0.55%) of 180 patients was positive for Microsporidia and she was a female patient.

Conclusions: On the basis of the frequency of this opportunistic infection, fortunately this parasite is not a common infection in these immune-deficient patients in spite using long time immunosuppressive drug.

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IMMUNIZATION CAMPAIGN FOR HIGH-RISK CHILDREN WITH PREVENAR-13

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Background and aims: Since 2001 the Department of Health of the Murcia Region provides pneumococcal conjugate vaccine to high-risk children. Since the license of Prevenar-13 we proceeded to the update of high-risk children who had received Prevenar previously. We evaluated: risk factor, compliance with the immunizations prescribed (pneumococcal, influenza and chickenpox) and the results obtained by passive and active uptake.

Methods: This campaign was done with two different strategies: passive (in June 2010 sent recommendations to all pediatricians and nurses) and active, since March 2011 to March 2012, we reviewed all high-risk children in our Immunization Registry contacting their parents through phone or mail.

Inclusion criteria were: less than 6 years at the start of the campaign and risk factors that indicate vaccination.

Results: A total of 685 children born between March 2005 and April 2009 took part of the campaign. The 95% of high-risk children accomplished the prescription with Prevenar but only 23.5% received the polysaccharide vaccine. 57.5% were vaccinated at least once against influenza and 71.1% against chickenpox (13.8% one dose, 57.3% two doses).

Immunization with Prevenar-13 by passive uptake was achieved by 17.4%, rising to 55% by active uptake. When telephone contact is achieved, coverage reaches 83%. There were a total of 20 deaths (2,9%).

Conclusions: Compliance with the vaccination of Prevenar is excellent but improvement over other prescribed vaccines is desirable. Passive uptake strategy is not effective and active strategy is required. Telephone contact is shown as the most effective strategy.

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SALMONELLA TYPHIMURIUM GASTRENTERITIS AS A RARE CAUSE OF RHABDOMYOLYSIS AND ACUTE RENAL FAILURE IN A CHILD

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Introduction: Rhabdomyolysis, a potentially fatal syndrome, has been described to be induced by Salmonella infections in adults. Salmonellosis in children has been rarely reported to be associated with such severe extraintestinal complications. Specifically, this is the first, to our knowledge, reported case of rabdomyolysis due to Salmonella typhimurium gastroenteritis in a child in Europe.

Case report: A 13-year old boy was referred to our institution from a rural peripheral hospital due to rhabdomyolysis and progressive impairment of renal function. At the regional hospital the child was presented with 12-hour fever, vomiting, diarrhea, oliguria, severe abdominal and muscular pain. The initial laboratory testing showed increased levels of CK (141,740 U/L), SGOT (3,020 U/L), SGPT, LDH (4,800 U/L), urea nitrogen (40mg/dl), and creatinine (1.4 mg/dl). The urine was reddish-brown, positive for myoglobulin. Stool specimens were positive for Salmonella typhimurium. Abdominal ultrasonography showed parenchymal renal damage and splenomegaly. Despite fluid replacement along with antibiotics the patient continued to be oliguric, developed generalized edema with increased body weight and progressive renal failure. On the fifth day of hospitalization the patient underwent hemodialysis and hemofiltration for 6 days. The patient gradually improved with increased urine output and normalization of the levels of CPK and serum/urine myoglobulin. He was discharged from the hospital three weeks later with normalization of renal function.

Conclusion: Despite the rareness of rhabdomyolysis due to Salmonella typhimurium, it can be a life-threatening complication due to the relatively high incidence of Salmonellosis. There seems to be need for stricter hygiene rules.

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NEONATAL GROUP B STREPTOCOCCUS INFECTION SURVEILLANCE STUDY IN WEST HERTFORDSHIRE, UK

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Background and aims: Group B streptococcus (GBS) remains the most important cause of neonatal morbidity and mortality in high income countries. In the UK, GBS accounts for 58% of early onset sepsis. In 2003, the Royal College of Obstetrics and Gynaecology established national guidance for intrapartum antibiotic prophylaxis, updated in 2012, to reduce neonatal infection rates.

We aim to undertake regional surveillance to estimate incidence in West Hertfordshire and changes over the last decade. We will evaluate service provision in the prevention of invasive neonatal GBS disease within our region.

Methods: A retrospective study from 1st January 2003 to 1st January 2013 of infants under 3 months with GBS culture positive sterile samples (blood, cerebrospinal fluid (CSF), urine, bone/joint aspirates) is underway. A standardised proforma will be completed by a clinician for each positive GBS culture including: infant demographic details (birth weight, gestational age, gender, post code, ethnicity), clinical information (risk factors for sepsis, presentation, ventilatory support), biochemical (C-reactive protein) and microbiological data (CSF microscopy, antibiotic sensitivities).

Results: The analysis will include; GBS Incidence, age at infection, clinical presentation, efficacy of intrapartum antibiotics and disease outcome.

Statistical analysis will utilise parametric or non-parametric methods after assessing data distribution and processed with STATA 9.

Conclusions: The incidence of neonatal GBS infection in West Hertfordshire is currently not known but rates of 1.15 per 1000 live births were reported in Bedfordshire almost 15 years ago. Knowledge of local GBS incidence rates will enable services to prioritise preventative strategies.

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STAPHYLOCOCCUS AUREUS PANTON-VALENTINE LEUKOCIDIN POSITIVE CAUSING COMPLICATED COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN

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Background and objectives: Diagnosis of community-acquired methicillin-sensitive Staphylococcus aureus (AC-MSSA), Panton-Valentine leukocidin (PVL) positive, pneumonia has increased in pediatric population from the beginning of XXI century. We report the clinical features, diagnosis, treatment and outcome of two children with complicated pneumonia by AC-MSSA secreting PVL.

Case reports:

Case 1: A 13 years old boy, with episodic asthma, fever, cough, night sweats, hyporexia, dyspnea and hemoptysis was admitted. He had hypoventilation in the base of left lung and rales in the base and apex of the right hemithorax. Multiple cavitary infiltrates were identified. In sputum culture grew MSSA PVL positive and blood cultures were sterile. Treated with IV clindamycin and cefotaxime, switched off to oral amoxicillin-clavulanate, 6 weeks of antibiotics, with gradual improvement. Afterwards he presented a pneumatocele.

Case 2: A 7 months old infant, previously healthy, with fever, irritability, increase work of breathing and low intake was admitted. On examination, hypoventilation in the right lung base. Condensation at medium and lower rigth lobes with loculated pleural effusion were seen. In the pleural fluid grew MSSA PVL positive and blood cultures were sterile. Treated with IV clindamycin and cefotaxime, switched off to IV cloxacillin and, afterwards, to oral amoxicillin-clavulanate, 4 weeks of antibiotics, pleural drainage and intrapleural fibrinolytics with good performance.

Conclusions: MSSA secreting PVL complicated pneumonia is a serious infection present in our environment that requires early and aggressive treatment. Their existence must be taken into account in the empirical antibiotherapy of community-acquired severe complicated pneumonia in previously healthy children.

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THE YIELD OF ROUTINE MONITORING OF CHILDREN WITH PERINATALLY ACQUIRED CHRONIC HEPATITIS C VIRUS INFECTION

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Children with hepatitis C virus infection (HCV) are often asymptomatic. This study assessed the yield from routine follow-up of such children attending the ID clinic in Dublin, Ireland.

Data for this retrospective cross sectional study was collected from patient charts, and radiology and laboratory reporting systems. Stata v12 was used for analysis. Confidentiality was ensured by numerically coding at input.

Sixty-nine patients with HCV were enrolled in the clinic in December 2012, 99% had perinatal transmission. Median age was 9 years [0.5-17 years] and 42(62%) were female. Blood was drawn a mean 1.4 times/patient/year for HCV RNA, liver biochemistry and haematology. 64 (93%) showed mild transaminitis and 6(9%) had hyperbilirubinaemia on at least one occasion. Mean maximum ALT was 107.98 [95%CI 89.77-126.18]. Patients at a mean of 20.27 [95% CI 3.03-37.5]. Iron deficiency anaemia was diagnosed in 16 patients. Abdominal ultrasound was performed on average every 2.8 years. Mild radiological abnormality was reported in seven patients (10%). Two patients reported symptoms and ten had physical signs. Psychosocial information was available on 57 patients. 26 [45.6%] were identified as 'vulnerable children'.29 families [50.8%] required ongoing psychosocial support. 33 children were aware of their diagnosis. In 17 cases [51.5%] disclosure was managed by the clinic team.

Routine clinical, laboratory and radiological monitoring has a low yield for disease progression and extrahepatic manifestations in our HCV infected population. Mild transaminitis is common but rarely clinically significant. Children with HCV are socially vulnerable and benefit from contact with specialist services including psychosocial support.

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DETECTION OF HUMAN HERPESVIRUSES IN FREQUENTLY ILL CHILDREN WITH ACUTE RESPIRATORY VIRAL INFECTION AND THEIR EFFECT ON THE DISEASE COURSE

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Introduction and aim: Data on the impact of herpesviruses in the incidence of acute respiratory infections (ARVI) is not enough. Our goal was to analyze the frequency of herpesviruses detection in frequently ill children with ARVI and to examine their effect on the severity and duration of disease.

Methods: 72 frequently ill children (at least 6 ARVI per year) aged 3 months - 3 years were studied. DNA of HSV1/2, CMV, EBV, HHV6 was detected by rtPCR in 181 samples: blood (n=68), urine (n=55) and saliva (n=58).

Results: DNA of at least one of the viruses was detected in 59.7% (43/72) children: CMV, in 33.3%; HHV6, in 38.9%; EBV, in 22.2%; HSV, in 2.8% cases.

Monoinfection was identified in 37.5% children. The detection frequency for DNA of HHV6 (19.4%) and CMV (13.8%) was significantly higher than that for DNA of EBV (4.2%) and HSV (0%). Mixed infection was detected in 26.3% children. In 19.4% children two viruses were detected: CMV+HHV6, in 8.3% of them; CMV+EBV, in 5.5%; EBV+HHV6, in 4.2%; EBV+HSV, in 1.3%. Three viruses were detected in 6.9% children: CMV+EBV+HHV6, in 5.5%; EBV+HHV6+HSV, in 1.3%. At high concentration of herpesvirus DNA (>10000 copies/ml) the disease was complicated by reinfection and lasted for a longer time period.

Conclusion: High prevalence of herpesviruses was demonstrated in frequently ill children with ARVI that manifests itself as mono- or mixed herpesvirus infections. High concentration of herpesvirus DNA was associated with complications of ARVI.

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INFECTIONS IN CHILDREN WITH LEFT VENTRICULAR ASSIST DEVICE (LVAD): THE EXPERIENCE OF EGE UNIVERSITY HOSPITAL

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Despite improvements in treatment of heart diseases with ventricular assist devices(VAD), infections are still associated with significant morbidity. Infections in patients with VAD described in three groups: left ventricular assist device(LVAD) related, non-LVAD related and sepsis. LVAD related infections includes driveline, pump pocket infections and defined as those that required treatment with antimicrobial therapy, when there is clinical evidence of infection such as pain, fever,drainage, and leukocytosis. We report in this retrospective study our three years of experiences (2009-2012) about infections in 12 pediatric cases with LVAD.

The patients had Berlin-Heart Excore LVAD (n=9) and Heart Ware LVAD (n=3). All patients had the diagnosis of dilated cardiomyopathy. The mean age of the patients was 8,33 years (range, 17 months-15 years). Five patients (55.5%) with Berlin Heart Excore LVAD had at least one episode of infection. Fever and drainage from the exit site were the most common symptoms. The most common type of LVAD related infection site was the exit of the drive line. The most common type of non-LVAD infections were urinary and upper respiratory tract infections. Most of the driveline infections remained superficial and were managed with local wound care and antibiotics until transplantation. Staphylococcus aureus was the most commonly detected microorganism in LVAD related infections. Only two patients died before transplantation, one of the patients died because of sepsis; coagulase negative Staphylococcus and Candida were detected in the blood cultures.

Although LVAD support is associated with improved survival and quality of life, infectious complications remain a major limitation.

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RSV INFECTION AMONG CHILDREN WITH UPPER OR LOWER RESPIRATORY TRACT DISEASES IN BULGARIA

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Background and aims: RSV is leading cause of respiratory diseases in infancy. The aim of this study was to determine the contribution of respiratory syncytial virus (RSV) to acute upper and lower respiratory-tract diseases (bronchiolitis and pneumonia) among infant and toddlers in Bulgaria.

Materials and methods: During the season 2010/2011 nasopharyngeal swabs were collected from 162 children aged ≤1 year who have been hospitalized for bronchiolitis and pneumonia in 4 regions of the country. In the next season 2011/2012 nasopharyngeal swabs of 45 children aged 0-2 years with ARI or ILI from different regions of country were investigated. RSV was detected using RSV Real Time RT-PCR kit (Liveriver, Shanghai).

Results: During the season 2010/2011 out of 108 tested children with bronchiolitis and 51 - with pneumonia, 43 (39,8%) and 20 (39,2%) were positive for RSV, respectively. The mean age of RSV infected children was 4,0 ± 2,9 months. RSV infections were predominating in December 2010 with peak in week 48/2010. 67% of the children with proved RSV infection have received antibiotics. During the season 2011/2012 RSV was not detected.

Conclusion: RSV is a common cause of bronchiolitis and pneumonia required hospitalization among children aged ≤1 year. Among children with upper respiratory tract diseases incidence of RSV infections was low. Real Time RT PCR is rapid, reliable, highly sensitive and specific method for diagnostics of RSV infection.

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SEVERE RSV INFECTIONS IN CHILDREN ADMITTED TO INTENSIVE CARE UNITS - RESULTS FROM A PROSPECTIVE SURVEILLANCE STUDY IN BAVARIA, GERMANY

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Background: We investigated the frequency and clinical characteristics of severe RSV infections in 22 paediatric intensive care units (PICUs) in Bavaria, Germany.

Methods: From October 2010 to April 2012, naso-pharyngeal secretions from children >1 month and < 17 years of age admitted with ARI to PICUs were tested by multiplex PCR for 20 respiratory viruses.

Results: A total of 279 ARI patients were reported. RSV was confirmed in 85 (31%) patients, by PCR (82%) or rapid test (18%). Median age of RSV patients was 2 months (IQR: 1-15); 50.6% were male. Underlying chronic conditions were reported in 36 (42%) cases (preterm birth 18 (21%)). Duration of PICU stay was 3 days (median; IQR: 2-5), of hospital stay 7 days (IQR: 6-10). Fifteen (18%) children were admitted in a life-threatening condition. The most frequent diagnoses were bronchitis/bronchiolitis (91%) and pneumonia (58%). Oxygen substitution was needed in 87%, CPAP in 26%, and endotracheal ventilation in 12% of patients. Two (2%) children had sequelae and 2 (2%) died. Viral co-infections were found in 27 (32%) children, most frequently with rhinovirus (9%) and coronavirus (8%). Clinical characteristics did not differ from infections solely with RSV.

Discussion: RSV was the most frequent viral pathogen leading to PICU treatment. One fifth of RSV patients were admitted in a life-threatening condition, but fatalities were rare. Thirty-two % of the RSV patients had a co-infection with another respiratory virus, but did not show a more severe course of disease compared to children positive only for RSV.

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THE DIAGNOSTIC AND TREATMENT OF HELICOBACTER PYLORI INFECTION IN CHILDREN - A SINGLE CENTER STUDY

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Helicobacter pylori is mainly acquired in childhood and in absence of therapy lasts for life in majority of cases.

To investigate the accuracy of diagnostic tests and treatment.

We conducted a prospective study of 145 children with active H pylori infection, who were diagnosed by invasive and non-invasive tests during 2009-2011.

They were randomized in 2 groups to receive one of the standard triple therapies for 7-14 days or a 10-days sequential treatment.

Of 145 children with H pylori infection, the urease test was positive in 115 children (sensitivity 85,19%; specificity 93,94%), histology in 129 cases (sensitivity 89,58%; specificity 99,36%) and culture in 108 cases (sensitivity 74,48%; specificity 100%). The H pylori virulence genotype was identified by PCR in 140 children (sensitivity 96,55%; specificity 100%), significantly higher compared with the other invasive tests. The cag A gene was positive in 96 cases, compared with vac A, which was identified in all cases. H pylori fecal antigen was identified in 132 children with a significantly higher sensitivity (92,96%), specificity (98,10%) compared with the most used biopsy-based tests.

Overall the eradication rate after the first treatment was 77,93%, with the best results for the sequential (86,3%) compared with that obtained by the three types of standard first line triple therapies (69,44%) $p = 0,0167$.

Our data suggest that among invasive test PCR, had a significantly higher sensitivity and specificity ($p < 0,0001$) compared with noninvasive ones. The eradication rate achieved with the sequential regimen was statistically higher compared with triple therapies.

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M. TUBERCULOSIS VS. M. BOVIS BCG - ELUCIDATING DIFFERENCES IN THE HOST GENE RESPONSE BETWEEN PATHOGEN AND VACCINE STRAIN

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Background and aims: BCG is the only available vaccine against tuberculosis (TB). It is routinely administered to infants in many countries worldwide and provides protection against disseminating and meningeal forms of TB, however protection against pulmonary TB is sub optimal. In order to understand how the host response to M. bovis BCG (BCG) differs from that to M. tuberculosis (MTB), we compared genome wide RNA expression in human blood in response to in vitro infection with BCG or MTB compared to controls.

Methods: Whole blood from non-BCG-vaccinated healthy donors was infected with either MTB or BCG and RNA recovered at five sequential time points up to 96 hours. After amplification and labeling, RNA was hybridized to Illumina HT12 microarrays. Genes showing significant differential expression in the infected samples compared to controls over time were identified using a novel in-house statistical method.

Results: 2064 genes were significantly differentially expressed in response to both MTB and BCG compared to uninfected controls. However, genes uniquely differentially expressed in response to either MTB (2576) or BCG infection (1642) were also identified. Biological pathway analysis (using Ingenuity, IPA) of the host response to BCG and MTB revealed reduced expression of genes involved in cellular interactions, T-cell signalling as well as phagolysosome maturation.

Conclusion: Elucidation of differences in gene induction in response to BCG or MTB may help to better understand the specifics of MTB infection as well as the characteristics of vaccine response to BCG.

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PRIMARY CYTOMEGALOVIRUS INFECTION AS A CAUSE OF HOSPITAL ADMISSION IN CHILDHOOD

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Background: Primary cytomegalovirus (CMV) infection has been occasionally associated with acute clinical manifestations in immunocompetent children.

Objective: To investigate the association between primary CMV infection and acute clinical manifestations in hospitalized children.

Methods: Three-hundred eighty-seven children (206 females), aged 3 months to 14.8 years (mean: 6.4), were admitted to San Salvatore Hospital, L´Aquila, between December 1, 2010 and November 30, 2012. CMV IgG, IgM antibodies and IgG avidity were measured along with blood, saliva and urine CMV DNA by RT-PCR in 282 patients (72.9%). Primary CMV infection was defined by the occurrence of increasing IgM levels, low avidity index and/or seroconversion.

Results: CMV IgG were detected in 67 (23,7%) patients. Primary CMV infection was found in 30 children (10,6%) and was associated with pneumonia in 8 (26,6%), urinary tract infection in 4 (13,3%), febrile convulsions in 3 (10%), lymphadenitis, arthritis, bronchiolitis, tonsillitis, and vasculitis in 2 each (6,6%), hepatitis in 1, mononucleosis syndrome, gastroenteritis, and unknown fever in 1 each (3,3%).

Conclusions: Primary CMV infection may be responsible for hospital admission in a significant number of patients who are mainly affected by respiratory diseases. In view of a possible routine diagnostic screening, a multicentre, larger study is suggested.

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HERPESVIRUS-ASSOCIATED URTICARIA: AN AGE MATCHED CASE-CONTROL STUDY

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Background and aims: Acute and recurrent acute urticaria are often associated with multiple factors including infections. We evaluated the association of herpesvirus infections with urticaria.

Methods: Thirty-seven patients aged 1 month to 15 years were age matched to 37 controls who were siblings or playmates of the patients. Patients and controls were followed for 1 to 6 years. Diagnostic studies included DNA detection by real-time PCR for herpes simplex virus (HSV) types 1 and 2, Epstein-Barr virus (EBV), cytomegalovirus (CMV) and human herpesvirus-6 (HHV-6). Tests for other infections included adenovirus, parvovirus B 19, respiratory syncytial virus, influenza A, group A streptococci, rotavirus, and parasites.

Results: The patients with acute urticaria or acute recurrent urticaria, compared to the age matched controls, had a higher prevalence of herpesvirus infections (65% vs 11 %, p=0.0003). HHV-6 was detected in 10 urticaria patients, CMV infection in 8, EBV in 5, and HSV-1 in 4.

Conclusions: In addition to an atopic predisposition and occasional allergens, herpesvirus infections, in particular HHV-6 and CMV, may play a triggering role in the development of acute urticaria in children.

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VARIATION IN RISK OF CLOSTRIDIUM DIFFICILE INFECTION ACROSS BETA-LACTAM ANTIBIOTICS IN CHILDREN WITH NEW ONSET ACUTE LYMPHOBLASTIC LEUKEMIA

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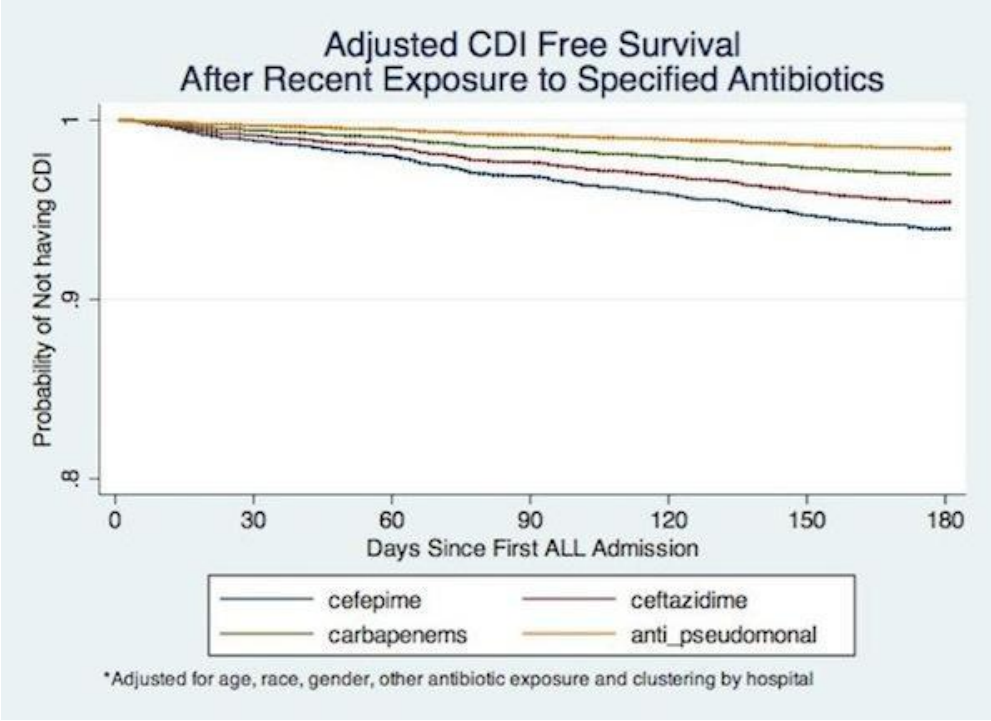
Background: Antibiotic exposure is common among children with leukemia. Limited data exist regarding variation in risk of Clostridium difficile infection (CDI) across antibiotic agents.

Methods: A multi-center cohort of children with newly diagnosed ALL between 1999-2009 was established using administrative data. Patients were followed until their index CDI event, defined by the CDI ICD-9-CM code plus a C. difficile test charge, or until 180 days from ALL diagnosis. CDI onset was defined by the C. difficile test date. Daily antibiotic exposures were captured using pharmaceutical billing records. A Cox proportional hazards model compared time to CDI in patients with recent exposure (prior 30 days) to anti-pseudomonal penicillins, carbapenems, cefepime, and ceftazidime, and adjusted for demographics, other antibiotic exposures, and clustering by hospital.

Results: A cohort of 8,268 ALL patients was assembled; median age was 5.5 years (range: 1.0-18.9) and 56% were male. 268 (3.2%) patients developed CDI within 6 months of ALL diagnosis. After multivariable modeling, recent exposure to cefepime was more significantly associated with CDI than exposure to anti-pseudomonal penicillins (HR: 4.54, 95% CI: 2.36-8.73) or carbapenems (HR: 2.29, 95% CI: 1.31-4.00). Risk of CDI following ceftazidime exposure was similar to cefepime (HR: 1.24, 95% CI: 0.70-2.20) (Figure).



[Figure]

Conclusions: Recent cefepime or ceftazidime exposure was associated with a greater risk for CDI among children with newly-diagnosed ALL than anti-pseudomonal penicillins or carbapenems. These findings, if confirmed, have potential implications for antibiotic choice during periods of fever and neutropenia.

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THORACO-ABDOMINAL MASS SECONDARY TO ACTINOMYCES INFECTION: AN UNUSUAL PRESENTATION

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Actinomycosis is an uncommon, indolent, invasive infection caused by Actinomyces species, opportunistic Gram positive organisms that normally colonize the oropharynx. Abdominal and thoracic districts are among the most common sites of involvment. Risk factors include dental caries and trauma. We describe a case of thoraco-abdominal acticomycosis in a 8-years-old-boy who was admitted to our hospital for left upper abdominal pain after a banal trauma, abdominal ultrasound was negative. Some days after he returned for shortness of breathing without fever and re-presentation of abdominal pain.

His physical examination was positive for left side abdominal and thoracic tenderness and several dental caries. The history was negative for severe infections and immunodeficiency. Abdominal ultrasound and computer tomography (CT), showed a pulmonary consolidation with pleuric effusion and vascularized perisplenic lesion. Routinary analysis showed leucocytosis with neutrophilia, an increased in C-reactive protein and mild anemia while lactate dehydrogenase (LDH), liver, renal function as well as cancer markers on the ipotesis of neoplastic lesion were normal. Ultrasound-guided biopsy of the lesion showed granulation tissue with abscesses. The culture came back to be Actinomyces. Antibiotic therapy was performed with a clinical improvement. Follow up CT scan showed a decrease of the thoraco-abdominal lesion.

Actinomycosis has been called “the most misdiagnosed disease” and it is rare in children and adolescent. The symptoms and routine blood tests are not specifics. The definite diagnosis of actinomycosis relies on Gram stain microscopy and culture. Furthermore radiological investigations are essential for diagnosis as well as for the follow up.

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REDUCING NEONATAL INFECTIONS IN SOUTH AND SOUTH CENTRAL VIETNAM: THE VIEWS OF HEALTH CAREGIVERS

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Aim: To examine the views of healthcare providers in provincial hospitals in south and south central Vietnam on how to improve neonatal infection prevention and control.

Methods: All fifty-four participants to workshop on infection prevention and control were asked to complete an anonymous, written questionnaire identifying their priorities for improving neonatal infection prevention and control in provincial hospitals in south and south central Vietnam.

Results: Hand washing, exclusive breastfeeding and safe disposal of medical waste were scored by participants as the highest priorities for preventing neonatal infections. Education through instructional posters and written guidelines, family contact, kangaroo-mother-care, limitation of invasive procedures and screening for maternal GBS infection received relatively low scores.

Conclusions: The opinions of neonatal healthcare providers at the workshop accurately reflect some of the current international recommendations for infection prevention. Some important recommendations were not however commonly identified by respondents. Our results will be used to design interventions to improve infection prevention in Vietnam, and may be relevant to other settings with limited resources.

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NEONATAL SEPTICEMIA - RETROSPECTIVE STUDY AT PREMATURE NEWBORNS

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Introduction: Neonatal septicemia occurs, especially, at premature newborns from the neonatal intensive care units. It is a serious affection with high mortality, even in the presence of a specific antibiotherapy.

Objective: The authors aimed to analyze the risk factors of the disease by grade of premature and starting age, correlated with clinical and biological signs , morbidity and mortality.

Material and method: The study was carried out between 2010 - 2011, on a lot of 50 premature newborn, hospitalized, selected by on anamnestic, clinical, epidemiologic and biologic criteria. The prevalence of the disease was 4.03 %.

Results: Neonatal septicemia with early start was present at 21 cases (42%). There were 13 cases associated with materno-fetal infection (61,9%), 8 cases with rupture membranes at 18 hours (38%). The mortality was high in 7 cases (14%), at big premature with intrauterine chronic affection and history of materno-fetal infection. The most present germs were: Serratia Marcensens, Pseudomonas Aeruginosa and Staphylococcus Coagulase-Negative.

Septicemia with late start was present at 29 cases (58 %) having a higher prevalence at premature with gestational age lower than 32 weeks and birth weight lower than 1500 g, with long hospitalization and associated malformative pathology. The same germs were involved.

Both groups presented classic signs of septicemia. Beyond positive hemoculture were present: positive PCR between 8,92 - 220 mg/l, leucocitosys between 17240 - 44000/mm^3 thrombocytopenia: 15000 - 120000/mm^3.

Conclusions: Neonatal septicemia is a serious affection with high mortality (14%) at premature newborns even if antibiotherapy was early started.

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THE ROLE OF HHV-6 IN THE PATHOGENESIS OF DRESS SYNDROME

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Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome, also named drug-induced hypersensivity syndrome (DIHS), is a delayed type IVb hypersensitivity syndrome. It is defined by the presence of fever, rash, systemic findings and haematological abnormalities. Several drugs are involved in the genesis of this syndrome including mesalazine. We report a case of a six year old boy who was admitted in our unit with persistent fever, rash, edema, icterus, hepatomegaly, lymph adenopathy, hyperemic pharynx with aphthous lesions and arthralgia. His past history was positive for hypogammaglobulinemia and colitis.

Laboratory investigations revealed leukocitosis with lymphocytosis, eosinophilia, mild anemia, thrombocytosis, hypoalbuminemia associated to an increase of liver enzymes, amylase, lactate dehydrogenase (LDH) and inflammatory markers. Blood smears as well as FACS analysis excluded lymphoblasts and confirmed exclusively an increase of activated lymphocites. Screening for various infectious agents on blood and saliva resulted negative except for human herpes virus-6 polymerase chain reaction (HHV6-PCR) which proved positive on saliva. Because all criteria were matched DRESS syndrome was diagnosed. Mesalazine was stopped. Corticosteroid therapy was started with an improvement of his clinical conditions and a normalization of laboratoristic parameters.

The pathogenesis of DRESS syndrome is unknown. Drug metabolites induced immunological alterations leading to an environment in which HHV-6 reactivates. Reactivation of HHV-6 plays a role in the complex pathogenesis of DRESS as well as in the development of immune inflammatory disorders. DRESS syndrome should always be considered in the differential diagnosis with infection which not respond to classic antibiotic therapy.

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IMMUNOGENICITY OF A CONJUGATE MENINGOCOCCAL SEROGROUP C BOOSTER DOSE FOLLOWING A REDUCED VACCINATION SCHEDULE IN INFANCY

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Background and aims: The immunogenicity of the Haemophilus influenzae type b (Hib) and serogroup C meningococcal (MenC) glycoconjugate vaccine following a reduced infant MenC vaccination schedule was investigated in a randomised controlled trial in the UK and Malta.

Methods: In the primary phase 509 infants were randomised to one of 4 groups to receive either MenC-CRM_{197}/MenC-TT, both at 3 months of age; or two doses of MenC-CRM_{197} at 3 and 4 months, or no MenC vaccine (control). The Hib-MenC-TT vaccine was administered to 483 participants when aged 12 months. Non-inferiority was reached if 4-6 weeks after Hib-MenC-TT vaccination the lower 95% confidence interval (CI) of the ratio of MenC rSBA geometric mean titers (GMTs) between the single and two-dose MenC-CRM_{197} groups was >0.45.

Results: MenC rSBA GMT after Hib-MenC-TT boosting in participants primed with one MenC-CRM_{197} dose was non-inferior to that after two MenC-CRM_{197} priming doses (GMT ratio 2.33 [LL95%CI:1.55]). No significant differences were noted in the percentage of participants with rSBA≥1:8 between the two-dose and single-dose MenC-CRM_{197} (Difference:1.38% [95%CI:-3.68-6.67]) or MenC-TT (Difference:-1.82% [95%CI:-6.57-3.52]) groups. Following the Hib-MenC-TT boost the percentage of participants with rSBA≥1:128 was significantly higher following one MenC-CRM_{197}/MenC-TT dose than two MenC-CRM_{197} doses. A significantly lower percentage of infants in the control group had titres above the protective thresholds.

Conclusion: Current MenC immunisation schedules incorporating two MenC infant priming doses may be reduced to a single priming dose without loss of immediate post-booster immunogenicity. Further evaluation of the duration of protection with different priming regimes is required.

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CAMPYLOBACTER INFECTION IN A PEDIATRIC POPULATION: PERSPECTIVE OF A NEW DIAGNOSTIC TOOL ON EMERGENCY DEPARTMENT

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Background and aim: Campylobacter infection is recognised as cause of diarrhoea in children. Culture detection on selective medium at 42°C lasts 2-5 days. Rapid-tests were developed to overcome this diagnostic delay. Aim of study is to evaluate impact of a new rapid diagnostic test (RDT - ImmunoSTAT CAMPY Méridian) developed by our bacteriology laboratory.

Material and method: Retrospective study performed in the emergency department during two years (2011 - 2012).

Results: Epidemiology - 62934 children were evaluated in ED. 2989 children younger than 3 years presented with enteritis, 340 admitted. In 380 stool-cultures and RDT were performed. 73[19.21%] had positive RDT for Campylobacter and 25 [6.58%] had positive cultures for Salmonella. Average age was 33.6 months (1.2-180), 41 were male (56%) and 41 (56%) were evaluated for the first time in ED during current episode. 41 (56%) were only in family, 24 (33%) were in day-care and 8 (11%) were returning from trip in an African country.

Clinical features - Bloody stools 50 (69%), fever 22 (68%), vomiting 28 (38%), abdominal pain 72 (98%) were present.

Bacteriology - 42 cultures were positive for Campylobacter jejuni/coli. Discordance was present in 31 (42%) with negative stool-cultures.

Treatment and evolution - 18[24.66%] of these patients were admitted, 27(37%) had only a complete blood count (beside stool evaluation) in ED and 56(77%) were treated with macrolide (azythromycine).

Conclusions:

1. RDT ImmunoSTAT CAMPY increased diagnostic accuracy by 73.81%.
2. The new RDT is cost-efficient, decreasing admittances and targeting antibiotherapy.

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RELATIONSHIP BETWEEN THE POLYMORPHISM OF IL28B AND RVR IN HCV INFECTED CHILDREN TREATED WITH PEGYLATED INTERFERON AND RIBAVIRIN

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Background and aims: Rapid virologic response (RVR) is defined as an undetectable hepatitis C virus (HCV) RNA at week 4 of treatment. RVR is used to predict 24-48 weeks therapy effectiveness.

Evaluation of relationship between the polymorphism of IL28B(rs12979860) and RVR in HCV infected children treated with pegylated interferon and ribavirin.

Methods: The study included 6 children (6,1-9,5 years): 4 girls, 2 boys, vertically HCV infected; 5 with genotype 1b(among them IL28B: CC-in 3, CT-1, TT-1) and 1 with genotype 4(IL28B: CT). All children underwent liver biopsy(LB), in 4 non-invasive FibroTest(FT) was performed. The baseline viral load (VL) and ALT activity was evaluated after 4 weeks of treatment. Therapy is continued in all children.

Results: High baseline VL(>600000IU/ml) was in 4/6 children, among them IL28B:CC-2,CT-1,TT-1. Low baseline VL(< 600000IU/ml) was in 2/6 children, among them IL28B: CC-1, CT-1. RVR was not attained. Decline of VL at 4 weeks was in all patients: < $2\log_{10}$ in 5(IL28B: CC-2, CT-2, TT-1), >$2\log_{10}$ in 1(IL28B-CC). Baseline ALT ranging from 46-85 UI/l(mean: 65) was elevated in all. At week 4 reduction of ALT was observed in 5/6 patients, among them normalization of ALT in 2(IL28B-CC). Girl with IL28B:TT, infected with HCV1b, had highest fibrosis score: LB(F2), FT(F1-F2), high baseline VL, at week 4 she declined VL< $1\log_{10}$ and did not normalized ALT.

Conclusions: RVR was not attained in any children, although half of them have IL28B:CC. The course of infection and response to therapy at week 4 were worse in girl with IL28B:TT.

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21ST CENTURY CONGENITAL SYPHILIS

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Introduction: Congenital syphilis is a challenge with neonatal morbimortality repercussions. Of all diseases transmitted during pregnancy and labour it has the greatest transmission rates, but can be prevented and/or treated if correctly screened for.

Aims: To assess neonates (NN) from VDLR-positive mothers: prenatal diagnosis and treatment, infection status, treatment and sequelae in NN.

Methods: Retrospective observational study, including all NN born in CHBM, ranging the last four years.

Results: Among 7325 NN, we identified 12 NN from VDRL-positive mothers, with a congenital syphilis risk prevalence at birth of 0,16%. Four NN (33%) were diagnosed with congenital syphilis, one of whom (8%) had thrombocytopaenia, long bone lesions, hepatitis and transfontanellar ultrasound and ocular fundus abnormalities. All NN belonged to high risk social groups, without appropriate pregnancy follow-up (40%), mothers with multiple sexual partners (30%), unemployed (100%) and none of whom had qualified further than 9 grade. Two (17%) of them were also infected with Hepatitis C. Ten (83%) were diagnosed during pregnancy and two during labour (17%); among these, seven were correctly treated for, however in three cases sexual partners were not treated and thus reinfection occurred. All NN from VDRL-positive mothers followed the national diagnosis and treatment protocols. Only the NN who had symptomatic congenital syphilis has minor sequelae.

Conclusion: Syphilis is still an important Public Health concern in Portugal, with social and economic repercussions. It is of the utmost importance to diagnose and provide early treatment to infected pregnant women and their sexual partners.

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ANTIBIOTIC PRESCRIBING FOR CHIDREN IN THE EMERGENCY ROOM (ER) - CONTINUOUS MONITORING AND OPPORTUNITIES FOR IMPROVEMENT

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Background and aims: The ER frequently represents the site for initiating antimicrobial therapy, sometimes inappropriate or unjustified. Our aim is to analyse and monitor trends of antibiotic use in this setting.

Methods: Retrospective analysis of randomly selected children admitted to the ER in 2004, 2008 and 2011, registering diagnosis and antibiotic prescription. Comparison of antibiotic use over the years was done.

Results: During the study period 161942 children were observed and 5067 (3.1%) included in the study. From 2004 to 2011, oral antibiotics were prescribed in 9, 14 and 16% of the children respectively; amoxycilin (49/67/61%) followed by amoxyclav (13/13/19%), flucloxacillin (15/8/4%), macrolides (5/6/7%) and cefuroxime (8/5/7%).

Amoxycillin was prescribed mainly for respiratory infections, cephalosporins for urinary tract infections (UTI), flucloxacillin for skin/soft tissue infections (SSTI), macrolides for pneumonia, amoxyclav for SSTI and UTI. Prescription occurred in 56/79/81% of the AOM cases, 0/7/5% of the fever of unknown origin, 4/5/1% of the upper respiratory tract infections, 0/1/0% of the bronchiolitis and 2/1/0% of the acute gastroenteritis in 2004-2008-2011 respectively.

AOM and tonsillitis were the main reasons for antibiotic use (17/25/18% and 16/20/22% of all prescriptions respectively). Amoxycilin was the choice in >80%.

Conclusions: There is an appropriate prescribing pattern however an increase in the total percentage of antibiotic use has been observed over the years. Decrease in flucloxacillin prescription in 2011 is probably related to it's discontinuation in pharmacies. AOM remains one of the most frequent reasons for antibiotic use and a reduction in prescription could be obtained.

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THE MEMORY B CELL RESPONSE TO A BOOSTER DOSE OF A 13-VALENT (PCV-13) OR 10-VALENT (PHID-CV) PNEUMOCOCCAL CONJUGATE VACCINE

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Background/aims: In the UK, children receive the 13-valent pneumococcal conjugate vaccine (PCV-13) at 2, 4 and 12 months of age. The purpose of this randomised controlled trial was to assess non-inferiority of a 10-valent pneumococcal conjugate vaccine (PHiD-CV) as an alternative 12-month booster. As a descriptive secondary objective, we assessed the memory B cell (MBC) responses to booster immunisation with either PCV-13 or PHiD-CV.

Methods: 178 children who had previously been vaccinated with PCV-13 at 2 and 4 months were randomised 1:1 to receive a booster dose of either PCV-13 or PHiD-CV at 12 months of age. Blood was taken before and 1 month following vaccination. MBCs were quantified using a cultured ELISpot assay for serotypes 1, 3, 4, 9V, 14 and 19A.

Results: 247 blood samples were available for analysis. A significant rise in MBC frequency was seen for 5 serotypes (1, 3, 4, 9V, 19A) in the PCV-13 group and 1 serotype (19A) in the PHiD-CV group. There was a particularly large increase in serotype 3-specific MBCs in the PCV-13 group (1.3 to 22.6 MBC/10^6 cells; $p< 0.0001$). Serotype 14 produced the smallest change in MBC frequency showing no significant increase in either group.

Conclusions: Following priming with PCV-13 in early infancy, a booster dose of PCV-13 results in a more pronounced peripheral blood MBC response than does a booster of PHiD-CV. However, correlation between MBC responses, (functional) antibody and clinical protection is unclear. Forthcoming IgG ELISA and OPA data may help further interpret these results.

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MICROARRAY BASED DETECTION OF ANTIBIOTIC RESISTANCE GENES IN ENTERIOBACTERICEAE

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Background and aims: MicroArray method is a very useful tool for the screening and detection of antibiotic resistance genes and the control of this phenomenon.

Aim: To evaluate the bacterial genes involved in the emergence of antibiotic resistance using MicroArray method.

Methods: Multiresistant antibiotic strains (more that 3 classes of antibiotics) of Enterobacteriaceae isolated in children (0-18 years) diagnosed with bacterial infections and admitted to Children Hospital, Timisoara, Romania between April 2010-September 2011 were studied. This bacteria were phenotyping with VITEK2. MicroArray method principle: 39 identified oligonucleotides sequences that define antibiotic resistance sequences were spot-on in duplicate with a controler on ArrayIt chip. The bacterial ADN was extracted using High Pure PCR Template Preparation (Roche), colored with Alexa Fluor and hybridized. Than the chip was scanned and analyzed with GenePixPro7 soft.

Results: Out of 51 multidrug resistant bacteria isolated, 17 Enterobacteriaceae (52.95% E. coli and 47.07% Klebsiella pneumoniae) were analysed using this method. The most frecquent genes identified in E.coli were amp C (100%), bla CTX-M12 (100%), bla TEM (77.77%), bla OXY-K1(33.33%) and sulII (33.33%). AmpC (75%), bla CTX-M12 (62.5%), tet (R) (62.5%), sulI (62.5%), bla OXY-K 1 (50%) were responsible for the most Klebsiella pneumoniae resistant strains. Other genes isolated were bla CMY-2, tet (A), mph (A), bla OXA -9, bla SHV-37, bla OXA-2b, ere (A) and ere (A2).

Conclusions: This study showed the great diversity of genes identified in bacterial isolates and that a single bacterial strain can simultaneously express multiple types of beta-lactamases.

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TEN YEARS OF CERTIFIED "POLIO FREE" STATUS IN GREECE: 2002-2012

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Background and aims: The last poliomyelitis case due to indigenous wild poliovirus occurred in Greece in 1996. From 1996-2002, 5 Vaccine Associated Paralytic Poliomyelitis (VAPP) cases were reported. Greece was certified "polio-free", with the WHO European region countries, in 2002. Poliovirus transmission is prevented by combining high immunization coverage and surveillance of acute flaccid paralysis (AFP) cases among children < 15 y.o.

Methods: To achieve and maintain the certification, following WHO's guidelines, an active weekly AFP surveillance has been set up to a national hospital level since 1998. An enterovirus stool study in high-risk subpopulation groups and environmental surveillance were implemented supplementary. Faecal and sewage specimens are tested for polioviruses/enteroviruses by the Hellenic National Polio Reference Laboratory.

Results: From 2002-2012, in total, 185 (11-24 per year) AFP cases were reported. No wild poliovirus case was identified. Annual incidence ranged from 0.95 to 1.43 per 100,000 population. AFP cases percentage with 2 faecal specimens (within 14 days from onset, < 1 day apart) ranged from 40.0-88.2%. Follow-up (60-90 days after onset) was 54.5-100%. The most prevalent definite diagnosis was Guillain-Barré syndrome. Since November 2010, stool samples were collected from 222 Roma children (< 15 y.o) with the addition of 110 sewage specimens during 2012. No wild or vaccine-derived polio viruses were isolated.

Conclusions: Sustained systematic and high quality AFP, stool and environmental surveillance is increasingly important for Greece to retain "polio-free" status and minimize the risk and consequences of polio re-introduction by immigrants from endemic countries.

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EFFECTS OF EARLY SKIN-TO-SKIN CONTACT MOTHER-INFANT ON BACTERIAL COLONIZATION OF THE NEWBORN

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Background and aims: Bacterial colonization at birth is object of numerous researches that study different factors implied in this process. The aim of our study is to analyze the neonatal bacterial colonization in two different kind of hospital practices: mother infant early Skin to Skin contact for the first hour after birth compared with normal routine policies that don´t apply this method.

Methods: A total of 19 women and their respective infants were randomly included in the study. Nine of them (Group A) undergo the Skin to Skin contact at birth and 10 did not. Five hundred swabs were collected from different mucocutaneous mother and infant districts; all of them have been plated and processed to analyze the different kind of bacterial growing.

Results: The main results indicate that at the first hour of life the Skin to Skin newborn group had oral mucosa significantly less colonized than the other group, even though their mothers, casually, reported a less contamination of the breast skin. This difference is reported also after three days from delivery, suggesting that the skin to skin contact may induce prolonged infant protection from nursery bacterial sources.

Conclusion: Even if we considered a small number of cases, we may hypothesize that newborn first bacterial colonization is strongly related also to different kind of hospital policies, with best results when applying early Skin to Skin contact. This suggests that improving more physiological hospital practices may promote mother and infant healthiness and wellbeing.

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CHEMOKINES RESPONSES IN CAMEROONIAN CHILDREN WITH PLASMODIUM FALCIPARUM MALARIA

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Background and aims: Malaria is an important parasitic infection. It causes significant mortality with children being more vulnerable. Chemokines regulate the host immune response to a variety of infectious pathogens. For instance, chemokines receptor CXCR3 and its ligand CXCL10 has been implicated as a biomarker in cerebral malaria in Ghanaian children. There is dearth of information on chemokines responses in malaria among Cameroonians children.

Methods: Chemokines in the serum of the 80 children with P. falciparum malaria and 16 control subjects were analysed by ELISA using the manufacturer's instruction (Abcam, UK). Also their haemoglobin was determined by an automated 5 Evolution Diana machine.

Results: Of 309 children examined, 238 (77.0%) had P. falciparum in their peripheral blood. They had a mean malaria load is 5384.94 parasite/µl with a mean haemoglogin level of 10.8g/dl.. The mean serum chemokines concentration of 80 P. falciparum infected children and their control subjects are chemokines 3 CX3CL 1.3±1.1 and 1.4±2.95 pg/ml , CXCL5 9618.8±2944.2 and 12013.3±4503.0, CXCL7 87.1±193.9 and 465.3±293.9; CXCL11 124.7±120.9 and 158.1±263.4; CCL28 88.9±217 and 1.73±6.71. The chemokines correlated negatively with the malarial loads (r = -0.23, -0.1 -0.04. -0.04. -0.1 and -0.2 respectively.

Conclusion: Elevated chemokines CXCL7 and CCL28 attempt to protect the children against malaria. Depressed chemokines CX3CL1, CXCL5, CXCL9 and CXCL11 may be indicative of suppressed immunity, thereby influencing the pathogenesis of P. falciparum malaria in Cameroonian children.

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EPIDEMIOLOGICAL ASPECTS OF MENINGOCOCCAL DISEASES (MD) PRE AND POST INTRODUCTION OF MENINGOCOCCAL C CONJUGATE VACCINE, PARANA(PR), BRAZIL(BR)

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Background and aim: Conjugate vaccine MCCV was introduced in the Brazilian Immunization Program for children less than 2 years of age in mid 2010. The Paraná State vaccination coverage is around 100%. This study presents an analysis of the epidemiological pattern of MD from 2008 to 2012, Parana, Brazil.

Methods: A descriptive study using data from epidemiological department of the Parana Public Health Department.

Results: A total of 484 cases were reported: 75 (15.5%) less than 1 year of age and 149 (30.8%) from 1 to 4 years. Serogroups were identified in 236 (48.8%) of the total of cases: 129 (54.7%) were C, 87 (36.9%) B and 20 (8.5%) W135. The most prevalent subtypes in children younger than 5 years were B:4,7:P1.19,15 and C:23:P1.14,6. For children less 1 year old the clinical manifestations were: meningitis 33.4%, 45.5% of meningococcemia and 21.5% of meningitis with meningococcemia and lethality rate was 15.4%, 45.5% and 7.75%, respectively. The proportion of C serogroup in 2008 was 5/20 MD cases and decreased to 1/18 in 2011. Lethality rate has decreased: 25% (2009), 20% (2010) to 11.8% (2011).

Conclusions: There was a reduction in proportion of MD cases by serogroup C in the vaccinated population. These encouraging results highlight the need of continued surveillance studies to assess the long term impact of this vaccination program.

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WHOLE EXOME SEQUENCING (WES) FOR THE IDENTIFICATION OF UNDEFINED PAEDIATRIC PRIMARY IMMUNODEFICIENCY (PID) DISORDERS PRESENTING TO A SINGLE SPECIALIST CENTRE

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Background: Many children presenting to a tertiary paediatric Immunology clinics with a history of increased susceptibility to infections do not have a clearly defined PID. Next generation DNA sequencing (NGS) has enabled rapid and reliable sequencing of whole exomes providing a powerful approach to studying variants in individuals.

Method: Whole exome sequencing (WES) was performed using Agilent 50Mb Sure Select exon enrichment and the HiSeq Ilumina platform.

Patients: All patients had been extensively investigated in a tertiary immunology clinic with no genetically defined PID diagnosed. Family 1 had 3 affected members with autosomal dominant inheritance pattern and a clinical phenotype of chronic mucocutaneous candidiasis (CMC). Family 2 had affected identical twins with a history of repeated respiratory tract infections. Family 3 had one affected member with an unusual autoimmune phenotype and family 4 had one affected member with a hyper IgE phenotype.

Results: Exome sequences of adequate depth (>20) and coverage (>82%) were obtained in the 8 individuals sent for sequencing. One concordant variant was observed in the 3 affected member of family 1, identifying the recently described STAT1 mutation (R274Q). No predicted candidate or previously described PID gene mutations could be identified in rest of the families. Further analysis has revealed 5, 4 and 3 novel variants for evaluation in families 2, 3 & 4 respectively.

Conclusion: The integration of NGS strategies for the diagnosis of 'non classical PID' will be an important development in paediatric practice over the next decade.

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NATIONAL "HEPATITIS B PERINATAL TRANSMISSION PREVENTION PROGRAM (HBPTPP)" IN THE REPUBLIC OF KOREA, 2002-10

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Backgrounds and aims: Since the introduction of hepB vaccine in Korea in 1982, the overall HBsAg+ rate in populations aged ≥10 years has declined from 7.25% in the early 1980's to 4.55% in 1998, and 3.0% in 2008. Specifically, HBsAg+ rate in those aged 4-6 years was 0.2% in 2006. National HBPTPP which supplies hepB vaccine, immunoglobulin and serologic test with free of charge into babies from mothers with chronic hepB has been started since July 2002. We reviewed the outcome of HBPTPP.

Methods: We analyzed the input data of enrolled cases of HBPTPP from July 2002 to December 2010 in a program server of Korea CDC.

Results: Total 125,855 cases (96.4%) were enrolled among the predicted 130,609 cases (estimated by maternal HBsAg+ rates with 3.4% in 2002-6; 3.2% in 2007-10). The serologic tests to identify the results of perinatal prophylaxis were done in 55.6% (n=69,999), the success or failure rate of prophylaxis was 96.86% (HBsAg-/anti-HBs+ 92.36%, HBsAg-/anti-HBs- 4.50%) or 3.14% (HBsAg+/anti-HBs- 3.08%, HBsAg+/anti-HBs+ 0.06%; n=2,198), respectively. After the initial administration of vaccine and immunoglobulin at birth, the enrolled rate of the 2nd or 3rd immunization were 89.9%, 81.7%, respectively. Among 46,887 pregnant women whose HBeAg status could be known, 36.7% were HBeAg positive. Methods of feeding (breast vs. bottle) or delivery (vaginal vs. C/S) did not impact the result of perinatal prophylaxis.

Conclusions: The failure rate of current HBPTPP was 3.14%. This program is playing an important role in reducing the cases with perinatal hepatitis B infection in Korea.

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A CASE OF SEVERE HEPATITIS DUE TO VARICELLA ZOSTER

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Severe hepatitis due to herpes virus in immunocompetent patients is a very rare event and can be rapidly fatal. Varicella is a common exanthematous disease that infects children primarily .The report represents an immune competent adult with severe hepatitis. A 16 year - old male without significant medical history was admitted to the infectious disease ward for evaluation of vomiting, abdominal pain, anorexia, low fever, and jaundice. Five days earlier he had developed fever, followed by common cold symptom. He had history of close contact with a chickenpox patient two week ego. On admission physical examination showed jaundice and fever.

Initial laboratory findings were:

WBC count 7700/µ L, platelet count 150000/ µ L,AST 3091 U/L, ALT 3289 U/L, LDH 841 U/L, ALP 550 U/L, bilirubin total 5.5 mg/dl, Direct billirubin 4.4 mg/dl, PT=19 seconds.

HBS Antigen, anti HBC-IgM, anti HCV, anticytomegalovirus (CMV) IgM, anti Epstein Barr virus (EBV)-IgM and anti -HAV-IgM was all negative.

CXR was normal. Ultrasonography revealed hepatospelnomegaly.

On the second day after admission coetaneous vesicles suggestive varicella were appeared on the face and trunk.

Serum VZV IgM antibody and serum VZV PCR assay were positive.

Treatment with intravenous acyclovir 10mg/kg three times /day was started on the second day.

This case underlines the importance of considering all herpes viruses as potential causes of severe hepatitis and liver failure. Treatment with acyclovir should be initiated as soon as possible.

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GROUP C BETA-HEMOLYTIC STREPTOCOCCUS IN CHILDHOOD - MORE THAN JUST COLONIZATION OF THE UPPER RESPIRATORY TRACT

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Background: Group A beta-hemolytic streptococcus (GAS) has been traditionally considered to be the main pathogen in acute bacterial pharyngitis. Group C beta-hemolytic streptococcus (GCS) is thought to be part of the normal flora of the upper respiratory tract but recent reports have demonstrated its potential role as a treatable pathogen in acute pharyngitis.

Methods: We recorded the presence of Centor criteria, white cell count, C-reactive protein (CRP), age and duration of symptoms before and after antibiotics in febrile children hospitalized in a tertiary unit in a three month period where GCS was isolated from throat swab and no other cause of fever was identified.

Results: 7 children (6 boys) with mean age of 5 years were included. 3 children were immunocompromised. All patients presented with fever, sore throat and unwell enough to require hospital admission. 4 of 7 patients had 2 of Centor criteria present, 2 patients had 3 criteria and 1 patient had 4 criteria. The average duration of symptoms before admission was 3,5 days. All patients had elevated acute phase proteins (mean CRP:10,8mg/dl) and 3 of them (immunocompetent) had elevated WBCs. All children were treated with antibiotics. In 5 children fever and symptoms resolved within 2 days after treatment.

Conclusions: Patients with tonsillitis caused by GCS have similar clinical picture as GAS. Although the benefits of treating non-GAS pharyngitis are yet unproven paediatricians may consider treating children with non-GAS pharyngitis especially those with underlying immunosuppression.

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HEMATOLOGIC COMPLICATIONS ASSOCIATED HEPATITIS A VIRUS INFECTION; HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS AND IMMUNE THROMBOCYTOPENIC PURPURA

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Acute hepatitis A virüs (HAV) infection is a common and worldwide infectious disease caused by HAV, seen most commonly in underdeveloped societies. HAV infection is a vaccine-preventable disease but it was not included in national vaccination programme of Turkey since November 2012. HAV infection is a self limited disease and extrahepatic complications of HAV infection seems rarely in childhood. Hematological complications are of HAV infection includes aplastic anemia, hemaphagocytic lymphohistocytosis, immun thrombocytopenic purpura and postinfectious thrombocytopenic purpura. Few pediatric reports have been published about hematological complications associated with HAV infection. We present two pediatric patient with different hematological complications including hemophagocytic lymphohistocytosis, immun thrombocytopenic purpura and transient bone marrow suppression.

Case1: A previously healthy eleven years old boy admitted to our hospital with mouth bleeding and petechial rash. His hemogram revealed thrombocytopenia and other series were normal. Bone marrow aspiration revealed no atypical lymphocytes and increased megacaryocytes. The diagnosis of immune thrombocytopenic purpura confirmed with bone marrow aspiration and poor response to platelet transfusion. Viral serologic studies were positive for anti-HAV IgM.

Case 2: A 14 months old girl referred to our hospital with prolonged fever unresponsive to wide spectrum antibiotic therapy, loss of appetite and cough. Her laboratory investigations revealed pancytopenia, high level of ferritin (>10000ng/ml) hypofibrinogenemia and hypertriglyceridemia. Viral serologic studies were positive for anti-HAV IgM. Hemophagocytosis seen in bone marrow. These clinical and laboratory findings fulfilled with diagnostic criteria of Hemaphagocytic Lypmhohistiositosis (HLH) triggered by HAV.

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THE INFLUENCE OF ANTIBODIES ON THE INNATE IMMUNE RESPONSE TO RESPIRATORY SYNCYTIAL VIRUS INFECTION

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Background and aims: Respiratory Syncytial Virus (RSV) can cause severe bronchiolitis in young infants. Not all cases of severe RSV infection can be explained by the known risk factors and the pathogenesis of disease severity is poorly defined. Evidence suggests that maternal antibodies might have an influence on severity of infection. This study tries to identify the influence of antibodies on the immune response to RSV infection.

Methods: Human mononuclear cells (MNC) were stimulated with RSV A2 in human serum (HS) containing neutralizing anti-RSV antibodies or antibody depleted HS. Secreted cytokines were measured after 24 hours in the supernatant.

Results: Stimulation of human MNC with RSV in combination with HS induced a synergistic increase in interferon-γ (IFN-γ) production. In the monocyte depleted fraction of the MNC this synergistic response persisted. This IFN-γ could be measured after 4 hours on mRNA level and after 24 hours on protein level, suggesting direct stimulation of T cells or NK cells. To study whether the enhanced IFN-γ production depended on immune complexes, other HS components or infectious versus antibody-neutralized virus, we stimulated human MNC with RSV and BPL-inactivated RSV in combination with HS and Ig depleted HS. Measurements of cytokine levels indicate that antibodies are the main cause of this synergistic increase in IFN-γ production.

Conclusion: Anti-RSV antibodies present in human serum enhances the induction of IFN-γ by MNC infected with RSV. This data indicates that the presence of (maternal) neutralizing antibodies during a primary RSV infection might enhance inflammation and effect disease severity.

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VARICELLA -RELATED HOSPITALIZATIONS IN CHILDREN IN THE PRE-VACCINE ERA IN TURKEY

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Background and aims: The aim of this study was to determine the indications of hospital admissions, complications of varicella infection and their clinical characteristics among immunocompromised and immunocompetent children in the pre-vaccination period in Turkey.

Methods: This study was carried out by retrospective evaluation of the files of 100 patients who were hospitalized for varicella infection between January 2004 and December 2010 in a tertiary care setting. Patient´ s demographics, immune status, clinical features, complications, treatments and the outcome were analysed.

Results: Of the 100 patients admitted to our hospital, 66% were immunocompetent, 34% were immunocompromised. Secondary bacterial infections were the most common complication identified in the both of groups. The other complications of varicella infections were neurological complications 21%, 0%, pneumonia 2%, 0%, hematologic complications 5%, 6%, hepatititis 12%, 38%, disseminated varicella infection 2%, 6% in immunocompetent and immunocompromised patients respectively.

Conclusions: Complications of varicella infection requiring hospitalization were more frequent than we thought even in immunocompetent patients for this reason a universal childhood varicella immunization may reduce the rate of varicella related complications and admissions in our country.

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VALUE OF HBC AB AND HCV AG SCREENING VERSUS HBS AG AND HCV AB IN MULTI-TRANSFUSED THALASSEMIC CHILDREN

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Background: Inspite of all efforts to guarantee saety of blood transusion, transfusion-transmitted HBV and HCV infections still occur particularly among multi-transfused. Occult hepatitis B virus (HBV) in blood is considered as a potential risk for transfusion. Similarly, hepatitis C antibody screening sometimes yields false positive and negative results. The aim of study was to screen multi-transfused thalassemic children for anti-Hbc Ab and HCV Ag compared with routine HBs Ag and HCV Ab testing.

Patients and methods: Two hundred children with thalassemia major (117 males) with mean age 10.59 +/-3.4 years were included. Hepatitis B core Ab, HBs Ag, HCV Ag and HCV Ab were done by Elisa for all.

Results: Anti-HBc Ab was detected in 23 (11.5%) while HBs Ag was positive in 58 (29%). Five HBs Ag negative patients were positive for Anti-HBc Ab (p,0.001). As regards HCV, HCV Ab was detected in 104 (52%) of paients with only 19 patients (9.5%) having positive HCV Ag. However, Six HCV Ab negative patients were positive for HCV Ag ($p < 0.001$).

Conclusion: Routine blood screening with HBs Ag and HC Ab are not sufficient for safe blood transfusion and may account for the high prevelance in multi-transfused. Use of Anti-HBc Ab and HCV Ag may add to safety.

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ANTIBIOTIC PRESCRIPTIONS AMONG CHILDREN AGED BELOW 3 YEARS: TRENDS FROM 2006 TO 2012 IN SOUTHEASTERN FRANCE

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Background and aims: In France, pre-school children frequently receive antibiotics for respiratory tract infections, particularly 3rd generation cephalosporins (3GC), known to generate microbial resistance. Efforts to curb antibiotic prescriptions began in Southeastern France in 2000 and were later extended nationwide. Trends in overall and 3GC prescription for children < 3 years were monitored in the Alpes Maritimes area from 2006 to 2012 both yearly among the overall population and in daycare centres in 2006, 2008 and 2012.

Methods: Volume and type of ambulatory antibiotic prescriptions by general practitioners and paediatricians were obtained from the National Health Insurance (NHI) for children < 3 years for the first semesters of 2006 to 2012 per aged-matched overall population in the Alpes Maritimes. Between January and April 2006, 2008 and 2012, antibiotic prescriptions were documented by parents of a random sample of < 3 year-old day-care attendees, and compared using chi-square tests.

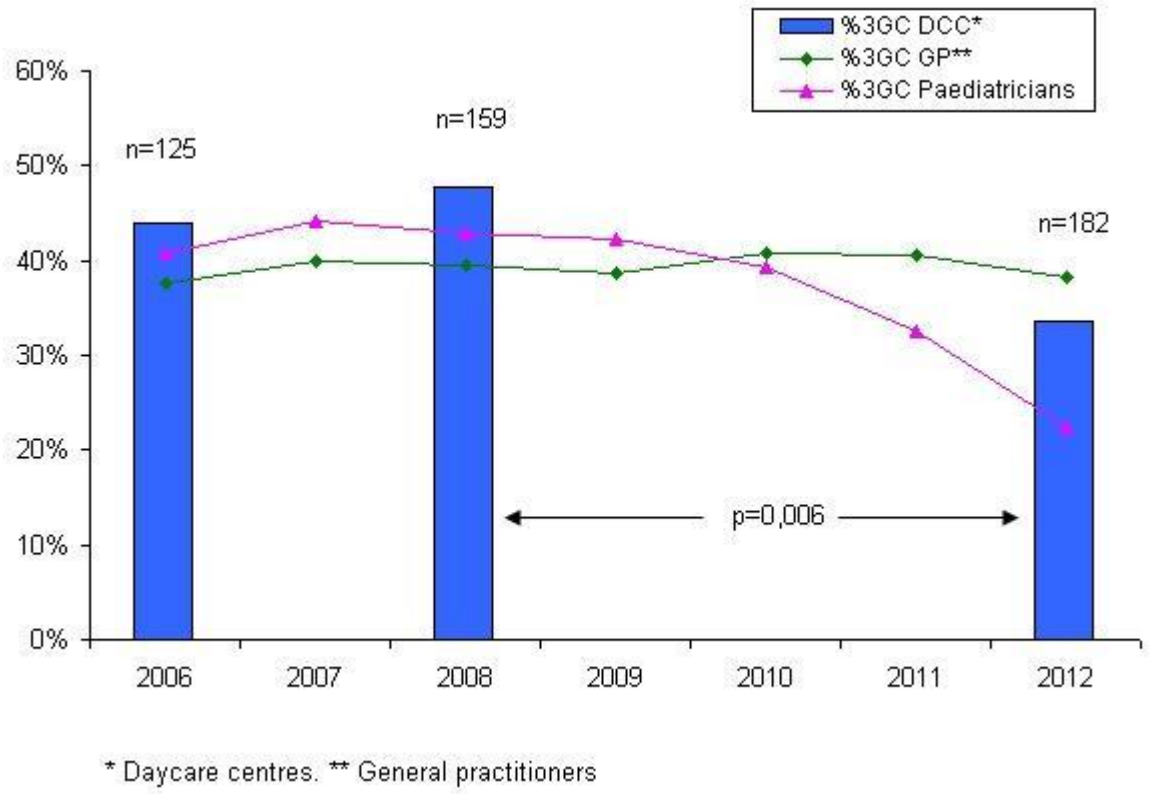
Results: Overall prescription/child peaked between 2009 and 2011 and was lowest in 2012. (Table1). Amoxicillin+/-clavulanate and 3CG accounted for over 80% of prescriptions. Compared to 2006, the study population increased by 5.3%, while prescriptions dropped by 4.5%. C3G prescriptions by paediatricians declined sharply as from 2011. Trends were similar in daycare centres (Figure 1).

Table 1: Population and antibiotic prescription trends for children < 3years of age in the Alpes Maritimes

	2006	2007	2008	2009	2010	2011	2012
# children < 3yrs*	34288	34898	35017	35662	35857	36481	36205
# prescriptions**	20215	20716	18945	22277	23688	22270	19345
% GP prescriptions***	57.7%	57.5%	56.2%	55.4%	54.6%	57.7%	60.5%
Prescriptions/1,000	590	594	541	625	661	610	534

*national population register (INSEE); ** national health insurance (AM PACA-Corse); ***general practitioners

[Table 1: Population and prescription trends]



[Figure 1: Trends in 3GC prescription]

Conclusions: Total antibiotic prescriptions decreased moderately over the 6-year period. Prescription of 3GC by paediatricians declined sharply. Reasons for the differences in prescription choices between GPs and paediatricians require investigation.

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RECURRENT INFECTIVE ENDOCARDITIS DUE TO PSEUDOMONAS AERUGINOSA IN A CHILD WITH WILLIAMS-BEUREN SYNDROME

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Background and aims: Infective endocarditis (IE) due to Pseudomonas aeruginosa is uncommon, but when it occurs, it is associated with existing risk factors, such as prosthetic heart valves.

Methods: The patient is a male child with Williams-Beuren syndrome, for whom surgical reconstructions were carried out for supravalvular aortic and supravalvular pulmonary stenoses, and coarctation of aorta at 6-7 months of age.

Results: The patient was hospitalized and treated for P. aeruginosa endocarditis at the ages of 9 months, 13 months, and 17 months. In the first admission, an ongoing growth of the organism was observed despite appropriate antimicrobials, which were then replaced with other effective agents. Surgery was performed for an mycotic aneurysm in the ascending aorta during his second admission. In his third hospitalization, P. aeruginosa endocarditis, which was successfully treated with ceftazidime+gentamicin, relapsed and the newly-grown P. aeruginosa strain necessitated meropenem+amikacin combination, to which addition of ciprofloxacin was deemed necessary.

Conclusions: To our knowledge, this is the only pediatric patient reported in the electronically-searchable literature with recurrent IE due to P. aeruginosa. Although care was taken to treat the IE with a beta-lactam antibiotic + an aminoglycoside with extension of antimicrobial therapy to at least 6 weeks, as recommended, the infection recurred. Therefore it may be prudent to change the recommended duration of antimicrobial therapy from “at least 6 weeks” to “at least 6 weeks of sterile cultures” and to switch to other antimicrobials to which the organism is susceptible in case clinical or laboratory failure occur.

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COMMUNITY SUPPORT FOR INTRODUCTION OF MENINGOCOCCAL B VACCINES

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Background and aims: Serogroup B meningococcal (MenB) vaccines are likely to be available soon. This study aimed to assess community knowledge, understanding and acceptance of MenB vaccines.

Methods: A large population survey of randomly selected metropolitan and rural households in South Australia was conducted by face-to-face interviews from October-December 2012 to assess community knowledge of meningococcal disease and attitudes to introduction of new MenB vaccines.

Results: A total of 3055 interviews were conducted with adolescents/adults, 15-97 years of age. Most adults (88.5% 2703/3055) considered meningococcal disease to be a severe or very severe illness. Concern about meningococcal disease was moderately high with 50.7% reporting moderate-severe concern (reporting 5-10 on a severity scale of 0-10) including 10.3% reporting extreme concern. Support for a MenB vaccine was high with 64.6% of adults indicating they would want to receive the vaccine themselves and 17.7% unsure. The majority of parents (83.9%) would want their child/ren to receive the vaccine. Parents who were more concerned about meningococcal disease were more likely to agree for their child/ren to receive a MenB vaccine ($p< 0.001$). For the majority of parents (80%), the requirement for an extra needle would not deter them from their child receiving a MenB vaccine, neither would potential for redness/swelling at the injection site (85.6%), nor mild-moderate fever (82.3%) following vaccination.

Conclusions: Public support for new MenB vaccines is high, particularly amongst parents, with support remaining high despite knowledge of the potential for fever, most of which is mild-moderate, or local reactions following immunisation.

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VALGANCICLOVIR TREATMENT IN PROTEIN- LOSING GASTROPATHY CAUSED BY CYTOMEGALOVIRUS INFECTION

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Background and aims: The association between protein- losing gastropathy (PLG) with cytomegalovirus infection has been documented. The disease in children is often self- limited but in some causes antiviral drugs are necessary to remit the illness.

The aim of this study is the description of a patient with PLG caused by CMV which disease was resolved after valganciclovir treatment.

Methods: We describe a case of PLG in which rapid clinical and laboratory remission was achieved with valganciclovir.

Results: A 3 months- old girl was admitted to our Pediatric Department because a 15 days history of vomiting, progressive abdominal distension and diarrhoea.

Physical examination revealed a generalized edema with severe ascites and hepatosplenomegaly. Laboratory test showed hypoalbuminemia of 1.8 mg/dl without proteinuria, and fecal alfa-1 protein antitrypsin level was not elevated. Immunological tests were normal. Ultrasound examination showed enlarged gastric fold. Gastric endoscopy revealed exudative erosions in corpus and antro of stomach and inclusion bodies were seen in histological examination. Postnatal CMV infection was confirmed by polymerase chain reaction in urine, blood and gastric tissue, with negative result in PCR to CMV in dried blood spots extracted in newborn age.

During the first three weeks the patient received infusions of albumin and diuretics without improvement. Treatment with oral valganciclovir (32 mg/kg/day) was administered for two weeks. Edema and hypoalbuminemia were resolved quickly, with no relapse.

Conclusions: Oral valganciclovir could be an effective alternative to intravenous ganciclovir in the treatment of PLG caused by a CMV infection in immunocompetent children.

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DIAGNOSIS OF SEPTICAEMIA IN EXTREMELY PRETERM INFANTS

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Background and aims: Neonatal septicaemia is one of the leading causes of morbidity and mortality in neonatal intensive care units (NICU). The early diagnosis is still difficult and represents a significant clinical problem in the early diagnosis of septicaemia ,especially in extremely preterm infants. The aim of the study was to assess biological markers such as C-reactive protein (CRP) level, white blood cell (WBC) count and platelet count together with clinical signs in diagnosis of neonatal septicaemia.

Material and methods: 176 infants were enrolled in this retrospective study. They were less than 28 weeks of gestational age (GA) and hospitalized in the NICU in Lund and Malmö between 2002-2011.Criteria for septicaemia were positive blood cultures or U-Arabinitol quota>5.Diagnosis was clinically compatible with biological markers of infection (CRP>8mg/l, total WBC>15000 or< 5000, platelet count< 100000u/L).

Results: Out of 176 infants 36,4% (95%CI 29,6-43,7%) were identified as infants with septicaemia. The median GA and birth weight (BW) was 26 weeks+1day and 810g respectively. The biological markers of infection most often were an increase of CRP 83%(95%CI 71,8-90,1%),followed by thrombocytopenia 44%(95%CI 32,3-55,9%), leukocytosis 9%(95%CI 4,4-19,1%) and leukopenia 5%(95%CI 1,6-13,1%).The most frequent clinical signs were cardiopulmonary: apnea 44%(95%CI 32,3-56,1%) and bradycardia 31%(95%CI 21,2-43,4%), abdominal distention 31%(95%CI 21,2-43,4%), respiratory distress 16%(95%CI 8,7-26,4%), hyporeactivity 9%(95%CI 4,4-19,1%) and vomiting 9%(95%CI 4,4-19,1%).

Conclusions: C-reactive protein is a good marker for the detection of septicaemia, response to therapy and development of complications. The most frequent clinical sign was apnea.

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RSV IMMUNOPROPHYLAXIS AT HOME VERSUS HOSPITAL SETTINGS: CLINICAL AND HEALTH ECONOMIC OUTCOMES- COMPARATIVE STUDY IN DEFINED BIRTH COHORT IN IRELAND

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Background and aims: Immunoprophylaxis (IP) has proved effective in reducing hospitalisation from respiratory syncitial virus (RSV) infection among high-risk infants. We aimed,

1. to compare the direct cost of RSV IP for high-risk infants allocated to monthly injections at home versus hospital settings,

2. to compare the compliance and 3. to analyse post-prophylaxis RSV hospitalisations.

Methods: Single-centre, multi-year retrospective review of RSV IP in defined birth cohort was undertaken. High-risk infants of Limerick university maternity hospital in Ireland, from 2003 to 2009 received IP through hospital and from 2009 to 2012 at home through a provider (TCP Healthcare®) purchased by the Health Service Executive (HSE) of Ireland. Compliance to IP was scored and post-IP follow-up conducted. Hospital Ethics Research committee approved the study.

Results: Unit cost of RSV IP session was € 300 and 520 for home and hospital groups respectively, taking into account IP failures and nosocomial admissions. Since introduction, home RSV IP programme prevented 12,700 hospital encounters in Ireland and under the base case assumptions a direct cost saving of €2.8 million for the HSE over 5 years. Compliance scoring was statistically significant for home group. Calculations are in addition to the drug cost of IP (Palivizumab®).

Conclusions: Significant professional hours in the hospital during winter time could be freed up by the 'outsourcing' of RSV IP to the 'home care'. In addition to the direct cost savings to the payer (Irish healthcare), prophylaxis at home offers significant indirect, opportunistic and societal cost savings as well.

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PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS WITH PALIVIZUMAB IN LATE-PRETERM INFANTS: OUR EXPERIENCE

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Background: Palivizumab is a humanized monoclonal antibody that binds to the respiratory syncytial virus (RSV) F protein and some recent studies seem to evidence its efficacy in the prevention of pulmonary infection by RSV.

Aim: To evaluate the prevalence of admission to our operative unit for pulmonary infection by RSV in two group of late-preterm newborns; the first group was treated with palivizumab (15 mg/Kg intramuscular once month for five months), while the second was characterized by absence of prevention with palivizumab.

Patients and methods: The first group was composed by 52 patients with a gestational age 33-35 weeks; the second group were composed by 47 patients with a gestational age 33-35 weeks.

Results: In the first group 2/52 patients (3.8%) were hospitalized for severe pulmonary infection by RSV during the first year of life, while in the second group 8/47 (17%) was admitted to our operative unit for severe pulmonary RSV infection. No case of adverse sides correlated to palivizumab were evidenced.

Conclusion: Our experience seems to demonstrate the efficacy and tolerability of palivizumab in the prevention of severe pulmonary infection correlated to RSV in late-preterm infants. This date is very important in relation to frequent respiratory sequels correlated to this infection.

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TINN2: TREAT INFECTION IN NEONATES 2 AZITHROMYCIN FOR THE PREVENTION OF BRONCHOPULMONARY DYSPLASIA IN PRETERM NEONATES

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Background: In neonates, pulmonary Ureaplasma colonization, and inflammation may play a role in BPD development, a multifactorial disease of prematurity. The macrolide antibiotic azithromycin may be effective in reducing the severity of BPD as it is active against Ureaplasma and has anti-inflammatory properties.

Objectives and clinical trial design: Therefore, the TINN2-project (www.tinn2-project.org) was submitted and financed by the FP7 program in order to evaluate azithromycin in neonates and obtain a PUMA. The TINN2 Pediatric Investigation Plan has been approved by the PedCo in January 2013.

Within the PIP, the randomised, double-bind, placebo-controlled trial was designed to assess the efficacy of azithromycin in increasing the rate of survival without BPD in preterm infants of ≤28 weeks gestation ventilated within 48hours of birth. The trial will include 810 preterm neonates, born at ≤28weeks of gestation requiring respiratory support within 12hours of birth will be recruited. The drug will be given at the daily dose of 10mg/kg for 10days.

Among the main secondary objectives the trial will assess changes in the overall neonatal mortality rate, safety and pharmacokinetics of azithromycin, pulmonary colonisation by Ureaplasma, and Ureaplasma resistance to treatment.

Expected outcomes and potential implications: TINN2 will provide the required information on the pharmacokinetics, efficacy and safety, of azithromycin in the newborn to apply for a PUMA.

TINN2 currently benefits from various paediatric drug evaluation initiatives across Europe, including the ongoing TINN1-project consolidating a network of units with experience in clinical research that will be used for additional drug evaluation in neonates.

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POPULATION PHARMACOKINETICS OF CIPROFLOXACIN IN NEONATES AND YOUNG INFANTS LESS THAN 3 MONTHS OF AGE

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Background: In the absence of pharmacokinetic and pharmacokinetic / pharmacodynamic studies, ciprofloxacin is used off-label in neonates with suspected or proven gram negative infection. Within the FP7 EU project TINN (Treat Infection in NeoNates), our aim was to evaluate the population pharmacokinetics of ciprofloxacin in neonates and young infants < 3 months in order to optimize ciprofloxacin treatment.

Methods: Blood samples were collected from treated neonates and ciprofloxacin plasma concentrations were analyzed by HPLC-MS.. Population pharmacokinetic analysis used NONMEM software to optimize dosing.

Results: Ciprofloxacin was administered as an intermittent infusion over 30 minutes or 1 hour at the dose of 10 mg/kg/dose twice daily in neonates and three times daily in young infants. Sixty two babies were included in the pharmacokinetic analysis and a total of 480 concentrations (pharmacokinetic or scavenged samples) were available for modeling to determine population pharmacokinetic parameters. Simulation was used to determine ciprofloxacin dose required to achieve the adequate pharmacokinetic-pharmacodynamics target ($AUC_{0\text{-}24}$/MIC ratio).

Conclusion: This is the first report of the population pharmacokinetics of ciprofloxacin in neonates and young infants < 3 months. The developed model will be used to optimize ciprofloxacin treatment in neonates and infants.

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IMPACT OF PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINES ON NASOPHARYNGEAL CARRIAGE: EXPERIENCE FROM CLINICAL AND EPIDEMIOLOGICAL STUDIES

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Background/aims: We review the impact of the 10-valent pneumococcal non-typeable Haemophilus influenzae protein D conjugate vaccine (PHiD-CV, GlaxoSmithKline Vaccines) and its 11-valent predecessor (11Pn-PD) on S.pneumoniae (Sp) nasopharyngeal carriage (NPC).

Methods: We reviewed data from 3 randomised controlled trials (RCTs)[1-3], and 1 non-randomised controlled trial[4] assessing the impact of PHiD-CV on NPC, as well as 1 RCT assessing the impact of 11Pn-PD[5,6]. Trial characteristics are summarised in the table. Results from 2 recent PHiD-CV effectiveness studies (Brazil[7], Kenya[8]) were also assessed. NPC was analysed using standard culture methods, except in Brazil where PCR was used.

Results: A consistent decrease in vaccine serotype (VT) Sp NPC was seen after PHiD-CV/11Pn-PD vaccination compared to vaccination with a non-pneumococcal control vaccine, with a maximum reduction of 31 to 56% (Table). In some studies, the decline in VT Sp NPC was already noticeable post-priming. Trends for elevated NVT Sp NPC were seen at some time points post-booster but these increases did not lead to complete replacement and an overall reduction in Sp NPC was seen in each study (maximum reduction: 11-36%). Similarly, the effectiveness studies showed reduced VT and overall Sp NPC 6-9 months after PHiD-CV was introduced in these countries' routine immunisation schedules.

Conclusions: In these studies, PHiD-CV vaccination resulted in a consistent reduction in overall/VT Sp NPC suggesting that herd protection may be expected with PHiD-CV. Further studies are required to evaluate the public health implications of reduced overall Sp NPC.

Table: Trial characteristics and vaccine efficacy of PHiD-CV in reducing pneumococcal nasopharyngeal carriage

	POET[5,6] Czech/Slovak Republics NCT00119743	COMPAS[1] Panama NCT00466947	Study 053[2] Finland NCT00839254	Study 014[4] Czech Republic NCT00496015	Study 027[3] The Netherlands NCT00652951
Trial characteristics					
Trial design	Double-blind Randomised	Double-blind Randomised	Double-blind Cluster-randomised	Open-label Non-randomised	Single-blind Randomised
Vaccines	11Pn-PD vs. HepA	PHiD-CV vs. HepB or HepA	PHiD-CV vs. HepB	PHiD-CV vs. MenACWY-TT	PHiD-CV vs. 7vCRM
PCV included in NIP before study start?	No	No	No	No	Yes (7vCRM)
Vaccination schedule	Priming: 3, 4, 5 mo Booster: 12–15 mo	Priming: 2, 4, 6 mo Booster: 15–18 mo	Priming: 3, 4, 5 mo (3+1) or 3, 5 mo (2+1) Booster: 11–12 mo	Priming: 3, 4, 5 mo Booster: 12–15 mo	Priming: 2, 3, 4 mo Booster: 11–13 mo
NPC swab sampling schedule	6 swabs between 6 and 24–27 mo	6 swabs between 7 and 24–27 mo	5 swabs between 3 and 18–22 mo	5 swabs between 12–15 and 24–27 mo	5 swabs between 5 and 24 mo
N per group	11Pn-PD: 191 Control: 190	PHiD-CV: 955 Control: 966	PHiD-CV 3+1: 1849 PHiD-CV 2+1: 1316 Control: 1928	PHiD-CV[a]: 209 Control: 336	PHiD-CV: 520 Control: 260
Highest point estimates of vaccine efficacy[b] and time points with highest point estimates					
VE (95% CI) against VT *S. pneumoniae*	**43%** (-17; 72) at 15–18 mo	**31%** (5; 50) at 18–21 mo	3+1: **56%** (47; 64) at 18–22 mo 2+1: **38%** (25; 49) at 14–15 mo	**54%** (21; 74) at 12–15 mo	**0%** (-87; 45) at 11–13 mo
VE (95% CI) against any *S. pneumoniae*	**23%** (-17; 50) at 15–18 mo	**11%** (-7; 25) at 15–18 mo	3+1: **28%** (20; 36) at 18–22 mo 2+1: **15%** (4; 25) at 18–22 mo	**36%** (9; 54) at 12–15 mo	**3%** (-19; 21) at 18–20 mo

[a]Only includes subjects who had not received prophylactic antipyretics at vaccination; [b]Results for total vaccinated cohorts; [1-6], see references; POET, pneumococcal otitis efficacy study; COMPAS, clinical otitis media and pneumonia study; HepA, hepatitis A vaccine; HepB, hepatitis B vaccine; MenACWY-TT, quadrivalent meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine; PCV, pneumococcal conjugate vaccine; NIP, national immunisation programme; 7vCRM, 7-valent CRM_{197}-conjugated PCV; mo, months; NPC, nasopharyngeal carriage; N, number of subjects (per group) in total vaccinated cohort; VE, vaccine efficacy estimated as 1 minus relative risk; VT, vaccine type; CI, confidence interval. [1]Tregnaghi, ESPID2011, abs. 1411; [2]Vesikari, ECCMID2013; [3]van den Bergh, Clin Infect Dis 2012; [4]Prymula, Vaccine 2011; [5]Prymula, Vaccine 2009; [6]Borys, ISPPD2012, abs. 189; [7]Andrade, ISPPD2012, abs.211; [8]Hammitt, ISPPD2012, abs. 242

Funding: GlaxoSmithKline Biologicals SA

[Table: Trial characteristics and vaccine efficacy]

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DEVELOPMENT OF IMMUNO-PCR ASSAY FOR THE DETECTION OF DIPHTHERIA TOXIN

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Diphtheria is frequent pediatric acute infection of the upper respiratory tract caused by toxigenic strains of Corynebacterium diphtheriae. Diphtheria toxin (DT) consists of two subunits: the enzymatically active, heat stable A subunit and the receptor-binding thermolabile B subunit. The most sensitive contemporary diagnostic methods for the C. diphtheriae reside on qualitative PCR detection of target DNA and fail in description of toxin level in a sample. Routine tests, such as conventional ELISA, have low sensitivity and usually require preliminary sample concentration. These drawbacks can be overcome employing immuno-PCR strategy, representing highly sensitive and specific diagnostic approach to identify proteinateous targets.

The purpose of the present study was the development of diagnostic assay for the detection of diphtheria toxin based on immuno-PCR techniques.

Recombinant non-toxic A subunit of diphtheria toxin was produced in E. coli, purified by metal-chelate chromatography (Talon matrix, Clontech), and used to raise murine monoclonal antibodies. Monoclonal antibodies (Mabs) were isolated from ascitic fluid by Protein G affinity chromatography. Mab specificity was confirmed by dot-blot analysis with a panel of recombinant proteins. Mab E6B9 was biotinylated to concentrate toxin by magnetic capture. Mab C2G5 was conjugated with a DNA fragment using Click chemistry reagents (Bioconjugate Technology Company) and employed for detection of the captured toxin by real-time immuno-PCR.

The assay was capable to detect up to 10 pg/ml of toxin, thus exceeding the sensitivity of conventional ELISA by three orders of magnitude. The developed immuno-PCR assay is suitable for the detection of diphtheria toxin in clinical samples.

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LONG-TERM IMMUNOGENICITY, SAFETY AND EFFECTIVENESS OF GARDASIL® IN THE NORDIC COUNTRIES

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Objectives: To evaluate long-term effectiveness, safety and immunogenicity of the quadrivalent HPV (qHPV) vaccine GARDASIL®, a pivotal randomized, placebo-controlled, double-blind, 4-year study (protocol 015-21) was extended up to 14 years in 4 Nordic countries. Interim analyses were performed at 8 years of total follow-up.

Methods: Nordic citizens are assigned a unique personal identification number (PIN) at birth, and are registered in a Civil Registration System in each country. A total of 2,750 subjects receiving qHPV and 2,097 receiving placebo at the start of study 015-21 are included in effectiveness and safety analyses. 4,344 participants consented for long-term immunogenicity analyses. Neutralizing and total IgG antibody response to HPV 6/11/16/18 were detected by competitive Luminex immunoassay (cLIA) and VLP-specific total IgG Luminex immunoassay (total IgG LIA), respectively.

Results: There were no cases of HPV 6/11/16/18-related disease observed through the current follow-up. There was no specific pattern of new medical conditions in the two cohorts and no evidence of an increase above background. In addition, 94.4%, 95.5%, 99.1% and 60.0% of patients remained seropositive to HPV 6/11/16/18 at year 8, respectively in the cLIA and 97.6%, 96.4%, 100% and 90.8% respectively in the IgG LIA. There was no evidence of HPV type-replacement against non-vaccine HPV types in young women.

Discussion: No breakthrough cases of disease related to vaccine HPV types have been observed among young women vaccinated with GARDASIL® through year 8. GARDASIL® continues to be generally safe and well tolerated. Immunogenicity to vaccine HPV types remains high 9 years following vaccination.

721

OUT-BREAK OF PROTEUS MIRABILIS PRODUCING VEB- EXTENDED SPECTRUM B LACTAMASE GENE IN NEONATAL INTENSIVE VARE UNIT NEW DELHI

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An outbreak of ESBL producing Proteus mirabilis septicaemia involving 5 babies in NICU was reported and the isolates showed an unusual synergy between Imipenem and ceftazidime.

Aim:

1. Examine molecular mechanisms involved in β-lactamase resistance.

2. Study molecular epidemiology of these outbreak strains and 3. Investigate source of outbreak.

Methods: The outbreak was investigated and all health care workers, non-infected babies and environmental samples were screened to study source of outbreak. The ESBL were screened with double disc synergy test using cefotaxime, ceftazidime and clavulanate. The ESBL typed were determine by PCR using specific primers for bla_{TEM-1}, bla_{SHV}, bla_{CTX-M}, $bla_{OXA.}$, bla_{PER}, bla_{VEB} followed by sequencing. Isolates were studied for clonality by ribotyping. The transferability was examined by conjugation.

Result: Proteus mirabilis was isolated from multi-dose vial of dextrose used for diluting antibiotics and also from the hands of the health care worker on duty. The outbreak strains and environmental samples were identical by ribotyping indicating that the source of infection was contaminated multi-dose vial. All isolates showed a marked synergy between cefoxitin and the 3rd generation cephalosporin and between imipenem , and ceftazidime and cefotaxime. PCR identified that gene to be $bla_{VEB.}$ The resistance was not transferrable by conjugation suggesting the VEB gene on the chromosome.

Conclusion: This is the first report of VEB producing Enterobacteriaceae in India and describes important phenotypic and molecular characteristics of ESBL.

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PEDIATRIC BACTERIAL MENINGITIS IN THE LAST DECADE IN A SPANISH TERTIARY HOSPITAL

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Background and aims: Describe the epidemiological, clinical and laboratory features of the pediatric bacterial meningitis in the last decade in a Spanish tertiary hospital.

Methods: Descriptive, retrospective study of bacterial meningitis in children admitted to the Hospital 12 de Octubre, Spain, Madrid, between 2002-2012.

Results: 43 patients had bacterial meningitis. 9 cases were excluded from analysis (nosocomial infections, all admitted at NICU: 6 E. coli, 3 S. agalactiae). Of the 34 remaining cases median age was 6.8 months (1.1-18.7), 38% were girls. 9% had history of concomitant disease and 11% were premature. The most frequent pathogens found were: S. pneumoniae (35%) and N. meningitidis (32%). E. coli and S. agalactiae were the most frequent bacteria in < 1 month-old, S. pneumoniae among 1-3 months-old, and N. meningitis over 3 months-old. 25% of S. pneumoniae had decreased susceptibility to penicillin. The most common symptoms were fever (82%), nuchal rigidity (66%), malaise (62%), headache (55%), irritability (52%) and vomiting (47%). On admission: median blood WBC: 13850/mm³ (6447-20825), median C-reactive protein: 9.1 mg/dl (4.4-17.5), median WBC count in CSF: 626/mm³ (70-3200), median neutrophils in CSF: 84% (75-90%). 41% had a positive blood culture. Diagnosis on admission was meningitis in 59% and sepsis in 21%. 18% presented pathological image test, 29% complications and 3% sequelae. PICU admission: 50%, mortality: 3%.

Conclusions: Bacterial meningitis remains a serious problem in pediatric population, with S. pneumoniae and N. meningitidis as the most common pathogens. We detected significant antibiotic resistance in S. pneumoniae meningitis.

723

INVASIVE PNEUMOCOCCAL DISEASES IN BIRTH COHORTS VACCINATED WITH PCV-7 AND/OR PHID-CV IN QUEBEC: AN UPDATE

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Background: In the province of Quebec, the 10-valent pneumococcal conjugate vaccine (PHiD-CV) was introduced in the summer of 2009, replacing the 7-valent vaccine (PCV-7) according to a 2+1 doses schedule. Transition to the new vaccine was recommended regardless of the number of PCV7 doses already administered. The objective of the study was to compare rates of invasive pneumococcal disease (IPD) in children exposed to different vaccines.

Methods: IPD cases were identified by the reference laboratory collecting isolates and specimen from all microbiology laboratories in the province. IPD rates were computed in cohorts of children born in 2007-2011 and observed up to the end of 2011 (maximum age = 48 months). The main vaccine used for the infant primary immunization series and the toddler booster dose was inferred from the Quebec City Immunization Registry data.

Results: IPD rate was significantly lower in the cohorts exposed to PHiD-CV (31/100,000 person-years) as compared with those exposed to PCV-7 (56/100,000; p=0.02). This was explained by a reduced frequency of 7F, 19A and other non-vaccine types. IPD rate also tended to be lower in children who had received PCV-7 for the primary series and PHiD-CV for the booster dose (24/100,000) as compared to those who had received PCV-7 only (36/100,000; p=0.14).

Interpretation: Results of this ecological analysis are compatible with a high level of protection induced by PHiD-CV against IPD caused by homologous serotypes and some level of cross-protection against other serotypes.

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RESISTANCE PATTERN FOR STREPTOCOCCUS PNEUMONIAE STRAINS IZOLATED IN DIFFERENT BIOLOGICAL SAMPLES IN A ROMANIAN HOSPITAL

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Background and aims: Streptococcus pneumoniae's resistance to antibiotics is continuously changing, especially in European countries, reaching 71% in Spain, France and Hungary; in the USA penicilline resistant strains are izolated in 44% of cases and in South-Eastern Asia (Hong Kong, South Koreea, Taiwan) antibiotic resistance reached alarming rates (78%). We aimed to analyse the sensitivity of Streptococcus pneumoniae strains izolated from different biological samples to the main antibiotics used in therapy in the Clinical Emergency Hospital for Children „Sfantul Ioan", Galati, Romania.

Methods: We used 45 strains of Streptococcus pneumoniae, izolated in pathologic products from children and adolescents (age: 0 months to 18 years) in the Bacteriology Department of the Clinical Laboratory of our hospital from January to December 2011.

Results: Out of all strains analysed, 60% (32/45) resulted from nose cultures and 40% (13/45) from different purulent colections (otic, conjunctival). Penicilline resistance was found in 71,1% (intermediate resistance in 37,8% and high resistance in 33,3%); ceftriaxone resistance was 9,1%. Am increased resistance to cotrimoxazol was noted (87,6%), clarytromycin (64,4%) and erytromycin (73,3%). Penicilline resistance was associated with cotrimoxazol and erytromycin resistance. All strains were vancomycin si ofloxacine sensible. Most of pneumococcus strains were chloramphenicol, tetracycline and rifampicin sensible.

Conclusion: The increased prevalence of multiresistant strains underlines the importance of the antibiotic sensitivity test when recommending antibiotic treatment. Continous monitorisation of antibiotic sensitivity of S. pneumoniae is necessary to elaborate an efficient guide for empiric therapy.

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THE MACROLIDE RESISTANCE AT STREPTOCOCCUS PYOGENES IN ISTANBUL, 2009-2012

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Aim: Group A beta hemolytic streptococcus (GAS) pharyngitis is a common childhood disease. The aim of this retrospective study is to evaluate prevalence of macrolide resistance among pharyngeal isolates of GAS from pediatric patients, who lived in Istanbul between 2009 and 2012.

Methods: The strains were isolated and identified by conventional methods. The susceptibility testing was performed by disc diffusion according to Clinical and Laboratory Standards Institude standards.

Results: We studied 9705 throat cultures and were isolated 867 (9 %) GAS in four years. In these GAS isolates, erythromycin resistance rates over the years were found 3 % (5 out of 177 strains) in 2009, 3 % (7 out of 214 strains) in 2010, 3 % (8 out of 283 strains) in 2011, 5 % (9 out of 193 strains) in 2012, respectively. Clindamycin resistance rates were found 2 %, 7 %, 4 % and 11 %, respectively.

Conclusions: GAS are still susceptible to penicillin, but have increasing resistance to macrolides. Reports of macrolide resistance rates varies regionally. In 2011, erythromycin resistance of GAS was determined as 1.3 % in first results of a pilot study from 8 centers in Turkey. Intermediate resistance of erythromycin and clindamycin were determined 2 % and 1.1 %, respectively. In our study, erythromycin resistance is found in low rate.

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PEDIATRIC URINARY TRACT INFECTIONS AT A GREEK HOSPITAL: RELATIONSHIP BETWEEN UROPATHOGENS, CLINICAL CHARACTERISTICS, GENDER AND AGE

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Background and aims: Pediatric urinary tract infections are a common cause of hospital admission and they usually appear in early childhood. The aim of this study was to determine the incidence of UTI in children, to analyze its clinical presentation and to evaluate the relationship between uropathogen, gender and age.

Methods: We examined retrospectively the hospital records of all children with UTI and positive urine cultures during January 2010-December 2011. We defined UTI by growth of a single pathogen of ≥50,000 colony-forming units (CFU)/mL of a specimen collected by bladder catheterization or ≥100,000CFU/mL by clean void or any growth by suprapubic aspiration.

Results: We identified 185 patients with positive urine samples: 96 females (52%) and 89 males (48%). The average age was 26.36 months. There were 92 (49.7%) cultures positive for Escherichia coli, 33 (17.8%) for Proteus sp, 24 (12,9%) for Pseudomonas sp., 17 (9.1%) for Klebsiella sp, 11 (6%) for enterococcus sp. Proteus mirabilis was more common in males than in females (23.9% vs 13.5%). During the first 3 months of life, the prevalence of UTI in boys exceeded that in girls (27.3% vs 16.7%). The most common symptoms associated with clinical UTI were fever (62.1%) and vomiting (31.5%).

Conclusions: The relative low percentage of E. coli as an uropathogen compared to other published studies is probably due to the small average age and the anatomical abnormalities found in our study group. In Greece, all male infants are uncircumcised probably accounting for the high male:female ratio found.

MICROBIAL CULTURE AND SENSITIVITY PATTERN IN URINARY TRACT INFECTIONS IN CHILDREN: EXPERIENCE WITH 281 URINE CULTURES IN SANANDAJ

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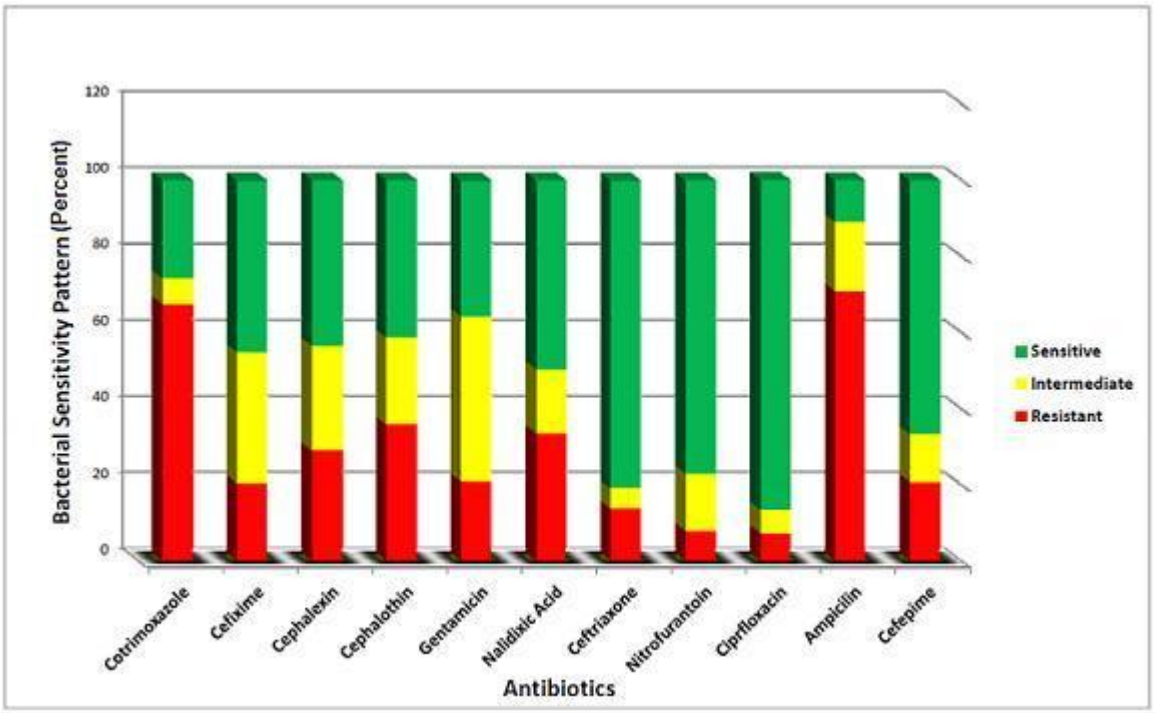
Background and aims: Urinary tract infections (UTIs) have been considered as an important risk factor for the development of vesicoureteral reflux and renal injury. Optimal empirical therapy of UTIs requires accurate knowledge of local susceptibility patterns, which vary with organism.

Methods: This cross-sectional study was conducted from January 2007 to September 2011 in Sanandaj in order to determine prevalence of bacterial types and the antibiotic resistance of urinary pathogens. Children aged less than 12 years who had signs and symptoms of UTI were selected. Urine samples were obtained by sterile urine bags (at least 2 consistent positive cultures), suprapubic aspiration and midstream sampling in older children. Sensitivity was measured by the disc diffusion method using the NCCLS protocol.

Results: A total of 281 positive urine cultures of children meeting inclusion criteria were included. 90% were females, and 28.1 were younger than one year. The most prevalent urinary pathogens were Escherichia coli (239 cases, 85.4%), Staphylococcus epidermitis (6 cases, 2.1%), Citrobacter spp. (4 cases, 1.4%), Enterobacter spp. (9 cases, 3.2%), Klebsiella spp. (14 cases, 5%). E. coli had a resistance rate of 67.7 to trimethoprim-sulfamethoxazole, 19.7% to cefixime, 28.3% to cephalexin, 33.8% to nalidixic acid, 4.8% to nitrofurantoin, 70% to ampicilin, 20.4% to gentamicine, 14.7% to ceftriaxone, and 22.7% to cefepime.



[Figure 1. Overall Sesitivity Pattern of Bacteria]

Conclusions: There were a high percentage of antibiotics resistances in Sanandaj. A national program is needed to provide judicious use of antibiotics and lower the bacterial resistance rates.

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BACTERIAL MENINGITIS IN CHILDREN, SEQUELS AND MORTALITY

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Background and aims: Bacterial meningitis (BM) remains a major cause of mortality and sequels.

Methods: An observational, descriptive and retrospective study was performed. We included patients from 30 days old to 15 years old, hospitalized at Hospital La Paz, from January 2000 to June 2011 with BM. Diagnosis was confirmed by blood or cerebrospinal fluid (CSF) culture, antigen detection, or polymerase chain reaction. Hospital-acquired infections, non bacterial pathogens and immunocompromised patients were excluded. Several variables were analyzed: age, sex, clinical presentation, laboratory test results, identified bacteria and sensibility to antibiotics, antibiotherapy; and patient evolution.

Results: 61 cases of BM were identified. The mean age was 2.5 years. The most common bacteria in our series was Neisseria meningitidis (44%), followed by Streptococcus pneumoniae (SP) (43%), Streptococcus agalactiae (10%), Enterococcus faecalis (1 case) and Haemophilus influenzae (1 case). 97% of diagnoses were made by blood or CSF culture. 76% of children debuted with neurological symptoms, 13% did with clinical sepsis and 11% had mixed symptoms. SP infection associates higher leukocytosis and neutrophilia. Total mortality was 8%. 73% developed sequels. Hearing loss was the most frequent (48%), both acute and permanent. Hearing and motor deficits reduced or even disappeared with the time, but visual deficits were permanent. Significant association between SP and development of sequels and mortality was found.

Conclusions: SP is the pathogen associated with higher amount of sequels and mortality. Hearing loss is the most frequent neurological sequel. Younger patients develop more frequently neurological sequels after a BM.

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EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF KAWASAKI DISEASE IN CYPRUS

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Background and aims: Kawasaki Disease (KD) is a systemic vasculitis of unknown aetiology, the leading cause of acquired heart disease in children. There are no previous published studies on KD in Cyprus. This study aims at investigating the epidemiology and clinical characteristics of KD in Cyprus.

Methods: This is a retrospective study on KD patients from all Cyprus hospitalised at Archbishop Makarios Hospital (AMH) the referral children's hospital in Nicosia. A chart review was performed.

Results: 56 children with KD from all Cyprus were hospitalized at AMH between 1/1/1989 and 31/12/2012. 4 of these cases were classified as atypical KD. 31 patients were boys (55.4%). 48 children were less than 5 years (85.7%). Liver enzymes were raised in 28/53 patients (52.8%) while median ESR value was 87mm. 54/56 patients received treatment with Intravenous immunoglobulin (IVIG) 2g/kg. 46/54 patients (85.2%) received IVIG within 10 days of onset of fever. Of those treated 7 (13.5%) did not respond and needed a second or even a third dose of IVIG. No one of them needed steroids. 5 developed cardiac complications (8.9%). 4 developed ectasia and one giant aneurysm. One case of ectasia occurred concurrently with myocarditis. Pericardial effusion was also detected in 5 cases (8.9%).

Conclusions: The epidemiology, clinical characteristics and outcome of KD in Cypriot children is comparable to other populations. Treatment was given in time, according to International guidelines in a significant percentage of patients. However, some cases still present late, therefore increased awareness of KD is needed.

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MANAGEMENT OF PAEDIATRIC TB IN LEADING UK CENTRES - UNVEILING CONSENSUS AND DISCREPANCIES

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Background and aims: National UK and international guidelines for the clinical care of children with TB differ in some fundamental aspects, with recommendations often based on expert opinion. We evaluated clinical practice in leading paediatric TB clinics in the UK.

Methods: A survey on diagnosis and management of latent and active TB was conducted in 12 specialist paediatric TB clinics in the UK using an electronic questionnaire.

Results: We had 100% response rate. Heterogeneous practice exists in use of IGRA and TST for screening (see table). Practice differs when choosing the age cut off for empirical TB prophylaxis for children: < 2yrs (69%) or < 5yrs (31%). In active TB, only 54% of clinicians do colour vision tests before prescribing ethambutol. Opinions divide on treatment duration of osteoarticular TB: 6 months (46%), 12 months (54%). There is consensus for conducting a routine HIV test, using drug doses recommended by British National Formulary (BNF) in treating active TB and monitoring MDR TB contacts without using chemoprophylaxis.

Conclusions: The survey shows marked variation in many aspects of clinical practice, highlighting the need to review their evidence base. Prospective paediatric studies are urgently required to unify clinical practice.

	TST alone	TST and IGRA	Either	Total
1mo-2yrs	4/12(33%)	8/12(67%)		12/12
2-5yrs	5/12(42%)	7/12(58%)		12/12
>5yrs	6/12(50%)	6/12(50%)		12/12
Immunocompromised		10/12(83%)	2/12(17%)	12/12

[Screening for latent TB in children, who had BCG]

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KINGELLA KINGAE SEPTIC ARTHRITIS - FIRST CASE DETECTED IN SLOVENIA

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Background: Kingella kingae (Kk) is reported to be a common cause of septic arthritis (SA) in children < 3 years of age. The organism is difficult to cultivate and inoculation of joint fluid (JF) in blood culture (BC) vials has been shown to increase diagnostic performance. Until now, inoculation of SA JF in BC vials has not been routine practice at our institution.

Methods: A 20-month old boy was adimtted to our Department with a 10-day fever. Three days before admission the child started to limp and complained of pain in the left knee. On admission, the left knee was swollen, red and painful, ESR was 36 mm/h, CRP 10 mg/L and WBC count was 18.5 x 10^9/L with normal differential. In the JF there were 43.4 x 10^9/L WBCs with neutrophil predominance and a negative Gram stain. BCs were drawn and JF was inoculated in a BC vial. The child was started on flucloxacillin.

Results: After Kk was grown in JF treatment was switched to penicillin G resulting in both general and local clinical improvement. Since echocardiography was normal the child was discharged on oral penicillin. Furher course was complicated by reappearance of high fever, gastroenteritis and elevated transaminases and the child made an uneventful recovery after cessation of penicillin treatment.

Conclusion: This is the first case of Kk SA detected in Slovenia. Current clinical algorithm for management of children with SA should include inoculation of JF in BC vials to enhance detection and guide antibiotic treatment.

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PARENTAL VIEWS ON CHILDHOOD INFLUENZA VACCINATION

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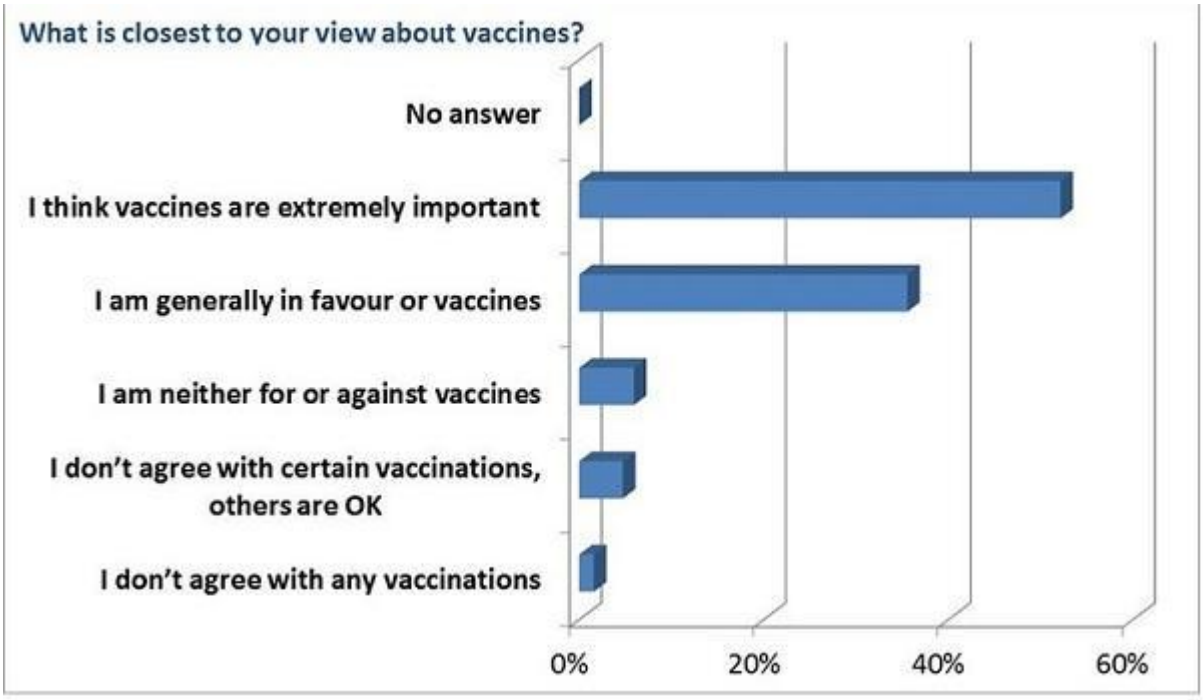
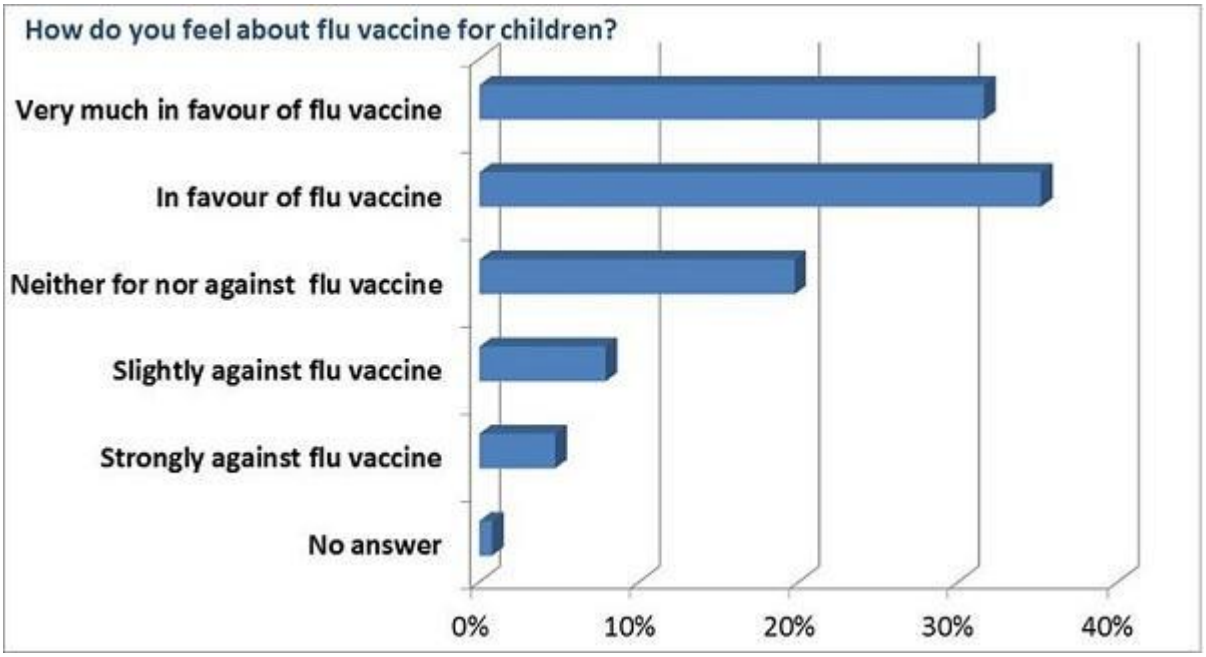
Background: Young children have high rates of influenza (flu) infection and are often significantly ill with high complication rates and prolonged viral transmission. Universal flu immunisation for children will be introduced in the UK. The study aim was to evaluate parental attitudes about childhood flu vaccination. A survey was used to assess their views and on vaccines in general.

Methods: A questionnaire consisting of background information and 8 questions was mailed to 2000 parents of children aged 2-11 years resident in Bristol, UK.

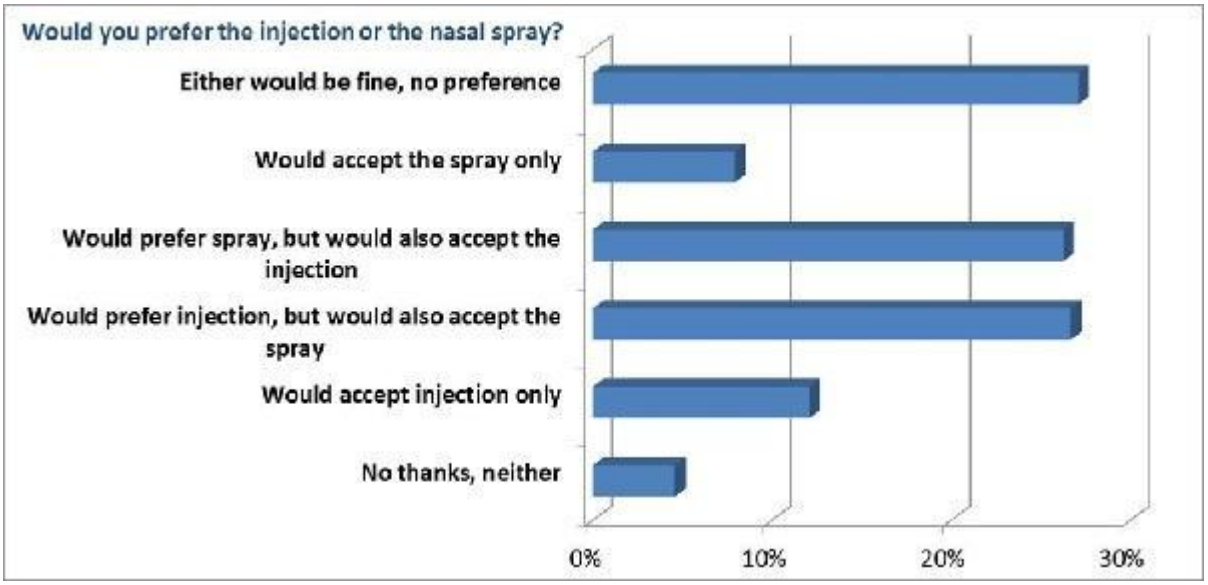
Results: Among 253 responses, 88% felt vaccinations are in general important and 67% were generally in favour of universal childhood flu vaccination with 20% undecided. If recommended by their doctor 92% would accept flu vaccine and of them, 12% would only accept injected vaccine. Almost 65% were willing to pay for flu vaccine for their child and most people (75%) would prefer to have it given at their GP surgery. The most important factors influencing acceptance were, in order, how well the vaccine works, stress for the child and serious side effects.



[General view on vaccines]



[Flu vaccine for children]



[LAIV vs TIV]

Conclusions: In this responding sample, parents generally had a positive attitude towards influenza vaccination. Further work using social networking sites will inform us about possible bias. Public education and involvement will be crucial for the success of the UK national flu vaccine programme.

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IS COMPUTED TOMOGRAPHY OBLIGATORY FOR THE FOLLOW UP OF ORBITAL CELLULITIS WITH MILD PROPTOZIS?

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Orbital infections require urgent diagnosis and treatment because the risk of severe complications such as vision loss and cranial tissue invasion. Despite preseptal and orbital cellulitis are different clinical conditions, often can be confused with each other or are seen in combination with. Usually clinical findings are helpful for diagnosis. Preferred imaging method is paranasal sinus and orbital computed tomography (CT). Because of high radiation risk of CT, we claim that the patients with mild proptosis can be treated without CT screening at presentation. We performed this study for determining the timing of CT scanning in the children with orbital cellulitis. A total of 71 patients with a diagnosis of preseptal or orbital cellulitis were enrolled in this study. Fifty of the patients (70.4%) were diagnosed with preseptal cellulitis, 21 of them (29.6%) were diagnosed with orbital cellulitis. Sinusitis was found 19 of 21 patients as an etiological factor with a diagnosis of orbital cellulitis (90.5%) and 22 of 50 patient with preseptal sellülitis (44%) ($p = 0.000$). Maxillary sinusitis rate was found 87.5%. We aimed to show that the patients who are in good general condition and have mild proptozis without limitation of eye movements can be followed with appropriate parenteral antibiotic therapy without CT scan. In the event of deterioration of general condition and eye globe findings and absence of fever response to the antimicrobial treatment, urgent paranasal and orbital CT must be taken. Thus we believe that this approach maintains children from the effect of irradiation.

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EVALUATION OF EFFICACY OF INTERFERON INDUCER IN TREATMENT OF THE RECURRENT ACUTE RESPIRATORY VIRAL INFECTIONS IN CHILDREN

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Background: It is known that recurrent episodes of acute respiratory viral infections (recurrent ARVI) are common for children attending nursery school.

Aim: To evaluate the efficacy of interferon inducer (IFN-i, anaferon), containing release active antibodies to interferon-γ in treatment of recurrent ARVI in children attending nursery school.

Methods: The open comparative prospective 2-center clinical trial of efficacy in parallel groups was conducted. The trial was performed in 141 children at the age of 1-5 years. 125 children included in group 1 received IFN-i in preventive regimen for 3 months. The 2-d group consisted of 16 children and they didn't receive medical prevention of ARVI. In case of appearing the ARVI symptoms all children received symptomatic medicines and the children of group 1 received IFN-i in treatment regimen - for 5 days. The duration of the first and recurrent episodes of ARVI in groups were estimated.

Results: The mean duration of ARVI was 8,9±0,92 days in 1-st group, and 14,6±1,79 days in control group respectively. The duration of the first ARVI episode was 9,5±0,53 and 15,8±2,1 days in 1-st and 2-d groups respectively. The duration of the second ARVI episode was 7,8±0,56 in 1-st group vs 14,2±2,11 days in 2-d groups. There were not registered any adverse effects in a children taking IFN-i during the trial.

Conclusions: The use of interferon inducer (anaferon) in treatment of ARVI leads to reduction of disease duration. In case of repeated anaferon administration its treatment efficacy isn't decreased.

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PERTUSSIS EPIDEMIOLOGY IN EL SALVADOR: A 10 YEAR REVIEW

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Pertussis is an important problem for public health in El Salvador (ES), continues causing significant morbidity and mortality, although its epidemiology has been studied in many developed countries, the current situation in Central America is unknown. This review summarizes the most important recent data concerning pertusis in ES.

Methodology: CDC diagnosis criteria were used. Age proportion of pertusis cases, immunization status and immunization coverage rate evaluated by Ministry of Health reviewed. Mortality and complications described. Bordetella pertussis isolate were characterized.

Result: From 2003 to nowadays, a steady increase of pertussis cases was observed.(5 to 40). Most of these correspond to patient younger than six month old (82%) who received less than two doses of vaccine (91%), but most of admitted (40%) and dead were younger than 4 month old (5% mortality). However cases in adolescent and adult have also been detected (5%). Several explanations have been proposed, among them the inability of current vaccines to induce long-lasting immunity is the most widely accepted as a cause of pertussing increasing. Positive culture was 20% of suspected cases.

Conclusions:

- Patient younger than 5 month old are in greatest risk of severe disease and death.

- Since pertussis is one of the vaccine preventable diseases on the rise, additional vaccine approaches include vaccination of newborns, additional booster doses for older adolescents and adult, and immunization of pregnant women with existing vaccines

- PCR is necessary to implement to improve the diagnosis of pertussis.

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PREVENTION STRATEGIES HAS BEEN EFFECTIVE TO LOWER THE INCIDENCE OF SEPSIS AMONG CHILDREN

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Background and aims: The aim of this study is to compare the incidence of bloodstream infections (BSI) in children 0-17 years during two 4 years periods, before and after the implementation of pneumococcal immunization and the introduction of the instituted risk-based intrapartum antibiotic prophylaxis (IAP) to mothers.

Methods: We retrospectively collected and analyzed data on blood cultures at yearly intervals during two 4 years periods, period 1; 20030701-20070630 and period 2; 20080701-2012.

Results: We identified 458 vs. 445 episodes of BSI during the two periods. The estimated incidence of invasive pneumococcal disease was 6.7/100.000 in children 0-17 years of age during period 1 and 2.4/100.000 during period 2. The incidence of BSI due to Streptococcus agalactiae (GBS) during period 1 was 0.56/1000 live born babies and 0.2/1000 in period 2. During period 1 57% of GBS was connected to early onset sepsis and 25% during period 2. Staphylococcus aureus increased from 10% (11/108) to 33% (34/103) of BSI among children 0-1 months of age. BSI at neonatal care units due to Candida spp. was halved during period 2. The occurrence of E.coli remained unchanged over the two periods. Staphylococcus aureus was the most frequently isolated pathogen and was found in 30% in period 1 and 37% in period 2 of all cases of BSI in children 0-17 year of age.

Conclusions: Implementation of the pneumococcal immunization programme and risk-based antibiotic prophylaxis has significantly decreased the incidence of BSI caused by Streptococcus pneumoniae and GBS. Staphylococcus aureus increases in relative importance.

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IMPACT ON SAVINGS AND REDUCTION OF IAS AFTER THE IMPLEMENTATION OF THE STRATEGY FOR HAND HYGIENE MULTIMODAL IN EL SALVADOR

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In the Benjamin Bloom Children`s Hospital the infection control committees (CPCIN) report that 85% of the IAS was located in 4 areas of the hospital with infection rates ranging from 10-36% with a mortality of 15-25%. In 2009 the CPCIN proposes the implementation of the strategy multimodal hand.

Descriptive study, transversal, analytic, it describes 4 years of experience:

Phase One: Hand washing (HW) change from soap and water for Alcohol Gel (AG)(2/4)

Second Phase: improving access to alcohol gel in ratio 1 / 1 and survillance.

Phase Three: to presents the results and impact of IAS rate and cost.

Results: 75% of the basins were suitable conditions for use. Compliance with HW increased 33.8% to 40.5% with better infrastructure.The rate of attachment to HW increased in almost all services: Infants: 54% to 81.3%, 50.6 to 65.5% NICU, PICU, 27% to 61%, Oncology of 36.8 to 72%. The IAS rate declined: from 2009 to 2012 as follows:NICU from 25% to 15% Neonatal 32 to 16%, UCI 16% to 9% and Oncology 8 to 5%

Reported an average of 3379.8 days ($ 638,782) of excess compared to 2010 with 1911.4 ($ 430.065).

Discussion: The overall rate decreased by 60% between year 2009 and 2012.These measures allowed savings of days attributed to IAS excess of $ $ 208,717.20, which proves to be cost effective, as the institution´s investment has been $ 10,000 per year.

A hand hygiene program must be planned, implemented and maintained to be successful and have the expected impact.

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A CASE OF VISCERAL LEISHMANIASIS WITH EBV AND HHV-6 CO-INFECTION

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Visceral leishmaniasis or kala-azar is a disseminated protozoan infection transmitted to human by the phlebotome sandfly. The prevalence is highest in southern Europe and central Africa and it is associated with mass migration, younger age and poverty. We describe a case of a Nigerian borne nine years old girl, always lived in Italy, transferred to our hospital for persistent fever, pancytopenia and epatosplenomegaly.

Routinary analysis showed pancytopenia, hight level of C-reactive protein (CRP) and lactate dehydrogenase (LDH), hypoalbuminemia, hypergammaglobulinemia and negative Coombs test. Epatosplenomegaly was confirmed by abdominal ultrasound. PCR (polymerase chain reaction) for EBV (Epstein-Barr-virus) and HHV-6 (human herpes virus-6) on blood and EBV IgG were positive. The diagnosis of visceral leishmaniasis relied on the demonstration of Leishmania in bone marrow aspirate and biopsy as well as on the positivity of PCR for Leishmania on blood and bone aspirate. She was treated with Ambisome for ten days with an improvement of his clinical condition and a slower improvement in bone marrow.

Differential diagnosis of visceral leishmaniasis includes infectives and autoimmunitary diseases, myelodisplastic syndrome, infiltranting tumors and macrophage activation syndrome.

The response to therapy is demonstrated by clinical improvement and not by the resolution of laboratoristic alterations. The severity of her clinical condition was likely influenced by EBV and HHV-6 co-infections, which determined an immunological impairment and a slow improvement in bone marrow.

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INVASIVE MENINGOCOCCAL DISEASE FOR THE LAST 17 YEARS

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Background: Meningococcal disease is one of the most common causes of death due to infectious diseases in childhood in developed countries. Universal meningococcal C vaccination is carried out in Spain since 2000.

Aim and method: Describe epidemiology and variables associated with outcome of confirmed invasive meningococcal disease in a terciary Hospital for the last 17 years (1996-2012).

Results: 230 cases were observed (120 male). Median age was 24 months (1-168 mo). Most cases (59%) were < 2 years. Main clinical forms were: septicaemia with meningitis (56%), septicaemia (24 %) and meningitis (19%). Distribution of serogroups was: 72% B, 29% C, 0.4% W135, and 7 % non-serogroupable. Most cases (75%) ocurred before 2005, no meningococcal C cases were detected since 2005. Sequelae were observed in 8.7% (4.5% neurological -hydrocephalus and seizures-, 3% distal necrosis, 1.3% others). Mortality rate was 7%. Poor prognosis (sequelae and mortality) was higher in children under 24 months ($p < 0.05$). In addition, this age-group of patients was associated with PICU admission, length of stay, and use of especial support, such as fluid resuscitation, vasoactive drugs use, mechanical ventilation and renal replacement therapy.

Conclusions: At least, 15% of children with meningococcal disease has poor outcome, above all those under 2 years of age. Important changes in the epidemiology of meningococcal infections have been observed during the last years, especially related to vaccination. The introduction of new vaccines, like meningococcal B or other combined meningococcal vaccines (A-C-Y-W135), is desirable.

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ACUTE DIARRHEA OF VIRAL ETIOLOGY IN CHILDREN AT UNIVERSITY HOSPITAL IN PRISHTINA, REPUBLIC OF KOSOVO

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Background: Rotavirus and adenovirus are the most common cause of childhood diarrhea, worldwide. The aim of this study was to determine the prevalence of these viruses as well as to analyze clinical presentation of the disease in children with acute diarrhea hospitalized at the Department of Pediatric Gastroenterology of the University Hospital in Prishtina, Republic of Kosovo.

Material and methodology: 100 randomly selected children, aged 0 - 5 year, hospitalized due to the acute gastroenteritis, were included in the study. Demographic data and clinical presentation were subjected to analysis. The presence of the viruses in stool was tested using standard tests.

Results: Of all children involved 50% were rotavirus and 9% adenovirus positive. The dominant clinical symptoms were diarrhea (94%) and vomiting (92%). The majority of the patients in study (80%) had the moderate dehydration.

Conclusion: Rotavirus was found to be the most common cause of acute diarrhea in children aged 0-5 year. Viral antigen analysis in stool is important to prevent unnecessary administration of antibiotics.

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TOXIC SHOCK SYNDROME: APROPOS OF A CLINICAL CASE

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Introduction: Toxic shock syndrome (TTTS) is an uncommon clinical entity so it´s important your timely recognition and appropriate treatment.

Case study: Male child of 18 months brought to the emergency department denied the motion, flushing the knee, rights thigh and leg edema and fever for 5 days of evolution. Objectively had antalgic position of the right thigh and pain when mobilize the lower limbs. Impetiginada lesion on the left forearm, bullous lesion on the left thumb and nonspecific macular rash on the limbs. Analytical study: normochromic and normocytic anemia, leukocytosis with neutrophilia and elevation 5 times the value of ALT. PCR 333 mg / L. Ultrasound articular: in the right hip joint effusion with about 3 mm, observed signs of cellulite around the right lower limb. Initiated empirical antibiotic with vancomycin and clindamycin. In D6 by persistent fever and identification of Streptococcus pyogenes in blood culture, initiated penicillin G and clindamycin. Developments complicated by the appearance of septic arthritis in his left ankle which required surgical drainage, cellulitis, and osteomyelitis of the right thigh in left tibia which resolved with conservative treatment. In D22 achieved clinical stability that allowed start with oral antibiotics amoxicillin and clavulanic acid.

Comments: SST should be part of the differential diagnosis of situations that occur with fever, rash, and shock. Although rare, have been described their association multifocal osteomyelitis and also cellulite. It is essential to start early antibiotic therapy and surgical drainage is sometimes necessary, as occurred in this patient.

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SURVEILLANCE OF PERTUSSIS IN A PEDIATRIC HOSPITAL IN BANGKOK, THAILAND

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Introduction: A resurgence of pertussis has been observed in countries with acellular pertussis vaccines are routinely provided. Few data have been from countries where whole-cell vaccines are still widely used. We performed hospital-based surveillance in a children hospital in Thailand to evaluate pertussis incidence, its clinical features and burden.

Method: We conducted surveillance at Queen Sirikit National Institute of Child Health, Bangkok by enrolling children age 0 - 18 years who had cough for ≥ 7 days with at least one of the followings; paroxysm**,** inspiratory whooping**,** post-tussis vomiting. Nasopharyngeal swabs were collected and tested for pertussis using RT-PCR.

Results: Ninety-six patients were enrolled, 58 (60%) were younger than 1 year. Eighteen children (19%) had pertussis confirmed by RT-PCR, 83% of them received none to 2 doses of DTP vaccine due to younger age than recommended schedule. Post-tussis vomiting, convulsion and cyanosis were significantly higher in pertussis PCR-positive than PCR-negative patients (94 vs. 65%, $p = .014$, 17 vs. 3%, $p = .044$ and 72 vs. 8%, $p < .001$ respectively). Mean duration of cough was 40.9 (range 14 - 67) days compared to 19.6 days in pertussis PCR-negative patients ($p < .001$). Fifteen (83%) of pertussis patients were hospitalized with mean length of stay was 10.67 days; mean medical cost was 594.4 USD that was not significantly different between groups.

Conclusion: Pertussis incidence was 19% in Thai children presented with prolong cough. Children with pertussis had significant longer coughing duration, and likely to develop symptoms such as convulsion and cyanosis resulted in high percentage of hospital admission.

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URINARY TRACT INFECTION IN A PAEDIATRIC DEPARTMENT OF A TERTIARY HOSPITAL

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Background and aims: Urinary tract infection (UTI) is a common condition in children. When empirical treatment is started is important to know the local patterns of antimicrobial susceptibility of major uropathogens. Profile of sensitivity and antimicrobial resistance may change with time, so periodic institutional epidemiological studies are needed. Characterize population of children admitted with diagnosis of UTI, known etiological agents, antibiograms and progress during hospitalization.

Methods: Retrospective study conducted by consulting medical records of patients admitted to an Emergency Room of a tertiary care hospital (November 2011-December 2012), with discharge diagnosis of ITU.

Results: 60 children were hospitalized. 75% younger than one year and 38.3% until 3 months. Reasons for hospitalization were oral intolerance (21.7%), previous disease (15%), unfavourable social context (5%) and germ resistant to oral antibiotic therapy (5%). Fever (92%) was the main complaint. 57% collected two urine samples, 70% by catheterization. Main antibiotics were cefuroxime (88.3%) and association with gentamicin (48.3%). E.coli was primary agent isolated (76.7%), P.mirabilis (8.3%) and K.pneumoniae (5%) next, with sensitivity to cefuroxime of 97.8%, 100% and 66.7%, respectively.

Conclusions: UTI was a frequent diagnosis in children under 24 months. In this age group most complaints are nonspecific. Timely diagnosis involves sterile urine collection, indwelling catheters was the method most used. Cefuroxime remains highly effective in UTI by E. coli. Evolution was favourable in all patients. Knowledge of local epidemiology and susceptibility allows the institution of effective treatment with relief of symptoms, eradication of infection and reduced renal complications.

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ORF INFECTION IN A PATIENT WITH CHRONIC MUCOCUTANEOUS CANDIDIASIS

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Chronic Mucocutaneous Candidiasis (CMC) refers to a group of immunodeficiencies, characterized by persistent or recurrent infections of the skin, nails, and mucus membranes caused by candida. A wide range of immunologic abnormality has been reported in CMC.

Orf is caused by a virus called the parapox virus, which infects mainly young lambs and goats who contract the infection from one another or possibly from persistence of the virus in the pastures. Human lesions are caused by direct inoculation of infected material. A 34 year old man who has been following CMC since 2004 cut his hand with a knife during slaughter; orf subsequently developed from those wounds and covered his right hand and right upper leg. The patient has STAT1 mutation which impairs IL-17 immunity and underlies chronic mucocutaneous candidiasis. He has been treated by cidofovir successfully (once weekly for eight consecutive weeks). This is the first report in the world that describes a case who has CMC and human orf infection treated by cidofovir.

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PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN A PATIENT WITH COMMON VARIABLE IMMUNODEFICIENCY WHO HAS LOW CD4 COUNT

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Progressive multifocal leukoencephalopathy (PML) is an opportunistic viral infection of the human CNS and appears to occur almost always as a consequence of immune dysfunction. It destroys oligodendrocytes, leading to neurologic deficits associated with demyelination. A nineteen year-old girl who has been followed as common variable immunodeficiency (CVID) since 2000 admitted to our outpatient clinic with the complaint of visual deficits, cognitive impairment, and motor weakness. She had gait disturbance, dysarthria, dysphasia, epilepsy and ocular palsy. Diagnosis was based on detection of JC virus in the cerebrospinal fluid by polymerase chain reaction, the clinical presentation, and demonstration of PML brain lesions on magnetic resonance imaging. She had a documented longstanding CD4 T-cell lymphopenia (250x 106/l). MRI shows multifocal, bilateral, asymmetrical lesions involving subcortical white matter. Lesions are principally located in supratentorial regions.

Cytarabine 2 mg/kg daily for 5 days and Cidofovir 5 mg/kg at 2 weekly intervals (3 cures) and mefloquine 250 mg weekly were administered. Subsequently, interferon alfa was started 3 MIU three times a week. Although these treatment, her control MRI showed that the lesions spreaded to deep periventricular white matter and the patient showed neurological deterioration.

JC virus infection should be considered in the differential diagnosis of the patient with CVID and signs and symptoms of multifocal leukoencephalopathy.

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COMPARISON OF TWO DIAGNOSTIC TECHNIQUES IN VENTILATOR ASSOCIATED PNEUMONIA IN A PEDIATRIC INTENSIVE CARE UNIT

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Background and aims: Ventilator associated pneumonia (VAP) is the second most common nosocomial infection in pediatric ıntensive care units. Multiresistant agents are an increasing problem causing VAP in hospitals worldwide. There is no optimal diagnostic test to discover the causative agent. The aim of the study is to compare two non-bronchoscopic techniques (endotracheal aspiration/ETA and mini-bronchoalveolar lavage/mini-BAL) for the diagnosis of suspected ventilator associated pneumonia (VAP) in pediatric cases.

Methods: Children mechanically ventilated in Pediatric Intensive Care Unit at Ege University Children´s Hospital were enrolled to the study. 42 patients had suspected VAP and specimens were collected with both methods, quantitative cultures were obtained and compared for pathogens.

Results: There was no spesific pathogen grown in specimen cultures of 14 patients in both techniques. On the other hand 14 patients had positive culture results in ETA specimens but their samples were negative when the aspirates were obtained via mini-BAL. There was no positive result with mini-BAL if ETA cultures were negative. And 13 patients had the same pathogens grown in their respiratory specimen cultures even they were collected with ETA or mini-BAL.

Conclusion: In comparison with ETA technique; mini-BAL seems more sensitive to avoid overdiagnosis and overtreatment of VAP in children similar to adults. Causes and correlations are discussed in the study.

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OVERWHELMING POSTSPLENECTOMY INFECTION SYNDROME IN CHILD WITH AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME: A CASE REPORT

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Overwhelming postsplenectomy infection (OPSI) syndrome is a life-threatening condition that occurs in splenectomized patients. Asplenic patients are at increased risk of generalized infections due to disorders of opsonization and phagocytosis of encapsulated bacteria.

A six year-old girl, who had splenectomy for hypersplenism at the age of two years, was admitted to an intensive care unit with septicemia and septic shock. The patient had a history of primary immunodeficiency, autoimmune lymphoproliferative syndrome. She had been vaccinated with the polyvalent pneumococcal vaccine in two years after splenectomy.

The first symptoms of the disease were nonspecific and included febrile fever, headache and nausea. Haemorrhagic rash arose on the third day of the illness. Physical examination revealed a toxemic appearance, presenting with fever, mottled skin, acrocyanosis, slow recoloration time, tachycardia and hypotension. Meningeal irritation findings were positive. Petechiae were localized on the on the face, trunk, extremities and oral mucosa. Laboratory tests revealed trombocytopenia with disseminated intravascular coagulation. Streptococcus pneumoniae were isolated from blood and normal cerebrospinal fluid.

Treatment comprised antibiotics, intravenous fluids, steroids, heparin, immunoglobulins. The patient was discharged from hospital with recovery.

The case demonstrated the successful experience of OPSI treatment in immunocompromised asplenic patient with primary immunodeficiency. We would like to emphasize that in case of necessary splenectomy, the patient should be given pneumococcal vaccine before surgery to reduce the risk of subsequent OPSI.

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INVASIVE FUNGAL INFECTIONS IN CHILDREN WITH ACUTE LEUKEMIA

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Invasive fungal infection (IFI) is an important cause of morbidity and mortality in children with leukemia.

The medical records of the patients with acute lymphoblastic (n=112) and acute myeloblastic leukemia (n=26) who were treated at Ege University Medical School, Pediatric Hematology Department between 2005 and 2012 were retropectively reviewed to determine the rate, causative agents, and the outcome of IFI.

All patients received nystatin oral solution since the diagnosis. None of the patients were given prophylactic antifungal treatment. A total of 53 IFI episodes were recorded in 51 (Male/ Female= 25/26) patients. The rate of IFI among the patients with acute leukemia was 36.9%. The median age of the patients was 8.2 (range 1.5-16) years.

IFI was classified as proven in 17 (32%), probable in 8 (15.1%) and possible in 28 (52.8%) episodes. Ten of the episodes (18.9%) were disseminated fungal infection, 37 (69.8%) were lower respiratory tract infection and 6 (11.3%) were sinonasal infections. The causative fungus was microbiologically documented in 21 episodes (39.6%). In 9 IFI episodes (42.9%) **Candida** spp. (2 albicans, 2 parapsilosis, 2 krusei, 1 kefyr, 1 gullimanti, 1 tropicalis), in 5 IFI episodes (23.8%) **Aspergillus** spp. (3 fumigatus, 2 flavus) and in four IFI episodes (19.1%) **Geotrichum capitatum** were isolated. **Acremonium** spp., **Mucor** and **Trichosporon asahii,** each were documented in one episode.

Three month survival of these patients after the diagnosis of IFI was (84.3%). IFI was the main cause of death in 4 patients (7.8%).

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EPIDEMIOLOGY OF STREPTOCOCCUS PNEUMONIAE AMONG HEALTHY CHILDREN AGED 1 TO 24 MONTHS IN LATVIA

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Background and aim: This study aimed to define the nasopharyngeal carrier rates and serotype distribution of S.pneumoniae among healthy children in Latvia aged 1 to 24 months.

Materials and methods: The study involved healthy children in a day care centre in Riga, and in University Children's Hospital in Tornakalns, Riga. Parents or caregivers were interviewed to collect the following demographic and medical information. On each child, physical examination was performed and nasopharyngeal swab was taken. The identification of the isolates was confirmed by optochin sensibility test and in questionable cases with VITEK GN. Serotyping was performed by multiplex PCR. Susceptibility results were interpreted according to CLSI standard.

Results: The study involved 68 children with average age 11.8 months (minimum age 2 months, maximum age 23 months). 44.1% were vaccinated (had received at least one PCV dose). Vaccination was complete in 8.8% (6) of children. 14.7% of the children were found to be carriers of S.pneumoniae. Among vaccinated children, 10% (3) were carriers. 70% of the carriers were not vaccinated (had not received a single dose of PCV), and only 13% (4) had been vaccinated according to their schedules. Serogroup 6 (serotypes A, B, C) was proven to be the prevalent (100%) and the majority of carriers were girls (25%, compared to 11.6% of boys). The age of the carriers varied from 9 to 20 months.

Conclusions: 14,7% were found to be carriers of S.pneumoniae. 44,1% of them were vaccined. 100% serogroup 6 was found.

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STREPTOTEST IN CHILDREN UNDER 4 YEARS OLD: ALWAYS NEGATIVE?

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Objective: Use of streptotest as a diagnostic tool in acute bacterial faringitis is not recommended under the age of **3-5 years** due to their low prevalence of Str.Piogenes. Our objective was to study the presence of positive streptotest in patients of that age

Material and methods: We studied all patients "**under 4 years"** that underwent a streptotest in the last three years suspecting acute bacterial faringitis **(n=236)** and we analysed them following a "case-control" method. The same process was carried out within our sample for patients **"under 3 years"**. Cases were furthermore studied analysing another 2 variables: presence or absence of rhinorrea-cough symptoms and presence or absence of tonsilar exudate.

Results: We obtained **31% positive** values in patients **"under 4 years",** and **18% positive values** in patients **"under 3 years"**, without statistical difference between both groups (X2, p< 0,05). **52%** of cases had rhinorrea-cough symptoms and only **23%** presented tonsilar exudate. Statistical relation between both variables was proven, where presence of the former decreased likeliness of the latter (X2 p< 0,05). We also had **7 positive** cases in children less than 2 years old (not statistically analysed)

Conclusions: We found surpisingly high streptotest positiveness in children less than **3** and **4** years old. We also found that amongst these a high proportion presented rhinorrhea and cough symptoms. This opens discussion regarding actual recommendations for the use of streptotest in patients under **3-4 years** as well as the usual symptoms we should expect to find in acute bacterial faringitis.

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IN VIVO ENDOSCOPICIMAGING OF ANCYLOSTOMIASIS-INDUCEDGASTROINTESTINAL BLEEDING: CLINICAL AND BIOLOGICALPROFILES

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Little data are available regarding the association of ancylostomiasis with overt gastrointestinal bleeding. This 6-year retrospective study describes the clinical and biologicalprofiles of unexpectedly identified ancylostomiasis in a 4-month-old baby and four adults; they presented with melena and were referred for urgent diagnostic gastrointestinal endoscopy, which confirmed numerous small intestine injuries with surrounding blood pools caused by Ancylostoma duodenale worms. Gastric erosions were also encountered in one patient. Uniquely, worm biological activities were recorded live in vivo, including mucosal invasion through a vigorous, rapid piercing process, repeated bloodsucking habits, and gut appearance during the stages of feeding, digestion, and excretion in male and female worms. In conclusion, ancylostomiasis-induced melena may occur in all ages from infants to the elderly. Worm bloodfeeding occurs after quick mucosal piercing, with blood loss being aggravated by a repeated feeding behavior. After treatment is started, bleeding stops rapidly in response to anthelmintic therapy.

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PREOPERATIVE STAPHYLOCOCCUS AUREUS CARRIAGE AND RISK OF SURGICAL SITE INFECTION AFTER CARDIAC SURGERY IN CHILDREN: A PILOT COHORT STUDY

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Aims: The objectives of this pilot prospective monocenter cohort study were to describe Staphylococcus aureus (SA) colonization in children before cardiac surgery and to compare the incidence of surgical site infection (SSI) and other nosocomial infections between preoperative carriers and noncarriers.

Methods: During 9 months, all children < 1 year undergoing cardiac surgery had preoperative methicillin-resistant (MRSA) and methicillin-sensitive SA (MSSA) screening by real-time PCR (genXpert System, Cepheid®). The only exclusion criterion was invalide PCR. All patients were followed regarding SSI and other nosocomial infections. The primary outcome was the comparison of incidence of SSI among colonized and noncolonized patients.

Results: Among the 42 studied patients (mean age 2.7+/-3 months, mean weight 4.4+/-1.6 kg, mean CBP time 120+/- 44 min, mean hospital length of stay 19.4+/20.9 days), overall rates of carriage of SA and of SSI were respectively 24% (21% with MSSA and 2.4% with MRSA) and 34.1%. Microorganisms were identified in 36% of the 11 cases of SSI (9% of MSSA, 9% of MRSA and 18% of coagulase negative staphylococci (CNS)). Incidence of SSI was not different between carriers and noncarriers (30% vs 25% respectively, p=0.29). Only 1 CNS bacteriemia and no pneumonia were documented in the cohort.

Conclusions: This study highlights that colonization with SA is frequent in our country whereas MRSA prevalence is low. At this stage, data are insufficient to conclude regarding the relationship between SA carriage and the risk for developing SSI.

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SUBCLINICAL ENDOTHELIAL DYSFUNCTION IN CHILDREN WITH TYPRE I DISBETES MILLETUS

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Introduction: Diabetes mellitus is an established risk factor for atherosclerosis. Preclinical atherosclerosis is more common in young subjects exposed to cardiovascular risk factors. Endothelial function and carotid IMT, known to be abnormal in preclinical atherosclerosis, have not been studied concurrently in a pediatric population exposed to a risk factor for atherosclerosis. . CD146, a novel cell adhesion molecule, localized at the endothelial junction.

Purpose was to detect subclinical endothelial injury by measuring carotid intimal thickness and its relation to biochemical markers in children with diabetes.

Methods: 30 diabetic children presented to pediatric diabetic outpatients' clinic of children university hospital during the first year of diagnosis. Clinical and laboratory investigations were done including total cholesterol, LDL, HDL, triglycerides, , HbA1c, CD 146, vit D, a CRP and vitamin C. 30 healthy volunteers were taken as control.

Results: Significant difference in HbA1c, CD 146, vit D, vit C, A CRP were found between cases and control. Carotid duplex measurements showed significant difference in IVSd, LVPWP, E velocity, E/A ratio, LVFS, IVRTand Max CIMT between cases and control. Significant -ve correlation between vit C, Vit D and E/A ratio. Also +ve correlation were detected between duration of illness and LVEDD and E velocity.

Conclusion: CIMT is simple, inexpensive, and reproducible noninvasive marker of global atherosclerotic disease. Early vit. C and D supplementation may help to decrease risk for vascular injury. Measurement of IMT may be used as a marker for future risk of clinical cardiovascular and cerebrovascular outcomes.

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OUTCOME OF CARDIAC ARREST IN PEDIATRIC INTENSIVE CARE UNIT IN ASSIUT CHILDREN UNIVERSITY HOSPITAL

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Introduction: Cardiac arrest is a clinical event that can occur suddenly, often without premonitory signs. Outcome of CPR is dependent on many factors, the site of event, quality of CPR, whether the event was witnessed, time to basic life support, time to advanced life support and initial rhythm.

Purpose: To determine the outcome of cardiopulmonary resuscitation in PICU and factors associated with unfavorable outcome.

Methods: Retrospective study of children with cardiac arrest and required CPR in PICU over a period from January to December 2010. Two outcome variables were measured (ROSC)) and survival to discharge from PICU.

Results: 700 PICU admission, a total of 172 (24.6%) patients developed cardiac arrest that required CPR. ROSC was achieved in 78 cases (45.3%), 25 patients (14.5%) survived to discharge and 94 patients (54.7%) did not respond to resuscitations. Success and survival were significantly higher in cases resuscitated for ≤20 mins than >20 mins (100% and 33.3% vs. 32.4% and 10.1% respectively). Success and survival were better for mechanical ventilation than those were not (48.1% and 17.8% vs. 37.2% and 4.7% respectively). Defibrillation was successful in 10 cases (25%) and survival was in 1 case (0.5%) and out of survivors 80% had good neurological outcome.

Conclusion: The frequency of cardiac arrest needed CPR was recorded in 24.6%. Improving the quality of CPR is an important factor to improve the outcome by implementing training programs. Studies using neurophysiolological methods to predict the neurological outcome are needed.

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ANTIMICROBIAL RESISTANCE IN INVASIVE GRAM-NEGATIVE BACTERIA IN CHILDREN IN EUROPE

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Background/aims: We aimed to compare AMR percentages in paediatric invasive isolates of Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa reported to the Antibiotic Resistance and Prescribing in European Children (ARPEC) project and the European Antimicrobial Resistance Surveillance Network (EARS-Net).

Methods: For each database, percentages of AMR in 2011 and 95% confidence intervals were calculated for isolates from patients aged < 18 years. Only data for the 11 countries reporting to both databases (Estonia, France, Germany, Greece, Italy, Lithuania, Netherlands, Portugal, Slovenia, Spain, and UK) were included.

Results: AMR percentages are presented in the table below. Approximately 1/4 E. coli, 1/3 K. pneumoniae and 2/5 P. aeruginosa isolates were resistant to one or more of the antibiotic groups under surveillance.

	AMR percentage [95% confidence interval] Microorganism (Antibiotic groups under surveillance)					
	E. coli - (Aminopenicillins, third-generation cephalosporins, aminoglycosides, fluoroquinolones, carbapenems)		**K. pneumoniae - (Third-generation cephalosporins, aminoglycosides, fluoroquinolones, carbapenems)**		**P. aeruginosa - (Piperacillin-tazobactam, ceftazidime, aminoglycosides, fluoroquinolones, carbapenems)**	
	ARPEC (n=164)	EARS-Net (n=1137)	ARPEC (n=88)	EARS-Net (n=446)	ARPEC (n=57)	EARS-Net (n=260)
No resistance	76.4 [69.5-82.4]	81.5 [79.2-83.7]	64.1 [53.5-73.9]	59.4 [54.7-64.0]	60.0 [46.5-72.4]	62.3 [56.1-68.2]
Resistance to 1-2 antibiotic groups	20.7 [15.1-27.5]	16.1 [14.0-18.4]	27.2 [18.4-37.4]	17.5 [14.1-21.3]	26.7 [16.1-39.7]	23.1 [18.1-28.7]
Resistance to ≥3 antibiotic groups	2.8 [0.9-6.4]	2.4 [1.6-3.4]	8.7 [3.8-16.4]	23.1 [19.3-27.3]	13.3 [5.9-24.6]	15.0 [10.9-19.9]

[Resistance patterns in Gram negative isolates]

Conclusion: Gram-negative isolates from European children are now frequently resistant to several antibiotics. With the exception of K. pneumoniae, resistance percentages were roughly concordant between ARPEC and EARS-Net. A potential explanation could be different types of hospitals surveyed by EARS-Net and ARPEC (integrated versus standalone paediatric) with consequent variation in clonal spread.

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ANTIMICROBIAL RESISTANCE IN INVASIVE KLEBSIELLA PNEUMONIAE ISOLATES: TOTAL POPULATION-LEVEL RESISTANCE PERCENTAGES DO NOT REFLECT RESISTANCE PERCENTAGES IN CHILDHOOD ISOLATES

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Background/aims: The European Antimicrobial Resistance Surveillance Network (EARS-Net, formerly EARSS) collects routine microbiological data on antimicrobial resistance in invasive isolates of selected pathogens. We compared resistance percentages in invasive Klebsiella pneumoniae isolates from different age groups to study potential age-related differences.

Method: Data for invasive K. pneumoniae isolates as reported to EARSS/EARS-Net in 2005-2011 were analysed. Resistance percentages by age class and 95% confidence intervals were calculated.

Results: Among 64 005 invasive isolates, the majority (97%) were from adults. Among the paediatric isolates, patients aged < 2 years predominated (73%). Resistance percentages in isolates from children differed considerably from those in isolates from adults, except for fluoroquinolones. In addition, isolates from children < 2 years showed significantly higher resistance for aminoglycosides and third-generation cephalosporins percentages than isolates from older children (Table).

	Resistance percentage [95% confidence interval]		
Age class	**Aminoglycosides**	**Third-generation cephalosporins**	**Fluoroquinolones**
Children (<18years)	29.3[27.8-30.9]	33.0[31.4-34.6]	21.0[19.6-22.4]
<2years	32.5[30.7-34.4]	36.6[34.7-38.6]	22.2[20.6-24.0]
2-4years	18.5[13.9-23.9]	22.1[17.0-27.9]	14.8[10.5-19.9]
5-18years	21.7[18.6-25.0]	23.6[20.4-27.0]	18.7[15.8-22.0]
Adults (> 18years)	16.7[16.4-17.0]	20.9[20.6-21.3]	21.6[21.3-21.9]
All ages	17.3[17.0-17.6]	20.1[19.8-20.4]	21.6[21.2-21.9]

[Resistance percentages in K.pneumoniae]

Conclusion: EARS-Net data mainly reflect the resistance situation in adults. The optimal method to report resistance percentages by age groups still needs to be determined.

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LOW LEVELS OF BORDETELLA PERTUSSIS AND BORDETELLA PARAPERTUSSIS CARRIAGE IN ASYMPTOMATIC ADOLESCENTS AND YOUNG ADULTS IN PORTUGAL

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Background: Like several other European countries with high uptake childhood immunisation programmes, Portugal has seen a recent upsurge in pertussis particularly in adolescents and young adults. The dynamics of pertussis transmission in this age group is poorly understood. In particular, whether an asymptomatic carriage state exists and plays a role in spread is unknown. We therefore undertook the first study to test this hypothesis and establish the rates of carriage of B.pertussis and B.parapertussis in asymptomatic adolescents and young adults.

Methods: We analysed oropharyngeal and nasopharyngeal swabs from 601 unselected young adults taken in May 2012 in Coimbra, Portugal. We performed monoplex and multiplex real time PCR (RT-PCR) assays using primers and probes to detect B.pertussis (IS481 and IS1002) and B.parapertussis (IS1001 and IS1002). Data were collected on the presence of cough in study participants. Ethical approval and consent were obtained.

Results: All 601 study participants had an oropharyngeal swab, 293 also had nasopharyngeal swabs taken. 168 (28%) participants were male, mean participant age was 21 years. 77% did not have cough when the swabs were taken. 1 participant was positive for B.pertussis. 3 participants were positive for B.parapertussis. Of the 4 individuals' positive for Bordetella.spp, 3 did not have a cough.

Conclusions: Low levels of B.pertussis and B.parapertussis carriage are detected by RT-PCR in the nasopharynx or oropharynx of asymptomatic adolescents and young adults. The findings of this study provide strong evidence that asymptomatic infection is not playing an important part in current pertussis dissemination among previously immunised teenagers.

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ANTIBODY RESPONSE TO STREPTOCOCCUS PNEUMONIAE, HAEMOPHILUS INFLUENZAE AND MORAXELLA CATARRHALIS PROTEINS AMONG CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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Background and aims: We aimed to investigate antibody responses to bacterial antigens in children with non-severe CAP and explore their use for etiologic diagnosis.

Methods: Acute and convalescent serum samples were collected from 733 children aged 2-59months with non-severe CAP. A fluorescent multiplexed microsphere immunoassay(FMIA) quantified IgG antibodies against 8 Streptococcus pneumoniae proteins: PcpA and PhtD(supplied by Sanofi-Pasteur), Ply, CbpA, PspA1,and PspA2(supplied by St.Judes Children's Research Hospital, Memphis,TN and University of Alabama, Birmingham,AL), SP1732-3,and SP2216-1; 3 Haemophilus influenzae proteins(NTHi-Protein-D, NTHi-0371-1,and NTHi-0830); and 5 Moraxella catarrhalis proteins(MC-Omp-CD, MC-RH4-2506, MC-RH4-1701, MC-RH4-3729-1,and MC-RH4-4730). Increase in antibody level was used for etiologic diagnosis. Continuous variables were analyzed using Mann Whitney test and categorical using Chi-square test.

Results: The rates of immune responses are depicted in table1. H. influenzae infection was more often among patients with paired samples collected 21-28 days apart(14.8%[n=31]vs.8%[n=42],p=0.005; and 10%[n=21]vs.4.4%[n=23],p=0.004) compared to patients with different time intervals by using≥1.5-fold and≥2-fold increase, respectively. By considering≥2-fold increase, children with infection by each bacterium were younger(median[25th-75thpercentile] months) than those without the infection by: S. pneumoniae:23.8[13.5-33.9]vs.26.1[14.1-41.6],p=0.02; H. influenzae:15[10-33.9]vs.26.2[14.3-40.4],p=0.003; M. catarrhalis 16.2[10.9-30.4]vs.25.8[14.1-40.2],p=0.04).

Conclusions: The frequency of immune responses varied widely by using different cut-offs of antibody level increases. Interval between paired serum samples and age also influenced the diagnosis of these bacterial infections.

Acknowledgements: We thank Intercell for supplying:SP1732-3,SP2216-1,NTHi-Protein-D,NTHi-0371-1,NTHi-0830,MC-Omp-CD,MC-RH4-2506,MC-RH4-1701,MC-RH4-3729-1,and MC-RH4-4730.

IgG increase	S. pneumoniae	H. influenzae	M. catarrhalis	Total recovery rate
≥1.5-fold	203 (27.7%)	73 (10%)	33 (4.5%)	256 (34.9%)
≥2-fold	111 (15.1%)	44 (6%)	20 (2.7%)	153 (20.9%)
≥4-fold	33 (4.5%)	10 (1.4%)	2 (0.3%)	42 (5.7%)

[Table1. Antibody responses using distinct cut-offs]

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CLINICAL PROFILE OF CARBAPENEM RESISTANT BACTERAEMIA AMONG PAEDIATRIC POPULATION-FIRST CLINICAL STUDY FROM INDIA

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Background: Carbapenem resistance is a growing burden especially in developing countries and is also associated with higher mortality. There is limited data available from these countries especially among the paediatric population.

Materials and methods: A retrospective observational study of carbapenem resistant bacteremic cases was done by medical record review among the paediatric population in tertiary care hematology, Oncology and Neurosciences center in South India during the period of January 2012 -13.

Results: Nine patients had carbapenem resistant bacteraemia and were included in our study. Six had leukemia, one myelodysplastic syndrome; one had thalassemia and one brain astrocytoma. Two among them had stem cell transplantation. Seven had central lines and two had PICC line. Five had recent hospitalisation history, and four received carbapenem in the previous admission. One had an invasive surgery 48hrs before bacteraemia. Among the isolates four were Pseudomonas aeruginosa, four Klebsiella pneumonia and one Acinetobacter baumannii. All isolates were carbapenem resistant, eight were sensitive to colistin, 5 sensitive to tigecycline, 4 were BL-BLI sensitive and one was aztreonam sensitive. One K.pneumoniae isolate was colistin resistant. Three among the nine patients recovered and were discharged. Four children expired and two couldn't be followed up.

Conclusion: Carbapenem resistant bacteraemia is a serious threat especially in paediatric oncology patients resulting in high mortality. Coordinated global efforts are needed to control the menace of antibiotic resistance.

PARAMETERS	AVERAGE
AVG. AGE	11 YEARS
AVG. CCU days	11.6 DAYS
AVG. APACHE	11.55
AVG. PITT'S SCORE	2.87
AVG. LENGTH OF STAY PRIOR TO ACQUIRING CARBAPENEM RESISTANT ORGANISM	58.3 DAYS
AVG. TOTAL COUNT	2100
AVG. TOTAL COUNTS AMONG NEUTROPENICS	340

[PARAMETERS]

TREATMENT GIVEN	NO. OF PATIENTS RECEIVED	OUTCOME
Colistin + Tigecycline	2	One recovered , One expired
Colistin + Aztreonem	1	Recovered
Colistin + Cefaperazone/Sulbactam	1	Recovered
Colistin	1	Expired within 24hours of starting colistin
Colistin + Meropenem	1	Expired before culture grew the organism
Colistin + Meropenem + Tigecycline	1	Colistin resistant bacteraemia was cleared with the combination therapy but subsequently patient developed another episode of carbapenem resistant bacteraemia and expired.
Not followed	2	

[TREATMENT]

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ANTIBIOTIC SUSCEPTIBILITY PATTERN OF BACTERIA ISOLATED FROM PEDIATRIC UNIT OF A HOSPITAL IN IRAN DURING 2011-2012

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A retrospective analysis of bacteria isolated from children hospitalized with urinary tract infection (UTI) was performed at the pediatric unit university hospital of Afzalipoor in Kerman, Iran from April 2011 to November 2012. Of 55 positive samples were examined, Escherichia coli (69%) was the leading uropathogen followed by Klebsiella spp. (18.8%), Proteus mirabilis (7.27%), Staphylococcus aureus (3.63%), Citrobacter frundii (1.81%), Enterobacter spp. (1.81%) and Enterococcus facium (1.81%) [P≤0.5]. Antibiotic sensitivity tests revealed that almost all uropathogenic E.coli were sensitive to carbapenems and amikacin (97.22% ±0.76), while majority were resistant to amoxicillin/clavulanic acid (63.88% ±0.34) as well as third generation of cephalosporins (38.88% ± 0.41). 44.4% ±0.74 were resistant to cefepime. Similarly, all Klebsiella spp. and P.mirabilis were sensitive to amikacin and carbapenems (100%±0.0) [P≤0.5]. C.frundii and Enterobacter spp. were sensitive to amikacin and carbapenems and third generation of cephalosporins (100%). In case of S.aureus and E.facium both were susceptible to methicillin and amoxicillin/clavulanic acid but they were resistant to gentamicin and cefepime. The ESBL confirmatory test for resistant isolates revealed that only E.coli isolates number 5, 6 and 20 were able to produce a detectable ESBL enzyme, while for the other resistant E.coli the ESBL test was negative.

From above results it can be concluded that E.coli was leading pathogen associated with UTI among hospitalized children in our hospital and amikacin, carbapenems were very effective drug for treatment of UTI in, while, care should be taken when third generation of cephalosporins, nalidixic acid and therimthoprime + sulfametoxazole are administered.

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SYSTEMIC INFECTIONS IN CHILDREN

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Objective: To track antibiotic susceptibility of Staphylococcus aureus isolates obtained from children with systemic infections and determine outcome of treatment.

Method: A 3-year prospective surveillance study of all invasive pneumococcal infections in children. Infants and children cared for at children´s hospitals in the with culture-proven systemic pneumococcal infection.

Results: One thousand one hundred eighty-five episodes of systemic pneumococcal infection were identified in 1050 children. An underlying illness was present in the children for 26% of the episodes. The proportion of isolates that were nonsusceptible to methicillin or ceftriaxone increased annually and nearly doubled throughout the 3-year period; for the last year the percentages of isolates nonsusceptible to methicillin and ceftriaxone were 18% and 7.3%, respectively. There was no difference in mortality between patients with methicillin-susceptible or nonsusceptible isolates. Only 1 of 672 patients with bacteremia had a repeat blood culture that was positive >1 day after therapy was started. All 24 normal children with bacteremia attributable to isolates resistant to methicillin had resolution of their infection; the most common treatment regimen was a single dose of ceftriaxone followed by an oral antibiotic.

Conclusions: The percentage of pneumococcal isolates nonsusceptible to methicillin and ceftriaxone increased yearly among strains recovered from children with systemic infection. Because empirical antibiotic therapy already has changed for suspected pneumococcal infections, antibiotic resistance has not been associated with increased mortality. Careful monitoring of antibiotic susceptibility and outcome of therapy is necessary to continually reassess current recommendations for treatment.

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EFFICACY OF LOCAL INTERFERON TREATMENT IN ACUTE RESPIRATORY INFECTIONS IN CHILDREN

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Objective: We aimed to study clinical and immunological effects of human recombinant α-2b interferon in the form of liniment for intranasal use (VIFERON®) in children with ARI.

Materials and methods: In double-blind, placebo-controlled RCT we evaluated clinical symptoms and markers of local immunity in 100 children with ARI. 60 patients were included into study group (SG), who recieved intranasal interferon in addition to basic therapy, 40 children from control group (CG) recieved placebo. Evaluation of local immunity markers in nasal wash-outs was performed before and after 6-7 days of treatment.

Results: Positive influence of VIFERON® on respiratory symptoms was confirmed by significant reduction of mean duration of dry cough and it's transformation into productive cough. The levels of α- and g-IFN increased 2,5 times while treatment with VIFERON®: from 4,31±0,47 pg/ml to 10,75±2,34 pg/ml and from 4,26±1,16 pg/ml to 9,75± 3,78 pg/ml ($p< 0,05$) and were significantly higher at recovery in SG when compare with controls. There were no significant changes in IL-8 concentration in SG during 6-7 days, while in CG the concentration of cytokine increased significantly: from 549,9±150,3 pg/ml to 651,48±170,3 pg/ml ($p< 0,05$). In SG we found increase of sIgA level while treatment (from 8,04±2,8 pg/ml to 13,2±4,17 pg/ml, $p< 0,05$), that appeared to be significantly higher at recovery when compare with controls. TNF-a level significantly decreased just in SG.

Conclusions: We confirmed that local therapy with intranasal interferon had positive influence on either clinical symptoms or immunological markers in children with ARI.

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ETIOLOGICAL STRUCTURE OF ACUTE RESPIRATORY INFECTIONS IN CHILDREN AND ITS CONNECTION WITH EFFECTS OF LOCAL INTRANASAL INTERFERON THERAPY

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Objective: We aimed to study efficacy of human recombinant α-2b interferon in the form of liniment for intranasal use (VIFERON®) in children with ARI depending on the etiology of the disease.

Materials and methods: In double-blind, placebo-controlled RCT we included 100 children aged 1-6 years with ARI. 60 patients from study group (SG) recieved VIFERON® in addition to basic therapy, 40 children recieved placebo (CG). Etiological verification of ARI in nasal wash-outs together with evaluation of local immunity markers was performed before and after 6-7 days of treatment.

Results: We identified viral agents in 89% cases: 12,4% patients presented with adenoviral infection, 6,7% - with parainfluenza virus, 12,4% - with RS, 18% - with rhinoviral infection, 50,6% - with mix-viral infection. In mix-infection IFN-a production was significantly lower (4,15±3,1 pg/ml) than in mono-infection cases (5,51±4,1 pg/ml), $p< 0,05$. Significant lack of IFN production we found in adenoviral and rhinoviral cases. At 6-7 day of treatment we confirmed viral elimination in 85,2% patients of SG and in 37,1% children from CG ($p< 0,05$) with significant difference in elimination rate either in mono-viral (90,1% vs. 18,2%) or in mix-viral infection (76,2% vs. 45,8%). In 36 children we detected re-infection while treatment but in SG it´s rate was significantly lower than in controls: 21,7% vs.57,5%, respectively ($p< 0,05$). The best protective effect of VIFERON® was found against adenovirus.

Conclusion: Local therapy with α-2b interferon has treatment and preventive effects on recurring viral contamination in children with ARI.

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CLINICAL AND LABORATORY RISK FACTORS OF ACUTE RENAL INVOLVEMENT IN CHILDREN WITH FEBRILE URINARY TRACT INFECTION

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Introduction: Urinary tract infection (UTI) is a common cause of fever without a source in childhood. Kidney involvement in these patients remains a major concern. However, little is known on the importance of clinical and laboratory findings for the prediction of renal lesions.

Purpose: To evaluate the predictive value of various clinical and laboratory parameters on the identification of acute renal involvement in children with febrile UTI.

Patients and methods: The medical records of 148 children aged (mean±SD)12±8 months (range:11 days-24 months) with a first episode of febrile UTI were analyzed. All patients were admitted to a Children's Hospital during a three year-period. Acute DMSA was used as primary outcome and clinical and laboratory parameters were evaluated.

Results: The mean±SD duration of fever before admission was 2.87±0.86 days (range:1- 168 hours). Seventy six children(51%) had abnormal findings on the acute DMSA. Among them 56 patients had moderate or severe findings (DMSA grade>/3), whereas 20 had minor findings (DMSA grade< 3). Patients with a DMSA grade>/3 were more likely to have shivering (OR 3.4), WBC>18,000/μL (OR 2.4), absolute neutrophil count (ANC)>9,300/μL (OR 4.4), CRP>50mg/L (OR 2.7) and PCT(procalcitonin)≥1.64 μg/L (OR diagnostic)**.** Among several risk factors associated with DMSA≥3 findings, PCT had the highest sensitivity and specificity (100%) at the cut-off level of 1.64 μgr/dl, while CRP (cut-off level:50 mg/dl) had lower sensitivity (49.3%) and specificity (73.3%) than PCT.

Conclusions: Shivering and elevated inflammatory markers increase the risk of acute kidney involvement in children with febrile UTI. PCT levels>/1.64μgr/dl are highly predictive of severe renal lesions.

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STUDY ON THE LEADING FACTORS AND DETERMINANTS OF THE URINARY TRACT INFECTIONS IN CHILDREN

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Introduction: Urinary tract infections (UTI) occupy third place in our entire pediatric infections pathology.

Objective: The study of the UTI leading factors and determinants among 0-16 year-old children hospitalized at the Pediatric Clinic no.2/Craiova Emergency Hospital, January 1st, 2011-December 31st, 2012.

Material and method: 139 children: 21 (15.1%) infants, 18 (12.9%) 1-3 year-old babies, 25 (18%) 3-6 year-old children, 75 (51%) > 6 year-old children.

Results: UTI represented 3% of the overall hospitalizations. The distribution according to gender (M/F): 17/4 in infants, 13/5 in 1-3 year-old babies, 10/15 in 3-6 year-old children, 21/54 in >6 year-old children. Urban/rural provenience: 11/10 infants, 8/10 in 1-3 year-old babies, 12/13 in 3-6 year-old children, 20/55 in >6 year-old children. The leading factors were most commonly represented by renal and urinary tract anomalies: 9 phimosis, 8 cases each of renal lithiasis and hydronephrosis, 3 cases each of pyelo-ureteral duplication and vesicoureteral reflux, 2 cases each of sole congenital kidney and hypospadias; 5 vulvovaginitis; 6 oxyuriasis; 4 constipation; 8 poor hygiene.

Bacterial leading factors: E. coli 81, Proteus 13, Klebsiella 9, Enterobacter 10, Pseudomonas aeruginosa 4; viral leading factors: 12 (acute viral hemorrhagic cystitis).

Conclusions: UTI were more frequent in the infants and 1-3 year-old babies of M gender and in the 3-6 year-old small children and >6 year-old children of F gender. E. coli was the leading factor in over 50% of the cases.

Renal and urinary tract anomalies favored the occurrence of UTI in approximately 1/3 of the cases.

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CORRELATION OF IL-6, C-REACTIVE PROTEIN, PROCALCITONIN AND NOVEL INFLAMMATORY CYTOKNES IN CHILDREN WITH SEPSIS

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Background and aims: Sepsis is one of the leading causes of death in children; being 7,8% among hospitalized healthy children. The most important factor of improving survival is early diagnostics. The aim was to reveal correlation of IL-6, C-reactive protein, procalcitonin and inflammatory cytokines to confirm their diagnostic value.

Materials and methods: In this prospective study (1.10.2010 - 1.10.2011) we included patients with SIRS and sepsis, based on the International Consensus Conference (2002) criteria. Levels of IL-6, CRP, procalcitonin, and experimental inflammatory cytokine panels were measured (Luminex-200, Millipore) at inclusion, after 24 hours, and on the day of discharge.

Results: In total, 24 patients were included. At the admission strong correlation was seen between IL-6 and IL-1β (r=0,67, p=0,016), IL-1ra (r=0,87; p< 0,001). After 24 hours positive moderate correlation was seen IL-6 and IL-10 (r=0,59; p=0,04); IL-6 (r=0,68; p=0,014); IL-6 (r=0,73; p=0,007); IL-6 (r=0,70; p=0,012), IL-6 (r=0,69; p=0,014), moderate negative correlation was seen between procalcitonin and IP-10 (r=-0,59; p=0,045). On the day of discharge found positive moderate correlations between CRP and GM-CSF (r=0,59; p=0,042); IL-1β (r=0,75; p=0,005), IL-1ra (r=0,82; p=0,001); procalcitonin and IL-1ra (r=0,67; p=0,018); sICAM-1 (r=0,76; p=0,004); negative moderate correlation was found between IL-6 and Eotaxin (r= -0,65; p=0,022).

Conclusions: IL-6 shown the best positive correlation rates with novel diagnostic inflammatory cytokines at the time of admission, whereas CRP and procalcitonin showed moderate correlations later, thus inflammatory cytokines can be used for early diagnostics.

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SERUM ZINC LEVEL IN HOSPITALIZED CHILDREN WITH RESPIRATORY OR GASTROINTESTINAL INFECTION

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Introduction: Zinc is one of the key element in all cells of the human body . Dietary zinc deficiency is a worldwide problem, and unfortunately, breast feeding and supplementary foods used in developing countries should not provide sufficient amounts.

Methods: This was a prospective study of 200 individuals with respiratory and gastrointestinal infections in patients admitted to children hospital of Bandar Abbass. Data Encoded and entered into the statistical software SPSS for windows 19 . For data analysis, descriptive statistics and Chi-square test and t-test were used. The significance level was set at less than 5 percent.

Result: Of 200 patients studied, 100 patients in the respiratory and 100 patients in gastrointestinal diseases were studied. Average age was 3/53 ± 2/04 years that in patients whose respiratory and diarreal diseases were 3/49 ± 2/26 and 3/58 ± 1/8, respectively. The study found that in older patients, serum zinc level was significantly decreased.

111 cases (55/5%) of patients were male and 89 (44/5%) were female. Mean serum zinc level in respiratory and gastrointestinal patients were 74/65 ± 27/7 and 54/1 ± 17/8, respectively. The study found that the level of zinc in patients with respiratory tract was significantly lower. Analysis of the data showed that patients with the lower Zinc levels, were more frequently infected patients.

Discussion: Zinc deficiency in developing countries is high due to lack of good diet. The daily use supplmentry Zinc led to further decreasing of the incidence of Gastrointestinal and respiratory infections.

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PAEDIATRIC EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) FOR CULTURE POSITIVE SEPSIS, INCIDENCE AND OUTCOMES : 20 YEAR REVIEW

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Background and aims: Paediatric UK ECMO began in the late 1980s. There are 4 UK centres. Sepsis data is limited for paediatric ECMO, figures suggest 37-55% survival.

This single centre retrospective review of referrals over 20 years aims to establish frequency, survival and organism significance on outcomes.

Method: Search included ECMO database, clinical notes, ECMO documentation and microbiological records.

Inclusion criteria: paediatric referral with infection, ECMO support initiated and confirmed microbiological diagnosis.

Results: 63 viral infection (60% survival), 69 bacterial infection (57% survival) and 15 had admission co-infection (73% survival). No survival difference over time.

Viruses: RSV was the commonest virus isolated (n=43) with best survival (70%). Other viruses were low frequency.

Bacteria: Commonest were Staphylococcus Aureus (n=16, survival 37.5%), Group B Streptococcus (n=12, survival 75%), Pertussis (n=12, survival 33.3%), Streptococcus Pneumoniae (n=8, survival 100%) and Meningococcus (n=8, survival 50%). Other bacteria were low frequency.

Co-infection: Small numbers. Viral+Bacterial infection at presentation survival 71% (n=14), other combinations were low frequency.

Conclusions: Overall series survival is higher than previously reported.

Neonatal pertussis is controversial and has poor survival figures. Staphylococcus Aureus has similarly poor survival rates.

Streptococcus pneumoniae has high survival and should be considered for ECMO. Group B Streptococcus has high survival, possibly due to age group, ELSO data suggests high neonatal survival rate.

Viral sepsis has high survival, particularly RSV+ children.

Paediatric ECMO should be considered for sepsis. Organism may indicate likely survival if known at referral and should influence discussions about suitability for extracorporeal support.

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CLINICAL COURSE OF MENINGOCOCCAL SEROGROUP B INFECTIONS IN THE NETHERLANDS BETWEEN JUNE 1999- JUNE 2011; A NATIONAL REPRESENTATIVE SURVEILLANCE STUDY

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Background: Invasive meningococcal disease in Europe is mostly caused by serogroup B (MenB), although its incidence has decreased considerably the last years. Recently, a four-component MenB vaccine received a positive opinion of the European Medicines Agency. Information on clinical course and mortality of MenB infections is useful to evaluate the cost-effectiveness of implementing a MenB vaccination.

Aim: To provide national representative information on clinical course and mortality of MenB infections in the Netherlands

Methods: A retrospective study using surveillance data on MenB infections in the Netherlands between June 1999 and June 2011. The surveillance data covered approximately 25% of the Dutch population and were representative for the total Dutch population. Clinical information on comorbidity, clinical manifestation, disease course, treatment, sequelae and fatality was retrieved from hospital records.

Results: A total of 711 cases of MenB infection were included in this study. 50.1% of the patients presented with meningitis, 16.0% with septic shock and 22.5% with both septic shock and meningitis. The median (IQR) number of days in the hospital was 9 (8-12). 232 (35.4%) patients required admittance to the ICU with a median (IQR) ICU stay of 3 (2-5) days. Overall mortality was 7.7% with the highest CFR among patients with septic shock (17.3%) and the lowest among patients with meningitis (1.9%). Among surviving patients 27.3% had either mild or severe sequelae at discharge.

Conclusion: MenB infections coincide with a considerable disease burden and mortality. The outcome of this study can be used for cost-effectiveness analyses on MenB vaccine implementation.

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VENTILATOR ASSOCIATED PNEUMONIA IN NEONATES GUEORGUIEVA R, NICU, UNIVERSITY PEDIATRIC HOSPITAL, SOFIA

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Aim of the study: To determine the incidence and etiology of ventilator associated pneumonia in neonates, treated in NICU, University Pediatric Hospital, Sofia for a period of three years (2010-2012).

Patients and methods: 889 high risk neonates were ventilated for three years. The diagnosis of ventilator associated pneumonia was made in accordance with clinical criteria and evidence of significant bacterial growth in samples of tracheal lavage fluid.

Results: Tke incidence of ventilator associated pneumonia was 14,6/1000 ventilation days in 2010, 6,2/1000 ventilation days in 2011 and 12/1000 ventilation days in 2012.The most common bacterial isolates were ESBL Klebsiella pneumoniae strains, sensitive in vitro to meropenem, imipenem, ciprofloxacin and rarely to some cephalosporins (cefoxitin and ceftazidime). All patients were successfully treated, according to these data.

Conclusion: Klebsiella pneumoniae is the leading cause of nosocomial ventilator associated pneumonia in neonates. The epidemiological and microbiological survey of neonatal ventilator associated pneumonia might have a positive impact on prevention strategy and the choice of empirical antibiotic therapy of severe nososcomial infections.

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BABY OR REPTILE? IT'S YOUR CHOICE. TWO CASES OF SALMONELLA MENINGITIS

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Background and aims: Salmonella infections in humans most frequently cause gastroenteritis but can result in invasive illness, especially in infants and the immunocompromised. Reptiles are a recognised source for salmonellosis. Salmonella infections have been identified in up to 0.9% of cases of neonatal bacterial meningitis. We describe two cases of reptile associated Salmonella meningitis in neonates.

Methods: Case review of two infants diagnosed with Salmonella meningitis.

Results:

Case 1: A 2 week old girl was admitted with 1 day history of high grade fever, lethargy and poor feeding. On examination, she was irritable with a bulging anterior fontanelle. Cerebrospinal fluid (CSF) examination showed WCC $555*10^9$/l (80% neutrophils), protein 2.43g/l and glucose < 0.5mmol/l. CSF and blood culture grew Salmonella monschau. She was treated with Amoxicillin, Gentamicin and Cefotaxime. The family had a bearded dragon lizard at home.

Case 2: A 3 week old girl was admitted with a 6 hour history of high grade temperature and poor feeding. She was irritable and febrile. CSF analysis showed WCC $900*10^9$/l (90% neutrophils), protein 13.2g/l and glucose 0.1mmol/l. Blood culture has grown Salmonella sp. (species awaited). She was treated with Amoxicillin, Gentamicin and Cefotaxime. Paternal grandmother had a tortoise at home and the baby's older sibling was in contact with it. He was unwell with diarrhoea.

Conclusions: Salmonella meningitis is very rare. When it does occur, there is a strong association with reptile contact. Always ask about pets when taking a history.

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URINARY TRACT INFECTION DIAGNOSED IN THE EMERGENCY DEPARTMENT AND REQUIRING HOSPITALIZATION - MICROORGANISMS AND ANTIBIOTIC SUSCEPTIBILITY

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Background: Urinary tract infections (UTI) in children, especially in the first year of life can lead to irreversible renal parenchymal lesions. Escherichia coli is the most frequently isolated, Proteus mirabilis, Enterococcus faecalis, Klebsiella pneumoniae and Pseudomonas aeruginosa more rarely. Once diagnosis of UTI empirical antibiotic therapy should be initiated, therefore it is fundamental to understand the epidemiology of population.

Objectives: Description of microorganisms and their antibiotic susceptibility, responsible for UTI diagnosed in the emergency department of a tertiary hospital requiring hospitalization, during the period 1 November 2011 - 31 December 2012.

Results: 60 children were hospitalized, 37 of which have two crops, which corresponds to 97 samples. 75% were younger than 1 year old. Urine collection was performed in 66.7% by catheterization, 20% midstream, 10% collection bag and 3.3% collection bag and catheterization. Germs most frequently isolated were: E. coli (71.1%), Proteus (5.1%), Klebsiella (5.1%) and Enterobacter (4.1%). Antibiotic treatment used was: association cefuroxime-gentamicin (48.3%), cefuroxime (40%), and amoxicillin/clavulanic acid (AM/AC) (3.3%). The sensitivities for E. coli, Proteus and Klebsiella have been 77.3%, 5.2%, 3.1% for cefuroxime; 73.2%, 4.1%, 3.1% for gentamicin; and 75.2%, 5.2%, 2.1% for AM/AC, respectively.

Conclusion: E. coli was the most frequently isolated bacteria, followed by Proteus and Klebsiella. The high use of cefuroxime-gentamicin association may be explained by the age of our sample, with high sensivity levels for E. coli. At this point, the antibiotic used empirically seems to be effective for the epidemiological characteristics of the study population.

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PLEOCYTOSIS IN CSF DURING TB MENINGITIS IN CHILDREN

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TB meningitis remains one of the rarely etiology proven CSF infection in developing countries. The aim of the study was to evaluate the duration of pleocytosis in CSF in children with TB meningitis.

Methods: This observational and prospective study included 202 children treated for TB meningitis over an eight-year period. Lumbar punctures (LPs) examined, were performed on days 1, 7 and 14, and 3 months after chemotherapy initiation. In 126 children were performed LPs each month until 12 months of treatment.

Results: Of the 202 children, the primary TB focus was found in 186 children (92%) while cultures of CSF were positive only in 10%. At initial LP, the mean value of pleocytosis in CSF was 332.4 ± 97.1 cells/mm^3 [224-506], in the second 391 [314-491], in the third 293 [156-593] and in the fourth 46 cells/mm^3 [27-68]. Lymphocytes were the dominant cell population isolated in all LPs. Proteins in CSF were elevated at all LP while glucose level at the fourth LP achieved normal values. The average duration of pleocytosis in CSF over the eight year study period was 70 days [56-92 days]. Elevated pleocytosis for one month had 36 cases (28.6%), two months 32 cases (25.4%), three months 28 cases (22.2%), four months 15 patients (11.9%) and five months 11 patients (8.7%). From 6 until 10 months, elevated pleocytosis had only 4 patients (3.2%).

Conclusions: Duration of pleocytosis in CSF in children with TB meningitis after five months of treatment was recorded in nonsignificant number of patients.

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RELEVANCE OF BRONCHOFIBROSCOPY IN THE DIAGNOSIS OF ATYPICAL RADIOLOGICAL IMAGES. A CASE OF ENDOBRONCHIAL TUBERCULOSIS

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Background: Endobronchial involvement occurs in 57% of the children with pulmonary tuberculosis. Right tracheobronchial tree is the most commonly affected site.

Case report: Female, age three, born and resident in Luanda (Angola) was sent to our unit because of a suspicious radiologic finding. There was a one month history of intermittent fever associated with weight loss, anorexia and asthenia. Her parents also reported a close contact with an uncle who had pulmonary tuberculosis, under treatment. Physical examination revealed some emaciation, without any further abnormalities. Immunization schedule was updated according to her place of residence, although without BCG. Previous chest radiograph showed a hypotransparency in the right upper lobe, with slight deviation of the trachea, and CT scan disclosed a right apical anterior mass with some contrast enhancement and areas of necrosis in contiguity with ipsilateral hilar engorgement. Mantoux test was positive (27mm induration). Bronchofibroscopy showed near-total obstruction of the upper right segmental bronchus by a mass, compatible with endobronchial tuberculosis. The remaining investigation showed normochromic normocytic anemia, elevated erythrocyte sedimentation rate and c-reactive protein. Bacteriological cultures and direct examination with Ziehl-Nielsen staining of gastric aspirates and bronchial secretions were both negative. Mycobacteria culture is currently in course. Antituberculosis triple therapy was started and included isoniazid, rifampicin and pyrazinamide associated with prednisolone. At discharge, the patient presented significant improvement of her general health and appetite, and chest radiograph revealed a decrease of the lesion's size.

Conclusion: In pediatric endobronchial tuberculosis, endoscopy has an important role in diagnosis and treatment.

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DISSEMINATED INFECTION BY SCEDOSPORIUM APIOSPERMUM IN ACUTE MYELOID LEUKEMIA

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Background: Scedosporium apiospermum is a rare pathogen in the immunocompetent, but it has been increasingly recognized as the cause of severe disseminated infection in the immunocompromised host, including patients with hematologic malignancies. Diagnosis and treatment are challenging because of histological similarities with more common filamentous species (Aspergillus and Fusarium) and multidrug resistance to the usual antifungals, with little response to empiric treatment.

Case report: The authors report the case of a child with acute myeloid leukemia diagnosed at the age of five, presenting first signs of Scedosporium apiospermum infection, initially localized to mandible and then disseminated, during bone marrow aplasia secondary to chemotherapy. Combinations of various antifungal agents were needed for disease control associated with surgical clearing where accessible. At present, at the age of twelve, after six years of antifungal, at present using posaconazole with clinical resolution and negative fungal cultures. As for her oncology disease, after five years post-treatment she is in complete remission.

Discussion: Authors point out that despite the challenge in diagnosis and treatment of a severe opportunistic infection by a resistant agent in an already fragile host, success can be achieved with combined antifungal therapy and follow up.

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KAWASAKI DISEASE: WHEN THE LAB DOESN´T FIT

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Background: The incidence of atypical Kawasaki disease (KD) is steadily increasing over the last decade. We report two cases presenting with coronary dilatation without complete clinical criteria and atypical analitic results.

Cases reports:

Case 1: 34-month-old boy, was admitted with irritability, anorexia, perineal desquamation and a facial and chest macular rash. He was diagnosed with scarlet fever seven days before admission, treated with amoxicillin; fever persisted for five days. Throughout this period he presented swelling of the hands and feet, conjunctival injection and cheilitis, with complete resolution before admission. Inflammatory markers and total blood count (TBC) were normal.

Case 2: 27-month-old girl, admitted with a persistent 3-week fever and cough, unsuccessfully treated with cefaclor for ten days. TBC showed pancytopenia and C-reactive-protein was raised. Chest x-ray revealed middle lobe pneumonia; she was started on ceftriaxone. She had serological evidence of recent EBV infection. Both had dilatation of coronary arteries (maximum 3mm diameter) that resolved after treatment with intravenous immunoglobulin (2 g/kg) and acetylsalicylic acid (50mg/kg/day).

Discussion: The authors present this two cases as an alert for not to discard KD when the laboratorial evaluation doesn't fit the diagnosis. The coronary abnormalities allowed the final diagnosis.

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ORBITAL CELLULITIS AND BACTEREMIA DUE TO EIKENELLA CORRODENS

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Introduction: Eikenella corrodens infections are usually associated with trauma, bites, and oral/upper respiratory tract disease. It's frequently isolated in co-infection with other oral pathogens. In a Pubmed review on OC and Eikenella corrodens there are only two children reported, in 1992.

Case report: A thirteen-year old boy, presented to the emergency department after three days of coryza and rapidly progressing unilateral periorbital redness and edema. On admission, he presented with fever, proptosis and exuberant inflammatory signs in the front and left orbit. Ophtalmologic examination was otherwise normal. CT-scan showed: left OC with subperiosteal abscess; maxilary, left frontal and etmoidal sinusitis. He was submitted to surgical drainage and started on ceftriaxone, clindamycin and prednisolone. Eikenella corrodens (penicillin susceptible) grew in both blood and pus cultures. Clinical resolution was confirmed by CT-scan with marked improvement on day seven. Antimicrobial therapy was adapted to amoxiclin-clavulanate that he completed for 14 days on oral formulaton.

Conclusion: Eikenella corrodens caused OC and bacteremia in an adolescent with no risk factors. The spectrum of antibiotic susceptibility is usually covered by empiric treatment used in OC. Amoxiclin-clavulanate was prefered due to the risk of polimicrobial infection. The outcome is comparable to that achieved with the usual agents responsible for OC.

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CHRONIC SEVERE MULTIFOCAL OSTEOMYELITIS DUE TO GROUP E SALMONELLA

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Background: Chronic osteomyelitis is a rare entity in children. Incidence is increased in those with functional hyposplenism, impaired complement activity or in necrotic bone.

Case report: 15-year-old African boy transferred from Guiné-Bissau, with sickle-cell disease and a 6-year-long history of inflammatory signs and purulent discharge of lower limbs, following trauma. Laboratory studies showed elevated inflammatory parameters; he was negative for HIV 1 and 2. Tuberculin skin test was positive; chest X-ray was normal. Bone scintigraphy and magnetic resonance imaging revealed multifocal chronic osteomyelitis, multiple bone sequestra in both tibias and necrosis of the left femoral head**.** The surgical approach was extensive removal of sequestra with longitudinal section of his tibias. Flucloxacillin and Ciprofloxacin along with HRZ were started after surgery. Group E Salmonella grew in bone cultures and flucloxacillin was stopped. Mycobacteria were not isolated in bone or sputum samples. At four weeks of treatment he shows both clinical and laboratorial improvement.

Discussion: Patients with sickle cell disease are particularly susceptible to bone infections caused by non-typhi Salmonella. This case is singular due to multifocal extension originating from the bone sequelae. The authors emphasize the role for adequate haematological management of these patients, and point out the need for covering Salmonella spp in the empiric treatment of osteomyelitis in patients with sickle cell disease.

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CLINICAL FEATURES AND OUTCOMES OF INFLUENZA A AND B IN CHILDREN

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Background: Influenza viruses are an important cause of disease of varying severity in humans. Complications of influenza may occur at any age, affecting mostly infants and children. The aim of the study was to describe the course of influenza among children aged 0-59 months.

Material and methods: The total number of 150 children with influenza-like symptoms (ILI): cough, fever > 37,8°C, sore throat was included into the observation. All children were tested with both rapid influenza detection test (RIDT) BD Directigen™ EZ Flu A+B® and RT-PCR. The total number of 64 cases of influenza was diagnosed (attack rate 40%): 19 (30%) cases of influenza caused by virus type B and 45 (70%) cases of influenza caused by type A virus. Children with influenza required more often follow up visits (p< 0,05, OR 1,99, 95%CI 1,03-3,85) and less often were administrated antibiotic therapy (p< 0,05, OR 0,25, 95%CI 0,044-0,97). The logistic regression analysis revealed that only positive result of rapid influenza detection test, not any of clinical symptoms, could be found as the independent predictor of influenza (OR 4,37, 95%CI 2,03-9,43). Patients with influenza type A more often reported muscle ache (p< 0,05) and complications (p< 0,05; OR 6,06, 95%CI 1,2-60,38). Otits media occurred more often among patients with than without influenza (p< 0,01), OR 15,5 95% CI 2,1-688,5).

Conclusions: Our results indicate that although influenza infections among children younger than 59 months were generally mild and self-limited, paediatric burden o the disease was significant.

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SEROPREVALENCE OF HEPATITIS B SURFACE ANTIGENAEMIA IN CHILDREN IN A TERTIARY HEALTH INSTITUTION IN THE NIGER DELTA OF NIGERIA

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Background and aims: There is paucity of data on the seroprevalence of HBV infection in children living in urban areas of the Niger Delta of Nigeria. The aim of this study is to determine the seroprevalence of hepatitis B surface antigenaemia among children presenting to the University of Port Harcourt Teaching Hospital (UPTH), to determine the trend in the seroprevalence of HBsAg over a five-year period and to correlate serological findings to clinical features.

Methods: A retrospective study of Serum samples from 251 children in UPTH aged > or = 16 years which were tested for Hepatitis B surface antigen using Clinotech HBsAg kits and confirmed using the Trinity Biotec enzyme linked immunosorbent assay based HBsAg kits. Medical records of the children were also obtained.

Results: The overall prevalence of HBsAg among children tested was 12.4%. HBsAg prevalence was highest in the 11-15 years age group (24.5%) and the lowest in the 6-10 years age group (11.0%). There was a statistically significant difference in the prevalence of HBV positivity based on age groups (/ 2 = 8.47, p = 0.014). Prevalence rate was relatively higher among males (13.7%) compared to females (10.7%). There is a statistically significant trend in the decline of HBsAg prevalence 1999 to 2004 (/ 2 for trend = 11.38, p = 0.001). The predominant symptoms among children positive for HBsAg were hepatosplenomegaly (75%) and jaundice (64.5%).

Conclusion: This study indicates a high prevalence of HBsAg among children presenting to a tertiary health facility in Port Harcourt.

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ANTIBIOTIC CONSUMPTION PATTERN IN A SINGLE SPECIAL NEONATAL CARE UNIT IN WARSAW (POLAND)

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Current and detailed knowledge of antibiotic use is essential in order to implement strategies for reducing the overuse and misuse of antibiotics and the spreading of resistant microorganisms. The objective of our study was to assess antibiotic consumption in the Special Neonatal Care Unit (SNCU) in a single district secondary level hospital in Warsaw (Poland) in 2011. Data on the quantitative and qualitative use of antibiotics was reported by the hospital's pharmacy. Antibiotic usage was calculated in daily defined doses (DDDs) per 100 patient days and DDDs per 100 admissions according to the Anatomical Therapeutic Chemical Classification (ATC) System. The antibiotics were ranked by volume of DDDs and the number of antibiotics that accounted for 90% and 100% of the total volume, DU90% and DU100% respectively (where DU stands for drug use). 15 antibiotics were used for treatment and prophylaxis at the SNCU, DU90% was 5 (ampicillin, amoxicillin with clavulanic acid, amicacin, gentamycin and ceftazidime). The total antibiotic use was 28,9 DDDs per 100 patient days (352,17 DDDs/ 100 admissions). Penicillins were the most commonly prescribed antibiotics (80,6%), followed by aminoglicosides (12%). The cost of penicillins and aminoglicosides accounted for 60,2% of the total antibiotic costs. The cost of third generation cephalosporins (18,6%) and meropenem (12,2%) was also respectively high. Our data indicates high antibiotic consumption in the SNCU and may serve as a background for comparisons with other hospital wards in Poland and other countries.

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PREVALENCE OF TICK-BORN SPOTTED FEVER, ANAPLASMOSIS, EHRLICHIOSIS AMONG PRESCHOOL CHILDREN IN CHENGMAI COUNTY, HAINAN PROVINCE, CHINA

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Background: On Oct 26, 2007, a six years old child (male) was etiologically diagnosed as infection with a novel spotted fever rickettsiae(SFGR) in Chengmai County, Hainan Province, China.We retrospectively went to the patients' village and conducted a filed epidemiologically investigation.

Methods: 12 suspected cases and 270 healthy preschool children were investigated. 2 ml of sodium citrate anti-coagulate and 2 ml of non anti-coagulate blood samples were collected from each patient for culture and molecular and serological analyses. The antibodies against the novel SFGR, A.phagocytophilum and E.chaffeenesis were detected by immunofluorescence assays. 570 ticks were collected and classified and grounds for extracting DNA to amplify the 16S rRNA genes of rickettsiae.

Results: All the 12 suspected patients were preschool children and 58.3% of patients had rash on their bodies .Five SFGR isolates were obtained . and the sequences of 16SrRNA(924bp) and ompA(542bp) were 100% identity with that of the novel SFGR isolates from the index patents in 2007. 7 of 12 cases had 4-fold increased titers of IgG antibody against the novel SFGR. The seroprevallence of the novel SFGR, A.phagocytophilum and E.chaffeenesis in 270 healthy preschool children were 37.5%, 6.3% and 12.5% respectively. 50% of patients' house had ticks and the total positive rates of the novel SFGR, A.phagocytophilum and E.chaffeenesis in 3 species of ticks including R. sanguineus, H. doenitzi and B. microplus were 23.7%, 6.9% and 12.7% respectively.

Conclusion: Differential diagnoses of rickettsia infection should be emphasized in local hospitals.

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RISK FACTORS FOR INFECTIONS IN BURN CHILDREN

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Risk factors for acquisition of nosocomial infections are not well known in burn children.

Objectives: Evaluate risk factors for acquisition of nosocomial infections of burn pediatric patients.

Material and methods: Prospective study.

Results: N: 110 patients. Mean age: 31.5 months (range: 1 to 204). Seventy one patients (65%) were male. The burn surface was between 1% and 95 %(median 25%). Type of burn was: A in 39 patients (36%), AB in 19 (17%), and B or full thickness in 52 (47%). Inhalatory injury was present in 52 patients (47%). In 63 patients 92 infections were diagnosed. Burn wound sepsis was the most frequent focus in 53 cases (46%). In 19 cases (16%) burn wound infection was without sepsis. Bacteremia related with intravascular catheter was found in 15 cases (13%) and bacteremia only, in 2 p (2%), pneumonia in 7 cases, (6%), osteomyelitis in 3 others (2%), urinary tract infection in 8 cases (7%), and other infections in 9 cases (8%). Forty- two infections (36%) were caused by P aeruginosa spp, and 11 (10%) by Acinetobacter spp. Fungal infections were detected in 22 cases (19%) The median length of hospital stay was 33d (r: 8-139 days) Ten patients (20 %) died of infections relates causes.By multiple logistic regression analysis invasive vascular catheters, requirement of graft, and antibiotic prophylaxis were risk factors for nosocomial infections.

Conclusion: Central venous catheter, requirement of graft and preoperative prophylaxis put burn children at high risk of infectious complications.

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SINGLE NUCLEOTIDE POLYMORPHISM OF IL-10 AND IL- 28B AS PREDICTORS TO THE RESPONSE OF INTERFERON THERAPY IN HCV INFECTED CHILDREN

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Background and aims: We aim to detect the relation between SNPs of IL-10 (-1082, -819, and -592) and IL28B gene (rs12979860) and prediction of response to Pegylated interferon (PegIFN) plus Ribavarin (RBV) in Egyptian pediatric subjects with genotype 4.

Methods: A RFLP-PCR and Real time PCR techniques were used to genotype 34 pediatric patients with HCV for IL-10 SNPs and IL-28B SNP respectively. Patients received (PegIFN) and (RBV) for 48 weeks subdivided according to their response to treatment into responders (20) and non-responders (14), and 20 healthy subjects.

Results: A significant difference ($p < 0.005$) was observed in IL-28B rs12979860 genotype frequencies between responders and non-responders. In responders CC genotype had greater frequency than CT and TT genotypes (60%, 30%, 10%) respectively with C allele in its wild genotype more likely to respond to treatment than in its mutant types. IL-10 at -819 showed significant difference in its genotype frequencies between responders and non-responders, TT genotype had greater frequency in responders than CT and CC (55%, 20%, 25%) respectively. Subjects with T allele (CT/TT) showed higher rates of response than those with no T allele (CC), its protective effect in both recessive and dominant forms.

Conclusion: Il-28B CC genotype as well as the IL-10 (-819) TT genotype are significantly associated with response to PegIFN and RBV for pediatric patients with HCV infection genotype 4. These SNPs can be used for predicting response to treatment before patient is prescribed to the expensive PegIFN-RBV therapy.

This work was supported by Cairo University.

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CASE REPORT: GRANULOMATOUS AMOEBIC ENCEPHALITIS CAUSED BY BALAMUTHIA MANDRILLARIS IN CHILDREN

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Background: Balamuthia mandrillaris (B.mandrillaris) is an emerging opportunistic protozoan pathogen, a member of the group of free-living amoebae. B.mandrillaris is known to cause serious cutaneous infections and fatal encephalitis with a case fatality rate of >98%. Since 1991, B.mandrillaris was associated with fatal human infection involving the central nervous system (CNS). Since then, more than 100 cases have been identified.

This is an 8 year-old previously healthy boy coming from a tropical area of Argentina. He was admitted for study of a 6 month history central face infiltrative non ulcerative painless plaque, with intranasal involvement without any other symptoms.

In his right arm he had a scarred round lesion compatible with previous cutaneous leishmaniasis. Montenegro intradermal skin test was positive for Leishmania.

Facial skin biopsy was performed for diagnosis. Pathology studies showed: necrotizing granulomatous dermatitis and protozoan images compatible with Leishmania. He began treatment with amphotericin lipidic formulation for 3 weeks with a favorable outcome.

One month later, he developed neurological symptoms, with headache and progressive consciousness involvement. MRI showed a diffuse CNS involvement and increased intracranial pressure. Amphotericin was reintroduced. Biopsy revealed graulomatous amoebic encephalitis, and infection with B. mandrillaris was confirmed with inmunofluorescent testing at the CDC, USA.

The boy´s level of consciousness deteriorated, from lethargy to coma, and he finally died 3 weeks later with extensive CNS involvement spite of the treatment.

Conclusion: Although rare, B.mandrillaris infection should be considered in a patient with chronic central face painless plaque and /or granulomatous encephalitis in tropical setting.

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NON-TYPHOID SALMONELLA GASTROENTERITIS IN PEDIATRIC PATIENTS IN NAJRAN REGION, SAUDI ARABIA

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Pediatric infection with non-Typhoid Salmonella (NTS) commonly causes acute gastroenteritis, which is a major cause of morbidity, worldwide. This study aimed to determine serotype distribution and resistance patterns of NTS strains isolated from pediatric patients with acute gastroenteritis in Najran region, Saudi Arabia. The study included 500 children aged < 5 years with diarrhea attending the outpatient clinic at Maternity and Children's hospital in Najran. Stool samples were collected from all patients and sent to the microbiology department of the Najran University College of Medicine for detection of Salmonella serotypes and antimicrobial susceptibility patterns. During the study period, a total of 42 NTS isolates were identified. The highest isolation rate (40.5%) was in the age group ≤12 months. The most prevalent Salmonella serogroup was serogroup B (47.6%) and D (38.1%). In this study, 9.5% of Salmonella isolates were resistant to one antimicrobial and 14.3% were multidrug-resistant. The highest resistance of isolates was to tetracycline (71.4%), followed by ampicillin (54.8%) and chloramphenicol (26.2%). The highest susceptibility was to ciprofloxacin (2.3%). In conclusion, Salmonella Serogroups D and B predominate as causative agents of pediatric salmonella gastroenteritis. The study highlighted an increasing salmonella resistance to commonly available antibiotics. Continuous monitoring of serotypes resistance to antimicrobials is necessary because of the public health implications of a potential spread of resistance clones.

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PHARMACOKINETICS OF CEFTRIAXONE IN SEPTIC NEWBORN FULL-TERM AND PRETERM

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Background: Klebsiella pneumonie and Escherichia coli are the leading cause of neonatal sepsis in Mexico and other developing countries.

Objective: To investigate the pharmacokinetics of ceftriaxone (CTRX) in Mexican neonatal patients suffering sepsis.

Methods: We performed a study in 19 term newborns and 7 preterm of the National Institute of Pediatrics of Mexico; they received intravenous infusions of (CTRX) to 75 mg/kg/day every 24 hours. The study was approved by the Institutional Ethics Committee. Blood samples were drawn by intravenous catheter (50 µL) to 0.25,1,2,4,6,8,12 and 24 hours after the first dose. Total plasma concentrations of (CTRX) were analized using HPLC-ultraviolet detector. The estimated pharmacokinetic parameters were studied using WINONLINE software.

Results: According to gestational age there were significant differences between full term newborns and preterm newborns: the t1/2β was 3 times longer in preterm newborns = 31.13 hours vs term newborns = 13.9 hours, $p< 0.01$. The AUC was 2 fold lower in term newborns = 2443 L/kg/h vs 4743 L/kg/h in preterm newborns. The differences in Cl and Vd in both groups were not significant, however the t1/2β was longer and Cl was more decreased in 7 hypotrophic newborns than eutrophic newborns who were matched for age.

Conclusion: The dose of (CTRX) in neonates should consider specific pharmacokinetic differences by gestational age and nutritional status, on the basis of decresed clearance in neonatal patients, it can argued that dose of (CTRX)should be decreased, or delay between doses should be increased.

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PREVALENCE OF INTESTINAL PARASITES AND POSSIBLE RISK FACTORS AMONG UNDER FIVE CHILDREN AT ABUNE SAMUEL SCHOOL IN GONDAR

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Introduction: Intestinal parasitic infections are amongst the most common worldwide. It is estimated that some 3.5 billion people and that 450 million are ill as a result of these infection, the majority being children.

Objective: To determine the prevalence of intestinal parasites and possible risk factors among under five children at Abune Samuel school in Gondar.

Methods: A cross sectional study was conducted among under five children at Abune Samuel School in Gondar, from Feb 5 up to Feb 28, 2012. Simple random sampling technique was used to select study subjects. From selected students stool sample was collect and examined for the presence of intestinal parasites using direct microscopy. The collect samples were check for its completeness and analyze with SPSS 16 Software Packages.

Results: From the total 384 samples 315 were volunteer and participated in this study. Of 315 included in the study 143(43.4%) were males and 172(54.6) females. The total prevalence of intestinal parasite in our study is 81(25.7%). Females are more affected than males with percentage of 42(51.8%) and 39(48%), respectively. The predominant affected age group was 4-5 years 38(46.9%) followed by 3-4 years 32(39.5%). From the study population 315(100%) were Christian religion followers. Age, family monthly income, maternal educational status and type of toilet were factors associated with the prevalence of intestinal parasitosis (P-value< 0.031).

Conclusion: There was a high rate of intestinal parasitosis among under five children in Abune Samuel kinder garden which alerts health intervention as soon as possible.

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PREVALENCE OF CLOSTRIDIUM PERFRINGENS INFECTION IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PILOT STUDY

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Backround and aim: Growing amount of scientific evidence suggests that superimposed infections of pathogenic bacteria may have deleterious effect on the clinical course of inflammatory bowel disease (IBD). Clostridium perfringens infection has also been detected in up to 15% of antibiotic-associated diarrhea cases; it has not been found in healthy people. The aim of the study was to investigate the prevalence of Clostridium perfringens infection in pediatric patients with IBD.

Methods: It was a prospective study evaluating pediatric IBD patients in Department of Paediatric Gastroenterology and Nutrition, Warsaw, Poland. All patients were diagnosed according to Porto criteria. Stool samples were collected at the day of admission. Clostridium perfringens infection diagnosis was based on a positive stool enzyme immunoassay (C. perfringens enterotoxin test kit TechLab).

Results: Between March 2011 and October 2012, 90 fecal specimens from patients with IBD were collected. The incidence of Clostridium perfringens infection was 9% (8/90). Average age of patients was 11.7 years. There was more Crohn's patients (6/8) in C. perfringens group.

Conclusion: The prevalence of Clostridium perfringens infection in pediatric IBD patients was 9%. Our pilot data add to the evidence base that Clostridia other than C. difficile may play a significant role in clinical IBD course, however further studies are needed to confirm this hypothesis.

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NEONATAL PURPURA FULMINANS AS A RARE CUTANEOUS MANIFESTATION OF EARLY ONSET GROUP B STREPTOCOCCAL INFECTION

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Introduction: Neonatal Purpura fulminans (PF) is a rare haematological emergency characterized by sudden onset of skin haemorrhage and necrosis with peripheral gangrene. Gram negative organisms are the commonest cause of acute infectious type and few cases of causative neonatal group B streptococcus (GBS) disease were reported worldwide.

Case report: A full term boy was delivered vaginally with a normal Apgar score, weighed 3100 grams and discharged at the age of 36 hours of life. The mother with an unknown GBS status antenatally came to the emergency department (ED) in active labour and no prophylactic antibiotics were given.There was no family history of haematological disorders. The mother brought him at the age of 43 hours of life to the ED with fever (39.5°C) and lethargy. Neonatal sepsis was suspected and started on intravenous Ampicillin and Gentamicin immediately. He rapidly deteriorated and required aggressive resuscitation then shifted to NICU. Two hours later, a purpuric rash developed over scrotum, upper and lower extremities with gangrenous fingers and toes. Initial workup revealed a disseminated intravascular coagulopathy and both blood and CSF cultures grew GBS. He had normal levels of Protein C and Protein S. Despite maximum support and proper antibiotics coverage, he developed multisystem-organ-failure and died 48 hours after admission.

Conclusion: Neonatal PF secondary to early onset GBS infection is a fatal condition that should not be missed. Screening of pregnant women for GBS colonization and implementation of the recommended guidelines are the most important preventative measures.

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NEUROLOGICAL SIGNS IN CHILDREN WITH CONGENITAL CYTOMEGALOVIRUS INFECTION

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Background and aims: Cytomegalovirus infection (CMVI) common congenital infection. It is known that the incidence of neurological disorders in children reaches up to 90%. We evaluated neurological features in children with congenital CMVI.

Methods: Verification of CMV was performed by PCR (determination of CMV DNA) of blood, urine, saliva and cerebrospinal fluid using the thermocycler ROTOR GENE 6000 with the use of test systems "The amplitude Sens SMV-FL» (Russia).

Results: We observed 96 patients with congenital CMVI. Neurological disorders were observed in 89 (92,7%) patients. Encephalopathy - 42 (43,8%), apnea - 13(13,6%), microcefalia-2(2,1%) were observed only in the neonatal period, hypertension syndrome - 38 (40%), hydrocephalic syndrome - 32 (33,3%) - in children aged 2-6 months. By 9-12 months among neurological signs were dominated motor and psychomotor delay -17(17,7%) and pathological changes in muscle tone with hypertonus -5 (5,2%).

Increased seizure activity-15(15,6%) was observed in all periods of the disease, its severity ranged from convulsive to general tonic-clonic seizures.

In our patients with microcephaly (2,2%), and calcification in the brain (4,4%) was observed in the future development of progressive sensorineural hearing loss, tetraparesis, deep psychomotor delay, development of atrophic chorioretinitis.

Conclusion: The central nervous system is involved in the pathological process in 90% patients with congenital CMVI and characterized by a variety of clinical manifestations, the absence of pathognomonic symptoms and development severe long-term complications.

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MORPHOLOGICAL RESEARCH IN PLACENTAE AT CYTOMEGALOVIRUS INFECTION

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Background and aims: Cytomegalovirus (CMV) infection is the most common congenital infection which is transmitted via placenta from mother to fetus. We evaluated morphological markers in placenta at CMV infection.

Methods: We examined 109 placentas wich included 79 placentas from women, whose newborns had congenital CMV infection and 30 - control group without CMV infection. Placenta's speciments were fixed by 10% formaline and than coloured by hematoxilin and eosin.

Results: We have found inflammantary features in placenta at CMV infection such as chorioamnionitis - 8,9% (p>0,05), deciduitis - 11,4% (p>0,05), choriodeciduitis - 8,9% (p>0,05), villusitis, intravillusitis -32,9% (p=0,0003) in comparison with control group. Petrifikates in placenta were detected in 16,5% (p=0,02) placentas in group with congenital CMV infection.

Conclusion: CMV plays a role in the development of villusitis, intravillusitis, petrifikates.

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THE INFLUENCE OF MATERNAL HIV AND MYCOBACTERIUM TUBERCULOSIS ON INFANT RESPONSES TO BCG VACCINATION

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Background and aims: Altered immune responses might contribute to the high morbidity and mortality observed amongst uninfected infants exposed to human immunodeficiency virus-1 (HIV) in utero. This study examined the influence of maternal HIV and Mycobacterium tuberculosis (Mtb) infection on infant immune responses to BCG immunisation.

Methods: 109 mother-infant pairs were enrolled from Khayelitsha, Cape Town, South Africa, and were followed for four months. Peripheral blood samples were collected from the mother-infant pairs at delivery and from the infant at 16 weeks of age. Responses to BCG antigens were measured using multi-parameter flow cytometry and multiplex enzyme-linked immunosorbent assays.

Results: At birth, HIV-exposed, uninfected infants had increased frequencies of BCG-specific proliferating T cells expressing TNF-α and increased levels of TNF-α protein in cell culture supernatants; levels were highest amongst HIV-exposed infants born to Mtb sensitised mothers. IFN-γ levels were lower amongst HIV-exposed, uninfected infants compared to unexposed infants. Maternal Mtb sensitisation was associated with increased infant IFN-γ levels; infants born to HIV-infected, Mtb sensitised mothers had similar levels compared to unexposed infants.

Following BCG vaccination at 6 weeks of age, the immune response to infant BCG vaccination was unaffected by maternal HIV infection or Mtb sensitisation.

Amongst mothers, Mtb sensitisation significantly influenced the response to BCG-antigens in HIV-infected, but not in HIV-uninfected mothers.

Conclusions: Antenatal HIV exposure was associated with some alteration in immune response to BCG antigens at birth, however HIV-exposed, uninfected infants had comparable potential to respond to BCG immunisation as HIV-unexposed infants.

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RANDOMIZED CLINICAL TRIAL TO EVALUATE THE IMPACT OF A FACT SHEET ABOUT INFANT VACCINATION PAIN MANAGEMENT ON PARENTAL KNOWLEDGE UPTAKE

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Background: Vaccination injections are the most common painful medical procedure that infants experience. We developed a fact sheet for parents summarizing evidence-based strategies for managing pain during vaccination.

Purpose: To determine maternal knowledge uptake from the factsheet; and the additional impact of administering the factsheet with a baseline knowledge test (i.e., pre-test).

Methods: New mothers at Mount Sinai Hospital, Toronto, Canada, were randomized to two study groups (factsheet) and two control groups (information on another new baby health topic). A pre-test was given to one of the study groups and one of the control groups. Following review of the fact sheet/control sheet, post-tests were administered to all four groups. The test consisted of 10 true/false questions about the effectiveness of various strategies for reducing pain and distress during infant vaccination injections and the level of confidence in the response (5-point likert scale: very sure, sure, a little sure, neither sure nor unsure, a little unsure, very unsure).

Results: 120 mothers participated. There were no significant differences ($p>0.05$) in maternal characteristics among groups. Mean knowledge test scores were higher in the intervention groups: 5.6 (SD=2.0) and 6.9 (1.6) compared to the control groups 3.2 (2.2) and 3.4 (2.5). A 2-way (study group, pre-test group) ANCOVA revealed a significant ($p< 0.05$) main effect of the study group and an interaction between the study group and pre-test group.

Conclusion: The factsheet improved maternal knowledge about effective pain management strategies for vaccination injections. Knowledge was augmented by the use of a pre-test.

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PREVENTION OF INFECTIONS ASSOCIATED WITH INTRAVENOUS CATHETERS IN VLBW-INFANTS: SURVEILLANCE OF SKIN DISINFECTION VIA PUNCTION SWABS

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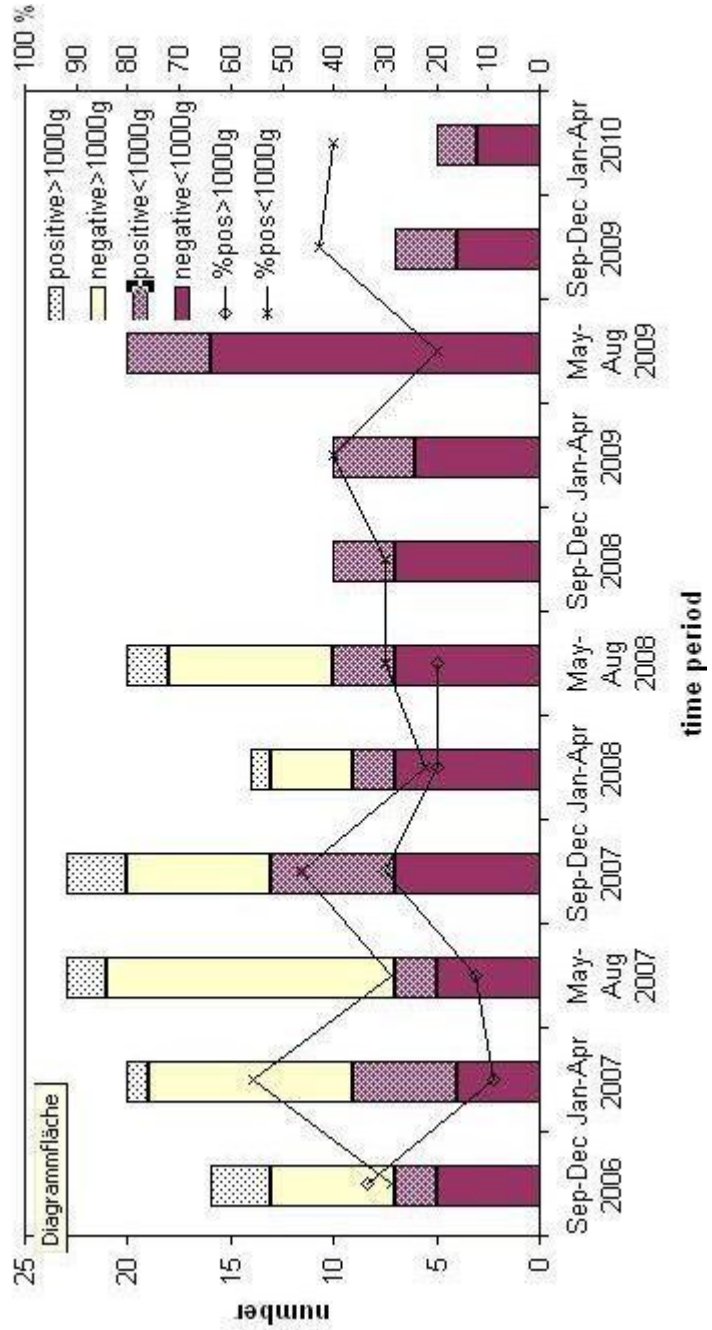
Background and aims: Premature infants with a birth weight under 1500g are at high risk to suffer from septic infections, mostly device associated. Our department participates in the german nosocomial infection surveillance system NEOKISS. Interpreting our outcome data of the years 2000-2005, our aim was to reduce the rate of intravascular catheter associated infections by checking adherence to line insertion practices. We chose post puncture skin smears as key indicator.

Methods: From Sept. 2006 to April 2010 170 VLBW-infants (after 09.2008 ELBW) were included in the study. After skin disinfection with Octenidin 0.1% or Octenisept and successful insertion of a peripheral intravascular cannula (PVC), before fixation a skin smear from the puncture site was drawn and cultured.

Results: In 68 from 911 swabs (7.5%) of 48 children (28.2%) smear germs were detected, most frequently (69%) coagulase-negative staphylococci. In 3 ELBW infants sepsis was diagnosed directly after a positive skin swab with the same germ, 2 children died.

There is no linear relationship between the smear result, the infants age when the smear was drawn, the infants maturity (gestational age), singleton or multiple birth, punction area location and antibiotic pretreatment.

Among children with a positive smear PVC-associated infections occurred significantly more frequent than in children without a germ in the punction swab. We observed no significant decrease of swab contamination during the observation period.



[Skin swab results]

Conclusion: Continuous education and surveillance of venipuncture hygiene is necessary. Coagulase-negative staphylococci are the most common contaminants.

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TT VIRUS INFECTION AMOUNG BETA-THALASSEMIA CHILDREN, SOUTH OF IRAN

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Background: Beta-thalassemic patients are high risk group to Transfusion Transmitted virus (TTV) infection due to repeated transfusions.

Objectives: To determine the incidence of TTV infection in beta-thalassemia children south of Iran.

Methods: This study was carried out on all beta-thalassemia children (452 children) of referring to beta-thalassemia centers south of Iran, June- July 2012. Serum samples from beta-thalassemia children were tested for the presence of TTV DNA by nested PCR using primer sets generated from N-22 region and from the untranslated region (UTR) of the viral genome.

Results: N-22 positive TTV DNA was detectable in 160 (35.40%) of 452 beta-thalassemia children.

Conclusions: It seems that the prevalence of TTV infection in beta-thalassemia children in south of Iran is lesser than the prevalence of TTV infection in the in beta-thalassemia patients in the most of other countries.

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VIRAL AETIOLOGICAL STUDY OF CHILDREN WITH ACUTE FEBRILE RESPIRATORY TRACT INFECTIONS IN TAIWAN, 2010-2012

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Background: Acute respiratory infection (ARI) is a leading cause of morbidity and mortality in children. This study aimed to determine the virological aetiology of acute febrile respiratory infections amongst children by a fast assay.

Methods: Clinical data and throat swabs were prospectively collected from children presenting with ARIs between August 2011 and October 2012. Viral aetiology was identified by the conventional cell culture and a fast assay (xTAG respiratory viral panel, RVP, Luminex Molecular Diagnostics, Toronto, Ontario, Canada).

Results: A total of 175 clinical samples obtained during the study period were analyzed. The RVP fast assay identified at least 1 respiratory virus in up to 60% specimens (105/175), whilst the traditional cultures 31.4% (55/175). Overall, rhinovirus/enterovirus was the most commonly detected virus (40/175, 22.8%), followed by human adenovirus (10.8%), parainfluenza virus (PIV) types 1-4 (8%), human metapneumovirus (HMPV; 6.8%), respiratory syncytial virus (RSV; 6.3 %), influenza type B (6.3%), influenza type A (4%), human coronavirus (HCoV) OC43, 229E, NL63, (3.4%), and human bocaviurs (1.1%). Coinfections were found in 18 of 105 positive specimens (17.1%). Despite the RVP assay showed higher detection rate, 5 culture-positive samples (4 of influenza B and 1 of RSV) were undetectable by this assay. During the study period, influenza virus and HMPV showed seasonal preference, whilst the other viruses were detected throughout the year.

Conclusions: The RVP assay is capable of detecting most of the viral pathogens timely for the children with febrile ARIs in Taiwan. Rhinovirus/enterovirus and adenovirus were the principal viral pathogens.

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EVALUATION OF HOSPITALIZED TURKISH PEDIATRIC PATIENTS WITH HEPATITIS A

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Hepatitis A is generally an acute, self-limiting liver infection transmitted through the faecal-oral route by a picornavirus, the Hepatitis A Virus (HAV). The clinical severity of the HAV infection varies from an asymptomatic infection to a fulminant fatal disease.

In this study pediatric patients younger than 18 years of age admitting between 01.01.2006-01.01.2011 to our hospital diagnosed as hepatitis A were evaluated. Of 427 patients, 49.4% were female and 50.6% were male. Hospitalisation rate of the patients was 28.3%. Reason of hospitalisation was vomitting in 58.7% of the patients and abdominal pain in 28%. Mean time of hospitalisation was 5,2 ± 4,5 (1-40) days. There was no significant difference in hospitalisation time by means of age. Vomitting and abdominal pain was significantly more common and PT and aPTT levels were significantly elevated in patients with elevated AST and ALT levels over 1000 IU/L ($p < 0.001$). PT elevation was present in 15.2% of the patients, aPTT elevation in 11.9%, leukopenia in 16.6% and thrombocytopenia in 2.6%. By means of atypical course, four patients (0.9%) had cholestatic hepatitis, 1 patient had recurrent hepatitis and 1 patient had fulminant hepatitis yet no mortality was observed.

In conclusion in this study it was observed that atypical course of hepatitis A was more scarce in pediatric patients, but careful follow-up of patients with AST and ALT levels >1000 IU/L is necessary.

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ROTAVIRUS A GENOTYPES CIRCULATING IN NIZHNY NOVGOROD (RUSSIAN FEDERATION) IN 2005-2012

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Background and aims: Rotaviruses (RVs) cause acute gastroenteritis (AGE) in young children with about 453 000 deaths annually, mainly in developing countries. Classification of RVs is based on G types (glycoprotein) and P types (protease sensitive), located in the outer layer of virion. In the USA, Europe and the European part of Russia the genotype G1P[8] was predominated during a long time. In several European countries vaccination program is implemented. Until 2012 RV vaccination was not used in Russia.

In this study we identified a change in G/P genotypes in the Nizhny Novgorod territory (Russia) during the years 2005-2012.

Methods: 5555 stool samples from children under 6 years hospitalised with AGE were studied. RVs were found by RNA-PAGE and RT-PCR in 30.1% of samples. P and G-genotypes of RVs were identified by RT-PCR and DNA sequencing.

Results: The study started in 2005, the first year when genotype G1P[8] dramatically decreased and other dominant genotypes appeared: G2P[4], G3P[8], G4P[8] and G9P[8]. By that time, other authors had already found that there had been 4 lineages of P[8] among the group A RVs. All strains in the Nizhny Novgorod territory were a variety of G-genotypes and the P[8]-3 allele. The G9 and P[8]-3 genotypes appeared there only in 2012 but in other countries it had been detected much earlier.

Conclusion: We suggest that strains are transferred from other territories rather than emerge locally as a result of reassortation or mutation. Our data should be considered when vaccination policy is revised.

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ANTIMICROBIAL UTILIZATION PATTERN IN THE PEDIATRIC INTENSIVE CARE UNIT OF A NORTHERN INDIAN TERTIARY CARE TEACHING HOSPITAL

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Background and aims: A retrospective study was conducted to evaluate the pattern of antimicrobial usage practices in a tertiary care pediatric ICU in northern India with an objective of obtaining baseline data, which could be utilized for designing an appropriate intervention to improve the antimicrobial use profile.

Methods: Relevant data was extracted from twelve hundred seventeen patient records who were admitted to the PICU between 2007-2009. Descriptive statistics were used to analyze the data.

Results: Seventy percent of the children were male. The reasons for admission were hemodynamic instability and ventilatory support due to critical illness,sepsis and multi-organ dysfunction syndrome. The mean duration of PICU stay was 9.1 ± 11.1days . Thirty three and 45.3%of the patients had negative and a positive cultures respectively. 26% and 19.2% of the cases were identified to have a gram positive and a gram negative bacterial infections respectively.The most common antibitiotic used was ceftriaxone (48% cases) followed by amikacin, vancomycin, ceftriaxone + sulbactum and cloxacillin. The most common antimicrobials commonly used as empirical therapy was co-amoxyclav followed by erythromycin and ticarcillin while cloxacillin, cefotaxime and itraconazole were prescribed for specific therapy. Results shwed diverse antibiotic prescription was common and based upon physician perception and choice.

Conclusions: In the absence of evidence-based hospital antibiotic policy, the risk of resistance leading to therapeutic failure can worsen financial burden, morbidity and mortality. Hence there is and urgent need to develop hospital and national antibiotic policy to suit the need of the majority.

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PERSISTENT NEONATAL CANDIDEMIA: A FOUR-YEAR RETROSPECTIVE STUDY IN A MATERNITY HOSPITAL

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Background: The prevalence and the clinical significance of persistent candidaemia among neonates are poorly understood. This study aim to describe the rate and the clinical relevance of persistent candidaemia over a four-year study period in Kuwait.

Study design: Retrospective chart review of infants admitted to the Neonatal Care Unit at the Maternity Hospital in Kuwait between January 2007 and December 2010, who had a positive blood culture for Candida species. Persistent candidaemia was defined as an isolation of the same Candida species beyond 6 days of initiation of the antifungal therapy or death due to candidaemia within 6 days of antifungal treatment.

Results: Of 89 neonates with candida infection included in the analysis, 54 (60.7%; 95%CI: 49.7-70.9%) had persistent candidaemia. Case fatality was 29 (54%) and 1 (3%) among persistent and non-persistent candidaemia; respectively ($p< 0.001$). Neonates with persistent candidaemia were more likely to be female and have central catheter at diagnosis and low platelets count.

All isolated candida species were susceptible for antifungal treatment and there was no difference in MIC between neonates with persistent and non-persistent candidaemia.

Conclusion: Persistent candidaemia is common and associate with increased risk of mortality. Drug resistance is unlikely explanation for persistent candidaemia but host-related factors seems to be more important and can be used to identify those at risk for preventive and treatment intervention.

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HIV1 VPR POLYMORPHYSMS ASSOCIATED WITH AA 77: A VIRUS HOTSPOT?

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Background: There are several HIV-1 Vpr polymorphisms that have been involved in biological functions of this viral protein that include replication and pathogenesis of virus, with direct influence in AIDS progression, namely in infants with perinatal acquired HIV-1 infection. The aim of this ongoing work was to study HIV1 Vpr polymorphisms at the position 77 in an HIV1-infected family, prompted by a clinical case of a perinatal-infected-5-year-old boy with repeated ear infections, but otherwise healthy.

Methods: Since July 2012, an HIV1-infected family (father, mother and son) has been studied in what regards HIV1vpr gene polymorphisms. The family members were clinically evaluated studying several clinical markers and other pathophysiological conditions.

Results: The analysis of HIV1 vpr sequences revealed two different mutations at the sequence that codes for amino acid position 77. Both parents were infected with virus carrying R77H mutation, while the child's-virus had R77Q variant. Both parents and child were considered asymptomatic, although the child had very high viral load (1,073,899 RNA copies/ml). Following therapeutic period to decrease the child's viral load, the child continues with no clinical signs of disease and interrupts therapy.

Conclusions: Our results show that different mutations associated with the aa 77 lead to non-progressive phenotypes. More, we identified a clinical case where the patient, a 5-year old child, remained with no visible signs of disease regardless of high viral load. With this study we aim to study Vpr not only as a bio-marker of disease progression, but also as an evolution flag of HIV1.

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NASOPHARYNGEAL CARRIAGE OF HAEMOPHILUS INFLURNZAE AND PNEUMOCOCCUS AMONG CHILDREN AFTER ATTENDING DAY-CARE CENTRES - INCLUDING THE EVALUATION OF VACCINATION

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Background: In Japan, while the rates of nasopharyngeal colonization by Haemophilus influrnzae (Hi) and Pneumococcus are high, the causative bacteria of meningitis are Hib and Pneumococcus. Hib vaccine and seven-valent pneumococcal conjugate vaccine (PCV7) started in February 2010 and in December 2008 as voluntary vaccines, respectively.

Objectives: To evaluate the carriage rate of Hi and Pneumococcus and the impact of both vaccines in children entering day-care centres.

Methods: Nasopharyngeal cultures of 46 healthy children between the age of one month and one year were conducted at three day-care centres. Reserch to determine the carriage rates and serotypes and the vaccines influencing the carriage was done.

Results:

① At the starting period, Hi was detected in 16 (34.8％) children. The carriage rates increased after entering day-care centres. Finally, it was more than 90% after eight months attending a day-care centre.

② At the starting period, Pneumococcus was detected in 17 (37.0％) children. The carriage rates increased, and then fluctuated. Finally, it was between 60 and 70 percent after nine months.

③ The carriage rates of PCV７ serotypes were low in vaccinated cases.

Conclusion: The carriage rates of Hi and Pneumococcus increased after attending day-care centres. Vaccination before entrance is important.

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PAEDIATRIC TB IN HIV ERA IN SUB-SAHARAN AFRICAN PERSPECTIVE

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TB is the number one cause of death in children with HIV in sub-saharan Africa. In the last three decade TB cases rates have increased dramatically in countries with high HIV prevalence. In South Africa alone 16% of children accounts for all TB cases of which 25-60% are HIV co-infected. Actual TB rates are much higher and have been under-reported in public health system.

Problems in detection and difficulties in diagnosis in children pose some challenges. The most widely used method of TB testing, the sputum smear, and show false negative in 87% of the cases. Overlapping lung diseases in HIV-positive children often lead to diagnostic error or delayed diagnosis of TB resulting in high infant mortality rate. This challenge is further compounded by the Multi Drug Resistant (MDR) strain of the disease.

In 2010, The World Health Organization endorsed PCR assay based diagnostic tools for TB such as Gene Xpert and MDR/RIP for children. These are more reliable diagnostic tools which have been used in adults with results obtained within hours.

In Paediatric patients evolution showed Gene Xpert detected twice as many cases (75.9%) as smear (38%). Unfortunately these are still not widely available owing to high cost.

Research, funding and trained personnel is needed for improving the diagnosis and treatment of smear-negative TB in children. TB is a multisystem disease and is correlated to HIV. If the HIV can be controlled, the TB will be decrease.

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INFECTIOUS CAUSES, COMPLICATIONS AND TREATMENT DURING PROTOKOL BFM-2000 IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN MACEDONIA

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Background: Infections are the most common complication and cause of death during the treatment of ALL as the most common malignancy in childhood.

Methods: We analyzed infections in 55 patients with ALL aged 0-14 years during treatment with BFM-2000 protocol (protocol I, protocol M, Protocol II and maintenance therapy) by determining the culture of each place of infection-sputum, urine culture, blood culture from a peripheral vein and/or CVC, tracheal aspirate, nasal swabs, throat and mouth and serological determination of antibacterial and antiviral antibodies.

Results: The most common infections during protocol I, protocol M, Protocol II and maintenance therapy is bacterial 77,3%, 57,7%, 71,23% and 82,8% respectively. The most common cause in the course of Protocol I, Protocol II and maintenance therapy is Streptococcus pneumoniae while in Protocol M Staphylococcus coagulasa negative. Febrile neutropenia occurring in 29.1% of patients during the protocol I, 7,3% in protocol M, 40% in protocol II and 5.9% in maintenance therapy. The total duration of antibiotic therapy during protocol I is averages 12,67±23,69 days, in protocol M ±11,4 13 days, in protocol II 9,3± 13,05 days and during maintenance therapy 6,4±3,5 days. The total number of treatment with G-CSF during the protocol I was 397 (average 4,79±7,22) in the course of the protocol M 134 (average 4,29±2,44) while in the course of Protocol II and maintenance therapy in 497 (average 5,65±9,20).

Conclusions: Identification and adequate treatment of infections during the protocol BFM-2000 directly affect the outcome of disease in patients with ALL.

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EVIDENCE OF CHRONIC IMMUNE ACTIVATION AND INFLAMMATION IN HIV-INFECTED CHILDREN

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Background: Persistent immune activation (PIA) and inflammation is known to be associated with non-AIDS events and mortality in HIV-infected adults; To date little data exists in children. The objective of this study was to compare serum levels of soluble biomarkers of inflammation (D-Dimer, CRP, beta2-microglobulin and IL-6) and cellular biomarkers of PIA ($CD45RA^+$ naive and $CD45RO^+$ memory T-cells, $HLA\text{-}DR^+$ and $CD38^+$ activated T-cells) in HIV-infected paediatric patients with those of healthy children.

Methods: Cross-sectional study including HIV-infected children (n=74) and healthy controls (n=32).

Results: D-Dimer, highly sensitive C-reactive protein and expression of $HLA\text{-}DR^+$ and $CD38^+$ on $CD4^+$ and $CD8^+$ T-cells were significantly increased in HIV-infected children with or without detectable viremia compared to healthy controls. Preservation of the $CD4^+CD45RA^+$ naive T-cell population in patients on effective HAART was found compared to patients with HIV viremia. A negative correlation between time with undetectable VL and $CD8^+HLA\text{-}DR^+$ and $CD8^+CD38^+$ T-cell percentages was observed.

Conclusion: PIA and inflammation occurs in HIV-infected children, especially in the setting of uncontrolled viremia. Soluble serum proteins such as D-Dimer, CRP and beta-2 microglobulin may be useful for monitoring PIA and inflammation in HIV-infected children on HAART.

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THE IMMUNOGENICITY AND SAFETY OF INACTIVATED TRIVALENT SPLIT INFLUENZA VACCINE IN YOUNG CHILDREN WITH RECURRENT WHEEZING

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Purpose: Influenza vaccination is recommended for children, but so far, active vaccination has not been achieved because most parents lack knowledge of vaccine safety and many doctors are reluctant to give vaccine due to concern that steroid may alter immunogenicity. The aim of this study is to compare immunogenicity and safety of inactivated trivalent split influenza vaccine(TIV) between children with recurrent wheezing and healthy children of the same age group.

Methods: 68 healthy children and 62 children with recurrent wheezing took part in this study. Seroconversion, seroprotection rate, geometric mean titer (GMT) and geometric mean titer ratio (GMTR) were measured by hemagglutination inhibition assay for assessment of immunogenicity. Solicited and unsolicited local and systemic adverse events were measured on a scale for assessment of safety.

Results: Regarding immunogenicity, seroconversion and seroprotection rate showed no difference between healthy children and children with recurrent wheezing over all. Also, no difference was observed between steroid treated and non-treated groups with the group with recurrent wheezing. GMT were higher in one-dose vaccination group and GMTR was higher in two-dose vaccination group in both healthy children and children with recurrent wheezing except for titers against H3N2 strain. And in safety, solicited local and systemic adverse events showed no difference between healthy children and children with recurrent wheezing, either.

Conclusions: This study demonstrates that inactivated split influenza vaccine can induce protective immune responses in healthy children, as observed in previous studies as well as in children with recurrent wheezing who require frequent steroid treatment.

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SINGLE DOSE PIPERAQUINE FOR WHOLE-PARASITE MALARIA VACCINATION

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Background: Malaria is responsible for a significant burden of morbidity in developing countries and thus, an effective vaccine is urgently needed.

Vaccination strategies based on the administration of whole parasites concomitant with prophylactic drug therapy have been shown to result in complete protection against malaria in rodent models and in humans. Single-dose regimens that can be co-administered with life wild-type malaria transmission stages, termed sporozoites will be a critical step towards clinical applications.To achieve this, further clinical development of a vaccination based on the administration of infectious malarial parasites under drug cover will in particular depend on the safety profile of the application. Most critically, single-dose regimens must reliably prevent potentially life-threatening breakthrough infections during vaccination.

Methods and results: We used piperaquine-tetraphosphate (PQ), a licensed antimalarial drug with a long half-life and favorable safety profile, to assess the feasibility of a single dose application in a rodent model. PQ was administered in drinking water (PQ-DW), orally through gavage tubes or by intraperitoneal injection. Our results indicate that a single dose of 7.5 mg PQ (oral or intraperitoneal) is sufficient to completely protect rodents from breakthrough infections after high-dose sporozoite inoculation. When calculated on the basis of body surface, this dosing is roughly equivalent to the drug dosing used for treatment of human P. falciparum infections.

Number of mice	sporozoite dosis used for immunisation (i.v.)	medication	drug dosis in mg *	dosis/m2 (0,007 m2/ mouse)	Protection
3	10000	PQ-DW	5,6	800	3/3 (100%)
3	50000	PQ-DW	5,6	800	2/3 (67%)
5	10000	PQ-DW	2,8	400	2/5 (40%)
5	10000	PQ-DW	1,9	271	2/5 (40%)
5	50000	PQ-DW	3	429	2/5 (40%)
5	50000	PQ-DW	3	429	1/5 (20%)
5	50000	PQ oral	7,5	1071	5/5 (100%)
5	50000	PQ i.p.	7,5	1071	5/5 (100%)

[graph 1]

Conclusion: Co-administration of a single dose of PQ together with live sporozoites might possibly be a simplified yet safe approach for whole parasite malaria vaccination.

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MULTIFOCAL SPLENIC ABSCESSES IN 2-MONTHS-OLD BOY AS A SIGN OF CHRONIC GRANULOMATOUS DISEASE

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Background: Primary immunodeficiencies are a heterogeneous group of inherited disorders of immune system with typical increased susceptibility to various infectious diseases (severe, persistent, unusual, and recurrent). Chronic granulomatous disease (CGD) is a rare primary immunodeficiency caused by a defect in the respiratory burst in phagocytes. Severity of clinical symptoms varies between patients, but in general these patients are in higher risk of recurrent infections and granuloma formation development.

Case report: We report a case of 2-months-old boy presented with multifocal splenic abscesses and other infectious complications.

Results and discussion: The clinical finding of splenic abscesses pointed the attention towards the possible inherited immunodeficiency. Visceral abscesses are typical clinical marker of phagocytic deficiencies. In our boy, autosomal recessive form of chronic granulomatous disease caused by the new, previously non-described mutation in NCF2 gene encoding p67phox protein of NADPH-oxidase complex. Subsequently, the prophylactic treatment with co-trimoxazole and itraconazole was started. The soon diagnosis of CGD led to the antimicrobial treatment with good clinical efficacy. The patient is now 4-years old and the clinical morbidity is within normal range. There is no available relative HLA-identical donor of hemopoietic stem cells.

Conclusion: In conclusion, although the splenic abscesses are rare in the clinical practice, their finding in the patients should focus the attention toward the diagnosis of chronic granulomatous disease. In general, visceral abscesses should be considered to be an important warning sign useful in the diagnostic algorithms of different primary immunodeficiencies.

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THE CMV SEROPREVALENCE AMONG PRESCHOOL CHILDREN WITH HEARING LOSS

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Background: The incidence of congenitally acquired HCMV in newborns ranges from 0.5 to 2.2% in developed countries. Up to 22% of neonates with hearing impairment are infected with HCMV. Auditory disability has pernicious effects on the development of speech and on the total development of the child. The age of onset of a child´s hearing impairment and the age at which the hearing impairment is diagnosed are crucial parameters for the further development of the child. This study was undertaken to determine the seroprevalence of CMV among preschool children with hearing loss.

Material and methods: The test group comprised 15 hearing-loss children of 3-6 years of age. The control group included accidentally selected 30 healthy children of the same age without any hearing complains. In both groups the CMV-specific IgG antibodies were determined in blood via the enzyme-linked immunosorbent assay “ELISA”.

Results: The excessive amount of IgG antibodies was found in 14 out of 15 children with sensorineural hearing losses being estimated objectively via computer registration of auditory brainstem responses, ABRs, and in 14 out of 30 children with normal hearing, being also inspected objectively via specialized screening procedure. The intergroup difference in CMV bearing rates 93.3% and 46.7%, respectively, has been confirmed to be statistically significant (p=0.007).

Conclusion: CMV bearing happens thus twice as much in sensoryneural hearing-loss than in normally-hearing children. Early assessment of CMV bearing and early detection of a hearing loss seem essential for immediate intervention and positive outcomes of specific treatment-rehabilitation means.

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THE ETIOLOGY OF ACUTE INTESTINAL INFECTIONS OF CHILDREN IN GRODNO IN 2012

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Aims: To study the etiological structure of acute intestinal infections of children in Grodno.

Methods: The etiological structure was studied on the basis of Grodno Region Infectious Hospital. There were cured 1571 children aged from 1 month to 15 years old having the given diagnosis in 2012. The following methods were used for diagnostics: bacteriological examination of stool, PCR for detection of antigens in feces, serological methods for isolation of specific antibodies.

Results: It was not able to decrypt a diagnosis of 673 (42,8 %) from 1571 patients and they were cured and were discharged from hospital with the diagnosis “acute intestinal infection of unknown etiology”.

The main cause of diseases among the left patients (898 or 57,2% from 1571) were diseases with viral etiology (641 from 898 or 71,4 %) such as: rotavirus infection - 559 (62,2 %) from 898; adenoviral infection - 20 (2,2 %); enterovirus infection - 9 (1%); norovirus infection - 16 (1,8 %); mixt-virus infection - 37 (4,2 %). There were diagnosed the following diseases of identified etiology: salmonellosis - 108 (12 %) from 898 patients; staphylococcal gastroenteritis - 33 (3,7 %); proteaceae gastroenteritis - 41 (4,6 %); escherichiosis - 7 (0,8 %); yersiniosis - 6 (0,7 %); clostridial infection - 5 (0,6 %). There was also diagnosed mixed viral and bacterial infection in 57 (6,2%) cases.

Conclusions: The proportion of children's acute intestinal infections of identified etiology is about half of all cases where the diseases of viral etiology are still prevailing.

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THERAPEUTIC LIMITATION FOR OSELTAMIVIR-RESISTANT H1N1(2009) IN A 2 YEAR OLD WITHOUT IMMUNOSUPPRESSION

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Case report: Oseltamivir resistant H1N1 (2009) is well described among immunocompromised patient. We report a case of resistance in a 2 year old with Epilepsy and developmental delay without underlying immunosuppression.

She was retrieved by our unit for respiratory failure following Status Epilepticus triggered by a severe H1N1 (2009) infection.

In PICU, CXR showed progressive airspace shadowing and a right pleural effusion needing a chest drain. She was ventilated for five days and required inotropic support. NPA for PCR confirmed H1N1 (2009).

She received a 10 day course of nasagastric Oseltamivir at 45mg twice daily and IV Cefotaxime and Clindamycin. Seizures were controlled on nasogastric Lamotrigine, Levetiracetam, and Sodium valproate. Although she showed improvement in her respiratory symptoms, temperatures continued to spike.This prompted a repeat NPA on day 8 for molecular analysis. Results revealed Oseltamivir resistant virus with H275Y neuraminidase mutation.

Our dilemma was either to give inhaled Zanamivir, an effective alternative to Oseltamivir which unfortunately isn't licensed for use in under five year old or to adopt a conservative approach with a risk of protracting duration of illness and a chance of onward transmission of a resistant virus. She improved on the later option.

Conclusion: Our case demonstrates the possibility of detecting resistant strains in children without a background of immunosuppression and the importance of molecular testing for Oseltamivir resistance in those with persistent symptoms. As there are no H1N1 (2009) resistant strains yet described to Zanamivir, safety and therapeutic trials should be performed in children under 5 years.

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THE FREQUENCY OF VARIOUS SPECIES OF MALARIAL PARASITES: THEIR CLINICAL AND HAEMATOLOGICAL FEATURES AMONG CHILDREN UNDER 14 YEARS OF AGE

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Introduction: Malaria is the world´s most important parasitic infection which poses major health challenges. Despite years of continual effort, malaria is still a threat to over two billion people, representing approximately 40% of the world´s population in about 100 countries.

Objective: To estimate the frequency of various species of malarial parasites and the clinical and haematological manifestations in children under 14 years of age

Methods A descriptive cross sectional study was conducted at clinics and the emergency room of the Aga Khan Hospital Karachi for six months. One hundred and eighty six patients met the selection criteria and were included in the study. The type of plasmodium species was recorded and clinical and haematological features were recorded by the principal investigator of different types of plasmodium species. In addition other relevant information such as age and gender were recorded in the proforma.

Results: Our study found that Plasmodium Vivax was found in 138 (74.2%) of the patients and Plasmodium Falciparum in 35 (18.8%). Almost 23 (12.4%) had shown a mixed type of plasmodium species. Most common clinical manifestation was fever > 38°C in 184 (98.9%) of the patients, while 167 (89.8%) of the patients had thrombocytopenia (platelets < $150x10^3/\mu L$).

Conclusion: The frequency and types of plasmodium, along with clinical and haematological manifestations have shown a prevalence that is in line with national and international studies, with obvious acceptable differences. We recommend further studies with large sample sizes to reach a firm conclusion.

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ARE TWO SETS OF BLOOD CULTURE USEFUL FOR NEONATAL SEPSIS IN DIAGNOSIS AND TREATMENT?

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Background: Appropriate sampling volume and frequency of blood culture are controversial in neonates. We have recommended routine sampling of two sets of blood culture in neonatal intensive care unit (NICU) as the most appropriate sampling technique since 2009. Therefore, the effectiveness of two sets of blood culture for the neonate admitted in NICU was studied retrospectively.

Methods: During the period Jun. 2006 to Dec. 2012, blood cultures were performed for 722 cases that were suspected of sepsis in NICU at Juntendo University Hospital, Japan. We investigated the number of blood culture, rate of positive culture per set, selection of antibiotics after blood culture identify positive and negative, retrospectively.

Results: After recommendation, the number of blood culture was increased 66.8%. Blood cultures were positive in a total of 127 neonates. The positive rate of blood culture was 17.5% in one set and 18.0% in two sets group. Selections of antibiotics based on pathogen that were detected are as follows: unchanged (43.4% vs. 20.0%); escalation (8.1% vs. 9.0%); de-escalation (38.4% vs. 64.0%); discontinuation (5.1% vs. 0%). When microorganisms did not grow from blood culture bottles during first 72 hours, two sets of negative blood culture were better to discontinue antibiotics than one set (29.6% vs. 10.4%).

Conclusion: By the education of appropriate technique and two sets of blood culture, the annual rate of two sets cultures has increased. There were no significant differences between positive culture rates in both sets. However, by undertaking two sets, it led to appropriate use of antibiotics.

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INDICATIONS FOR OSELTAMIVIR TREATMENT IN HOSPITALIZED CHILDREN WITHOUT UNDERLYING DISEASES. IS IT ALWAYS NECESSARY?

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Aims: To analyze if treatment with oseltamivir in hospitalized children without underlying diseases and influenza confirmed infection improved the outcome of the diseases.

Methods: Multi-centric, retrospective study was performed in Madrid between September 2010-June 2012. Children admitted with confirmed influenza infections were included. Children with underlying diseases were excluded. Patients who received and who do no received treatment with oseltamivir were compared. Fever duration, oxygen support, antibiotics administration, length of hospital stay, intensive care admission and bacterial complications were analyzed. To compare variables Chi-square, Fisher´s exact test, ANOVA or Mann Whitney U were used.

Results: 287 children were included, 93 of them treated with oseltamivir (32%). There were no significantly differences among treated and untreated patients in most clinical data studied. Patients with asthma presented no differences in the outcome variables between both groups.

	Treated (n=93)	No treated (n=194)	p
History of asthma	34 (36.6%)	49(25.5%)	NS
Antibiotic treatment	41 (44%)	98(51%)	NS
Hospital stay	4.7± 3.6	4.9 ± 3.2	NS
Fever duration	1.2 ± 2	1.6 ± 2.4	NS
Hypoxia duration	1.6 ± 2.3	2.1 ± 2.9	NS
Intensive care admission	6(6.5%)	3 (1.6%)	NS
CRP > 60 mg/L	10/69 (14.5%)	21/113 (18.1%)	NS
Typical pneumonia	5/45 (10%)	13/76 (17%)	NS

[Clinical characteristics of the groups]

Conclusions: We have not found benefit in treating with oseltamivir any hospitalized pediatric patient without underlying diseases or risk factor for developing a serious illness.

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ASSESSMENT OF WATER CONTAINER OF INCUBATORS OF NEWBORN WARDS FOR DETERMINATION THE FREQUENCY OF MIP GENE IN CONTAINED LEGIONELLA PNEUMOPHILA

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Background and aims: Water of incubators in newborn wards and water of respirators are main transferring source of legionellosis in hospitals. The mip gene is main virulence factor of legionella pneumophila. Aim of the present work was to study the frequency of mip gene in all legionella of water of newborn incubators in Guilan province hospitals.

Methods: Samples were collected directly in sterile containers and concentrated by centrifuge, then transferred to yeast extract broth containing L-cyctein, Fe^{2+}, Glycin, and vancomycin and incubated for 3-4 days. DNA was extracted using boiling-percipitation method and PCR was performed to investigate legionella and mip gene using two pair primers. By using universal primer 16S rRNA, contamination with other bacteria were investigated in all negative samples.

Results: About 11.1% of samples had Legionella pneumophila. One third of Legionella pneumophila had the mip gene. About 84.9% of negative samples showed bacterial contamination with universal primer 16S rRNA.

Conclusions: Present study indicate in spite of using stilled water for incubators, legionella pneumophila contamination is considerable but it seems that most of the bacteria are less pathogenic because frequency of mip gene is not considerable. In addition, other bacterial contamination is very high. It might be related to the length of time that water remains in incubator container which is a predisposing factor for biofilm formation.

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PALATIBILITY OF A NEW PAEDIATRIC FORMULATION OF VALACYCLOVIR

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Background and aims: Valacyclovir is available in tablets with doses that are too high for small children. Many children dislike the taste of the crushed tablets or are unable to swallow the tablets. We have developed a liquid formulation with three different flavours. An essential step in this process is palatability testing. The primary aim of this pilotstudy was to determine which formulation is accepted best in children. Also, it was determined whether parents could predict the palatability preference of their child.

Methods: Three extemporaneously prepared formulations (plain, orange or raspberry flavour) were presented in randomized order to children with primary immune deficiency or cancer, and one of their parents. A 100mm facial hedonic (VAS) scale was employed to indicate the palatability of each formulation. Also, a choice had to be made which of the formulations was most palatable.

Results: Eight children that participated in the study had evaluable results. VAS scores of the flavours were not significantly different (P>0.50). The mean VAS (SD) in children of respectively plain, raspberry and orange flavoured formulation were 38.4 (31.4), 33.3 (18.6) and 25.4 (17.9) mm.

Three children preferred the plain formulation, raspberry and orange was preferred by each two children, and one child was unable to choose. Two (25%) parents were able to predict the palatability preference of their child.

Conclusions: The palatability of the new valacyclovir formulation is low, even when flavours are added. Further research will be performed in another target population.

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SUCCESSFUL TREATMENT WITH SPLENECTOMY FOR HIV-RELATED THROMBOCYTOPENIA

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Background: Thrombocytopenia, alone or in association with anemia and/or leucopenia, is frequently seen in approximately 40% of HIV-infected patients in the course of their disease. We report on the case of a patient with acquired immune deficiency syndrome- and thrombocytopenia in which splenectomy was successfully used to be safe and effective in refractory to treatment of IVIG and steroid.

Case: A one-month old boy was referred to our hospital because of sepsis. He was diagnosed as HIV positive with a RNA copy number of 1,968,000 copy/mL and bicytopenia (anemia and thrombocytopenia) was treated with IVIG and HAART. In laboratory test direct Coombs negative, reticulocyte %2.7. During his follow-up he had CMV hepatitis in 1 year old and lung tuberculosis in 4 years old. IVIG therapy was intermittently received up to 8 years of age for thrombocytopenia. Then count of platelets persisted to 9000-20000 µ/L although IVIG therapy. We checked the patient for all etiology of secondary thrombocytopenia. Bone marrow aspiration was showed that megacaryocyts have increased. Metilprednizolon therapy was applied for 2 years. But count of thrombocyte persisted below 100000 µ/L. He had splenectomy at 10 years old. Count of platelets increased to 650,000 and there was no complication due to splenectomy. At last outpatient visit (11.5 years old) count of platelets was 480,000.

Conclusion: The most common cause of thrombocytopenia in HIV infection is HIV-related autoimmune thrombocytopenia, which is clinically indistinguishable from classic immune thrombocytopenia purpura. Splenectomy has proven to be safe and effective in refractory patients.

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BRUCELLOSIS OF THE CHILD IN CONNECTION WITH AN EPIDEMIC

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Summary: Human brucellosis is closely related to the animal infection, brucella reaches primarily the ruminants which are at the origin of the near total of the human contaminations.

The interest of the communication is to determine the atypie and the gravity of the clinical picture, as well as the antibiothérapie with good cellular diffusion.

Materials and methods: Retrospective study made on files of patient of: January 1st - December 31st, 2005.

Results: 18 cases were identified, with 80% having fever, 90% having sweats, 16cas have pains, 03 cases occurring in the ostéo-articular hemophiliacs with attack.

Conclusion: Brucellosis became increasingly frequent in the child, and it is necessary to know to pose the diagnosis in endemic zone in front of feverish pains.

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CUTANEOUS LEISHMANIASIS IN THE CHILD; ONE YEAR EXPERIMENT

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Summary: Leishmaniases, one of six (06) parasitosis which WHO regards as a world problem of public health. The cutaneous leishmaniasis is in resurgence in the world.

In ALGERIA: endemic disease in two of its forms:

- Very old L.C (nail of Biskra remained a long time contaminated to the steppe area (Biskra and Abadla)

- The area of the AURES beside Biskra is strongly touched by the epidemic with 11000 cases of 2004 - 2005 only the infantile population represents more than half of declared cases

Objective: To determine the frequency of the cases, as well as the impact on the clinical departments.

Material and methods: Retrospective study made on files of patients of January 2003 in December 2004 with recruitment of 139 cases.

Results:

- 57 cases hospitalization, with parenteral therapy.

- 82 Infiltrations.

- The wet form is most frequent.

- Relapse was found at 07 cases.

Conclusion: New areas located more at north of the usual hearths are touched.

- Is it about an extension of the vectorial surface? And why?

- It is of the extension and/or the pullulation of the animal tank?

- It is of a new animal tank or a crossing of the barrier of species?

- Is this the result of a climate change?

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EPIDEMIC OF TYPHOID FEVER 2004 FOR BATNA (ALGERIA)

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Summary: Disease of féco-oral transmission, the typhoid fever remains very narrowly dependant on the level of general hygiene of the country, and more particularly of the access a drinking water and of an adequate basic cleansing has

Objective: To determine the clinical profile in the child during an epidemic blaze.

Material and methods: Retrospective study made on files of patient during the epidemic.

Results: 73 cases were compiled with a rate bordering the 25% of the epidemic with a atypie bearing on the mode of installation, the signs functional, dissociation pulse temperature was found in 60% of the cases.

No digestive complication was noticed, in parallel of the rare complications retained and even exceptional such as: Bulbite 1 cases, PNA 2 cases were announced.

Conclusion: The found rate of 25% did not correspond to the awaited value, the atypie of the clinical picture (respiratory disorders, urinary disorder, fever insulated) must encourage the clinician in front of an epidemic blaze to evoke the diagnosis.

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THE MILD CLINICAL COURSE OF CHILDREN WITH CRIMEAN CONGO HEMORRHAGIC FEVER: CAN IT BE EXPLAINED BY CYTOKINE RESPONSE?

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Background: This study aimed to determine the differences between the cytokine levels of pediatric and adult patients with Crimean-Congo hemorrhagic fever (CCHF), the influence of cytokines, and the disease course which seems to be milder in children.

Material and method: Thirty-four children and 36 adult patients diagnosed with CCHF between 2010 and 2011 were included in this study. Diagnosis was performed serologically and/or by polymerase chain reaction for CCHF virus. IFN-γ, TNF-α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12 p70, IL-13, IL-17A, and IL-22 were determined in all the serum samples.

Results: Although the disease had a fatal course in 3 adult patients, there was no fatal outcome in children. No statistically significant differences were observed between the cytokine concentrations of the adults and children. No differences were detected between the serum cytokine levels of the children with moderate and severe clinical course of the disease. In the adult patients with fatal outcome, significantly higher serum levels of IFN-γ, IL-1β, IL-2, IL-5, IL-9, IL-12 p70, IL-13, and IL-22 were determined compared with cytokine levels of the patients who survived after the infection. No differences were detected between the serum IL-17A, IL-10, IL-6, IL-4 and TNF-α levels of the patients who died and those who survived after the infection.

Conclusion: The milder clinical course of children with CCHF could not be explained by only cytokine network. The uncompleted maturation of immune system and timing and scale of immune responses could change the outcome dramatically, particularly in acute viral responses.

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PLASMA OXIDATIVE STRESS AND TOTAL THIOL LEVELS IN CRIMEAN-CONGO HEMORRHAGIC FEVER

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Objective: In this study, we investigated the pro-and antioxidant status of patients with Crimean-Congo hemorrhagic fever (CCHF) in terms of their role in the pathogenesis of the disorder.

Methods: Between April 2010 and September 2011 with a diagnosis of 34 children and 41 adults were diagnosed with CCHF during the study period.The control group consisted of healthy children and adults matched for age and gender.Serum levels of total antioxidant capacity (TAC), total oxidant status (TOS), oxidative stress index (OSI) and plasma total thiol (TTL) were evaluated and compared between groups.

Results: The difference between CCHF patients and healthy controls in terms of mean TAC value was not statistically significant ($p>0.05$).Mean values for TOS, OSI and TTL were significantly lower in CCHF patients compared to healthy controls ($p< 0.001$ for all). Following two-group comparisons, no difference in TAC was observed between groups ($p>0.05$), whereas mean TOS and OSI values were significantly lower in adults with CCHF compared to their healthy counterparts ($p< 0.001$ for both comparisons).Similarly, mean TTL levels were lower in both children and adults with CCHF when compared separately with healthy controls ($p< 0.05$ for both comparisons).There was no difference between children and adults with CCHF with regard to mean TTL levels ($p>0.05$).

Conclusions: Our study results suggest that TTL may play a more important role in the pathogenesis of CCHF than the other parameters investigated. As a surprising finding in this study, mean TOS and OSI values were higher in the control group compared to CCHF patients.

RESPIRATORY VIRAL ETIOLOGY OF INFLUENZA-LIKE ILLNESSES DURING THE INFLUENZA SEASON BETWEEN DECEMBER 2011 AND APRIL 2012

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Background: The aim of this study was to determine the frequency of respiratory viruses responsible for respiratory tract infections during the 2011-2012 influenza season.

Methods: Nasal swabs were obtained from patients with symptoms suggestive of an influenza-like illness (ILI) between December 2011 and April 2012.Specimens were evaluated by RT-PCR to help identify the causative viral pathogen.Participants were followed-up for 10 days after initial presentation, and information regarding clinical course of illness was recorded.

Results: A total of 200 patients with ILI were enrolled in the study. A respiratory virus was successfully detected in 102 (51%) children;influenza A H3N2 in 39.2%,influenza B in 23.5%,RSV in 15.6%,rhinovirus in 13.7%,bocavirus in 2.9%,coronavirus in 2.9% and metapneumovirus in 0.9% of patients. A statistically significant difference in mean age of presentation was observed between the various viral pathogens ($p < 0.001$). Patients with RSV were significantly younger whereas children infected with the influenza viruses were significantly older. Comparison of symptoms revealed fever and headache to occur more frequently with the influenza viruses compared to the other viruses combined ($p < 0.001$ and $p < 0.05$,respectively), whereas durations of symptoms such as fever, cough, nasal congestion and rhinorrhea were also significantly longer in the influenza group ($p < 0.001$,$p < 0.005$,$p < 0.001$,$p < 0.005$,respectively). Only school/daycare attendance was found to be associated with a significantly increased risk for influenza infection.

Conclusion: With an overall viral pathogen detection rate of 51%, findings of our study suggest other respiratory pathogens may also result in hospital visits due to ILI in children during influenza season.

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ABSOLUTE EFFECTIVENESS OF ACELLULAR PERTUSSIS VACCINE AND RELATIVE EFFECTIVENESS IN COMPARISON TO WHOLE-CELL VACCINE DURING EPIDEMIC YEARS IN QUEENSLAND, AUSTRALIA

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Background and aims: In Queensland, Australia, 2009-2011 were epidemic years for pertussis with notification rates highest in late childhood. Peak notifications coincided with the first birth cohorts primed with acellular pertussis vaccine, which replaced whole-cell pertussis vaccine in 1999. We investigated the relative effectiveness of acellular to whole-cell pertussis vaccine by comparing notification rates of children born in 1998, primed with either, or a mixture of, acellular and whole-cell pertussis vaccine. We also assessed acellular pertussis vaccine effectiveness (VE) against hospitalisation and notification in Queensland children in 2009 and 2010.

Methods: Queensland notification, hospitalisation and vaccination register data were linked.

Among children born in 1998, notification rates during 2009-2011 were calculated by receipt of ≥3 doses of either purely acellular, purely whole-cell, or mixed pertussis vaccine, before the first birthday.

VE was calculated using the screening method, for 3, 4, or 5-doses of pertussis vaccine among children aged 1-3, 5-7, and 7-11 years, respectively, by year of birth. Population vaccination coverage figures were provided from the Australian Childhood Immunisation Register.

Results: Notification rates were higher in children primed with acellular compared to whole-cell pertussis vaccine: IRR 3.29 (95%CI:2.44-4.46).

VE point estimates against hospitalisation and notification in 1 to 3-year-olds were 84%-89% in 2009 and 2010. VE point estimates against notification among 5 to 11-year-olds were 71%-88% in 2009, and 36%-71% in 2010.

Conclusions: Although less protective than whole-cell vaccine, acellular pertussis vaccine provided very good protection against pertussis in 1 to 3-year-olds, and, generally, good-to-moderate protection in 5 to 11-year-olds.

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ENGINEERED LACTOBACILLUS RHAMNOSUS GG CAPTURING ROTAVIRUS-SPECIFIC HYPERIMMUNE BOVINE COLOSTRUM ANTIBODIES PROTECT AGAINST DIARRHEA IN AN INFANT ROTAVIRUS INFECTION MODEL

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Background and aims: Rotavirus-induced diarrhea cause more than 500,000 deaths annually in the world and new effective treatment strategies should be considered due to the partial protection of current therapies in developing countries. Purified antibodies derived from hyperimmune bovine colostrum (HBC) of cow immunized with rotavirus were previously used for treatment of rotavirus diarrhea in children. A combination of HBC antibodies and the probiotic strain of Lactobacillus rhamnosus GG (LGG) was also found to be more effective than HBC alone in reducing diarrhea in a mouse model of rotavirus infection. In order to further improve the treatment, LGG was engineered to display IgG-binding domains of protein G which capture HBC-IgG antibodies and target rotavirus.

Methods: The expression of IgG-binding domains on the surface of LGG, their binding activity to HBC-IgG and to rotavirus (simian strain RRV) was assessed by western blot, flow cytometry and EM. The prophylactic activity of modified LGG and HBC was evaluated in the neonatal mouse model of RRV infection.

Results: Efficient binding of modified lactobacilli to HBC and rotavirus was observed. Compared to HBC alone or a combination of wild type LGG and HBC, a combination of LGG expressing IgG-binding domains and HBC was significantly more effective in reducing the prevalence, severity and duration of diarrhea.

Conclusions: The combination therapy with engineered LGG and HBC reduces the effective dose of HBC by nearly 100-fold and could decrease treatment costs considerably. This antibody capturing platform strategy could also be used to target other gastrointestinal pathogens.

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PERSISTENCE TO 12, 18 AND 24 MONTHS OF BACTERICIDAL ANTIBODIES INDUCED BY INFANT IMMUNISATION WITH A SEROGROUP B MENINGOCOCCAL VACCINE

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Background: We evaluated the persistence of antibodies beyond 12 months of age following infant immunisation with 4CMenB (a serogroup B meningococcal vaccine recently recommended for European licensure).

Methods: In this follow-on study, children previously receiving 4CMenB at 2, 4, 6 or 2, 3, 4 months of age with routine vaccines (M246R and M234R, respectively) and without routine vaccines (M246), received 4CMenB at age 12, 18 or 24 months. 4CMenB-naive controls received 4CMenB at 12 and 14, 18 and 20 or 24 and 26 months. Serum bactericidal activity was determined before and one month after each immunisation using human complement (hSBA, protective correlate ≥1:5).

Results: At 12 months, prior to any booster doses, 116/157(74%: 95% CI 66%-81%) of the M246R group had hSBA ≥ 1:5 for strain H44/76 compared to 121/143 (85%: 78%-90%) for M246, 50/87 (57%: 46%-68%) for M234R and 25/199 (13%: 8%-18%) for controls. For 5/99 these proportions were ≥ 95% for all 4CMenB recipients compared with 1% for controls. For NZ98/254 these were 21% for M246R, 19% (M234R), 35% (M246) and 1% for controls. By 24 months these proportions in 4CMenB recipients were 11% - 21% for H44/76, 83% - 96% for 5/99 and 7-9% for NZ98/254, and in control participants were ≤4%.A booster dose of 4CMenB resulted in ≥ 97% of participants having hSBA ≥1:5 for H44/76 and 5/99, and 77%- 97% for NZ98/254.

Conclusions: A booster dose of 4CMenB is required to maintain elevated hSBA titres. The persistence of the post-booster hSBA increase is being evaluated.

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ANTIBODY RESPONSE OF VARICELLA-ZOSTER VIRUS FOR POSTEXPOSURE VACCINATION IN 6 TO 11 MONTH-OLD INFANTS

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Background: Varicella continuously occurs in epidemics among children in Japan from the low Varicella-Zoster Virus (VZV) vaccination coverage at 30-60%. VZV exposures in hospital are problematic for infection control. The postexposure prophylaxis is vaccine administration within 72 hours in immunocompetent children, however little is known regarding to the efficacy in infants. Our aim of study is to evaluate the postexposure vaccine efficacy in 6-11 month-old infants.

Method: We included immunocompetent infants exposed to VZV in wards at Tokyo Metropolitan Children´s Medical Center from March 2010 to June 2012. We administered Oka strain VZV vaccine in ≧6 month-old for prophylaxis. We prospectively registered the 6-11 month-old infants and evaluated VZV IgG titers with Enzyme Immunoassay at >1 month from vaccination. We interpreted the values according to manufacturer's definitions; negative as < 2.0, indeterminate as 2.0 to 3.9, and positive as ≧4.0.

Results: Twenty eight infants received VZV vaccination in 24 occasions of VZV exposures in hospital. Of those, 17 infants had VZV-IgG measurement. Eleven Infants (64.7%) had positive titers ranging between 4.3 and 17.8 (median 5.8). Four infants had indeterminate titers and two infants had negative titers. No infants developed VZV diseases.

Conclusion: The seroconversion occurred at 64.7% in the 6- 11 month-old infants. It was lower than 80-85% reported in ≧12 month-old children. However, no infants developed VZV diseases subsequently. VZV vaccine might be a choice for exposed children who are ≧ 6 month-old.

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CMV-RELATED MILLER FISHER SYNDROME AND CD4+ LYMPHOCYTOPENIA REVEALING RAG1 HYPOMORPHIC IMMUNODEFICIENCY IN A 1 YEAR OLD CHILD

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Introduction: In the last years several genes responsible of Severe Combined Immune Deficiency (SCID) have been described. Mutations in recombination activating genes (RAG1 and RAG2) are well known to cause T-cell-B-cell-SCID and Omenn-syndrome. Hypomorphic mutations allow residual function and thus partial T/B-cell differentiation resulting in highly variable clinical phenotype.

Case: AD is 1 year old child presenting with a 4-days history of progressive ascending paralysis. The neurological examination showed axial hypotonia, absent tendon reflexes in the lower limbs, ptosis and ophthalmoplegia. For the deterioration of clinical conditions a respiratory support with a continuous positive airway pathway was started. Laboratory-tests showed: hypergammaglobulinemia, hypertransaminasemia, normal total lymphocyte, CD8+, NK and CD19+, low CD4+(4%;80#;CD45%RO/RA=3.3/0.1) and expansion of TCRγδ-T-cell population. HIV,HHV6, HHV8, toxoplasma, EBV, enterovirus, flavivirus, parvovirus, flebovirus and TBC resulted negative. Cytomegalovirus(CMV) IgM/IgG were positive and were confirmed by PCR (sera/blood=2071/85750cp/mL).

Cerebral Magnetic Resonance Imaging showed impregnation of cranial nerves and mild impregnation of the optic chiasm leading to diagnosis of Miller-Fisher-Syndrome. Combination therapy with Ganciclovir, immunoglobulin and corticosteroid was started. Considering the severe CD4+penia associated with CMV-infection, RAG1-mutation was suspected and genetic analysis revealed a homozygous mutation (c.368_369delAA;p.K86fsX118). According to autoimmune phenotype, in order to control autoreactive B-cells, several plasmaferesis cycles and once weekly anti-CD20-antibodies were started with a progressive improvement of the general conditions.

Conclusions: This case points out the high variability of the clinical presentation of hypomorphic RAG1-mutation, therefore, diagnosis of SCID should not be excluded in a context of normal B-cells or if the ability to form antibodies is preserved.

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KNOWLEDGE OF TURKISH FEMALE UNIVERSITY STUDENTS ABOUT HPV INFECTION AND HPV VACCINATION

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Background and aims: Female students are supposed to have sufficient knowledge about HPV infection and HPV vaccination because they are in the risk group for HPV infection and the related complications. This study was descriptively conducted in order to determine knowledge of female university students about HPV infection and HPV vaccination.

Methods: This study was conducted with 380 female students of Bozok University, Yozgat, Turkiye during September-December 2012. All of the female students were informed verbally and they participated voluntarily. A questionnaire was used to collect data. Percentage distributions and Chi-square test were used to evaluate data.

Results: Mean age of the participant students was 20.17±1.84. It was found out that 60.0% of students had an income equal to expenses, 49.2% lived city center most and 56.3% stayed at public university dormitories.

It was discovered that 59.5% of the students did not hear about HPV infection, 72.4% did not know how HPV infection was transmitted, 90.0% did not know health problems caused by HPV infection, 23.4% heard about HPV vaccination but nearly all of them did not have HPV vaccination.

In this study, there was statistically significant difference between mothers' educational level, school, class and living-place, and HPV infection and HPV vaccination; and between transmission ways, knowing probably health problems and wish to have vaccination ($p < 0.05$).

Conclusions: In light of our study results, it was determined that female students did not have sufficient knowledge about HPV infection and HPV vaccination.

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CLADOPHIALOPHORA BANTIANA PHAEOHYPHOMYCOSIS WITH PULMONARY AND CEREBRAL DISEASE IN A PAEDIATRIC PATIENT WITH IDIOPATHIC RETROPERITONEAL FIBROSIS. A CASE REPORT

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Background: Cladophialophora bantiana phaeohyphomycosis is associated with potentially fatal cerebral infections but can also involve other sites. Both healthy and immunocompromised human hosts can be affected and prompt treatment with antifungal therapy is needed to affect a cure. Despite treatment, the outcome can be poor.

Method: Case report of a paediatric patient with idiopathic retroperitoneal fibrosis and pulmonary and cerebral Cladophialophora bantiana phaeohypomycosis.

Results: A 12 year old boy with idiopathic retroperitoneal fibrosis and previously treated aspergillius lung infection and cytomegalovirus viraemia presented with 3 week history of fever, cough and haemoptysis. He was on prophylactic Voriconazole and Valganciclovir with oral Prednsiolone at the time. Brownish- black sputum was obtained on review and fungal elements were noted on microscopy. Liposomal Amphotericin was added for the presumed recurrence of Aspergillus. Intravenous Teicoplanin and Ceftriaxone were also commenced when Actinomyces odontolyticus was cultured. He subsequently developed left sided weakness from a right sided cerebral lesion, confirmed on neuroimaging, that was suggestive of infection. By this time, initial sputum culture confirmed Cladophialophora bantiana, thus treatment was adjusted to Posaconazole , with intravenous Micafungin and Liposomal Amphotericin. This was later converted to oral Flucytosine and Posaconazaole. After 18 months of treatment, there is clinical improvement but with residual neurological and respiratory sequelae.

Conclusion: Cladphialophora bantiana is a rare cause of cerebral and pulmonary fungal infection. This report illustrates a rare paediatric case with phaeohyphomycosis caused by this organism and its successful treatment using a prolonged course of multiagent antifungal therapy.

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IMPLEMENTING ISONIAZID PROPHYLAXIS IN CHILD-CONTACTS OF ADULT TUBERCULOSIS CASES IN A DEVELOPING COUNTRY SETTING

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Background and aims: Although WHO universally recommends Isoniazid (INH) prophylaxis for children under-5 exposed to adults with sputum smear positive tuberculosis (TB), this is generally not being done in resource-poor settings. In 2012, a TB Reach grant enabled us to assess feasibility of INH prophylaxis. We describe the associated challenges and opportunities in our West African setting.

Methods: Contact tracing was conducted in households of consenting adult smear positive TB cases. All symptomatic and / or TST positive (≥10mm) children were evaluated at the childhood TB clinic of the Medical Research Council, The Gambia. All children < 5years without TB disease received INH 10mg/kg daily for 6 months, administered by primary care-givers (mainly mothers). Adherence to prophylaxis was monitored monthly from October in a randomly selected sample of children using the urine Isoscreen method.

Results: Of 1014 child contacts seen, 409 (40.3%) were < 5 years of age. By December 2012, 318 (77.8%) of these had been placed on INH and 168 children had completed prophylaxis. Adherence increased from 54.9% in October to 73.7% in December. 1 child died of confirmed malaria while on prophylaxis and 5 children dropped out as their parents moved from study areas. None of the children on INH has been diagnosed with active TB disease so far.

Conclusion: This ongoing study shows that Isoniazid prophylaxis in vulnerable child contacts can be implemented in a resource-poor country, but additional resources to National TB programs would be required. Mothers play a major role in ensuring adherence.

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EFFICACY AND SAFETY OF VALGANCICLOVIR ORAL THERAPY FOR CONGENITAL CYTOMEGALOVIRUS INFECTION: PRELIMINARY DATA

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Background: Congenital cytomegalovirus is the leading non-genetic cause of sensorineural hearing loss in childhood. Symptomatic infections have been typically treated with iv ganciclovir. Nowadays valganciclovir is available as oral syrup and its use for the prevention of cytomegalovirus-related sequelae in asymptomatically infected newborns is growing. However, its best use is still controversial.

Aims: prospective evaluation of the efficacy of a personalized valganciclovir treatment on cytomegalovirus viral load in blood, urine and pharynx, hearing function and its side effects.

Methods: valganciclovir syrup 15 mg/kg bid for 6 weeks was administered to all newborns and repeated if blood viral load returned positive during the first year of life.

Results: 22 newborns with cytomegalovirus infection were enrolled. 68% children needed more than one course of valganciclovir therapy to have a persisting negative blood PCR. Newborns with a pre-treatment blood viral load of < 1000 copies/ml needed only one course of valganciclovir, those with pre-treatment blood load of 1000 to 10000 and > 10000 copies/ml needed a third cycle in 50% and 67% cases (p 0.01).

Neutropenia developed in 16% of all cycles (nobody reached less than 500/dl) and more frequently in children with higher blood cytomegalovirus load (p 0.44) and in children who underwent more treatment courses (p 0.07).

None showed worsening of the baseline hearing function and no new late-onset hearing-loss were detected.

Conclusions: The tolerability of oral valganciclovir along with its poor microbiological control when administered for six weeks, should advice us to think for longer/personalized treatments.

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UNDERSTANDING PARENTAL ACCEPTANCE OF A NOVEL MENINGOCOCCAL SEROGROUP B VACCINE FOR INFANTS

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Background: N. meningitidis serogroup B (MenB) is responsible for the majority of invasive meningococcal disease (IMD). A novel MenB vaccine may soon be licensed.

Objectives: To assess parental concerns, intention to vaccinate, and determinants of intention to vaccinate their infant with novel MenB vaccine.

Methods: Parents of infants aged 2 to 6 months, presenting for scheduled “healthy-baby visits,” were interviewed before and after physician interaction during which information about IMD and MenB vaccine was provided. Parents responded to measures of spontaneously elicited beliefs concerning positive and negative aspects of infant immunization, and the new MenB vaccine, sources of social support for vaccinating their infants with MenB vaccine, knowledge about IMD and MenB vaccine, and direct measures of attitudes, social, and physician support, and intention to vaccinate their infant with MenB vaccine.

Results: Parents' (N = 115 at 19 Canadian clinics) baseline knowledge of IMD and MenB vaccine was low but increased significantly following the physician visit. Parents' attitudes and perceptions of social and physician support for MenB vaccination strongly predicted their intentions to vaccinate their infants with the new vaccine, Rmult = .81. The majority of parents intended to vaccinate their infants with MenB vaccine. Neither number of injections nor the vaccine adverse event profile influenced intentions, but price of the vaccine had a negative impact on intentions to vaccinate.

Conclusions: Parental attitudes, perceptions of support from significant others, and perceptions of physician support strongly predict parent´s' intentions to immunise their infants with a novel MenB vaccine.

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RESPIRATORY VIRUSES IN PEDIATRIC ONCOLOGIC PATIENTS WITH FEBRILE NEUTROPENIA

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Introduction: Pediatric oncologic patients with neutropenia and fever frequently do not have etiologic agents determined. Viral infections are the most comon cause for fever in healthy subjects. In this study we search for respiratory viruses in upper airway samples of pediatric oncologic patients admitted due to fever and neutropenia. In our hospital there is no risk stratification and all patients are admitted to the hospital.

Methods: We have included pediatric oncologic patients admitted to the hospital with fever and total neutrophil count lower than 500/mm3 or lower than 1000/mm3 with expected decrease in the next two days. From those patients we collected nasal and oropharyngeal swabs, and also a saliva sample. These samples were tested for respiratory viruses with RT-PCR, using the FTD respiratory 21 multiplex kit.

Results: We have included 16 patients with a total of 23 febrile neutropenia episodes. Respiratory viruses were found in 8 (34,7%) of these episodes, mostly through nasal swabs (87,5%). Coronaviruses were the most comon viruses found, present in 7 episodes (87,5%). The viruses found included Coronavirus OC43, (3 cases), Coronavirus 229E (5 cases), Coronavirus NL63 (2 cases), Parainfluenza 2 (1 case), Rhinovirus (1 case) and SRV (1 case). There was viral coinfection in 4 episodes. Only in 3 episodes the patients had respiratory symptons.

Conclusion: Respiratory viruses are definetly to be considered when determining the cause of fever in pediatric oncologic patients with neutropenia, but they can also be found in asymptomatic subjects.

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DEWORMING OF CHILDREN AT DEPLOYED MILITARY HEALTHCARE FACILITIES: AN OPPORTUNITY NOT TO BE MISSED?

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Introduction: Soil transmitted helminths (STH) affect over 1 billion people, and infection is more common in areas of conflict. Despite recent controversy about the benefits of mass deworming, the World Health Organization (WHO) advocates mass anti-helminthic treatment of school-age children in areas of high prevalence. STH prevalence in Afghanistan is 20% - 50%, but a high proportion of children do not attend school, and are missed by deworming programmes. The WHO encourages programme managers to find innovative means of reaching those in need. Deworming children must reach beyond a school-based approach to exploit all opportunities.

Discussion: The primary function of military medical facilities in a theatre of war is to provide life, limb and eyesight-saving treatment. Additional humanitarian aid in the form of non-emergency treatment has also been provided in Afghanistan for thousands of civilian children. Furthermore, children represent 3% - 15% of the patients treated at deployed military medical facilities. We report recent experience of deployed multinational surgical teams in Afghanistan who noticed high levels of STH in combat casualties. Military medical facilities may provide an opportunity to integrate a policy of deworming of children into existing humanitarian support. Treatment is inexpensive, simple, and has a very small risk of harm, presenting a compelling case for deworming those unfortunate enough to require humanitarian care at deployed facilities. As military bases hand over control to Afghan personnel, the continuity of healthcare to the local communities could be enhanced by the education and training that will result from this legacy.

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NEUTRALIZING ANTIBODY TITERS AGAINST JAPANESE ENCEPHALITIS VIRUS ABOVE 15 YEARS OLD IN KOREA: A PROSPECTIVE MULTICENTER STUDY

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Background and aims: Japanese encephalitis(JE) patients with JE have been reported intermittently in adult. Therefore, reliable data on the neutralizing antibody titers above 15 years old in Korea are required through a prospective study.

Methods: The 1,603 specimens were collected from clinically healthy adolescent and adult above 15 years old in five geographically distant hospitals in Korea, prospectively. We measured the neutralizing antibody(NTAb) values by pseudotyped virus test(PVs). To verify that PVs and plaque reduction neutralization test (PRNT) were associated, we performed linear regression analysis using boostrapping. We also compared geographical differences of NTAb values statistically using ANOVA and Holm-Bonferroni method.

Results: NTAb titers equal or greater than 1:50 were considered to be positive in the PVs method. The JE antibody-positive population was more than 95% for ages the age of 15 to 29 years, gradually began to decrease for the age of 30 to 44 years, then 75.24% for the age of 55 to 59 years, 80.82% for the age of 65 to 69 years, and 59.77% above 70 years old. In geographical NTAb results, the highest titer in Seoul population was reported among all age groups.

Conclusions: Positive rate and titer values for NTAb tests revealed appropriate levels for all age group above 15 years old. But, there is constant need for consecutive study of NTAb titers against JE virus and continuous surveillance for JE cases so as to determine proper immunization schedule.

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EPIDEMIOLOGY CHARACTERISTICS OF CHICKENPOX HOSPITALIZATIONS IN CHILDREN´S HOSPITAL IN PERU, 2001-2011

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Objective: To determine the epidemiology of chickenpox hospitalizations in the National Institute of Child Health in Peru from 2001 to 2011.

Design: Case series were studied hospitalizations for chickenpox treated at the National Institute of Child Health (INSN) in Peru, a country without vaccination against this routinely infection, we identified patients who were discharged or diagnosed with chickenpox deaths according data from statistical office.

Results: We had studied 1566 children hospitalized for chickenpox, with an average of 142 patients per year, with the median age 2 years 6 months, 46.4% (727/1466) were female, the median hospital stay was 6 days (IQR: 9.4). The most affected group was 0 to 2 years corresponding to 55% (864/1566). We could take note there were many continuously cases, with a seasonal distribution in the frequency curve for months, with an increasing trend annually. Cases of chickenpox with some complication were 68.5% (1073/1566). The deaths accounted for 0.8% (12/1493) this corresponds to a rate of 0.3 deaths per 100,000 people. We would suggest researching to value effectiveness cost of the chickenpox vaccine introduction in the national immunization schedule.

Key findings: Hospitalizations for chickenpox in the INSN is a major cause of morbidity with a seasonal trend, being more frequent since November to February, with a tendency to increase annually, moreover it represents a significant economic burden.

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CHARACTERISTICS OF PNEUMONIA IN CHILDREN HOSPITALIZED FOR INFLUENZA AH1N1/2009 PANDEMIC, PERÚ

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Objective: Determine the clinical and demographic characteristics of pneumonia caused by influenza virus pandemic AH1N1/2009 in the Institute National Children.

Methods: Retrospective case series in children hospitalized for influenza pneumonia pandemic AH1N1/2009 in pediatric hospital. Reviewed the medical records between the months of June to September 2009. All cases had virological confirmation, we describe the clinical characteristics and conditions of severity. Compared with negative pneumonia influenza pandemic AH1N1/2009.

Results: A total of 74 children with influenza pneumonia AH1N1/2009 pandemic, of those 50 were community acquired pneumonia (CAP) and 24 were pneumonia nosocomial (NN), 16 required mechanical ventilation. There were 12 deaths, all had preexisting factors. The NN had statistical association with mortality. Pre existing factors were frequent malnutrition, respiratory infections, congenital heart disease and neurological deficits.

The cases NAC were under 6 years accounted for 72%. The most frequent symptoms were fever, cough, runny nose. Received oseltamivir 82%. Protein c reactive (PCR) more than 10mg/L was significantly associated with respiratory failure ($p < 0.05$).

Fever and lymphopenia were associated factors of the NAC by influenza AH1N1/2009 pandemic compared with other pneumonias.

Conclusions: The results of this study show that fever and lymphopenia are associated with NIV-p; There is an increased risk of death among cases NVIp-NN, The high PCR and presentation of pre-existing condition is associated with severe NVIp-NAC, we suggest prospective studies to confirm the results.

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MATERNAL ATTITUDES AND FACTORS INFLUENCING PERTUSSIS BOOSTER VACCINATION TO NEW MOTHERS ON THE POSTNATAL WARD

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Background/aims: Cocooning aims to protect vulnerable infants from pertussis by vaccinating caregivers. Health message framing is a novel intervention strategy we used to promote postpartum vaccine uptake. We sought to describe maternal attitudes towards pertussis and perinatal vaccination at baseline as well as identify factors influencing vaccine acceptance and completion.

Methods: Subjects were recruited in an Australian public postnatal ward. They completed a paper-based knowledge and attitudes baseline questionnaire in English. Sequential block allocation by week was used to allocate the interventions (gain or loss-framed pamphlet) or control (government Pertussis fact-sheet). Subjects were then offered a free Pertussis vaccination (dTpa), given by midwives if accepted. A short follow-up questionnaire was completed prior to discharge. Women unable to give written informed consent were excluded.

Results: 1080 (77%) of the 1404 mothers enrolled (November 2010-July 2012) did not meet the current Pertussis immunisation recommendation (dTpa < 10years). Pertussis vaccine uptake was 70% (754/1080), with 'Loss' framing promoting a non-significant increase in coverage (72% vs. 69 % vs. 69%, P=0.624). Vaccination was associated with perceived vaccination benefits (OR1.61, P< 0.0001), baseline intention to be vaccinated (OR2.33, P< 0.0001) and pertussis vaccination recommendation (OR1.62; p=0.03). Influential factors at follow-up included: protecting the newborn, vaccine recommendation, family/friends, pertussis awareness, and convenience.

Conclusion: In the largest known perinatal attitudinal survey, strategies to encourage provider recommendation and promoting Pertussis vaccination benefits may increase postpartum uptake. Further analysis of framing effect on vaccine uptake may indicate sub-groups where this communication method is effective for clinicians to implement.

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OBSTACLES FACTORS FACING ADEQUATE TUBERCULOSIS TREATMENT IN CHILDREN LIVING IN A DEVELOPING COUNTRY: A HOSPITAL-BASED STUDY

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Background and aims: Despite availability of antituberculosis treatment and application of Directly Observed Treatment Short-course (DOTS) strategy, default in tuberculosis (TB) treatment is still a problem, especially in TB high-burden countries. Defaulted TB treatment in children has not been much studied and reasons may likely be different. The aim is to determine factors influencing defaulted TB treatment and describe its reasons.

Methods: This retrospective cohort study was performed based on 1,350 documented TB in pediatric DOTS registry from January 2009-June 2012 in Hasan Sadikin General Hospital. We contacted by phone to parents of 102 identified defaulted TB treatment. Documented data covered the age, sex, distance of the patient's dwelling to hospital, payment methods, type of TB, and antituberculosis formula given. Chi-square analysis was performed to determine influencing factors of defaulted TB treatment with $P< 0.05$.

Results: Of the 102 parents of identified defaulted TB treatment consisting of 43 (44%) girls and 54 (55%) boys with median age 60 months presented with pulmonary TB (85%), there were five children who had completed TB treatment at their nearest health facility. Defaulted rate was 7.5%. The general problems encountered was financial (22.7%), time clash of working parents (16.5%), and far dwelling (16.5%). Far dwelling ($P=0.027$) and single drug formulations ($P=0.001$) are the significant factors influencing defaulted treatment.

Conclusions: Problems encountered in TB control may likely be different among countries as we find the urge to take into account using TB-9 form and fixed dose combinations.

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COMPARISON OF VIRUS SHEDDING AFTER VACCINATION WITH LIVED ATTENUATED HUMAN ROTAVIRUS VACCINE AND PENTAVALENT HUMAN-BOVINE REASSORTANT ROTAVIRUS VACCINE

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Background: Transmission of rotavirus vaccine or vaccine-reassortant strains to unvaccinated contacts has been reported. Therefore, it is essential to evaluate and characterize the nature of vaccine-virus shedding among rotavirus vaccine recipients.

Material and methods: Two groups of healthy infants who received a complete course of RotaTeq or Rotarix were enrolled (between March 2010 and June 2011) to compare fecal shedding for one month after each vaccine dose. Shedding was assessed using both enzyme immunoassay (EIA) and real-time reverse transcription-polymerase chain reaction (RT-PCR).

Results: Eighty-seven infants (34 girls and 53 boys) were enrolled in the study. After the first vaccine dose, the peak time of virus shedding occurred between day 4 and day 7, with positive detection rates of 80-90% by real-time RT-PCR and 20-30% by EIA. The shedding rate detected by real-time RT-PCR was higher than that detected by EIA. Mixed effects logistic regression analysis of real-time RT-PCR data showed no significant differences between infants receiving RotaTeq and Rotarix when shedding rates were compared after the first vaccine dose (P=0.71) or after the second vaccine dose (P=0.99). However, infants receiving Rotarix shed significantly higher viral loads than those receiving RotaTeq when compared after the first vaccine dose (P=0.001) and after the second dose (P=0.039).

Conclusions: In terms of shedding rates detected by real-time RT-PCR, vaccine uptake of RotaTeq or Rotarix among infants in Taiwan was comparable. Clinical significance of higher shedding viral loads in Rotarix should be further observed.

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EPIDEMIOLOGY OF RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN IN CYPRUS DURING THREE CONSECUTIVE WINTER SEASONS (2010-2013)

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Background and aims: Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections among infants and young children. The aim of the present study was to determine the epidemiology of RSV infection in paediatric patients over three winter seasons in Cyprus (November 2010 to March 2013).

Methods: 391 nasopharyngeal swabs were collected from children diagnosed with respiratory infections and tested for the presence of 15 respiratory viruses using Real-time RT-PCR. Furthermore, RSV-positive samples were subjected to sequencing of the second hypervariable region of the G gene in order to genotype individual RSV isolates.

Results: RSV was detected in 96 samples as a single pathogen and in further 32 samples as a co-infecting pathogen in multiple infections along with other respiratory viruses. The age distribution of RSV positive children was: < 1 month 11 (8.6%); 1-3 months 32 (25.0%); 3-6 months 24 (18.8%); 6-12 months 17 (13.3%); 12-18 months 13 (10.2%); 18-24 months 9 (7.0%); 24-36 months 7 (5.5%); >36 months 15 (11.7%). Typing of RSV isolates revealed that during the first winter season of the study (2010-2011), the only RSV subtype circulating was GA2, which was subsequently replaced by subtype BA in the next winter season (2011-2012) with only few sporadic cases of GA2. The newly emerged RSV subtype ON1 was the only subtype circulating during the last winter season of the study (2012-2013).

Conclusions: RSV is a major cause of lower respiratory tract infections in children younger than 2 years old, predominantly in winter and early spring. Active epidemiological surveillance is important to monitor the pathogenicity of circulating subtypes and to update epidemic preparedness and response plans accordingly.

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CAPSULAR TYPES OF EXTENDED-SPECTRUM B-LACTAMASES PRODUCING KLEBISELLA PNEUMONIAE STRAINS FROM PEDIATRIC PATIENTS

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We collected 64 Klebisella pneumoniae strains isolated from blood or CSF of pediatric patients. Among them, twenty-one were extended-spectrum β-lactamases (ESBL)-producing strains. Capsular types of the ESBL-producing strains were determined by a new bacteriophage/enzyme typing system. The results revealed that two strains were K17, and eight strains belong to K2, K12, K16, K23, K28, K30, K47 and K62. The remaining eleven untypable strains were probably to be four new types and 8 of them belong to the same capsular type (KN2). Therefore, we found that 8 of the 64 ESBL-producing K. pneumoniae strains from pediatric patients belong to a new type KN2 which could be a prevalent type in ESBL-producing strains.

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ROTAVIRUS VACCINATION COVERAGE AMONG INFANTS IN FLANDERS (BELGIUM) IN 2012

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Background and aims: The Belgian Superior Health Council (SHC) recommended rotavirus vaccination in October 2006. Both vaccines (Rotarix™ and RotaTeq™) are partially reimbursed. Through a retrospective survey (2012) we estimate the coverage rate of the rotavirus vaccination in Flanders among infants born in 2010.

Methods: Through a randomized cluster design 946 toddlers were selected from 125 clusters assigned to 105 municipalities in Flanders. After consent of the parent(s), we interviewed 874 (92.4%) families at home. The requested information included demographic characteristics, socio-economic background and documented vaccination history (with update through medical files and vaccination database). Predictive factors for vaccination status were identified through multiple logistic regression. Adherence to official (SHC) age at vaccination recommendation was also assessed (8-12-16 weeks of age).

Results: The coverage rate for 2 doses rotavirus vaccination was 92.2% (95% CI: 90.2-93.8). Only 8 (1 %) children were vaccinated after the permitted 26 weeks of age. In 57.3% of the vaccinated children, there was a late start regarding the administration of the first dose (i.e. at age 9 weeks or later). Incomplete vaccination was often a deliberate choice of the parents.

The following factors were identified as being related with incomplete vaccination: living in the province of Antwerp, unemployed mother, 3 or more older siblings in the household.

Conclusions: Surprisingly very high coverage rates were found for a vaccine not free of charge, already 4 years after recommendation, but was lower compared to other recommended infant vaccines, offered free of charge.

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2006-2012: FOLLOW-UP OF PERTUSSIS PAEDIATRIC SURVEILLANCE, IN PRIVATE PRACTICE, IN FRANCE

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Background and aims: Between 1966 and 1998, French children received a primary-vaccination and one booster with an efficacious pertussis whole-cell (Pw) vaccine. The duration of protection of this vaccine strategy was estimated to be around 10 years. In 1998, a second booster at 11-13 years of age was introduced with pertussis acellular (Pa) vaccines. Between 2002 and 2006 surveillance in private practice (ACTIV) confirmed this duration of protection. However, Pa vaccines replaced totally Pw vaccine in 2005. ACTIV surveillance continued in order to evaluate the duration of protection induced by Pa vaccines.

Methods: Paediatrician´s enrolled children suspected of pertussis and completed standardized questionnaire. Biological confirmation was obtained using specific Bordetella pertussis, B. parapertussis and B. holmesii diagnosis.

Results: Completed questionnaires and biological diagnoses were obtained for 228 children over 292 enrolled by 64 paediatricians, between 2006 and 2012 (78% instead of 59% during the first period). Pertussis was confirmed for 70 children, parapertussis for 6 children and bordetellosis for 43 children. Among the 70 children with pertussis, 18 children were too young to receive their vaccinations, 6 children received only Pw vaccines for their primary vaccination and their first booster, 18 children received a mix of Pw and Pa vaccines, 28 children, aged 7.2y±1.8, received only Pa vaccines.

Conclusions: Our surveillance indicates

(i) a better recognition of the disease by the paediatricians

(ii) the importance of a specific biological diagnosis

(iii) a duration of protection induced by Pa vaccine of around 7 years of age.

However, surveillance needs to continue.

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PASSIVE SURVEILLANCE OF SYNCOPE AND SEIZURES AFTER HUMAN PAPILLOMAVIRUS VACCINE IN THE VALENCIAN REGION, SPAIN: A CASE/NON-CASE STUDY

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Aims: To assess the association of syncopes and seizures following qHPV administration in female adolescents in the Valencian Region, Spain.

Methods: Case/non-case study performed from the Valencian Pasive Surveillance database (Pharmacovigilance Centre) between September 2007 and December 2011. This study included reports of syncope and seizures related to the administration of qHPV in girls aged 13 to 15 years.

Case/non-case study can use the Reporting Odds Ratio (ROR) as a measure of disproportionality. ROR assesses if an adverse event (AE) is reported more frequently for a drug to another.

Results: The Pharmacovigilance Centre received 193 reports related to qHPV and 27 reports related to other vaccines.

There were 33 cases of syncope, 6 cases of presyncope and 6 cases of syncopal seizures. There were no reported cases of non syncopal seizures.

The Reporting Rate for syncope was 17.6/100,000 doses administered and 3.2/100,000 doses administered for presyncope and syncopal seizures.

The ROR for syncope was 0.14 (95% CI: 0.06-0.33); for presyncope was 0.07 (95% CI:0.02-0.04); for syncopal seizures was 0.83 (95% CI: 0.09-7.21).

Conclusions: The increased reporting of AE following qHPV compared with the reporting related to other vaccines could be explained by the recommendation for reporting any AE of a new drug in the first 5 years of marketing.

The low number of reports for other vaccines may bias the disproportionality measures. ROR seems not to be a useful tool for assessing association between syncopes and seizures and qHPV in the Valencian Region.

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BORDETELLA HOLMESII IS NOT DETECTED IN SWISS PATIENTS WITH PERTUSSIS-LIKE SYMPTOMS

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Background and aim: Bordetella holmesii has recently been identified as the cause for bacteremia and other invasive infections, and is also responsible for pertussis-like illness. Routine diagnostic assays for Bordetella spp. relying on PCR amplification of IS481 are not species-specific: this can have an impact on epidemiological surveillance. The aim of our study was to assess the prevalence of infection due to B. holmesii among Swiss patients suffering from pertussis-like symptoms.

Methods: Samples positive for B. pertussis by routine IS481-PCR in 2011 were subjected to a triplex real-time PCR able to discriminate B. pertussis (IS481+, IS1001-, hIS1001-), from B. holmesii (IS481+, IS1001-, hIS1001+) and B. parapertussis (IS481-, IS1001+, hIS1001-).

Results: Of the 196 samples tested 189 (95%) were confirmed as B. pertussis, 5 (3%) were B. parapertussis and 2 were negative for all three targets. No B. holmesii was identified.

Conclusions: Although B. holmesii is circulating in neighbouring countries, this species was not identified in our symptomatic cohort. Because B. holmesii has a higher potential for invasive disease than B. pertussis, and misdiagnosing B. holmesii for B. pertussis could falsely suggest vaccine failure, it is important to continue to monitor the epidemiology of B. holmesii using discriminative diagnostic tools.

Acknowledgements: We thank Pr N. Guiso for providing B. holmesii DNA for validation of the PCR, and Dr N. Liassine from DianaLabs® for providing samples.

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TRENDS IN HUMAN PAPILLOMAVIRUS IMMUNIZATION COVERAGE OF GIRLS AGED 14. 1994 - 1997 BIRTH COHORTS. VALENCIAN COMMUNITY (SPAIN)

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Background and aims: The immunization coverage against human papilloma virus (HPV) in our community has not reached the results expected.The aim of the study is to evaluate the trend in HPV inmunization coverage of girls from 1994 to 1997 birth cohorts in the Valencian Community.

Methods: Retrospective study of HPV vaccine acts of girls reported in the Immunization Information System of the Valencian Community. The analysis has been done by dose and by birth year.

Results: The first dose of HPV vaccine in girls of 1994 cohort, was administered at the health centers in 41,6% of the health departments. Girls born in 1995 and 1996 were vaccinated in health centers. 21148 doses of HPV vaccine were reported in girls aged 13-15 (86% girls aged 14) in 2008. 63036 doses were reported in 2011(72,6% girls aged 14).The HPV coverage is showed on table 1.

Birth Cohort	Dose 1	Dose 2	Dose 3
1994	85,76%	82,02%	75,14%
1995	74,15%	71,71%	70,24%
1996	81,11%	79,26%	77,88%
1997	76,92%	74,78%	70,03%

[HPV immunization coverage by birth cohort and dose]

The drop-out rates between the first and third doses were 10.6% (1994 cohort), 3.9% (1995), 3.2% (1996) and 6.9% (1997).

Conclusions: The number of HPV doses reported had increased. The coverage for the third dose is over 70% for all the cohorts. Drop-out rates are higher for 1994 and 1997 cohorts. Health departments where vaccination was carried out in schools had achieved better coverage.

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COMPARISON BETWEEN TWO POSOLOGIC SCHEMES OF AQUEOUS PENICILLIN G GIVEN FOR CHILDREN WITH PNEUMONIA

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Background and aims: This study assessed the differences in evolution between children with pneumonia treated with 6- or 4-daily doses of aqueous penicillin G.

Methods: Patients aged from 2 months to 11.5 years were retrospectively followed up. Pneumonia was radiologically diagnosed based on detection of pulmonary infiltrate or pleural effusion on the chest radiograph taken on admission and read by a pediatric radiologist blinded to clinical data. The total daily dose of aqueous penicillin G was 200,000IU/Kg. Data on admission, during evolution up to the 7th day of treatment and final outcome were recorded. Result of hospitalization, daily frequency of symptoms, signs and treatment items were assessed.

Results: The subgroups comprised 120 and 144 children who received aqueous penicillin G in 6- or 4-daily doses, respectively. On admission, very severe pneumonia was more frequent in the 6-daily doses subgroup (17.5% vs. 9.0%; p=0.04) in which children were younger (median [25th-75th]: 17 [9-29.5] vs. 24 [12-49] months; p=0.001). No association between age and severity was detected. There was no difference between the compared subgroups regarding final outcome, hospitalization and aqueous penicillin G use length, as well as frequency of aqueous penicillin G substitution. Children in the 6-daily doses subgroup presented more vomiting on D1 (8.3% vs. 2.8%; p=0.045), D3 (8.3% vs. 2.5%; p=0.049) and D4 (12.2% vs. 3.3%; p=0.03). This association was modified by absence of severe pneumonia.

Conclusion: Irrespective of differences on admission, the studied posologic schemes were similarly effective in treating children hospitalized with radiologically diagnosed pneumonia.

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DISTRUBUTION OF RHINOVIRUS GENOTYPES IN NASOPHARYNX AMONG SYMPTOMATIC CHILDREN WITH ACUTE OTITIS MEDIA OR UNCOMPLICATIED RESPIRATORY TRACT INFECTION

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Background and aims: Rhinoviruses are the most common respiratory viruses which have recently been classified into A, B, and C genotypes. Our aim was to investigate if the distribution of these genotypes is similar or different between symptomatic young children diagnosed with acute otitis media (AOM) and uncomplicated respiratory tract infection.

Methods: We enrolled children (6-35 months) with acute symptoms suggestive of AOM. AOM group showed middle ear effusion and acute inflammatory signs in pneumatic otoscopy along with acute symptoms, while non-AOM group had no abnormal otoscopic signs or only middle ear effusion.

We took nasopharyngeal samples from each child and analyzed the samples for rhinovirus by PCR and further sequenced the rhinovirus positive samples to determine if the rhinovirus genotype was of A, B, or C.

Results: We sequenced altogether 202 samples which had been positive for rhinovirus by PCR. Sequencing gave genotype result from 137/202 samples (68%), 77 samples in AOM group and 60 samples in non-AOM group. The distribution of rhinovirus genotypes A, B, and C was following: 33/77 (43%), 4/77 (5%), and 40/77 (52%) in AOM group and 25/60 (42%), 5/60 (8%), and 30/60 (50%) in non-AOM group, respectively (p=0.763).

Conclusions: The distribution of rhinovirus genotypes is similar in symptomatic young children diagnosed with acute otitis media and uncomplicated respiratory tract infection suggesting that each rhinovirus genotype similarly predisposes young children to the development of AOM.

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TRENDS IN INFLUENZA IMMUNIZATION COVERAGE OF CHILDREN AT HIGH RISK FROM 2007-08 TO 2011-12 SEASON IN VALENCIAN COMMUNITY (SPAIN)

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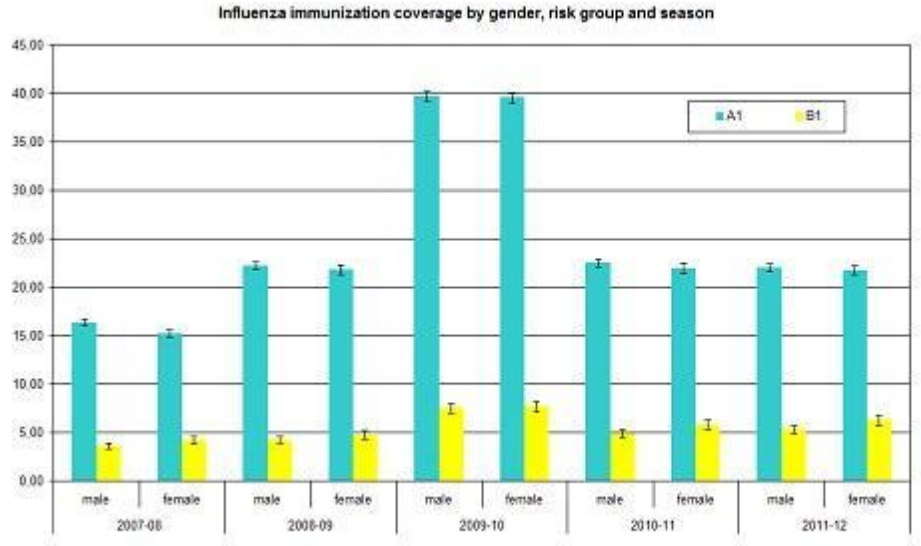
Background and aim: Children with chronic medical conditions (CMC) are at high-risk of suffering from serious complications due to influenza. Although routine annual influenza immunization is recommended in these children, few of them fulfil the recommendation. In Valencian Community (Spain) influenza vaccination in children is recommended in children older than 6 months who are diagnosed with any risk factors. The aim of the study is to analyze vaccination coverage against seasonal influenza in children aged 6 months to 14 years who have chronic cardiorespiratory processes (A1) and patients with renal disease, diabetes, immunocompromised or morbidly obese (B1), from 2007-2008 to 2011-2012 season.

Methods: A retrospective study has been done. Vaccine coverage and confidence intervals at 95% by gender for A1 and B1 risk groups have been calculated.The data of vaccinated people were obtained from Vaccine Information System (SIV) and diagnoses from Information System Primary Care Ambulatory (SIP) coded according to ICD9.

Results: Cumulative incidence rates per 100,000 children of the seasonal influenza for the 6 months to 14 years group reported in the Sentinel Network of Valencian Community (RCSCV) from 2007-2008 to 2011-2012 were 2500, 2250, 8950, 2650 and 2250 respectively.Vaccination coverage against influenza for A1 risk group were 15.87%, 22.05%, 39.66%, 22.28%, 21.88% respectively for the seasons of the study. Influenza vaccination coverage is showed on graph 1.



[Graph 1]

Conclusions: Influenza coverage of children of A1 risk group is similar to literature data (10-23%), however, it would be desirable to implement specific strategies to achieve 75% coverage.

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SCREENING NEWBORNS FOR CONGENITAL CHAGAS DISEASE (AMERICAN TRYPANOSOMIASIS) IN GENEVA, SWITZERLAND

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Chagas disease is caused by Trypanosoma cruzi. Vector-borne transmission occurs exclusively in the Americas, where millions are infected. Transmission can occur vertically with a risk of mother-to-child transmission of 1%-10%. Children are often asymptomatic at birth. The risk of developing cardiac or gastrointestinal disease in their life time is estimated between 20% and 30%. In Europe, vertical transmission of Chagas disease has recently emerged in the context of international migration.

Since 2008, a Chagas screening program is performed in our institution. All pregnant women followed in our hospital and coming from an endemic area are tested. If the mother is positive, neonates are screened at birth (direct exam and PCR on cord blood) and at nine months (serology). Treatment is started if any test is positive.

Between January 2008 and December 2011, 22 pregnant women were tested positive. We tested 26 children (4 of the mothers had 2 children each). Four (19%) were positive for Chagas disease. Two children were treated with nifurtimox and two with benznidazole. Both were well tolerated. Two patients were not tested at nine months (lost to follow-up). The serology will be repeated in two other children because of unclear results.

The Chagas disease screening program allowed treating mothers, detecting and treating four vertically infected children, and screening previously born children from infected mothers. Pediatric Chagas disease in non-endemic countries is an under recognized entity. Most of the patients are asymptomatic but can develop serious complications later in life; therefore, a mother-baby screening program is warranted.

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SAFETY OF PENTAVALENT ROTAVIRUS VACCINE IN HEALTHY PREMATURE INFANTS: AND OBSERVATIONAL STUDY

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Background and objectives: Premature infants (PI) seem to be at greater risk of severe forms of rotavirus (RTV) gastroenteritis and hospitalization. The risk increases as the lower gestational age (GA) and lower weight. To date, studies on safety and efficacy of the pentavalent vaccine against RTV reflect similar results in preterm and term infants, which has led to the different societies to recommend.

Methods: Longitudinal observational epidemiological study to assess the safety of Rotavirus Pentavalent Human-Bovine vaccine in premature infants less than 32 weeks GA by studying the occurrence of adverse effects in the vaccinated population. All infants were to be followed for clinical adverse events for 42 days after each dose.

Results: The vaccine has been administered to 186 infants under 32 weeks. First dose was administered at 6 or more weeks of life, after discharge, and ended before 22 weeks.

There were no serious adverse events. No case of intussuspection occurred.

There have been mild side effects as: 2 vomiting, 4 irritability / crying , 2 bronchiolitis VRS negative, similar rate to control groups prior published in clinical trials. There have been no hospital admissions or emergency room visits for gastroenteritis so far.

Conclusions: Vaccination against RTV has shown to be as safe in prematures than in term infants.

Vaccination should be considered as an option in neonatal units after discharge.

We need to have more experience in real life data substantiating the safety and efficacy that trials have provided.

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CONTROLLING HEAD LICE IN IRANIAN PRIMARY SCHOOLS FOR GIRLS

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Background: A research study showed that in spite of spending a huge budget by the sanitary and medical centers for procurement and distributing of antipedicular shampoos, prevalence of pediculosis in girls primary schools continuous.

Objective: Efficacy of antipedicular shampoos lindane 1% and permethrin 1% on the pediculosis control among students was studied.

Methods: 1242 contaminated school girls in 31 girls schools were randomly exposed to shampoos (520 students treated using lindane1% shampoos and 722 students treated using permethrin1% shampoos). One hundred twenty five contaminated school girls were exposed to placebo shampoos. Efficacy of shampoos was studied after twice use within one week apart. Before distribution, an educational pamphlet was distributed among all students discussing methods of prevention and directions for use of shampoos. The study was statistically analyzed.

Results: We found that shampoo treatments resulted in 52.9% overall recovery. With lindane it was 50.96% and with permethrin 54.29%. The highest level of recovery was observed among grade five primary school girls. Recovery in the central zone of the city and in private schools was greater. Furthermore, the efficacy level of shampoos was influenced by different factors such as parasite load, type of school, school location, level of education, level of awareness and cultural factors.

Conculusion: Antipedicular shampoos are effective but socio-cultural factors are also important.

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CHRONIC CHAGAS DISEASE: A CASE REPORT

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Aims and background: Chagas disease is becoming a global problem due to migration of populations where the infection is endemic. In our country, congenital transmision is the most common. Treatment in first months of life is very effective (almost 100% cure) so many neonatal units have established protocols for its early diagnosis. However, many children (not Spain born) will be diagnosed in later stages. They used to be asyntomatic and treatment efficacy is uncertain. We report a case of a 6 years- old child.

Case report: 6 years-old child, asymptomatic, born in Spain, dispatched for a Trypanosoma cruzi positive serology. He had a normal physical examination by organ and systems. Family history included the death of his grandmother in Bolivia for Chagas disease. It allowed the diagnostic of the disease to the mother, who had cardiac involvement. Additional tests showed an Ig G (ELISA) and IgG (IFI) to Trypanosome Cruzi (TC) positive. Echocardiogram, EKG and gastro-esophageal-duodenal transit were normal. With the diagnosis of recently chronic Chagas disease was decided to start treatment with nifurtimox.

Conclusions:

-Several studies show higher cure rates if the treatment starts in the earlier age. So that WHO recommends, under 15 years, treatment in both symptomatic and asymptomatic patients.

-For the diagnosis of Chagas disease two different techniques TC positive serology are required.

-In adition of neonatal screening, it would be necessary to make it to all children from endemic areas of Chagas disease.

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PHARMACOKINETICS OF CIPROFLOXACIN (FLUOROQUINOLONE) IN NEONATES ADMINISTERED FOR SUSPECTED GRAM NEGATIVE SEPSIS (TINN TREAT INFECTION IN NEONATES EUROPEAN CONSORTIUM)

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Background: Ciprofloxacin is prescribed off-label in 25% of European neonatal units for suspected sepsis particularly if known resistance to first line antibiotics. There is insufficient data to define a rational neonatal dose regimen.

Aim: To obtain neonatal pharmacokinetic data of ciprofloxacin for preterm to term neonates.

Methods:

Design: A population PK study with sparse informative sampling supplemented by scavenged clinical samples. Recruited on neonatal and paediatric intensive care units/ wards at Liverpool Women´s and Children´s Hospitals UK.

Eligibility - administered ciprofloxacin for clinical care for suspected sepsis 24-52 weeks PMA.

Sampling schedule: 3 samples day 1 and 5 within 3 to 10 minutes of 3 set times following the infusion (6 per baby plus scavenged). **PK parameters** - AUC, Cmax/Cmin, volume of distribution and clearance).

Results: 62 recruits stratified into 4 week age bands between 24-48 weeks PMA.

A minimum of 7 babies per age group (except PMA 48-52 as none were eligible).

36 recruits completed both day 1 and 5 samples (42% day 5 samples missing as treatment had stopped or mortality). These were supplemented by 183 scavenged clinical bloods with exact times (4.3 on average per recruit).

10 samples from clinically required LP were obtained to determine the CSF level of ciprofloxacin.

6 /62 babies had confirmed Gram negative infection in blood cultures.

52 DNA buccal or blood samples were obtained for pharmacogenomic analysis.

Conclusion: A pharmacokinetic sampling strategy was achieved that will capture changes in absorption, distribution, metabolism and excretion throughout neonatal age range.

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MONITORING OF STREPTOCOCCUS PNEUMONIAE STRAINS SEQUENCE TYPES (ST) ISOLATED FROM MENINGITIS PATIENTS AND CARRIERS

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Background: To conduct monitoring of S. pneumoniae strains sequence types.

Methods: Multilocus sequence typing (MLST) was performed for gene locus: aroE, gdh, gki, recP, spi, xpt, ddl of 23 S. pneumoniae isolates (serotypes: 1, 4, 17F, 14, 19F, 18C, 9N/9L, 6B, 6A). For investigation of STs UPGMA and eBURST were used.

Results: MLST allowed identifying allele profiles and STs for each profile. According to allele profiles of 23 isolates 19 closely related and belonging to one cluster STs were identified. eBURST analysis revealed 4 subcluster ST groups, closely related in origin. The group I included 2 isolates from nasopharynx and CSF (serotype 19F and 320 ST); group II-ST 3104 (from nasopharynx) and ST 517 (from CSF) which belonged to serogroup 9N/9L; in group III-3 isolates belonged to serotype 6A and 473 ST (2 isolates from CSF and 1 from nasopharynx); group IV- ST 246 and 244 ST (from CSF, serotype 4). When assessing the data on S. pneumoniae isolates in MLST base it was identified that the following STs were registered in Russia earlier: 423, 3104, 4841, 239. The STs: 490, 146, 7196, 473, 1227, 320, 3750, 517, 246 and 2436 were not registered in Russia, but were found in other regions.

Conclusions: S. pneumoniae strains, which cause of bacterial meningitis and those found in carriers belonged both to STs circulating on the territory of Russia and to STs which were not registered earlier. The data suggest that migration of STs from other regions take place.

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PERTUSSIS AREA HEALTH OF GRAND CANARY. 1999 TO 2012. INCREASE IN CASES IN THE LAST TWO YEARS

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Background: It presents a descriptive epidemiological study on the evolution of pertussis in the island of Gran Canaria, during the time period 1999-2012, analyzing in detail the increase in cases verified that year.

Methods: We studied cases of laboratory-confirmed pertussis by PCR techniques, and reported on the island to the Epidemiological Surveillance Network Canaria, from 0 hours of January 1, 1999, at 24 pm on December 17 , 2012. The information was obtained through the established epidemiological tab for the declaration of a suspected case, and supplied by the Microbiological Information System Canary (SIMCA) were studied all the processes, reporting year.

Results: During 1999-2010 105 confirmed cases were reported (44% of total cases reported during the study period), while in 2011 89 confirmed cases were detected (37% of total cases reported in the period), and in 2012, 46 (19% of total cases reported in the period). Of the latter, 41% had less than 1 year of age, 15% between 1 and 4, and 9% between 5 and 9. 20% were between 10 and 29 years, and 15% between 30 and more years. During the period 1999-2010, the bulk of reported cases occurred in 2006 with a total of 18 cases.

Conclusions: There is still a considerable number of the disease process, mainly in people age have not been vaccinated or have incomplete vaccination we must emphasize the importance of monitoring of these processes, to determine new needs for new prevention strategies.

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FINANCIAL BENEFITS AFTER THE IMPLEMENTATION OF ANTIMICROBIAL COPPER IN INTENSIVE CARE UNITS (ICUS)

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Aim: Aim of this study was to evaluate the reduction on Intensive Care Unit (ICU) microbial flora after the antimicrobial copper alloy (Cu^+) implementation as well as the effect on financial - epidemiological operation parameters.

Methods: Medical, epidemiological and financial data into two time periods, before and after the implementation of copper (Cu 63% - Zn 37%, Low Lead) were recorded and analyzed in a General ICU. The evaluated parameters were: the importance of patients´ admission (Acute Physiology and Chronic Health Evaluation - APACHE II and Simplified Acute Physiology Score - SAPS), microbial flora´s record in the ICU before and after the implementation of Cu^+ as well as the impact on epidemiological and ICU´s operation financial parameters.

Results: During December 2010 and March 2011 and respectively during December 2011 and March 2012 comparative results showed statistically significant reduction on the microbial flora (CFU / ml) by 95% and the use of antimicrobial medicine (per day per patient) by 30% ($p = 0,014$) as well as patients hospitalization time and cost.

Conclusions: The innovative implementation of antimicrobial copper in ICUs contributed to their microbial flora significant reduction and antimicrobial drugs use reduction with the apparent positive effect (decrease) in both patients hospitalization time and cost. Under the present circumstances of economic crisis, survey results are of highest importance and value.

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A CASE OF SERRATIA MARCESCENS OSTEOMYELITIS IN A NEONATE AFFECTED BY CHRONIC GRANULOMATOUS DISEASE

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Background and aims: Chronic granulomatous disease (CGD) is a genetically heterogeneous primary immunodeficiency resulting from mutations in any of 4 subunits of phagocytic cell nicotinamide adenine dinucleotide phosphate (NADPH) oxidase. Patients with CGD are at risk for infections with catalase-positive bacteria and fungi. Serratia marcescens infection of bone and soft tissue is a common presentation of CGD in infancy.

Methods: We describe the case of a 12 days old neonate affected by CGD who developed an osteomyelitis at the third finger of the right hand during an episode of cellulitis by serratia marcescens on the same hand as well.

Results: An evident large tumefaction between the second and third finger of the right hand with involvement of the hand's-breadth and back was notable at admission. Initial blood screen showed an elevation of inflammatory markers and white blood cells. Culture from the finger abscess grew Serratia marcencens. X-ray showed an osteomyelitis process affecting the second phalanx of the third finger. He was treated with i.v. antibiotics for 4 weeks and was discharged on prophylactic trimethoprim and itraconazole with complete remission. Considering the family history, molecular and immunological investigations led to the diagnosis of X-linked CGD in the infant.

Conclusions: Osteomyelitis by Serratia marcencens, particulary in infancy, should raise the suspicion of the presence of CGD as an underlying condition. Few are the cases reported in literature during the neonatal period. In these patients aggressive therapeutic treatments, should be strongly encouraged.

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IMMUNIZATION COVERAGE AND SOCIAL MEDIA AS TOOLS FOR IMPROVEMENT

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Introduction: To improve these hedges were put in place, first a recruitment campaign targeted at girls who are 14 years old, in order to improve coverage against vaccine HPV campaign was called: "If you are 14 call 012 "(The 012 is a telephone information), which began in 2011 On the other hand, a website, misvacunas.es, which began operation in May 2012, and from which the user can register anonymously, data that the system needs to, for example, by SMS or remind email vaccines public health system recommends to his children. We present the results obtained after acceptance implementing these campaigns.

Methods: The first campaign was conducted in three social networks: Tuenti, Facebook: and Youtube. For the second, we evaluated the number of web users, the mobile users, the number of mobile and SMS messages sent.

Results: One month after the start of the first campaign, the number of active users was of 1,204, this means that the read and access the daily profile. Of these 84 visits were voluntarily affiliated users. The purchase of advertising reported that the ad created, was seen by 1,200,000 people. At 8 months into the second season, the number of web users was 1072, the mobile users of 193. Furthermore, the number of ads to mobile was 181 and 809 sent SMS.

Conclusions: We believe that these campaigns have worked well, by way of information from those interested, and which users access the profile and website, and read the information.

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HYPER IGE SYNDROME: A CASE REPORT

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Background and aims: The hyper IgE syndromes (HIES) are rare primary immune deficiencies characterized by elevated serum IgE, rash, and recurrent bacterial infections of the skin and lung.

Methods: We report a case of a 13-year old boy from Sri Lanka. The boy has been suffering from atopic dermatitis since first months of life, and from recurrent allergic asthma since the age of 2. Pustular lesions with a tendency toward formation of multiple abscesses appeared all from August 2011 and were always treated with antibiotic therapy.

Results: In June 2012, the child was admitted to our department due to fever and abdominal pain that started 5 days prior to admission. Blood test results: PCR= 93,4 mg/L (normal value < 10 mg/L), Mycoplasma pneumoniae serological Immunoglobulin (Ig) M positive, Ig E level = 10,428 UI/mL (normal value < 100 UI/mL). Mantoux test was negative. Chest X-Ray showed a consolidation area, which looked like a pulmonary abscess. CT imaging confirmed the diagnosis. Clinical and radiological improvement was not achieved despite antibiotic treatment with ceftazidime and clarithromycin. The abscess was drained and Methicillin resistant (MRSA) Staphilococcus aureus was isolated. Considering the clinical features, IgE values and etiology of abscess, a diagnosis of hyper-IgE syndrome was stated. Antibiotic therapy with vancomycin was started, and clinical condition improved. Identification of STAT3 mutation is still ongoing.

Conclusion: Complications of pulmonary infections are the most common causes of death in hyper-Ig E syndrome. Introduction of comprehensive treatment, including prophylaxis, decreases the recurrences.

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ANTIMICROBIAL COPPER (CU +) IMPLEMENTATION AND ITS INFLUENCE TO THE EPIDEMIOLOGICAL DATA IN ELEMENTARY SCHOOL POPULATION

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Aim: The aim of this study was to evaluate the epidemiological data in elementary school students after implementing Cu^+ in multi- touch surfaces.

Methods: Antimicrobial copper alloy (Cu 63% - Zn 37%, Low Lead) was used to cover or replace multi-touch surfaces (handrails, stair railings), in five elementary schools (N = 1596 students). Epidemiological surveillance of flu-like symptoms was conducted from the 40th week of 2011 to 15th week of 2012 and recorded absenteeism among students based on a specific protocol.

Results: A significant reduction of pathogenic strains and viruses after the implementation of antimicrobial copper Cu^+ influenced the occurrence of respiratory infections of viral etiology. A decrease of seasonal influenza (Influenza Like Illness) was recorded on the students of these schools. Clinical morbidity index of students was recorded at 36, 01% (average 5 schools), while in the community the same period (2011-2012) the rate was 48, 8%.

Conclusions: The use of antimicrobial copper in places with great population concentrations and crowded places such as schools is an innovative application, which in combination with hand hygiene contributes significantly to the reduction of viral respiratory tract infections and emerging as one of the most important allies to the Public Health.

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AN UNUSUAL CASE OF PYREXIA OF UNKNOWN ORIGIN, PAROTID ENLARGEMENT AND RENAL IMPAIRMENT IN A 3-YEAR OLD AFRICAN CHILD

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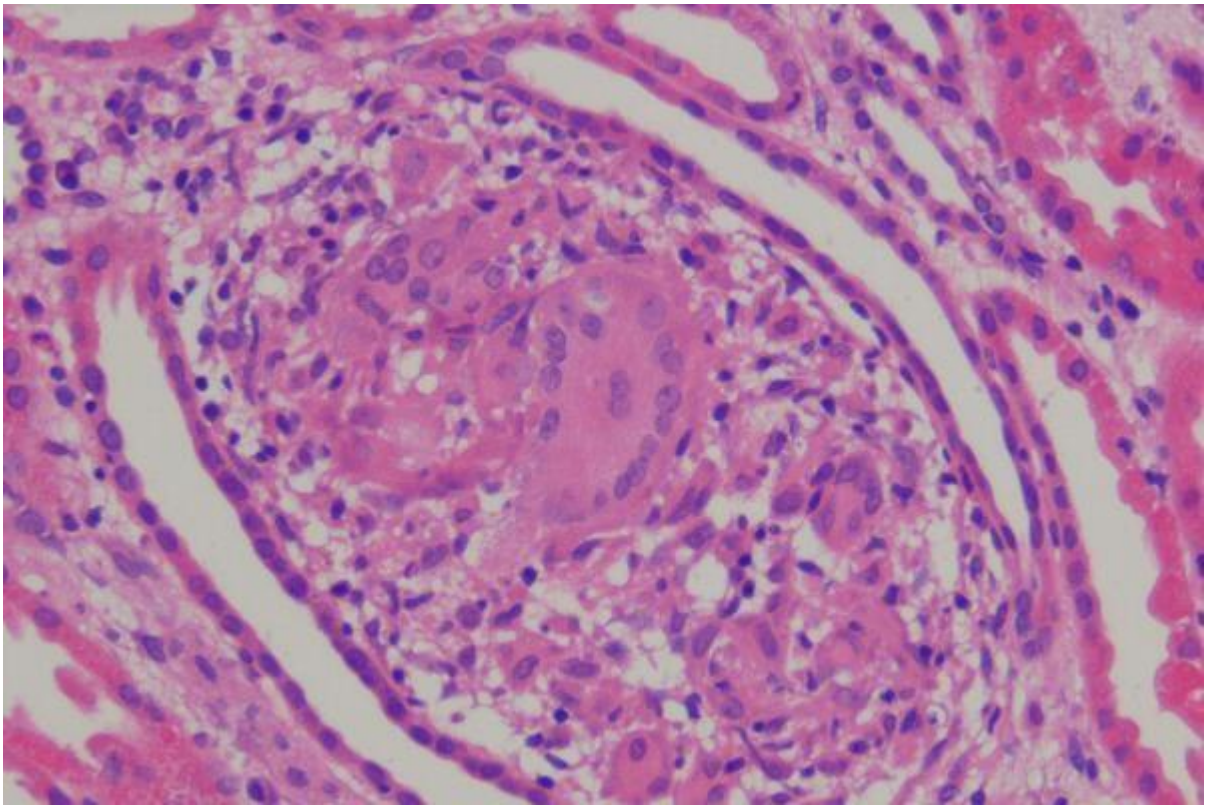
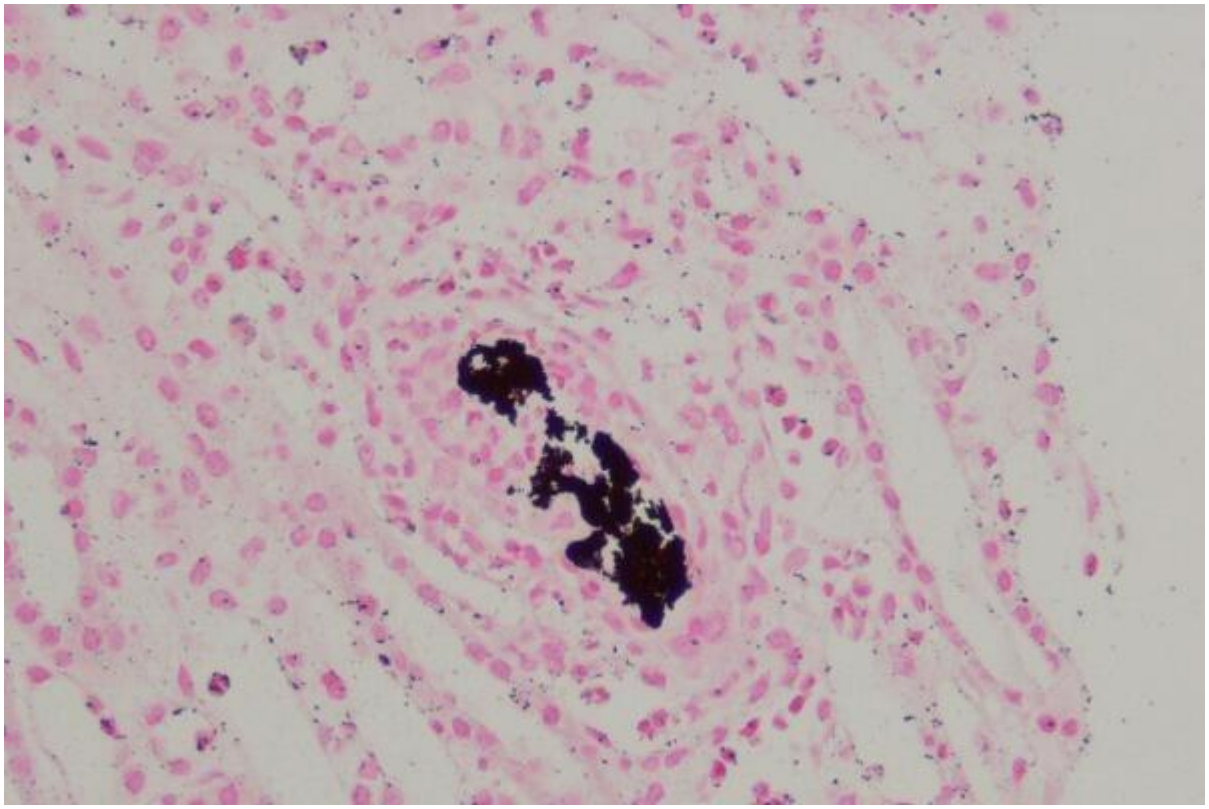
Background: Pyrexia of unknown origin (PUO) poses a diagnostic dilemma to the infectious disease specialist. Early-onset sarcoidosis may present with fever and a triad of arthritis, uveitis and rash; in older children pulmonary symptoms predominate.

Methods: We describe an unusual case of early-onset paediatric sarcoidosis presenting as PUO with renal, parotid and pulmonary involvement in a Nigerian 3 year old girl with a history of 3-months of intermittent high fevers, weight loss, fatigue and acute generalised rash settling on her lower legs at the onset of illness. She had received antibiotics for presumed lower respiratory tract infections. On examination she had bilateral parotid enlargement and hyperpigmented patches on her lower legs.

Results: At admission she had hypercalcaemia, raised inflammatory markers and anaemia. Chest x-ray was unremarkable. Over the course of admission her renal function became profoundly impaired with a protein-losing nephropathy and hypercalciuria. Serum angiotensin-converting enzyme (ACE) levels were slightly raised. Malignancy, vasculitis, endocrinopathy, HIV and sepsis were excluded. HRCT chest showed diffuse parenchymal abnormalities supporting a diagnosis of sarcoidosis. Renal biopsy showed florid granulomatous tubules and mild tubular calcification in keeping with sarcoidosis. Parotid gland biopsy revealed granulomatous lymphadenitis.She was treated with pulsed methylprednisolone and cyclophosphamide with good response; fever settled after 3 weeks of immunosuppressive treatment. Renal function returned to normal.



[Renal biospy showing florid renal granulomas]



[Renal biospy showing nephrocalcinosis]

Conclusions: This case highlights that parotid enlargement may suggest an inflammatory diagnosis rather than infectious. A multidisciplinary approach aided in confirming the diagnosis of sarcoidosis in this unusual case of PUO with florid renal involvement.

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LABORATORY INVESTIGATION IN VACCINATED PATIENTS WITH VARICELLA

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Background: Accompanying varicella vaccination in children in Germany recommended with one (2004) and two (2009) doses, sentinel surveillance of varicella with a sample (n~1000) of private physicians was established in 2005. Laboratory investigation of skin lesions of vaccinated patients was performed to identify varicella-zoster virus (VZV) and confirm diagnosis. We analyzed the impact of vaccination frequency on laboratory results.

Methods: Skin lesion samples were obtained with a cotton tip and sent together with a case-based questionnaire to the reference laboratory. VZV wild-type and vaccine-type DNA was identified by polymerase chain-reaction (PCR) and pyrosequencing methods. Case-based data and preliminary laboratory results were descriptively analyzed.

Results: From April 2005 to December 2012, of all monthly reported vaccinated cases in the sentinel-system (n=4499), 18% (n=832) had samples sent to the laboratory. Of those, 653 (168) patients had received one (two) varicella doses; 11 had no vaccination recorded. PCR remained negative in 21% (n=138) cases vaccinated once, in comparison to 68% (n=115) cases vaccinated twice. VZV was confirmed in 510 (49) patients vaccinated once (twice); identification of VZV wild-type, vaccine-type, or no further differentiation was possible in 495 (41), 8 (6), and 7 (2) cases, respectively. Number of lesions (classified by < 50/>50) did not differ between individuals vaccinated once or twice.

Conclusion: In vaccinated patients with clinical varicella symptoms PCR might fail due to low virus load or misdiagnosis, particularly in patients vaccinated twice. More detailed clinical data than number of lesions and serological investigations are necessary to complement sentinel surveillance.

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«HALO» PHENOMENON (PHENOMENON "STEFANIS") IN RELATION WITH ANTIMICROBIAL COPPER IMPLEMENTATION

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Aim: The aim of this study was to evaluate the antimicrobial action of copper alloys in the form of a 'circle' ("halo" phenomenon), resulting in a further reduction of microbial loads in non antimicrobial copper implemented multi-touch surfaces.

Method - Material: In a Neonatal Intensive Care Unit (NICU) with the capacity of 26 beds (boxes) of a pediatric hospital implemented with antimicrobial copper Cu^+ (Cu^+63% Zn - 37% low lead) and certified for the antimicrobial activity of objects and surfaces, samples and cultures were taken within 50cm distance from the Cu^+ implemented objects and surfaces, in order to measure the microbial flora. This process took place the period before, during and 2 months after Cu^+ implementation. Parameters such as Operational Protocols and staffing of the NICU during the research were not differenciated.

Results: The reduction of microbial load on multi-touch surfaces of Cu^+ was recorded at 90%, and at a distance of 50 cm from the Cu^+ implemented objects or surfaces the reduction of microbial loads (cfu / ml) was recorded at a rate of 70-75% ($N = 36$-$P < 0,05$). Microbial strains found were: Klebsiellaspp., Staph. Epidermidis, Staph. Aureus, Sphingomonaspaucimobilis.

Conclusions: The recorded 'radial action' of the Cu^+ alloys in a circular form ("halo" phenomenon) provides further confirmation of copper's antimicrobial ability. The «halo» phenomenon enables Cu^+ to reduce microbial flora and increase its beneficial effects on health sector and sets the bases for further comparative.

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IMPLEMENTATION OF ANTIMICROBIAL COPPER IN NEONATAL INTENSIVE CARE UNIT (NICU)

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Aim: The aim of this study was to investigate the effectiveness of the application of antimicrobial copper alloys (Cu +) in a Neonatal Intensive Care Unit (NICU) in relation to the reduction of microbial flora.

Materials and methods: At a Level III Neonatal Intensive Care Unit of a pediatric hospital, with the capacity of twenty-six (26) incubators, antimicrobial copper (Cu +) was implemented on touch surfaces and objects. The copper alloy contains Cu 63% - Zn 37% (Lead Low). Microbiological cultures were taken in three different time periods, before and after the application of Cu^{+}, using dry and wet method technique.

Results: In the above NICU, the reduction of microbial flora after the implementation of the antimicrobial copper (Cu +) on the selected surfaces and objects was statistically significant ($n = 15$, $p < 0,05$) and was recorded at 90%. The pathogens isolated at high rates (CFU / ml) prior to copper implementation were as follows: Klebsiella spp., Staph. Epidermidis, Staph. Aureus, Enterococcus spp.

Conclusions: This study highlights the positive impact of antimicrobial copper (Cu +) and demonstrates that copper implemented surfaces and objects are effective in neutralizing bacteria, which are responsible for Health Care Acquired Infections in the nosocomial environment (HCAIs).

The innovative implementation of antimicrobial copper in the NICU and the significant reduction of microbial flora heralds the reduction of antimicrobial drugs use, and a possible reduction of hospital acquired infections and hospitalization time.

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THE ANALYSIS OF VANCOMYCIN SERUM TROUGH CONCENTRATION IN NEONATES AND INFANTS

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Background: Vancomycin (VCM) serum trough concentrations of 15-20 mg/L were recommended to improve clinical outcome for Staphylococcus aureus complicated infections by practice guidelines from Infectious Diseases Society of America. In newborn and infant patients, however it is unclear whether the current VCM dosages are enough to achieve this target concentration.

Methods: We analyzed the correlation of VCM dosages and trough concentrations , and the ratio of achievement for target trough in NICU of Juntendo University Hospital, Japan. Medical records of neonate and infant inpatients with VCM treatment were investigated from January 2010 to October 2012. Cases such as insufficient for duration of the treatment before the monitoring, changed dosage, and serum creatinine levels were > 0.5 mg/dL were excluded. Current dosages were based on Nelson Textbook, Red book and Sanford Guide (Neonates, 20-30 mg/kg/day; Infants with mild to moderate and severe infection, 30-40 and 60 mg/kg/day).

Results: Subjects were 69 patients, twenty of whom were excluded. Trough concentrations were 13.2 ± 3.5, 7.9 ± 4.2 and 9.1 ± 4.7 mg/L, for neonates, mild to moderate and severe infants. The ratios of achievement for trough concentrations 10-15 mg/L were 83.3%, 29.2% and 55%, and for 15-20 mg/L were 33.3%, 4.1% and 0%. In addition, trough concentrations correlated negatively with postnatal age and weight in neonates with dosages 20-30 mg/kg/day.

Conclusions: It was difficult for neonates and infants to achieve the target trough concentrations by current initial dosages. Further research is required to confirm the appropriate VCM dosing regimen.

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PREVENTION OF MOTHER-TO-CHILD HIV TRANSMISSION IN COIMBRA FROM 2000 TO 2011: ANALYSIS OF THE COHORT

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Background and aims: One of the major advances in the fight against HIV was the prevention of mother-to-child transmission (MTCT) by implementation of measures and specific therapeutics in infected pregnant and newborn. This study aims to assess MTCT rate of VIH and its risk factors.

Methods: Longitudinal cohort study of children from HIV infected women born in Coimbra between 2000 and 2011. Complete protocol compliance was defined by the following measures: antiretroviral therapy (ART) during pregnancy (at least three weeks), delivery and the newborn, as well as elective cesarean section.

Results: A total of 180 infants and their HIV positive mothers (HIV-1 in 90,6%) were followed. In 64,5% (98/152) the risk factor for HIV infection was heterosexual transmission. Co-infection was present in 61 women (85,2% with hepatitis C). Mothers HIV infection status was diagnosed in pre-gestational period in 57,2% of cases, during pregnancy in 42,2% and at delivery in 0,6%. Complete protocol compliance was found in 67,2% of cases. During pregnancy 86,7% received ART and 94,9% (169/178) during delivery. All newborn did ART prophylaxis. One newborn, whose HIV mother status was known after delivery, was breastfed. The overall rate of HIV infected children was 1,7% (n=3: normal delivery, failure of ART during pregnancy, HIV virus resistant to ART). Since 2005 no child was infected.

Conclusions: Effectiveness of MTCT preventive measures is high. Continued efforts are needed to ensure that all women know their HIV status before pregnancy to ensure appropriate supervision of pregnancy and early beginning of prophylactic measures.

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BCG HEALING AND TETANUS ANTIBODY LEVELS AFTER PRIMARY IMMUNIZATION IN INFANTS EXPOSED TO IMMUNOSSUPRESSORS DURING GESTATION

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Background and aims: Immunosuppressors used during gestation are known to interfere with the fetus' immune system development. However, little is known regarding their influence on the response to the infant's immunization. We evaluated BCG adverse events and scar development as well as tetanus antibodies in children born to renal transplant women.

Methods: 24 renal transplant women and neonates and 30 healthy women and neonates at term (Control) were studied. All transplant mothers received azathioprine, prednisone and either tacrolimus (71%) or cyclosporin (29%). T, B and NK cells were evaluated at birth in 17 neonates of transplant group and from all controls. BCG was administered at birth or as early as when they reached 2Kg; DTwP vaccine was administered at 2, 4 and 6 months of age. Children were followed up and the evolution of BCG scar was registered. At 7 months of age, tetanus antibodies were measured by ELISA.

Results: Infants of transplant group had lower median CD4 T cells/mm3 (1238x1646, p=0.037) and B lymphocytes/mm3 (119x517,p< 0.001) than controls, but similar CD8 T cells/mm3 (633x667,p=0.288) and NK cells/mm3 (774x764,p=0.432). No BCG adverse events were observed. Median time for BCG scar development was 1.8 months in both groups(p=0.919). All children had protective tetanus antibodies (>0.1 IU/mL) and similar tetanus antibody levels (1.680 IU/mL in transplant and 1.609 IU/mL in control group, p=0.553) after vaccination.

Conclusions: Despite low numbers of CD4 T and B cells at birth, children exposed in utero to immunosuppressors have adequate BCG healing and response to tetanus vaccine.

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ACUTE CEREBELLITIS AND ENCEPHALOPATHY ASSOCIATED WITH INFLUENZA A (H3N2) VIRUS INFECTION: A CASE REPORT

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Aims: To describe an unusual neurological complication of Influenza A H3N2 virus infection in a child.

Methods: Case report.

Results: A previously fit and well 3-year-old girl was admitted to hospital with high fever, drowsiness, irritability and delirium. She had a 3-day history of upper respiratory tract infection diagnosed as tonsillitis in primary care.

On examination, she had a temperature of 40°C; she was encephalopathic with a decreased level of consciousness. Routine investigations revealed a WBC 6.7×10^9/L and raised CRP 41 mg/L. Initial CT brain imaging showed no abnormalities. A subsequent CSF examination revealed 1 WBC/µL, 30 RBC/µL, normal protein 0.19 g/L and normal paired glucose; no viral DNA/RNA or influenza A RNA was detected by PCR. A contrast-enhanced MR brain imaging demonstrated high T2 signal within the dentate nuclei of the cerebellum with restricted diffusion suggestive of acute cerebellitis. The throat swab on admission revealed only influenza A (H3N2) RNA by PCR.

The patient received oral Oseltamivir, IV Acyclovir and Ceftriaxone. By the third week of admission her encephalopathy had improved and signs of cerebellitis became apparent with ataxic gait, limb tremor and speech disturbance. These symptoms gradually resolved. She was discharged after one month in hospital with mildly depressed cognitive function and neuro-rehabilitation in the community.

Conclusion: Clinicians should be aware that Influenza A is a rare potential cause of encephalopathy/encephalitis and cerebellitis of significant morbidity and mortality.

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BURDEN OF COMMUNITY-ACQUIRED PNEUMONIA IN HOSPITALISED CHILDREN BETWEEN 6 WEEKS AND 5 YEARS OF AGE IN POLAND

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Background and aims: The burden of community-acquired pneumonia (CAP) was evaluated in hospitalised children in Poland.

Methods: This observational, retrospective study was conducted in two hospitals in Bialystok and one in Trzebnica. Children aged 6 weeks to 5 years who had been hospitalised between January 2006 and December 2010 with CAP as primary or secondary discharge diagnosis were identified based on ICD-10 codes. Identified cases were matched to standardised case definitions of suspected, confirmed, or likely bacterial CAP used in a previous pneumococcal conjugate vaccine efficacy study (COMPAS),[1] which included outpatients and inpatients.

Results: 4766 hospitalisations classified as suspected CAP were reported; 4730 were included in the according-to-protocol cohort with a median length of hospitalisation of 9 days. Percentages of confirmed CAP were 76.7% (3208/4180) in Bialystok and 26.0% (143/550) in Trzebnica. The difference between centres likely reflects the Polish hospital referral system and its consequent impact on the diagnostic process.

Incidence rates of hospitalisations due to CAP (according-to-protocol cohort)

Site	Number of hospitalisations	Population under surveillance during 2006–2010 [Persons-years]	Incidence rate per 100,000 persons-years (95% CI)
Suspected CAP			
Bialystok	4180	86510	4832 (4686–4981)
Trzebnica	550	20546	2677 (2458–2910)
Confirmed CAP			
Bialystok	3208	86510	3708 (3581–3839)
Trzebnica	143	20546	696 (587–820)
Bacterial CAP			
Bialystok	397	86510	459 (415–506)
Trzebnica	50	20546	243 (181–321)

[Incidence rates of hospitalisations due to CAP]

Proportions of hospitalisations due to all suspected CAP were 11.63% (95% confidence interval: 11.30-11.96) in Bialystok and 13.78% (12.73-14.89) in Trzebnica. No deaths were reported.

Conclusions: Incidences of hospitalisations due to CAP were high in Polish children (especially in Bialystok) compared to other developed countries.[2] Our data provide an important addition to the relatively scarce data available on CAP incidence in developed countries, and could help inform future preventative strategies**.**

Funding: GlaxoSmithKline Biologicals SA

[1]Sáez Llorens, ESPID 2011, Abstract 1412

[2]Madhi, Pediatr Infect Dis J 2012

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DR. GOOGLE: WHAT ABOUT THE HUMAN PAPILLOMAVIRUS VACCINE?

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Background and aims: To assess and analyse the information and recommendations provided by Google® in relation to web searches on the HPV vaccine, its indications for females and males, and its possible adverse effects.

Method: Descriptive cross-sectional study of the results of 14 web searches. Comprehensive analysis of results based on general recommendation given (favourable/dissuasive), as well as compliance with pre-established criteria, namely design, content and credibility. Sub-analysis of results according to site category: general information, blog / forum and press.

Results: In the comprehensive analysis of results, 72.2% of websites offer information favourable to HPV vaccination, with varying degrees of content detail, versus 27.8% with highly dissuasive content in relation to HPV vaccination. The most frequent type of site is the blog or forum. The information found is frequently incomplete, poorly structured, and often lacking in updates, bibliography and adequate external quotes, as well as sound credibility criteria (scientific association accreditation and/or trust labels).

Conclusions: Google®, as a tool which users make use of to locate medical information and advice, is not specialised in providing information that is necessarily rigorous or valid from a scientific perspective. Search result and positioning based on Google´s generalised algorithms can lead users to poorly grounded opinions and statements, which may impact HPV vaccination perception and subsequent decision making.

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CIPROFLOXACIN AS ANTIPSEUDOMONAL TREATMENT IN CHILDREN WITH CYSTIC FIBROSIS

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Background: Respiratory exacerbation is the most common cause of morbidity and mortality among patients with cystic fibrosis (CF).

Aim: Assessment of ciprofloxacin effectiveness as antipseudomonal treatment in children with CF with mild respiratory exacerbations.

Methods: We studied 28 patients with CF younger than 15 years of age, who were admitted at Children´s new clinic. To assess severity of the exacerbation were used following signs: intensity of cough and expectoration, activity level, malaise, dyspnea, Auscultative phenomena - changes in chest sounds, decrease in FEV1/FVC and radiographic changes. Choice of antibiotic was based on sputum culture results. 17 patients were randomly assigned to oral ciprofloxacin alone (Group I) and 11 received ciprofloxacin plus inhaled colomycine (Group II). The general duration of antibiotic therapy was 14 days.

Results: Both regimens were well-tolerated. Negative sputum cultures were achieved in 17 patients (61%) at the end of 14 days therapy (8 Group I and 9 Group II) and 4 after 28 day therapy (14%) in Group I and 3 (11%) in Group II . Sputum isolates at the end of therapy (resistance to ciprofloxacin) was found in 4 (14%). There was no correlation between clinical outcome and either elimination of Pseudomonas aeruginosa from sputum culture or development of ciprofloxacin resistance. There were no severe or serious adverse events, no signs of quinolone-related arthropathy and no growth impairment.

Conclusion: Ciprofloxacin is efficacious, safe and well-tolerated as antipseudomonal therapy in pediatric patients with CF.

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EPIDEMIOLOGY OF COMPLICATED PNEUMONIA IN A TERTIARY UNIVERSITY MEDICAL CENTER IN LEBANON

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Pneumonia is still a major mortality and morbidity causative agent in both life extreme ages. Recently we are treating more complicated pneumonia in our institution. We conducted a retrospective observational study searching for predictive paraclinical tools for complicated pneumonia. 460 children were hospitalized for pneumonia confirmed radiologically. 40 patients (8.6%) with complicated pneumonia, with a mean age of 3.9 years (1 to 15 years) were included.

The most common presenting symptoms were fever (92.5%) and cough (85%). 12.5% presented with septic shock, and 67.5% were previously treated with antibiotics. Laboratory exams upon admission revealed a mean WBC count of $17.2x10^9$/l (range 0.9-$35x10^9$/l) and a CRP of 21.9mg/dl (range 2-58 mg/dl). 20% had a stage 1, 22.5% stage 2 and 55% stage 3 pleural effusion. 67.5% had chest tube inserted with a mean duration of 6.03 days (range 2-28 days). During stay 22.5% had a pneumatocele, 15% developed a pneumothorax and 10% had emphysema. Upon discharge only 5 % had a normalized chest X-ray.

There were neither correlation between chest tube duration and hospital stay nor correlation between age and duration of stay. No correlation was found between WBC upon admission and hospital duration. A positive correlation between hospital duration and CRP upon admission with a $p< 0.001$ was the only relevant finding.

In our study we found a positive correlation between increased CRP and prolonged hospital stay.

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THE SHORT AND LONG OUTCOME IN CHILDREN HIV INFECTION IN ALGERIA

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The HIV/infection emerged in paediatric in Oran from 1995; it remains underestimated and diagnosis remains late.

Objectives: Study forecast with short and long term of the HIV children, describe various therapeutic; study clinical and biological outcome and insertion in the normal life.

Methodology: 187 children; 119 alive and followed from 1995 till 2012, the others died and/or lost sight. Of the follow-up; every 3 months with clinical and biological data.

Results: 76 % were < 5 years old at diagnosis (1 month 10 years), sex ratio: 1.4 and vertical transmission 94 %, breast-feeding was noted in 83 %. Diarrhea (61 %), lung infections (46 %), the tuberculosis (26 %), the low development (42 %), lymph nodes (61 %), molluscum contagiosum (34 %), oral candidosis (63 %), bad teeth (43 %), fever (23 %), pneumonia lymphoïde (22 %), parotiditis (16 %), otitis (51 %), neurological signs (9.1 %), were the most suggestive signs. The HAART was established at 52 % of the children, (22 %) died and (15 %) have Were lost sight.

Conclusion: Transmission of the virus is vertical in almost all of the cases. The infected children become symptomatic in a mean age of 23 months. Lymph-nodes, respiratory and digestive signs were the most frequent signs. Parotiditis, Pneumonia, Molluscum contagiosum and the tooth decays were signs which characterized these children. In front of child´s chronic symptomatology, don´t limit to classical diseases (allergy; coeliac). 22 % of them died. The forecast of these children was clearly improved thanks to HAART.

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ELECTROPHEROTYPES AND G-TYPES OF GROUP A ROTAVIRUSES DETECTED IN DIARRHEIC CHILDREN IN LAGOS, NIGERIA

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Background and aims: It is estimated that over 500 000 children die annually due to severe dehydrating diarrhea caused by rotaviruses. The virus is a double stranded RNA (dsRNA) virus with 11 segments. Group A rotaviruses show a characteristic 4-2-3-2 migration pattern following electrophoresis. This work was embarked on to evaluate the prevalence of rotavirus infection among children under 5 years with diarrhea in Lagos, and to determine the circulating genotypes and electropherotypes of the rotavirus isolates.

Methods: Three hundred and two (n=302)stool samples from children below 60 months were collected from different hospitals and health care centers in Lagos and subjected to enzyme immunoassay (EIA) to determine presence of group A rotavirus, RT-PCR to determine the G types and polyacrylamide gel electrophoresis (PAGE) to determine the electropherotypes.

Results: The result shows that 60.3% of the samples showed distinct RNA migration pattern having long electropherotypes (55.3%) of seven variations dominated over the short electropherotypes (44.5%). Six different G types were detected (G1, G2, G3, G4, G9 and G12). Serotypes G1 and G12 show long electropherotypic pattern while G2, G3 and G9 either exhibited short or long electropherotype. All G4 detected show short electropherotypic pattern.

Conclusions: Information on the genomic diversity of RNA electropherotypes and serotypes of rotaviruses detected in diarrhea children in Lagos is reported in this study.

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ORAL AMOXICILLIN IN TWO OR THREE DAILY DOSES TO CHILDREN 2-59-MONTHS-OLD WITH NON-SEVERE PNEUMONIA: A RANDOMISED TRIPLE-BLINDED PLACEBO-CONTROLLED EQUIVALENCE TRIAL

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Background and aim: Oral amoxicillin in 3 doses is the first-line therapy for non-severe pneumonia. If 2 daily doses prove equally efficacious, compliance could be enhanced. We assessed whether oral amoxicillin (50mg/kg/day) given in 2 or 3 doses were equivalent in non-severe pneumonia.

Methods: This randomised (1:1), placebo-controlled, triple-blinded investigation was conducted at one tertiary-care centre in Salvador, Brazil. Children aged 2-59 months with non-severe pneumonia diagnosed by trained paediatricians based on respiratory complaints and radiographic pulmonary infiltrate/pleural effusion received 2 bottles named Amoxicillin 1 and Amoxicillin 2: one bottled contained amoxicillin and the other placebo. Participants were randomly assigned to receive one bottle in 2 doses and the other in 3 doses. Follow-up assessments were done at 2, 5, and 14 days. Chest radiograph were later read by three independent radiologists. Primary outcome was treatment failure (development of danger signs, persistence of fever, tachypnoea, development of serious adverse reactions, and withdrawal from the trial) at 48h.

Results: 412 and 408 received amoxicillin in 3 and 2 daily doses, respectively, between Nov 8,2006, and Apr 25,2011. Treatment failure was detected in 94(22.8%) and 94(23.0%) in intention-to-treat analysis (risk difference 0.2%;95%CI-5.5% to 6.0%) and in 80(20.1%) and 85(21.3%) in per protocol analysis (risk difference 1.2%;95%CI-4.4% to 6.8%). Pneumonia was radiologically confirmed by concordant reading in 277(33.8%) cases among whom treatment failure was registered in 25/133(18.8%) and 27/144(18.8%) (risk difference-0.05%;95%CI-9.2% to 9.3%) participants from compared groups.

Conclusion: Oral amoxicillin given at standard dose (50mg/kg/day) is equally efficacious in 2 or 3 daily doses.

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INFLUENCE OF HOSPITAL TRANSFER TO NEW BUILDING ON HEALTHCARE-ASSOCIATED INFECTIONS IN CHILDREN

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Background and aims: Healthcare-associated infections (HAIs) are among the most important threats to patient safety. In March 2011, Chung-Ang University Youngsan Hospital (CAUYH) has been transferred to new building of Chung-Ang University Hospital (CAUH). We aimed to accumulate local healthcare epidemiologic data and check any change in pattern of HAIs after hospital transfer.

Methods: We performed a retrospective analysis of databases of patients who were diagnosed with HAIs at CAUH from 2007 through 2011. The data on prevalence of HAIs in various wards and its annual trends were compared to previously reported nationwide data. Moreover, we analyzed the patterns of antibiotic susceptibility results for HAI pathogens.

Results: A total of 181 HAIs were identified in 122 patients. The HAI rate among pediatric patients at CAUH was 2.4/1,000 person-hospital days. Urinary tract infections (UTIs) (53 episodes, 29.3%) were the most common, followed by pneumonia (33 episodes, 18.2%). Staphylococcus aureus was found to be the most common causative organism, and methicillin-resistant S. aureus (MRSA) comprised 84% of the S. aureus infections. There was continuous decline in annual incidence of HAIs until 2011, the year when CAUYH merged into CAUH. Although no change in strategy for managing HAIs, annual incidence increased from 1.5 in 2010 to 3.0 in 2011.

Conclusion: Between 2007 and 2011, UTIs were the most common type of HAIs, and MRSA was the most common pediatric HAI pathogen at the CAUH. Hospital transfer should be considered as a risk factor of HAI.

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MOLECULAR CHARACTERIZATION OF GIARDIA LAMBLIA ISOLATES IN SOUTHWEST OF IRAN USING PCR - RFLP METHOD

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Aims: Giardia lamblia is one of the most common enteropathogenic parasites all over the world, including Iran. Recently, molecular assays have been developed to help in understanding the complex epidemiology of this infection. The study was carried out to characterize Giardia lamblia isolates from subjects with Giardiasis and investigate the correlation of socio-demographic factors and clinical manifestations of infection with the parasite's assemblages in southwest of Iran.

Methods: Eighty nine Giardia-positive stool samples were included in this study. Giardia cysts were isolated and purified by the 85% M sucrose method. The genomic DNA of the cysts was extracted using a genomic DNA extraction-kit .The PCR-RFLP assay, targeting the glutamate dehydrogenase (gdh) and triose phosphate isomerase (tpi) genes, was applied to characterize assemblges and sub-assemblages of the parasites. A questionnaire was used to collect the socio-demographic data and clinical manifestations of the subjects.

Results: Out of 89 samples **,** 43 were positive for the 148 bp-tpi amplicon (assemblage A), 36 (40.4%) for the 81-bp tpi amplicon (assemblage B) and 10 samples for both tpi gene amplicons (assemblages A+B). PCR-RFLP assay using showed that 4.5%, 39 43.8%, 32.6%, 7.9% and 11.2% of the samples had the sub-assemblages, A_{I}, A_{II},B_{III}, B_{IV}, and $A_{II+}B_{III}$, respectively. There was also a close relationship between G.lamblia assemblage A and diarrhea, loss of appetite and weight loss. $p< 0.05$.

Conclusions: Our findings indicated that no zoonotic infection was occurred and only the assemblages A and B were infectious for humans.

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PREVALENCE OF ASYMPTOMATIC URINARY TRACT INFECTION IN BOROUJERD CITY PRIMARY SCHOOL FIRST-GRADE CLASS IN 1391

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Background and purpose: Asymptomatic urinary tract infection is a condition that an infected person does not have a clear clinical symptom; however, more than one hundred thousand unit colonies are formed in urine and after a while some complications such as pyelonephritis, renal scarring and renal failure will occur. Due to the fact thatdud no research has been done yet in this field in Boroujerd, this study aims is estimating the prevalence of urinary tract infection in Boroujerd city.

Methods: In This cross - sectional study from 4240 boys and girls at the primary school first-grade class, 300 students by the use of cluster sampling were selected, then by trained personnel, urinary samples from middle stream urine were taken and samples immediately were sent to the lab. Data Analysis spss (version 17) was performed by spss (version 17).

Results: 4 girls and 1 boy due to having symptoms of urinary tract infection were excluded and research was conducted on 146 female students and 149 male students. Eight girls (5.47%), and 3 boys (2.01%) stricken by asympthomatic urinary tract infection meanwhile, all those who had positive culture results were affected by one of the following: Positive nitrite test, hematuria, pyuria or bacteriuria.

Conclusions: Due to the potential complications of urinary tract infection, in order to promote the community public health level, it is better to set screening of school children at the beginning of school, and Supervisors through health official programs must support it.

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FASCIOLA HEPATICA INFECTION IN A 2½ YEAR-OLD BOY

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Introduction: Fascioliasis is an infectious disease caused by Fasciola hepatica or liver fluke. Humans are accidental hosts to these flatworms. The World Health Organisation considers fascioliasis an important human parasitic disease. Even though in Europe, Australia and Northern America, the disease is extremely rare, it should be taken into consideration in patients who have lived in or travelled to endemic areas.

Case presentation: Our case report refers to a 2 ½ - year-old boy from Kuwait, who recently spent his holidays in Ethiopia and was admitted to our hospital with fever, diarrhoea, cough, cervical lymph adenopathy and night sweats. Initial complete blood count revealed leucocytosis, hypereosinophilia, elevated alkaline phosphatase (AP), high values for aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT) and a high Epstein-Barr VCA IgM titer. The abdominal ultrasound scans revealed multiple irregular nodular lesions in the liver and enlarged abdominal lymph nodes. Clinical, radiological signs and continuous hypereosinophilia led to an extensive stool examination, where a large number of ova from Fasciola hepatica were detected. Fasciola hepatica infection could also be confirmed by serology. Two courses of Triclabendazole 10 mg/kg for 2 days were administered in combination with steroid therapy. Under this treatment the clinical and laboratory signs improved. **Discussion:** Fasciola hepatica infection in children should be considered in the differential diagnosis of patients coming from high risk countries with hepatic or biliary disease associated with eosinophilia. Interestingly our patient presented with an EBV co-infection. Treatment of fasciola hepatica infection in young children is challenging.

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EVALUATION OF INFLAMATORY MARKERS IN THE ASPHYXIATED PREMATURE INFANTS

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Introduction: The aim of this study was to to correlate early neonatal inflammatory response in the critically ill neonates after suffering severe asphyxia, no signs of infection at start and development of further problems in the CNS

Methods: A retrospective cohort study was carried out on 30 inborn preterm infants. Clinical symptoms for perinatal asphyxia (low Apgar score) verified on ultrasound and negative hemoculture. First sample was blood from vein taken at check in and/or shortly after, second sample was 48-72h after hospitalization and third 5-7 days after hospitalization. CRP value above 5 mg/L is considered as pathological.

Results: There is statistically significant correlation between the cytokines and asphyxia in premature infants. There is no statistically significant correlation between asphyxia and elastase, except the first 24 hours slight increase and equal values 2-3 days later due to hypoxic-ischemic support of the neutrophyles. In asphyxia cases there is an obvious edible elevation of Il-6 values in the 1^{st} measurement and of elastase values in the 2^{nd} measurement, using Friedman's test and Wilcoxon's test with a statistical significance ($p< 0.01$). Ischemia and haemodynamic disturbances in the 1^{st} days activate the cytokines, especially in infants with asphyxia, and promote increasing levels of Il-6.

Conclusion: Measurement of serum IL6 concentrations provides important clinical information on early anti-inflammatory processes, before histopathology can confirm fetal involvement in amniotic infection. Ischemia and haemodynamic disturbances in the first days activate the cytokines, especially in infants with asphyxia, and promote increasing levels of Il-6.

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CURRENT PERTUSSIS EPIDEMIOLOGICAL SITUATION IN LATIN AMERICA AND ASSOCIATED VACCINATION STRATEGIES

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Background: Increasing pertussis in Latin America is affecting infant mortality rates (MR).

Methods: MEDLINES and National Ministry of Health websites were reviewed (2005-2012) epidemiological data.

Results:

Argentina: The incidence rate (IR) increased 46% in 6 years, ranging from 5.7/100,000 (2005) to 8.3/100,000 (2011), 374/100,000 < 1 year of age (MR=2.4%). A pregnant women vaccination strategy was implemented in 2012.

Brazil: 867 confirmed cases occurred in 2007, and 2,247 in 2011 (77% < 1 year of age) (MR=2.2%).

Chile: IR increased 275% in 2 years, (4.0/100,000 in 2009 and 15/100,000 in 2011). 50.2% of cases occurred in children < 1 year of age (MR=0.6%). A cocoon strategy was implemented in 2011.

Colombia: 1,720 cases reported in 2009, 1,325 in 2010 and 1,805 in 2011. 56% occurred in children < 6 months of age (MR=1.7%).

Costa Rica: In 2006-7 outbreaks caused 12 deaths. A post-partum vaccination strategy was implemented in 2007 with no deaths reported in 2010-11.

Mexico: 579 cases reported in 2009, 401 in 2010 and 495 in 2011. 85% occurred in children < 12 months of age.

Central America: El Salvador, Honduras and Guatemala reported very low IR.

Conclusions: Pertussis has been increasing in many Latin American countries in recent years, specifically in children < 1 year of age. Improvements in the sensitivity of surveillance and diagnostics might explain part of this increase. Nevertheless, this has lead to novel strategies like post-partum, cocoon, and pregnant women vaccination for which effectiveness studies should be put in place to measure their impact

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TUBERCULOSIS PREVALENCE IN CHILDREN AND ADOLESCENTS OF EASTERN UKRAINE: TREND ANALYSIS

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Aim: To study the dynamics of pulmonary tuberculosis prevalence (TBP) in children and adolescents of the Eastern region of Ukraine.

Materials and methods: The analysis of TBP rates in children and adolescents in Lugansk region during 2005-2011 was conducted according to Lugansk Regional TB Dispensary data.

Results: TBP remained high during the period of observation: the lowest rates of TB were detected in 2009-12.5 per 100000 children, highest - in 2006-16.3. TBP in adolescents was highest in 2009-50.8, lowest - in 2011-24.4, average - 42.4 per 100000 adolescents, which is 1.3 times higher than national average rate (31.4 per 100000 adolescents). Pulmonary TBP rate in children was highest in 2011-14.3, lowest - in 2005-9.7, average - 11.7 per 100000 children. Highest pulmonary TBP rate among adolescents was in 2006-50.5, lowest - in 2011-21.4 per 100000 adolescents. In the structure of disease morbidity major form was TB of intrathoracic lymph nodes (TBILN) with rates 35,0 and 66,7 per 100000 children as highest and lowest for the 7 years. In the structure of pulmonary TBP in adolescents infiltrative TB (ITB) was revealed more often with highest rate in 2011-71.4, lowest - in 2006-55.8 per 100000 adolescents. TB was detected during preventive examination in 72.1% of children and 65.2% of adolescents.

Conclusions:

1. TBP among children and adolescents in Lugansk region remains high.

2. TBVGLU prevails in the structure of pulmonary TB in children, in adolescents - ITB.

3. Quality of preventive examinations needs to be improved with introduction more sensitive tuberculin test.

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CORRELATION BETWEEN ANTHROPOMETRIC DATA OF INTERNATIONALLY ADOPTED CHILDREN IN A MONOGRAPHIC UNIT ADOPTION

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Introduction: About 12% of the Spanish-population is foreign. In the last 10-years our country has adopted 42,805-children. These children come mainly from developing-areas, most of them from orphanages; presenting high-risk of malnutrition, retarded-development and emotional-deprivation by medical and social-factors. The initial study includes anthropometric-measures as nutritional markers. In the first evaluation of the adopted-children in a Reference Unit of International-Adoption (IAU), our objective was to determine the standard-deviation (SD) of weight, height and head-circumference according to World-Health-Organization(WHO)-graphics compared to the foundation-Orbegozo(FO) spanish-graphics.

Materials and methods: We performed a cross-sectional-study of the adopted- children from January 2011-June 2012, in the IAU, Hospital-Carlos III; Madrid. Data were collected from the medical-records, in the first-visit after the adoption, including demographic, anthropometric-data and SD according WHO and FO-graphics. A difference > 0.5 SD between the WHO and FO was considering significant. Statistical-analysis was performed by SPSS15.0

Results: 171 children; median age 2.2 years (5-11years); 50.3% (86/171) females. Origin: 39.8% (68) Asia, 25.7% (44) Africa, 24% (41) Eastern Europe and from South America 10.5% (18). Statistical-association was found in the weight

(considering as acute nutritional marker), between WHO and FO data, more than 0.5 SD ($p < 0.05$) SD, but not in the height nor head circumference (nutritional chronic markers). We did not find a statistical association for height and head-circumference.

Conclusion: The evaluation of the adopted-children is complex but, it could be analyzed by standard-percentiles from adopting-Countries. Initially it could be completed by the WHO-graphic's for measures such as weight, considering acute malnourishment.

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APPROACHES TO THE CHOICE OF EFFECTIVE ANTIBACTERIAL PREVENTION OF POSTOPERATIVE INFECTION IN CHILDREN WITH PENETRATING INJURIES OF THE EYEBALL

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Background: It is well known that clinical strains of S. aureus are widely spread microorganisms, causing nosocomial purulent infections in pediatric ophthalmology.

Methods: We studied the sensitivity of S. aureus clinical strains (n-131), obtained from children with infectious complications of the eyes' penetrating injuries, to antibiotics, used in pediatrics (by means of disc-diffusion method) and to antiseptics decasan 0,02%, miramistine 0,01%, chlorhexidine 0,05% (by the way of serial dilutions' method).

Results: We found low sensitivity of S. aureus to penicillins (26,79-53,57%). The resistance to oxacillin (44,50%) has shown a presence of methicillin-resistance among studied strains of S. aureus in children with infectious postoperative complications. We registered resistance to aminopenicillins (48,21%), carbenicillins (30,40%), ureidopenicillins (30,36%). About 91,07 % of strains were sensitive to amoxicillin/clavulanate. Cephalosporins of the 1st (cafazolin-83,93%), the 3rd generations (ceftriaxone-89,28%, ceftazidim-80,36%) were of high effectiveness against S. aureus. Strains of S. aureus were sensitive to meropenem (87,5%) aminoglycosides (14,29 -89,29%). Only in 46,72% of cases S. aureus was sensitive to vancomycin.

We found decasan as the most effective antiseptic against S. aureus with minimal bactericidal concentration (MBcC) - 1,45±0,8 mkg/ml; MBcC of miramistine varied 8,04±4,24 mkg/ml; as for chlorhexidine its MBcC was 13,01±10,60 mkg/ml.

Conclusions: Administration of aminopenicillin/clavulanat, cephalosporins of the 1st, 3rd generations, meropenem, gentamycin, tobramicin can be used to prevent eye infection in children with penetrating injuries, associated with S. aureus. High sensitivity of S. aureus to antiseptic decasan proves its usage as alternative method of antimicrobial prevention of postoperative Staphylococcus infection.

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NEONATAL INFECTION IN NEWBORN INFANTS WITH A MATERNAL HISTORY OF PREMATURE RUPTURE OF MEMBRANES

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Premature rupture of fetal membranes (PROM) occurs in approximately 2÷10% of all pregnancies. Both mother and fetus are at greater risk of infection after rupture of membranes.

Aim: Compared with regard to infectious morbidity and the role of the time duration of rupture of membranes between preterm (< 37 weeks gestational age) and term infants.

Methods: It is a retrospective study from University Hospital of Obstetric Gynecologic “Geraldine Queen” in Tirana Albania during a period September 2010 to September 2011, for neonates with history of PROM ≥ 18 hours. The two groups were compared, preterm and term group.

Results: 6420 newborn infants were born alive during the study period. 206 (3.2%) infants had a maternal history of PROM ≥ 18 hours. From them 92 (44.7%) was preterm. Rupture of membrane of more than 24 hours duration occurred in 86 (41.7%) of the patients. Only 41 of 92 (44.5%) infants in preterm group had probable infection comparative with 29 of 114 (25.4%) infants in term group (RR=1.95, P=0.0005 95% CI =1.33÷2.85). Overall neonatal infection was diagnosed in 13 of 206 (6.3%) infants with maternal PROM $\geq$ 18 hours. 11 of 92 (11.9%) infants in preterm group had infection comparative with 2 of 114 (1.7%) infants in term group (RR=9.16 P=0.003 95% CI =2,11÷39.7).

Conclusions: Incidence of neonatal infection is (6.3%) in infants with maternal history of Premature Rupture of Membranes $\geq$ 18 hours. Comparison between preterm and term neonates showed significant differences in rate of infection (p= 0.003).

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CHRONIC PLASMODIUM MALARIAE INFECTION: AN UNUSUAL PRESENTATION

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Background and aims: To describe an unusual clinical case of chronic Plasmodium Malariae infection focusing on the importance of rare tropical diseases in immigrated children.

Methods: A 16 years old boy was admitted to our paediatric department due to a persistent daily fever started 3 weeks before. Arrived in Italy from Pakistan 7 months before the admission, no particular problems were reported since then. Blood test showed only a significant C reactive protein increase (13 mg/dL) with a normal white cells count. Before the admission, an empiric antibiotic treatment with amoxicillin+clavulanate (1 gram three times a day for 10 days) was administered without any benefit. The malaria wide drop test resulted positive to Plasmodum malariae with a low concentration (< 0.01%). The patient was treated initially with clorochine for 3 days and then with primachine for other 14 days with success (apyrexia immediately the day after the first dose of clorochine). No other causes of infection or fever were found.

Results: Despite the clinical presentation was unusual for a chronic malaria case, this was the only etiologic cause found: immediately after starting the anti malaria treatment, the patient promptly recovered and the blood tests gradually brought back to normal.

Conclusions: With the increasing rate of immigration is important to think about tropical and unusual diseases, in particular in all patients with persistent signs or symptoms without a response to usual treatment. Country of provenience and epidemiological local data could be very useful in their management.

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QUALITY OF CARE INDICATORS FOR THE CARE OF HIV-INFECTED INDIVIDUALS ADAPTED TO THE PEDIATRIC AGE

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Background and aims: Since infection with human immunodeficiency virus (HIV) was firstly described there have been many advances in its diagnosis, monitoring and treatment. However, few contributions are related to the area of health care quality. In this sense, the Spanish Study Group on AIDS (GESIDA) has developed a set of indicators of quality of care for adult patients living with HIV infection that includes a total of 66 indicators, 22 of which are considered to be relevant. Standards were calculated for each of them in order to reflect the grade of quality of care offered to these patients. Similar documents for pediatric patients are currently lacking.

Methods: Elaboration of a set of quality of care indicators applicable to pediatric patients based on the GESIDA´s document and the Spanish Guidelines for monitoring of pediatric patients infected with HIV. We analyzed each of the indicators with respect to the required standards in all patients below 18 years of age followed-up in our Unit with the aim to evaluate the quality of care provided.

Results: A total of 61 indicators were collected (51 from the GESIDA´s document and 10 from current available pediatric guidelines), 30 of which were considered to be relevant. A global compliance of 81% - 83% when assessing relevant indicators - was obtained.

Conclusion: The availability of health care quality standards is essential for the attention of pediatric HIV-infected patients. The assessment of these indicators in our Unit yielded satisfactory results.

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CHANGES IN PERTUSSIS OCCURRENCE IN SLOVAKIA DURING YEARS 2006 - 2012

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Aim: To analyze pertussis occurrence in association with vaccination.

Methods: Pertussis is obligatory reported communicable disease based on the standard criteria of ECDC in Slovakia. The data on pertussis morbidity are from the Epidemiological Information System (www.epis.sk). Used laboratory methods were PCR, real-time PCR, and ELISA.

Results: The significant increase of the morbidity rate from 0.4 (2006) to 17.5 (2012) with maximum of 29.5/100,000 (2010) was observed. The highest increase was in the age group 15 -19 from 2.6 (2006) to 48.8 (2012), maximum of 128.7/100,000 (2010). The age group 10-14 revealed an increase from 1.1 (2006) to 15.2 (2012), maximum of 57.04/100,000 (2010). The morbidity in the age group 0 continuously rose from 1.9 (2006) to 36.6 (2012). Only a moderate increase of the morbidity was in the remaining age groups.

National childhood vaccination schedule of pertussis 3-doses (3-5-11 months), revaccination in 3 and 6 years of age using whole cell pertussis vaccine (wP) has been used in the period 2006-2007. Replacement of schedule of wP to aP (acellular pertussis vaccine) started in 2008. The revaccination in 3 years of age closed and the aP has been introduced in the 6 (2009) and 13 years (2010).

Conclusion: The introduction of the aP vaccine did not affect the increase of the pertussis morbidity. Revaccination by aP vaccine (13 years of age) indicates a positive impact on the pertussis morbidity in the most vulnerable age groups.

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THE CLINICAL AND EPIDEMIOLOGIC CHARACTERISTICS OF CHILDREN'S INFLUENZA ILLNESS IN EMERGENCY ROOM DURING 2011-2012 INFLUENZA SEASON

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Introduction: We investigated clinical and epidemiologic manifestation of influenza-like illness in Korean children during 2011-2012 influenza season.

Method: Children who visited emergency room (ER) with influenza-like illness (ILI) and were diagnosed as influenza by rapid antigen test (RAT) were included. The RAT was performed with nasal aspirates from all consented children who visited ER with ILI for 6 months (Dec 2011 to May 2012). The clinical and epidemiologic data were taken by survey form and medical records.

Results: Total 1720 patients were enrolled. The RAT results were positive in 300 (17.5%) patients and negative in 1420 (82.5%) patients. Among 300 positive patients, 127 (42.3%) were type A, 164 (54.7%) were type B, and 9 (3%) were positive in both type A and B. There were no statistical differences between positive and negative groups in age, sex, degree of fever, duration of fever, number of leukocytes, and chest X-ray findings. The statistically significant variables were presence of chilling, cough, sputum, sore throat, chest pain, abdominal pain, headache, myalgia and general weakness. Antimicrobial agents were more frequently used in RAT negative group (45.7 % vs, 61.8%).There was no significant difference in previous influenza vaccine history between two groups. There also no differences in passive smoking, number of family member and attendance of daycare or school.

Conclusion: This study showed that it was hard to discriminate true influenza infection in ILI patient only by clinical manifestations in emergency room. Further investigation like PCR or culture should be necessary.

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SURVEILLANCE OF OTITIS MEDIA AND NASOPHARYNGEAL CARRIAGE IN HIGH-RISK AUSTRALIAN INDIGENOUS CHILDREN DURING PCV7- AND PHID-CV10- VACCINATION ERAS

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Background: Less than 10% of Australian Indigenous children living in remote communities have normal middle ears and around 20% have chronic suppurative otitis media (CSOM). Medical, surgical and audiological services are inadequate and families do not cope with management of CSOM.

Aims: To monitor prevalence of otitis media, nasopharyngeal carriage and risk factors in high-risk Australian Indigenous children.

Methods: Surveillance occurred between September 2008 and September 2012. PCV7 (2,4,6 + PPV23 at 18mo) was replaced by PHiD-CV10 (2,4,6,18mo) on 1st October 2009. Children included in this report were 0 to < 36 months of age. Parents were asked to consent to their child's clinical assessments, swabs, medical record reviews and a lifestyle questionnaire.

Results and discussion: Mean ages of 362 PCV7- and 401 PHiD-CV10-vaccinated children were 18.6 and 18.3 months, respectively.

OM was diagnosed in almost all children (91% vs 90%) whereas tympanic membrane perforation (TMP) was 20% [16 to 25] in PCV7 group and 14% [10 to17] in the PHiD-CV group. Pneumococcal carriage was 75% vs 80%, and NTHi 75% vs 78%, respectively. Prevalence of risk factors were similar between groups although household crowding (number of children < 5 years of age) was significantly less prevalent, and child care attendance and recent antibiotic use were significantly more prevalent in the PHiD-CV10 group.

Conclusions: Prevalence of CSOM has declined from 20% to 14% (p=0.057) in recent years. Randomised controlled trials are needed to confirm the role of PHiD-CV10 in this reduction.

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MOTHERS´ KNOWLEDGE AND PERFORMANCE ABOUT DIAPER RASH IN INFANTS WITH DIARRHEA (2011)

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Diaper rash is one of the most common skin disorders, occurring in 50% of infants, with 5% having severe rash. The aim of this research is assess the Mothers´ knowledge and performance about caring diaper rash in infants´ with diarrhea.

Methodology: This is a descriptive-analytical research. We assess 231 mothers whom have infants 6-60 months with diarrhea. Data gathered through a researcher- administered questionnaire and interview by a professional. . Data analyzed by experts through SPSS version 16.00.

Findings: Finding showed that the majority of mothers (%90) have not knowledge about caring of diaper rash after diarrhea. Their knowledge was weak and they did not know how they treat or behave with diaper rash. About gaining information about skin care of diaper said we have not more information and knowledge to care it effectively (%76). Analysis of questions about knowledge and performances highlighted that the mothers´ knowledge about care of diaper rash was weak and their performances was weaker. Those mother who had diploma and higher, have more knowledge. The results after teaching through interview, showed that their knowledge was increased and they said this interview is more effective than others teaching methods.

Discussion: Considering the weak result about knowledge and performance of mothers about diaper rash in infants with diarrhea and its complications, promotion of their knowledge suggested through health workshop and others training meeting by professional and governmental official is necessary.

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ANEMIA IN ANTIRETROVIRAL THERAPY EXPOSED INFANTS

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Background and aims: Maternal antiretroviral therapy (ART) reduces the risk of HIV vertical transmission from 30-40% to 1-2%. Can ART be blamed for the anemia developed in the HIV exposed newborn, at 6 weeks, after postnatal HIV prophylaxis? Our aim was to evaluate from January 2009-July 2012 the hematological findings in HIV exposed infants from our Pediatric Clinic.

Methods: 68 infants born from infected HIV mothers were analyzed. Two infants (2,94%) are now HIV infected. We analyzed the erythrocyte line (Hemoglobin level and red cell indices) at birth and 6 weeks of age, maternal ART during pregnancy (Highly Active), gestational age, birth weight, ART prophylaxis (Zidovudine, Lamivudine), presence/absence of coexisting infections.

Results: ART during pregnancy was successfully administered to 53 of the mothers (78%). Almost half of infants (48.52%) presented anemia at birth, only 5 of them from non-medicated mothers. All infants received postnatal HIV exposure prophylaxis. At 6 weeks of age 95.23% of infants presented anemia, with a mean hemoglobin value of 9g/dL. Macrocytosis incidence increased from 7.35% in newborns to 25% after 6 weeks of treatment. Meanwhile the incidence of microcytosis decreased from 27.94% at birth to 9.5% at 6 weeks of age. Mostly, anemia was asymptomatic and needed only multivitamins/iron supplements, but in 25 cases blood transfusion was required.

Conclusions: Exposure to maternal ART can be associated with newborn anemia (RR=1.7), and macrocytosis (RR=2.48). Meanwhile postnatal HIV vertical transmission prophylaxis can significantly enhance the incidence of infant anemia, with a trend of increased mean corpuscular volume.

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MASSIVE PERICARDIAL EFFUSION AS AN UNUSUAL MANIFESTATION OF KIKUCHI - FUJIMOTO DISEASE

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Kikuchi - Fujimoto's is a rare self limiting disease usually characterised by cervical lymphadenopathy and fever.The aetiology of this disease is unknown.It can be confused with SLE, lymphomas and tuberculosis. Lymph node biopsy and a self limiting course are of help in diagnosing this disease.

We report a 7 year old male child who was admitted with complaints of fever for 1 month, skin rash for 10 days and difficulty in breathing for 2 days. On examination child was in congestive heart failure. Left cervical lymph nodes were significantly enlarged.X-ray chest showed cardiomegaly. Echocardiography revealed massive pericardial effusion with impending temponade. Pericardiocentesis with pig tail catheter insertion was done. Lymph node biopsy was suggestive of kikuchi-fujimoto disease. Child responded well to oral corticosteroids.

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MOLECULAR EPIDEMIOLOGICAL ANALYSIS OF THE BURKHOLDERIA CEPACIA COMPLEX STRAINS, ISOLATED FROM THE CYSTIC FIBROSIS PATIENTS IN THE RUSSIAN FEDERATION

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Background and aims: Cystic fibrosis (CF) is one of the most common monogenic hereditary disease with multiple organ pathology requiring complex treatment throughout the patient´s life. In Russia, according to the newborn screening the incidence of CF ranges from 1:2500 to 1:17000. 80% of mortality in cystic fibrosis is associated with lung disease. Burkholderia cepacia complex (Bcc) is associated with the deterioration of lung function, bacteremia and higher mortality. It was shown an increase in the frequency allocation Bcc more than 7 times in hospitalized patients, compared with outpatient. Genotyping of Bcc strains isolated from the Russian CF patients and their molecular epidemiology analysis was the aim of this research.

Methods: MLST protocol (Spilker T. et al.) for Bcc strains genotyping, software packages SplitsTree, LIAN, BURST, PHYLIP, MEGA 5 for multilocus sequencing data analysis.

Results: Bcc strains collected in 14 hospitals of the country from 1998 were analyzed and registered in the database PubMLST under id 1150-1153, 1155, 1189-1268. Strains were characterized by 9 new ST 708, 709, 710, 711, 712, 714, 727, 728, 729. Most strains were referred to the ST709 B. cenocepacia and were isolated from patients of all federal districts, except for the Far East. The genotypes of 241 and 729 are defined only in strains from patients of the Far East region. ST708 strain, previously marked as nosocomial, identified in CF patient together with the strain of epidemiologically significant ST709.

Conclusions: ST 708, 728, 709 are genetically similar with major epidemic lines: ST28 and ST32.

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TREATMENT OF UPPER RESPIRATORY INFECTIONS CAUSED BY STREPTOCOCCI FROM 2010-2012 IN DRACEVO AND ITS SURROUNDING

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Background and aims: Infections of upper respiratory tract are prevalent in pediatric age.Viruses are most common cause but also bacterial infections especially streptococcus pneumonia and infections caused by streptococcus pyogenes.These are difficult to treat because their recurrent nature although they are treated with antibiotics according to sensitivity pattern and because of resistant nature of these germs due to antibiotic abuse. After the treatment consequences in child development can be found.

Materials and methods: This study was undertaken in period of 2010 - 2012 and includes 1215 children aged from 1-15 years.Data was collected from health card-index. Quick strep-test is most often used method, blood count, CRP, RF, ASO, microbiology tests.

Results: In 551 child streptococcus pyogenes type A was found,treated with penicillin type drug for 10 day, microbiology check performed on day 7 from beginning of treatment without withdrawal of antibiotic.On day 10,526 children had negative results from microbiological check and repeating of test (ASO,CRP,RF) after 7 days shows negative or normal values .25 children had some abnormalities:20 with higher values of ASO,higher CRP and RF normal and in those children another 10 day regiment of treatment was taken.Prophylactic doses of oral penicillin was prescribed in 3 month period and has shown as successful treatment.5 children were streptococci positive all the time despite 10 day treatment and prophylactic treatment-germ carrier.After three weeks 1 child develops ASPGN.

Conclusion: Timed diagnosis and rational use of antibiotics may diminish the incidence of complications.Rapid strep test is an important tool to distinguish those who need antibiotic treatment.

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MANAGEMENT OF PEDIATRIC ORBITAL AND PERIORBITAL CELLULITIS

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Background: Orbital and periorbital cellulitis formation in pediatric patients usually arises as a complication of acute sinusitis and if untreated may cause visual loss or life-threatening intracranial complications. In this study we reviewed the current evaluation and management of this condition in pediatric unit.

Methods: A two year retrospective patients files analysis was performed on all hospital admissions to a tertiary children´s hospital with the diagnosis of orbital and periorbital cellutis. We have detected 28 children who were hospitalized for the treatment of orbital and periorbital cellulitis.

Results: Between 2011 and 2012, seven patients with orbital cellulitis and 21 patients with periorbital cellulitis had been followed. Among them 19 were boy and 9 were girl. Mean duration of hospitalization and treatment were 10.4 days and 17.8 days, respectively. None of the patients needed surgical intervention or had complications. The most important predisposing factor was sinusitis and the other predisposing factors were thooth abcess, conjunctivitis, varicella zoster infection and leukemia. Twenty five patients were treated with intravenous ampicilline-sulbactam and/or seftriaxone. Only in 3 patients this therapy did not result in full-recovery and therapy was switched to vancomisin+meropenem, vancomisin+cefoperazone-sulbactam, and vancomisin+piperacilline-tazobactam, respectively. All patients have discharged with cure without complications.

Conclusion: This study showed that ampicillline-sulbactam was effective in the treatment of orbital and periorbital cellulitis.

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VENTRICULOPERITONEAL SHUNT INFECTION AND TREATMENT IN PEDIATRIC PATIENTS WITH HYDROCEPHALUS: SINGLE CENTER EXPERIENCE

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Infection remains the most significant complication of ventriculoperitoneal (VP) shunt surgery and the reported rates of VP shunt infection vary widely across studies in patients with hydrocephalus. The objective of this study is to review and evaluate the infections complicating VP shunt surgery in pediatric patients with hydrocephalus.

Children who underwent VP shunt surgery for hydrocephalus between 2010 and 2012 were evaluated. Medical charts and clinical follow-up evaluations were reviewed and analyzed retrospectively. Between 2011 and 2012, 36 patient who were between 3 days of age and 16 years old have followed with VP shunt infections. Among them 24 boy and 12 girl. The most frequent indications for VP shunt surgery were conjenital malformations-myelomeningocele, tumor and intraventriculer hemorrhage. Among 36 patients bacteria grew in CSF culture of 19 patients and others were consistent for cerebrospinal fluid (CSF) inflamation. The most common growing bacteria was coagulase negative staphylococcus (%78). The other microorganism grew in culture were Staphylococcus aureus, Enterococcus faecalis, Enterococcus gallinarium, Pseudomonas stutzeri, Candida albicans, Streptococcus mitis, and ESBL (-) Klebsiella pneumonia. Among 36 patients VP shunt were removed and external ventriculer drainage was replaced in 24 patients and in 12 patients VP shunt were not removed. The mean duration of treatment was 14.7 days (range:4-56 days). Only one patient died during the treatment and others were fully recovered with treatment. In a case of a shunt infection the timely usage of appropriate antibiotics and removal of the shunt appear to be essantial for successful treatment of VP shunt infections.

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THE USE OF INTRAVENOUS COLISTIN AMONG CHILDREN: SINGLE CENTER EXPERIENCE

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Multidrug-resistant (MDR) gram-negative infections recently increasing thus leads to usage of colistin. Although it is well described in adults, tocixities of colistin in children are not well known. We report findings of pediatric intravenous colistin usage. We evaluated 28 children prescribed intravenous colistin. The mean age of children was 5.5 years (range: 4 days to 17 years). The most commonly targeted organisms were MDR Acinetobacter baumanii (82%) and MDR Pseudomonas (18%). MDR Acinetobacter baumanii growth were detected in blood culture in 15 patients, urine culture in one patient, wound culture in one patient, and endotreacheal aspiration fluid culture in one patient, respectively. MDR Pseudomonas growth were detected in respiratuar cultures in 4 patients, and blood cultures in one patient. The median duration of intravenous colistin therapy was 11 days. Additional antimicrobial therapy was given to all children, the most common given concomitant antibiotics were carbapenems in 13 children, sulbactam-ampicilin in 5 children, ciprofloxacin in 4 children and aminoglycosides in 3 children. During the intravenous colistin therapy one patients died due to infection. None of the children developed nephrotoxicity. This study showed that effectiveness and safety of intravenous colistin therapy in MDR gram-negative infections in children. Moreover, we found that nephrotoxicity in children may not be as high as described in adults.

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METABOLIC ACTIVITY OF INTESTINAL MICROFLORA WHILE ANTIBACTERIAL THERAPY

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Background and aims: To evaluate the effect the antibiotic therapy on the metabolic activity of intestinal microflora depending on the use of probiotics.

Methods: 74 children receiving antibiotic therapy (ABT) were included into the study. Children were divided into 2 groups. The 1st group of 25 children received probiotic (B.bifidum, B. longum, L. casei) from the first day of ABT. Patients from the 2nd group (21 children) received ABT without probiotics. Metabolic activity of intestinal microflora wasevaluated based on the level of short chain fatty acids (SCFA) with gas-liquid chromatography analysis on the first and 21st days.

Results: At baseline, children from the 1st and 2nd groups showed increasing level of propionic acid (0,222±0,009 U and 0,219±0,009 U respectively) and butyrate (0,103±0,006 U and 0,108±0,007 U respectively), as well as decrease in acetic acid (0,675±0,011 U and 0,673±0,010 U respectively). Anaerobic index (AI) was changed to negative values (-0,481 ±0,014 U in the 1st and -0,486 ±0,015 U in the 2nd groups).

Three weeks later, a group of children who received probiotic from the first day of ABT showed a normal level of C2-C4 fatty acids due to the stabilization of microflora content and removing the negative impact of antibiotic therapy. In the 2nd group changes in SCFA worsened due to microflora disorders while antibiotic therapy.

Conclusion: SCFA levels in stool can be an objective marker of the state of intestinal microflora. Preventive use of probiotics to protect against activation of proteolytic microorganisms.

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CLINICAL FEATURES OF PATIENTS HOSPITALIZED WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION

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Background and aim: RSV is one of the most common causes of respiratory tract illness among infants and young children. There are limited data on the epidemiology of RSV in Turkey. The aim of this study is to document the epidemiology and clinical characteristics of patients hospitalized with RSV infection.

Methods: We reviewed the medical records of 71 hospitalized children due to acute respiratory illness who had RSV PCR positive in nasopharyngeal specimens from 1st January 2012 to 1st June 2012 at the Department of Pediatric Infectious Diseases in Ankara University Medical School, Turkey.

Results: The age ranged from 1 to 192 months with a median age of 9 months and male-to-female ratio was 1.95:1. Bronchiolitis-pneumonia was the leading diagnosis followed by, pneumonia, upper respiratory tract infection, pertusis like and laryngotracheobronchitis. The most common isolated antigenic group was RSV type B. Increased risk factors for severe RSV disease include infants under the age of 6 months, gestational age < 37 weeks, birthweight < 2500 g, underlying disease were detected 38 %, 26.7%, 28.1%, 29.5% of patients respectively. Seven patients (%9,8) were admitted to the PICU. Underlying medical conditions were determined in three critically ill patients. Three patients (%4,2) who were previously helthy had needed mechanic ventilation support. There was no death due to RSV infection.

Conclusions: RSV infection causes a serious disease that provides a significant social and economical burden on the health system. The development of safe and effective vaccine for RSV requires to achieve effective control of RSV infection.

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CAN WE RELY ON A NEGATIVE RESULT OF PCR IN DRIED BLOOD SPOTS TO RULE OUT A CONGENITAL CYTOMEGALOVIRUS INFECTION?

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Background and aims: Congenital cytomegalovirus (CMV) infection (cCMV) may be devastating and its retrospective diagnosis is usually troublesome. The usefulness of real time polimerase chain reaction (rtPCR) for the detection of CMV in dried blood spots (DBS) has been demonstrated in many studies but none was performed in our country. Our aim was to evaluate its sensitivity in patients with a confirmed CMV congenital infection when retrospectively assessed.

Methods: All patients followed up in our Unit between 2007 and 2012 with the diagnosis of confirmed cCMV were enrolled. cCMV diagnosis was made by the finding of DNA of CMV in any body fluid in the first two weeks of life. Real time-PCR using nucleic acid extraction by an automatic system (EZ1 Qiagen®), amplification of two targets and DNA detection with molecular beacon probes (Smartcycler Cepheid® termocycler) was used to investigate the presence of CMV DNA in the DBS of Guthrie cards collected as newborn metabolic screening.

Results: Fourteen patients with confirmed cCMV were enrolled (10 males, median age 2.8 years). Only 7 studies were positive (sensitivity=50%). When analysing the correlation between the results and the viral load at birth (bVL), the difference between the two groups was statistically significant (median bVL was 6390 copies/ml for the positive results and 499 copies/ml for negative ones; p= 0.005)

Conclusions: At least in our centre, and despite the low number of analyzed specimens, rtPCR of CMV-DNA in DBS is suboptimal for the diagnosis of cCMV, especially in cases with low bVL.

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NEONATAL HEPATITIS HUMAN CITOMEGALOVIRUS CHARACTERISTICS AND COMPLICATIONS IN INFANTS AT DR. HASAN SADIKIN GENERAL HOSPITAL BANDUNG, WEST JAVA INDONESIA

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Background and aims: Neonatal hepatitis is inflammation of the liver that occurs in early infancy or neonates, often between one and two months after birth, when the mother as vertical transmission rate ranges from 40%-50% has a primary infection (or reactivation) during pregnancy. Human Cytomegalovirus (HCMV) is one of the causes. Developing country such as Indonesia have level of infection by HCMV is high. Cholestasis jaundice cause by intrahepatic (2/3 cholestasis) and extrahepatic .The aim this study to determine how the characteristics and complications that may occur in infants who suffer from hepatitis HCMV.

Methods: This study was descriptive research, comprised consecutive infants submitted with cholestasis jaundice and neonatal hepatitis between Januari 2011 and December 2012 by Gastrohepatology division at Child Health Department Dr. Hasan Sadikin General Hospital Bandung, infants age 1-19 months, neonate's identification, history, symptoms, physical examination, clinical findings, and results of laboratory testing was documented.

Results: All 50 infant obtained boy 30 (60%) and girl 20 (40%), the most ages was 2 month 15 (30%). Levels of ALT (alanine aminotransferase) ranged between 27-1093 U/L and direct bilirubin 6.41-18.21 mg/dL, with overall complaints jaundice 50 (100%), Hepatomegaly 47 (94%), Splenomegaly 10 (21%), accompanied by biliary atresia 9 (18%), cirrhosis 5 (10%), 1 (2%) baby had cortical blindness, Hearing impairment 4 (8%), Hydrocephalus 1 (2%), 4 (8%) palsy cerebral, and 1 (2%) intracerebral calcifications

Conclusions: From this study we found that patients with neonatal hepatitis HCMV can be associated with the biliary atresia and severe complications such as cirrhosis, cortical blindness, and hearing impairment are frequent.

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SURVEILLANCE OF ROTAVIRUS GASTROENTERITIS HOSPITALIZATIONS IN CHILDREN < 5 YEARS OF AGE IN SPAIN, PERIOD 2005-2010

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Background and aims: This study aims to assess time trends in hospitalizations for rotavirus in children < 5 years during the period 2005-2010. Rotavirus vaccines were marketed in Spain in 2007 and vaccination coverage was 17% in 2007, 35% in 2008, 38% in 2009 and 18% in 2010 (Rotarix was suspended since March 2010, and Rotateq between June and November 2010).

Methods: Retrospective survey by using the National Spanish Surveillance System for Hospital Data. Hospitalizations for infectious gastroenteritis and, specifically, for rotavirus infections were selected. The annual rate of hospital admissions was calculated. Results were gathered by age.

Results: A total of 31,179 hospital admissions for rotavirus in children < 5 years were recorded in the period 2005-2010. 86% were in children < 23 months of age. Rotavirus hospitalization rates for rotavirus were 300 per 100,000 in 2005, 256 in 2006, 264 in 2007, 193 in 2008, 174 in 2009 and 194 in 2010. Among the study period, the hospitalization rate decreased globally by 37% from the prevaccination period (2005-2006) to 2009. This decrease was more remarkable (43%) in children < 12 months of age. Between 2009 and 2010 hospitalizations rates related to rotavirus increased. This was not observed for all-causes gastroenteritis.

Conclusions: Non-systematic use of rotavirus vaccine in Spain had driven a reduction in the burden of hospitalizations by rotavirus disease in young children. In 2010 this trend was not observed, but it should be taken into account that vaccines were suspended and the vaccination coverage decreased significantly.

908

NECROTIZING (MALIGNANT) OTITIS EXTERNA (NOE) AS THE PRESENTING DIAGNOSIS IN A 2-YEAR OLD PATIENT WITH UNDERLYING AUTOIMMUNE NEUTROPENIA

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Background: NOE is usually found in elderly diabetic patients, whilst it is rare in childhood. Paediatric cases are described in context with severe immune suppression often associated with haematologic malignancies. Pseudomonas aeruginosa is isolated in >90% of cases. Autoantibodies against neutrophil antigens lead to autoimmune neutropenia (AIN) which is characterized by chronic neutropenia and mild infections.

Case presentation: A previously healthy two-year old girl presented with a two-month history of purulent right ear discharge without other systemic symptoms and despite receiving several courses of amoxicillin without a satisfactory response. Clinically a red and painful swelling behind her right ear was detected and intravenous flucloxacillin and penicillin was commenced. Full blood count showed neutropenia (300/µl) and treatment was switched to Piperacillin-Tazobactam, Gentamicin and topical Ciprofloxacin following isolation of Pseudomonas aeruginosa from ear swab. Because of persistent neutropenia (lowest count 10/µl) Piperacillin-Tazobactam was substituted by Teicoplanin. A CT-scan revealed extensive inflammation involving the right pinna, cartilaginous and bony ear canal and an associated 1,2x1,2cm collection. The abscess was drained and HNA-1a antibodies were detected, confirming the diagnosis of AIN. A four-week course of oral Linezolid, Ciprofloxacin and G-CSF (5µg/kg) thrice weekly achieved good responses. Because of persistent severe neutropenia G-CSF was increased (10µg/kg) leading to the recovery of neutrophil counts.

Commentary: To our knowledge this is the first case describing NOE as the presenting disease in AIN. The management consists in prolonged antibiotic treatment with/without surgery. G-CSF use in AIN is controversial but might be indicated in patients with serious invasive infections.

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SEVERE PULMONARY INFECTION WITH SCEDOSPERMIUM APIOSPERMUM IN A PATIENT WITH CYSTIC FIBROSIS AND ITS TREATMENT WITH SYSTEMIC AND NEBULIZED VORICONAZOLE

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Background: Infections with Scedospermium are rare complications in patients with chronic pulmonary disease or immunodeficiency. Prognosis is often poor and the long-term antifungal treatment difficult.

Methods: The case of a seventeen year old patient with cystic fibrosis and respiratory failure, secondary to an infection with scedosporium is reported. Its antifungal treatment with voriconazole and amphotericine B is described and the literature for antifungal nebulizations and treatment of scedosporial infections is reviewed.

Results: Secondary to decreasing lung function (FEV1% dropped from 50% to 35%) and rising aspergillus antibodies, the patient was suspected to have allergic bronchopulmonary aspergillosis (ABPA) and was treated accordingly (steroids and itraconazole). After four weeks his condition worsened and he developed respiratory failure (FEV1% 19) with hemoptysis.

CT-scans revealed severe cavernous pulmonary destruction. Finally Scedosporium apiospermum was isolated from bronchoalveolar lavage.

Respiratory stabilization and regression of the infection was achieved with intravenous and nebulized voriconazole and intravenous amphotericine B. After successful lung transplantation three months later and continuation of voriconazole for one year, no relapse occurred in the following two years.

Conclusion: Scedosporial infections, primarily resistant to Itraconazole, are difficult to treat. Scedosporium apiospermum usually still responds to Vori-/ Posiconazole; Scedosporium proliferans is naturally resistant to most antifungals. Pharmacokinetics of nebulized voriconazole have been described in the mouse model for prevention of pulmonary aspergillosis.

For the first time the safe use of nebulized voriconazole for treatment of severe pulmonary infection with Scedoporium apiospermum in an adolescent with cystic fibrosis and his survival after lung transplant is reported.

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EPIDEMIOLOGICAL DATA OF CHILDREN WITH FEBRILE SEIZURES DURING A FIVE YEARS PERIOD. DOCTOR OF SCIENCE EDMONT LAHO. REGIONAL HOSPITAL CENTER ELBASAN ALBANIA

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Aim: To present the epidemiological data of the children with febrile seizures, the underlying infections and recurrences.

Material and methodology: This is a retrospective study for the period 2005-2011. In this study there have been taken all the cases of children hospitalized at the pediatric service of regional hospital of Elbasani hospitalized with febrile seizures. All the cases that have been studied for epidemiological and clinical data registered.

Results: There were 12,214 children hospitalized with various disease. 263 cases or 2, 15% of total hospitalized had the admission diagnosis of febrile seizures. 48 out of them (18%) of them had recurrent episodes of seizures. The age group more affected was 1-4 years old (45%). Viral respiratory infections were the main underlying diseases regarding even the seasonal distribution was mainly during Autumn and Winter (67% compared to those cases of Spring-Summer by 33%).

Conclusion: Febrile seizures are common in children mainly represented with infections. The most affected age group resulted that over 1 year.

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VARICELLA HOSPITALIZATIONS BY AUTONOMOUS REGIONS IN SPAIN, PERIOD 2009-2010

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Background and aims: Two Spanish Regions (Madrid and Navarra) and two cities (Ceuta y Melilla) have routine vaccination programs against varicella at 12-15 months of age since 2007. In the rest of Regions, routine immunization targeted susceptible 10 to 14 years of age. In addition, varicella vaccination of infants is prescribed by pediatricians in a non-routine basis reaching different vaccination coverage.This study was aimed to assess the epidemiologic situation of serious varicella cases in Spain during the period 2009-2010.

Methods: Retrospective, descriptive study based on the national surveillance system for hospital admissions (Conjunto Mínimo Básico de Datos). All hospitalizations with a varicella diagnosis in any diagnostic position were selected. Demographic and diagnostic data were collected. The Spanish population data were used for the hospitalization rate calculation. Vaccination coverage data was estimated for each region using distribution data.

Results: Varicella hospitalization rate during the study period was 3.27 hospitalizations per 100,000. Overall, 0-4 years of age children showed the highest annual hospitalization rate (41.4 admissions per 100,000). Navarra and Madrid showed low hospitalization rates in the period 2009-2010 (1.37 and 1.99 per 100,000, respectively). These regions had vaccination coverage of nearly 90% in the period 2007-2009. Cantabria registered the highest hospitalization rate (5.70 per 100,000). This is one of the regions with lower vaccination coverage (16% in the period 2008-2010).

Conclusions: Varicella still causes a significant burden of severe disease in Spain. Regions with systematic vaccination programs in young children showed to have lower rates of varicella serious cases requiring hospitalization.

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INSTRUMENT FOR MEASURING PSYCHOLOGICAL VULNERABILITY IN CHILDREN AND PUBERTAL HIV

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Background: In the Hospital Muñiz we serve children and teens which contracted HIV. The life of patients depends on their adherence to treatment. Adherence aspects are both objective and subjective. Between these last mentioned, is usual to refer to inherent vulnerability to the condition of living with HIV, or to the resilient attitude according to the case. We tend to capture in our patients a conflict between resilient attitude (AR) in where the adversity becomes an effective stimulus to increase vitality and the behaviour of passively surrendering to the adversity (RPA). This conflict lasts the whole life.

Resilient attitude managed to process losts of topics (they are detailed on the score).

Objetives: Building a score to detect the level of vulnerability/resilient in the required moment.

Methods: Psychologic interview, playtime to extract the simple. Concepts of vulnerability and resilient were operationalized to build the score.

Results: Table

Horizontal cathegories:

- Patient
- Score
- RPA prevails: topics not detected
- AR prevails: personal issues topics are detected
- Intermediate condition: themes are detected, absence of personal commitment

Vertical cathegories:

- Disease nature and origin
- Distinction between objects and toxic and nutritional substances
- Family trauma
- Cronical nature of disease
- Mental disposition to what is different: envious attack / creativity

Conclusions: This score allowed us to distinguish patients with resilient attitude from others which surrender to adversity, while it guides clinical work.

913

ENCEPHALOPATHY RECOVERY OF A CHILD SECOND-GENERATION INFECTED WITH HIV/AIDS THROUGH VERTICAL TRANSMISSION, THAT RECEIVED A NON RECOMMENDED ANTIRETROVIRAL THERAPY

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Objectives: The objective of this work is to describe the neuro-developmental recovery of a child, which is the second-generation infected with HIV/AIDS through vertical transmission, that received a non recommended antiretroviral therapy. These drugs were delivered since the patient didn't show congenital resistance to other drugs when the diagnosis was done.

Methods and patients: We made a descriptive and observational study of the case, based on the child's medical history. His mother shows bad adherence to the treatment, before and during the pregnancy, and was treated with AZT during the childbirth. He also received AZT the first 15 days of life. The HIV PCR test showed two positive results. The genotyping test informs the resistance to the nucleoside and non nucleoside inhibitors of the reverse transcriptase, and sensibility to the proteases inhibitors.

Present: CV >750000 (log>5,7) and CD4 2062 (20%). He started the treatment ARV with Lopinavir/Ritonavir, Fosamprenavir y Enfivurtide.

Results: When admitted, he presented progressive encephalopathy by AIDS C3, developmental delay, pyramidal syndrome and spastic paraparesis. Brain TAC test showed diffuse brain atrophy. He received early stimulation, physical rehabilitation and antiretroviral treatment. He showed the progressive improvement in immune status and the recovery of the maturational patterns according to his age. Nowadays: NMR without brain atrophies' signs, and CV< 34 (log< 1,53), CD4< 2611(39%).

Conclusion: Lopinavir/Ritonavir, Fosamprenavir and Enfivurtide, not recommended drugs in pediatrics, promote the neuro-maturational recovery in an infant (2 months old), with a high congenital resistance to antiretroviral drugs and without adverse effects to the present.

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SINGLE CENTER EXPERIENCE OF PEDIATRIC CANDIDAL INFECTIONS

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Pediatric Candidal infections increasing in numbers since more children and neonates need more intansive care and more usage of broad-spectrum antibiotics. This study aimed to describe the epidemiology of pediatric candidal infections in Marmara University Hospital during 2011-2012 periods. We detected 29 children who had candidal infections. Among them 17 (59%) were male and 12 were female (41%), 11 (38%) of them were under age one, 9 (31%) of them were between age 1-5 years and 9 (31%) of them were older than 5 years old. The most common underlying diseases were malignancies, congenital heart diseases and neurological diseases. Candida growth detected blood culture in 17 children, urine culture in 10 children and cerebrospinal fluid culture in 2 patients. Candida albicans were recovered in 17 (59%) children. Among all children 2 had a hepatosplenic candidal infection, one had candidal endocarditis, and 2 had candidal pulmonary infection. None of the patients revealed ophtalmic and renal involvement. For therapy, 11 children received caspofungin, 15 children received flucanazole and 1 children received amphotericin B. None of the candidal isolates was resistant to any of antifungal agents. During the therapy one patient died because of infection. Candida albicans still the most common Candida species isolated in children. Flucanazole still remains efective antifungal agent since no resistance was detected in our study population.

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CLINICAL FOLLOW-UP OF CHILDREN WITH VERTICALLY-ACQUIRED HIV/HCV CO-INFECTION IN SPAIN- A CROSS-SECTIONAL STUDY

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Background and aims: Little data exist regarding the clinical evolution of patients with HIV/HCV co-infection acquired by vertical transmission. This study aims to give further information on the current clinical situation of this patient group and alert about the liver damage.

Methods: A cross-sectional study was performed to describe vertically-acquired HIV/HCV co-infected children, included in Node 1 of the Spanish Paediatric HIV Cohort (CoRISpe-1). Data collected included the clinical state, diagnostic procedures and treatment.

Results: Information was obtained from 26 patients, of whom 19 are still being followed in pediatric units. The median age at the last visit was 16,5 years (IQR 14-19.25); 58% were female. All patients received HAART. The median CD4 count was 761 cel/mm3 (IQR 492-929), 76% had >500 cel/mm3 CD4 and 88% more than 25% of CD4. 69% have undetectable HIV viral load. HCV genotypes were: 46% genotype 1, 15% genotype 3 and 27% genotype 4 (11% unknown). 42% had increased ALT (> 40 U / L). 15% were seronegative for HCV antibodies. Liver biopsy was performed in 8 of 26 patients, 5 of whom had some degree of fibrosis. FibroScan was performed in 20 patients being abnormal in 40% (stiffness >7.6 kpa). One patient died of hepatic cirrhosis. 8 patients were treated for HCV infection (RBV+Peg-IFN); virological response was sustained in only 2 of them.

Conclusions: Whilst HIV infection in vertically-acquired HIV/HCV co-infected children appears to be well controlled, an important proportion of these patients suffer from progressive liver disease at adolescence or young adulthood.

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INFECTIONS IN PEDIATRIC EMERGENCY DEPARTMENT AND THE INFLUENCE OVER HOSPITAL ADMISSIONS

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Background and aims: Without protocols and specific criteria for admission of pediatric infectious pathology in tertiary hospitals, we want to analyze the foremost diagnostics in pediatric emergency department (PED) and the total number of main infections, using Diagnosis-related group (DRG) classification, reported in the last year (2012) by the biggest children hospital from western part of Romania.

Methods: We include all the records from PED in the last 12 month and analyzed the main categories from DRG groups, using data from SNSP - the national reference system - that we exploit to compare and report hospital activity about admitted patients in the same period of time.

Results: Among the total number of 25870 (urban/rural-18336/7354) cases in the unique PED from Timis county, in 2012, 9376 were cases with diagnostic of one of the important pediatric infectious. From this, the majority were upper respiratory infections/inflammations 5524 cases - 58.91%, interstitial lung disorders (694) 7.40%, otitis media (545) 5.81 %, entero-colitis (1239) 13.21%, urinary tract infections -UTI (417) 4.44%. The admitted cases in hospital departments were 19421 in 2012. From all, 4.52% were upper respiratory infections/inflammations, otitis media - 2.85%, UTI - 1.39%, interstitial lung disorders - 1.06%, entero-colitis 1.01%.

Conclusions: The main causes of admission in hospital departments from PED are interstitial lung disorders, UTI and otitis media. From those infectious diagnosis in pediatrics the vast majority of cases can be solved as outpatients or in extremis - in the PED (with all the lost of resources, influencing efficiency).

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ACUTE BRONCHIOLITIS: ASSESSMENT OF RISK FACTORS FOR SEVERE EVOLUTION

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Introduction: Bronchiolitis is a common disease in children under 2 years old causing ER presentation and sometimes admission. Severity of bronchiolitis (do to acute respiratory failure) accounts for admission criteria. Children with one or more risk factors for severe bronchiolitis (prematurity, dysmaturity, environmental factors, neurological disease, cardiac disease, airways anomalies, immune deficiency, chronic lung disease, age under 3 months old, formula feeding, RSV infection) are among those usually admitted.

Objectives: To reveal the correlation between admissions do to bronchiolitis and the presence of the risk factors.

Methods: A retrospective study was conducted, including 96 children under 2 years old, admitted in our hospital between November 2011 and January 2012. The admission criteria were Wang severity score for bronchiolitis (> 6). We have correlated the hospitalization lasting > 5 days and/or the Wang score for severity > 10 with the number of risk factors.

Results: All 96 children admitted had at least one risk factor for severe bronchiolitis. Children with Wang score >10 and hospitalization lasting > 5 days (34 children) associated at least 2 risk factors, most frequent of them being crowded living condition (94%), male sex (73,5%), prematurity (50%), age under 3 months (47%) and other comorbidities (29%).

Conclusion: Severity of bronchiolitis is correlated with number of risk factors that coexist for the same child.

918

HOSPITAL ADMISSIONS FOR PERTUSSIS IN CHILDREN IN A SECOND LEVEL HOSPITAL IN MADRID, SPAIN, 2005-2012

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Background and aims: Pertussis or whooping cough is far from erradication, and the incidence is increasing. Although mortality rate is less than 1 %, the morbidity is high, and involves a high cost to society.

The aim of this study is to estimate the rate of hospital admissions in children due to whooping-cough in a peripheral area in Madrid.

Methods: We carried out a retrospective epidemiological survey. Data were obtained by review of clinical electronic history. All hospital discharges in children under 5 (ICD-9- CM 033) between January 2005 and December 2012 were analyzed.

We estimated the annual incidence of hospitalization for pertussis and average length of stay.

Results: The annual incidence during the period of the study was 34 per 100.000 children under 5. Up to 25% of the cases ocurred at 2011.

Table 1 shows the annual incidence per year and percentage.

	2005	2006	2007	2008	2009	2010	2011	2012
Cases per 1000 children under 5	0.34	0.17	0.17	0.26	0.43	0.43	0.68	0.26
Percentage of the global cases	12.5	6.2	6.2	9.4	15.6	15.6	25	9.5

[Table 1. Annual incidence per year and percentage]

97% of children were less than 1 year of age, average age: 3,1 months (SD: 1,6).

More than half (56%) was referring familiar symptoms.

Average length of stay was 6,1 days (SD: 3,5) and 6,2% of patients needed critical care assistance. There were no mortality cases.

Conclusion: Rate of hospital admissions in children due to whooping-cough is increasing.

Adolescents and adults immunization programs should be taken into account.

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DOES THE INCREASE IN INCIDENCE OF MUMPS IN VACCINATED POPULATION REPRESENT A SERIOUS HEALTH ISSUE?

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Backround and aims: Mumps vaccine was introduced into Czech routine immunization schedule in 1985, the second dose was added two years later, which has led to significant decrease of the incidence. However, recently there has been identified increase in the incidence of mumps with higher risk of development of complications. The aim of this study was to evaluate clinical features and complications of mumps in paediatric patients.

Methods: This is a retrospective study of paediatric cases of mumps diagnosed at Hospital Na Bulovce in Prague in the years 2009-2012.

Results: During the study period there were identified 117 cases of mumps (75 boys, 42 girls). The age median was 15 years (IQR 8-17), 84 (71.8%) were treated as outpatients [median age 14 (IQR 7-17)] and hospital stay required 33 (28.2%) patients [16 (IQR 13.5-18), p=0.001]. The clinical course was complicated in 32 (27.4%) patients: orchitis (21; 17.9%), meningoencephalitis (11; 9.4%) and acute pancreatitis (2; 1.7%). Interestingly, 32 (27.4%) patients were treated with antibiotics in the primary care settings prior to diagnosis of mumps. The vast majority of patients (111/114; 97.4%) were vaccinated against mumps with 2-dose schedule.

Conclusions: Presented study confirmed the increasing trend in the incidence of complicated cases of mumps requiring hospital stay. There are several possible explanations of this trend: disappearance of vaccine-induced antibodies, circulation of more virulent viral strains or vaccine failure. Due to the significance of these findings, it is important to monitor this trend and eventually improve the vaccination strategy.

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INFLUENZA VACCINATION RATES AMONG SWISS CHILDREN DURING 2011/12

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Background and aims: In 2011, the Federal Office of Public Health in Switzerland recommended vaccinating children suffering from chronic diseases aged 6 months-9 years without previous influenza vaccination. However, little is known about influenza vaccination coverage rates (VCRs) in children. This study aimed to determine the number of vaccinations administered to children< 18 years during 2011/12.

Methods: Telephone interviews conducted among Swiss pediatricians from May-June 2012. The survey collected demographic data and data on the number and type of influenza vaccinations administered to children aged 6 months-17 years from September 2011-January 2012. Data were weighted by workplace and linguistic region.

Results: Included in the survey were 220 pediatricians from the German (61.8%), French (34.5%) and Italian (3.6%) regions. On average, 23.72 children were vaccinated per pediatrician (=5218 vaccinated children). In total, 28.8% (95%CI: 25.8-31.4%) of children aged 6-35 months, 27.4% (95%CI: 23.4-31.5%) of those aged 36-60 months, 22.1% (95%CI: 19.4-25.1%) of children aged 6-8 years, and 21.7% (95%CI: 19.8-23.6%) of children aged 9-17 years were vaccinated. By extrapolating these results to the Swiss population, we assume that ~27004 children were vaccinated in 2011/12. In Switzerland there are 1.4Mio children aged < 18 years, thus a theoretical VCR of 2% would have been achieved. One of the most frequently used vaccines was the virosomal adjuvanted influenza vaccine (39.9%).

Conclusions: During the influenza season 2011/12, the VCR of children in Switzerland seems to be very low. Although those are preliminary results, measures should be undertaken to improve VCR of children.

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LIPOSOMAL AMPHOTERICIN B VERSUS PENTAVALENT ANTIMONY SALTS FOR VISCERAL LEISHMANIA IN CHILDREN

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Objective: The aim of this study was investigate the efficacy of a 21 day schedules of Liposomalamphotericin B, compared to pentavalent antimony salts for the first episode of visceral leishmaniasis.

Methods: seventeen cases of visceral leishmaniasis who were admitted to Dr Behcet Uz Children's Hospital between January 2005 to April 2012 were retrospectively reviewed. One group included eleven patients who were treated with pentavalent antimony salts, sodium stibogluconate or meglumineantimoniate, intramuscularly for 28 Days. Second group was treated with amphotericin B intravenously at a dosage of 3 mg/kg on 1-5,10 and 21^{th}days (a cumulative dose of 21 mg/kg/day).

Results: The mean duration of hospital stay was 16 ± 2,7 days in liposomalamphotericin B group, while it was 30,18 ± 0,98 days in pentavalent antimony salts group and significantly longer in pentavalent antimony saltsgroup (p=0,000). The mean time required for recovery of fever in amphotericin B was 2.17 ± 0,753 days and 4,45 ± 1,508 days in pentavalent antimony salts group and significantly longer in pentavalent antimony salts group (p=0,000). Statistically significant durational increase was present in Hemaglobin levels in both of the drug groups; however significant durational difference was present in white blood cell, platelet counts and albumin levels only in pentavalent antimony salts.

Discussion: While pentavalent antimony salts were found to increase biochemical and haematological findings; liposomal amphotericin B was responsible for rapid recovery in fever and shorter hospital stay. As a result, our study shows the advantages of both medications independent of their costs.

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A CASE OF SEVERE COMPLICATION MANIFESTED AS A MASSIVE OEDEMA AND SECONDARY INFECTION AS A RESULT OF PRETERM NEONATE VACCINATION

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Background and aims: In the Department of Neonatalogy and Intensive Care of Neonate, Medical University of Warsaw preterm neonates are vaccinated after obtaining stable living functions and gaining appropriate mature age. The aim of the study was to determine the frequency of severe massive oedema as a complication of vaccinations scheduled for preterm infants.

Methods: In the period 04.2011-10.2012 there were 264 children born before 32nd Hbd in our department. They were vaccinated as follows: 105 against pneumoccoci (on the 71st day of life), while 94 against DTaP, HIB, Poliovirus and Hepatitis B (75th day of life), respectively. Children were observed at least for 48h, taking under special consideration oximetric parameters, local reactions and general condition.

Results: In a single case a massive oedema of the lower part of the body was observed in an infant born in 28 Hbd. It was vaccinated against DTaP, HIB, Poliovirus and Hepatitis B in 57 th day of life (36 weeks of postconceptional age). Blood tests revealed elevated markers of inflammation: WBC- 11,7 x10e3/uL, CRP- 17 mg/L, PCT < 0,5 ng/ml, and positive blood cultures (S. coagulase negative MRCNS). Vaccination against pneumococci was performed in 47th day of life and no side effects were noted.

Conclusions: Described complication was the only one so severe observed in our department, which, however, did not need any intervention and resolved spontaneously.

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CORONARY ECTASY IN KAWASAKI-LIKE SYNDROME DUE TO NON-INVASIVE STAPHYLOCCOCUS AUREUS INFECTION

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Introduction: Superantigens produced by Staphylococcus aureus have been classically associated with food poisoning and toxic shock syndrome (TSS). Numerous studies have also shown their possible role in other diseases such as Kawasaki disease (KD).

Case report: A 9 year old child presenting with 48 hours fever and mild respiratory symptoms was admitted and initially treated with endovenous ampicilin. A plaster placed several days before to treat an ankle sprain was removed, revealing an infected pressure ulcer. A swab for culture was collected, before switching to endovenous amoxicillin-clavulanic acid, in which Staphylococcus Aureus meticilin-sensitive (MSSA) was isolated. 24 hours later, fever disappeared and patient was discharged with oral treatment against MSSA. On the 10th day of this clinical picture, being afebrile and the ulcer in resolution, patient presented macular rash in the face and both hands, with extended subungueal desquamation. New analysis were taken, not meeting clinical criteria nor for TSS neither for KD (not even atypical). Nevertheless, given the characteristic desquamation, an echocardiogram was performed, showing left coronary ostium ectasy. Patient was readmitted, and treated with endovenous gammaglobuline (IVIG), clindamycin and aspirin, with immediate rash resolution, and progressive coronary ectasy improvement.

Discussion: Differential diagnosis between TSS and KD may be difficult. Both may benefit from IVIG administration, the former in severe cases, the later to prevent and improve the evolution of coronary abnormalities.

Conclusions: In order to ensure an appropriate clinical management, Kawasaki-like disease may be considered in a patient with non-invasive S. aureus infection presenting any criteria of KD.

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A VOLUNTARY PERFORMANCE AND QUALITY SURVEY OF A REGIONAL PAEDIATRIC HIV CENTRE

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Background: With the improved survival HIV has become a chronic condition. The development of centres delivering a high quality service is therefore a priority.

Aim: To evaluate the quality of our Paediatric HIV service using relevant markers of published quality dashboard.

Methods: Markers from the East Midlands Paediatric HIV Quality Dashboard and the CHIVA Standards were selected. All children attending a Regional Paediatric HIV Centre for at least 1 year were included. The survey was undertaken by a retrospective note and Patient Administration System (PAS) review.

Results: All 97 eligible patients were included.

Quality Markers	Compliance
1. Clinic Appointment within 2 weeks of HIV Diagnosis/Referral Letter	86%
1. CD4 count 4 weeks after HIV Diagnosis/Referral Letter	88%
Undetectable Viral Load 1 year after commencing treatment	81%
CD4 > 200 copies/ml after 1 year since 1. appointment	100%
Clinic letters send to GP	93%
Children & young people aware of their diagnosis	93%
Average Did Not Attended (DNA) Rate in 2012	19.5%

[Service Evaluation]

Conclusion: This service evaluation provided a useful exercise in understanding mechanism of service delivery. Caution has to be exercised with the interpretation when applying current quality markers on previous practice.

The evaluation is best performed prospectively to avoid incomplete data collection.

Some markers are not suitable to meassure quality and have to be worked out with commissioners, clinicians and service users.

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SEVERITY OF RESPIRATORY TRACT DISEASE IN PEDIATRIC PATIENTS POSITIVE FOR HUMAN RHINOVIRUS/ENTEROVIRUS IN RESPIRATORY SPECIMENS

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Background and aims: Human rhinovirus/enterovirus (HRV/ENT) is commonly identified in acute respiratory infections (ARIs) in children, although data on its clinical severity remains limited. We aimed to compare clinical severity between HRV/ENT, respiratory syncytial virus (RSV), influenza A/B (FLUA/B) and other common respiratory virus infections in children.

Methods: Retrospective study of children presenting in a tertiary care hospital with ARIs and confirmed single positive viral infections on mid-turbinate swabs by molecular assays. Outcome measures for clinical severity included hospital admission and, for inpatients, a composite end-point consisting of intensive care admission, hospitalization greater than 5 days, oxygen requirements and death.

Results: A total of 118 HRV/ENT, 104 RSV, 104 FLU A/B and 65 other common respiratory viruses were identified. Compared to children with RSV, FLUA/B and other common respiratory viruses, those positive for HRV/ENT were more likely to have underlying cardiorespiratory comorbidies (respectively 32.2% vs 14.4%, $p< 0.001$; 32.2% vs 9.6%; $p< 0.001$; 32.2% vs 16.9%, $p< 0.001$). In multivariable analysis adjusting for underlying diseases and age, children with HRV/ENT infections had increased odds of hospitalization compared to those with RSV (OR 2.6, 95% CI 1.37-4.76, p=0.003) and FLU A/B (OR 2.6, 95%CI 1.37-5.0, p=0.003) infections and increased odds of severe clinical disease (OR 2.39, 95% CI 1.28-5.0, p=0.006) only when compared to those with FLUA/B infections.

Conclusions: Children presenting with HRV/ENT had a more severe clinical course than those with RSV and FLUA/B infections, thus suggesting the importance to consider HRV/ENT infections in children with severe ARTIs.

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ROUTINELY SCREENING OF HIV IN CHILDREN IN COTE D'IVOIRE

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Background and aims: In Africa, AIDS is a public health problem in our countries. So many governments created a ministry only for AIDS. Several control policies are then developed and the disease has enormous financial resources. In Côte d'Ivoire, the ministry is called “Ministry of population and for fighting against AIDS”. One of these policies is the systematic screening of all children in pediatric consultation. This study aims to improve the fight against HIV in children. The specific objectives are to:

· Determine the seroprevalence of HIV in children

· Determine the rate of acceptance by parents of their child´s screening for HIV.

Methods: This cross-sectional study was conducted from June 2012 to December 2012. It concerns 393 children aged 0-15 years old from consultation in paediatric Jacqueville General Hospital. After information of their parents, children gave blood sample for HIV serological testing using rapid tests in accordance with current national algorithm.

Results: Among the 393 children received, 390 were authorized by their parents to undergo the test. 201 children were male and 192 female. HIV seroprevalence was 1.5% with 6 children aged from 13 months to 7 years old with a female predominance.

Conclusion: Children should be screened routinely for HIV. HIV seroprevalence among children remains high and could be even lower if the prevention of transmission from mother to child was properly followed. Strict policies must be applied in order to have no new HIV infection in 2015 like the objectives of WHO.

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RABIES POSTEXPOSURE PROPHYLAXIS IN THE INTERNATIONAL TRAVEL CLINIC OF THE NATIONAL MEDICAL CENTER FROM 2006 TO 2012, KOREA

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Background and aims: Rabies is an acute fatal viral disease generally transmitted through bite of infected animals to human beings and is widely distributed across the globe. Recently, Korean people who traveled to rabies-endemic countries and also were bitten by animals are increasing annually. Thus, we investigated international travelers who got rabies vaccine and/or rabies immunoglobulin at the National Medical Center (NMC) for obtaining data of appropriate or inappropriate rabies postexposure prophylaxis (PEP).

Methods: This study was performend through retrospective review of 106 patients who visited the International Travel Clinic of NMC and got rabies PEP from July 2006 to December 2012.

Results: 12 among 106 were children under 18 years of age and median age was 10.8 years (3.7-18.0). 20s, 30s, and 40s of 94 adults were 37 (39.3%), 29 (30.8%), and 10 (10.6%) respectively. The children traveled to China (4), Philippines (3), Indonesia (3), Thailand (1), and Vietnam (1) and of the 94 adults 36 (38.3%), 14 (14.9%), 13 (13.8%), 9 (9.6%), and 4 (4.3%) traveled to Thailand, China, India, Indonesia, and Nepal respectively. The most common mammal of biting animals is a dog(8 children, 63 adults). Within 7 days all children and 74 adults received the first rabies vaccination and 4 children and 47 adults got a rabies immunoglobulin injection. 11 (2 children, 9 adults) of 106 took the inappropriate rabies PEP.

Conclusion: Appropriate rabies PEP for overseas travelers who were bitten by suspected rabid animals is very important to prevent human rabies.

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VISCERAL LEISHMANIASIS IN CHILDREN: CLINICAL FEATURES AND DIAGNOSTIC METHODS

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Background: We examined the cases of visceral leishmaniasis (VL) admitted in an Italian children´s hospital, focusing on diagnostic approach.

Methods: We reviewed the files of all children discharged with VL diagnosis between October 2006 and October 2012.Diagnostic methods were: serological test using indirect fluorescent-antibody assay, PCR on peripheral blood (PB) and bone marrow (BM) and microscopical evaluation of BM aspirates, as gold standard.

Results: Data of patients are listed in fig1. In all cases serological determination of Leishmania antibodies was positive, with a median title of 1:1280. PCR on PB was performed in 87.5% of cases, with a positive results in 64%. In 57% of patients BM aspiration was performed. All samples underwent microscopic examination, while only 77% were tested with PCR: both methods obtained 100% of positive responses. In particular among the five patients with negative PCR on PB, three underwent BM aspiration confirming diagnosis and two were treated based on serology with recovery.

Patients characteristics	
o Mean age	2 y and 9 m
o Male: Female	10:6
o Time among symptoms onset and diagnosis	3,5 weeks (2-32w)
o Mean length of hospital permanence	13 days (6-24d)
Clinical and Laboratoristic findings	**Frequency %**
o Fever	94% (15/16)
o Splenomegaly	100% (16/16)
o Hepatomegaly	75% (12/16)
o Lymphadenomegaly	73% (11/15)
Emocromocytometric parameters	**Frequency %**
o Pancytopenia	81% (13/16)
o Anemia	100% (16/16)
- less than 8 g/dL	43% (7/16)
o Leukocytopenia	87.5% (14/16)
Relative Linfocytosis	53% (8/15)
o Thrombocytopenia	87% (13/15)
- less than 100.000/µl	47% (9/15)
Other laboratoristic features	**Frequency %**
o AST and/or ALT elevation	75% (12/16)
o LDH elevation	81% (13/16)
o Alteration of sieric protein concentration	87.5% (14/16)
- inversion of albumin/γglobuline ratio	50% (7/14)
o CRP elevation	93% (14/15)
o VES elevation	75% (6/8)
Diagnostic methods	**Frequency %**
o Bone-marrow aspiration	57% (9/16)
- microscopic examination	100% (9/9)
✓ positive	100% (9/9)
- *PCR*	77% (7/9)
✓ positive	100% (7/7)
o Sierology	100% (16/16)
✓ positive	100% (16/16)
o PCR on peripheral blood	87,5% (14/16)
✓ positive	64% (9/14)
Therapy	**Frequency %**
o Liposomal amphotericin B	100% (16/16)
- 5 days + booster	44% (7/16)
- 10 days + booster	25% (4/16)
- 10 days	25% (4/16)
- not specified	6% (1/16)
o Relapses	6% (1/16)
o Side effects	6% (1/16)

[Patient's data]

Conclusion: In developed countries VL is a rare but still challenging infective disease, especially for diagnostic issues. Our study shows a high diagnostic performance of serological test, although the poor discrimination between active and past infections has to be taken into account. PCR on PB, on the contrary, failed to diagnose VL in 31% of patients. This suggests that a negative result in presence of signs and symptoms of VL should recommend the execution of BM aspiration for microscopical examination, PCR and cultural isolation.

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THE ROLE OF IL-17 ON OCCURENCE OF PLASMA LEAKAGE IN DENGUE HAEMORRHAGIC FEVER THROUGH ACTIVATION OF PRO INFLAMATORY CTYTOKINE

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The role of IL-17 in virus infection has been evaluated, but there is no data its role in dengue hemorhagic fever. First aim was to evaluate the effect of shock in dengue hemorhagic fever into Th17 and IL-17 level. Second aim was to known the effect of IL-17 recombinant exposure on macrophage activation through expression of TNF-a, IL-8 and MMP-2. Third aim was to analysis an effect of activated macrophage by IL-17 on plasma leakage on human umbilical vascular endothelial cells (HUVECs) culture marked by albumin level.

Methode: Expression of Th17 was done by flow cytometry. Expression of IL-17 was done by ELISA. Expression of TNF-a, IL-8 and MMP-2 from activated macrophage exposed to IL-17 recombinant was evaluated by ELISA. Albumin level was evaulated by spectroscopy.

Results: There are significant increase on Th 17 and IL-17 in DHF with shock than without shock ($p< 0.000$). There is significant increase on TNF α between group in IL-17 recombinant exposure on macrophage at 16. 24 and 48 hour. There are significant different of MMP-2 between groups in IL-17 recombinant exposure macrophage 16. 24 and 48 hour. Post hoc test showed significant different of IL-8 between exposures 16. 24 and 48 hours; ($p< 0.000$), There is significant different of albumin level between 2. 4 and 8 ng/mml dose of IL-17 and time of exposure 48 hour ($p< 0.000$).

Conclusion: There is role of Th17 in pathomechanisms of plasma leakage in dengue hemorhagic fever via macrophag activation and secretion proinflammatory cytokine.

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PEDIATRIC HIV/TB SURVEILLANCE IN UKRAINE: CURRENT CHALLENGES AND NEEDS

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Background and aims: As of January 1, 2012 HIV prevalence among population 0-17 years in Ukraine has reached 2,906 and 91 (3.13%) were diagnosed with TB. Data on main HIV/TB epidemiological indicators (incidence, prevalence, mortality) in children is significantly biased due to surveillance, diagnosis, and reporting concerns, and artificial factors. Public health attention is needed to clarify main gaps in pediatric HIV/TB surveillance.

Methods: We conducted and analyzed focus group discussions on priority issues in pediatric HIV/TB surveillance among specialists and researchers in the area of HIV and TB in August 2012.

Results: Prioritized gaps include:

1) underdeveloped HIV/TB/MDR-TB case notification procedures including postmortem diagnosis with substantial differences in HIV/TB data among TB and AIDS care systems and that of regional/national departments of statistics;

2) absence of nationwide electronic registry of TB patients (currently under development);

3) outdated and unsecured mechanisms of personal data exchange between health care facilities:

4) artificial underestimation of HIV/TB incidence, particularly in postmortem diagnosis:

5) overestimation of HIV incidence among children with TB aged 0-18 months born to HIV (+) mothers.

Conclusions: Comprehensive approach to HIV/TB and MDR-TB surveillance regarding case definition, case notification, postmortem HIV/TB surveillance, and data security is needed to obtain a clear picture of epidemiological situation. Application of an electronic TB registry and its link with HIV registry might optimize the system. The use of direct methods of HIV diagnosis may resolve the issue of HIV incidence overestimation among TB-diagnosed children aged 0-18 months.

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MYCOBACTERIUM PHOCAICUM BACTEREMIA: AN EMERGING INFECTION AMONG PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS

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Background and aims: Non-tuberculous mycobacteria (NTM), specifically the rapidly growing (RGM) are ubiquitous in soil, dust, bio-aerosols, and water. NTM may cause Central venous catheter (CVC) associated bacteremia. Heat-shock protein 65 (hsp65) and 16S rRNA genes sequencing is increasingly used for identification of these pathogens. Mycobacterium phocaicum (MPo) was first described in 2006, is closely related to M.mucogenicum. To our knowledge, no clinical cases were described so far. We describe hereby 4 cases of MPo bacteremia among pediatric hematology-oncology patients.

Methods: Cases with NTM bacteremia and clinical data were retrieved from hospital charts. Isolation of NTM was done using BACTEC 9240 and isolates identified by hsp65 and 16S rRNA genes sequencing.

Results: Between March 2011- October-2012, eight patients had NTM bacteremia. Four were from MPo. Ages were 3- 15.5 years. Primary diagnosis was leukemia, Burkitt, neuroblastoma and lymphoblastic lymphoma. CVC´s were inserted 14-63 days before bacteremia; duration of bacteremia was 1-15 days. Antibiotic treatment consisted of Meropenem, Clarithromycin and Ciprofloxacin. Lung CT scan was abnormal in 3/4 patients, mainly with ground glass appearance. All patients recovered. No positive blood culture was documented after removal of CVC. One patient died 2 months later from neuroblastoma.

Conclusion: MPo is an emerging RGM, may cause bacteremia in pediatric oncology patients with CVC as was previously described with other RGM. In our cases, possible pulmonary involvement was common. Removal of CVC seems important for clearance of bacteremia. More data is needed for the evaluation of the full pathogenic spectrum of these emerging pathogens.

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GRANULOCYTE COLONY-STIMULATING FACTOR AMELIORATES CORONARY ARTERY LESION BY UP-REGULATING ENDOTHELIAL PROGENITOR CELLS IN A MICE MODEL OF KAWASAKI DISEASE

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Objective: To investigate the feasibility to prevent the coronary artery lesion by using granulocyte colony-stimulating factor (G-CSF) in Kawasaki disease (KD), and the effects on endothelial progenitor cell (EPC).

Method: To induce KD C57BL/6 mice were given an i.p. injection of L. casei cell wall extract. The coronary artery lesions were dynamic observed; meanwhile, the number of circulating EPC and the function of bone marrow EPC were assessed.

Result: The mice model of KD by using an i.p. injection of L. casei cell wall extract was shown similar natural progression on coronary artery inflammation and the elastin broken with KD patient. Furthermore, the number of circulating EPC and the function of bone marrow EPC were decreased in different level. Administration of rhG-CSF could up-regulated the number of circulating EPC and the function of bone marrow EPC effectively, and prevented the elastin broken of coronary artery.

Conclusion: G-CSF could prevent the coronary artery lesion by up-regulating EPC number and function in mice model of KD.

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SAFETY MONITORING IN THE NETHERLANDS IMMUNISATION PROGRAMME. SPONTANEOUS REPORTS IN 2011

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Background and aims: In the Netherlands Childhood Immunization Programme 2,2 million vaccine doses are administered annually. Surveillance of Adverse Events Following Immunization (AEFI) is prerequisite for vaccine acceptance.

Methods: Since January 2011 the Netherlands Pharmacovigilance Centre Lareb does review and registration of individual spontaneous AEFI reports. Before, this was done by the National Institute for Public Health and the Environment (RIVM).

Results: In the Netherlands, AEFI of childhood vaccinations are commonly encountered at community health centers. The majority of the reporters were primary child health care professionals (75%). In 2011 Lareb started a campaign to stimulate patients and parents to report AEFI because their involvement in vaccine safety surveillance is considered important. Now, the proportion of parents reporting AEFI has increased over 50%.

In 2011 Lareb received 1103 reports, with 1774 AEFI. According to international CIOMS criteria 88 of them were assessed as serious. No death were reported. The number of reports is comparable with the numbers reported to RIVM prior to the transition. Figures of 2012 will be included later. The types of reported AEFI are in line with past years. The majority represent well-known AEFI as injection site reactions, pyrexia, skin discolourations and symptoms of general discomfort. Remarkable is the already known adverse event 'extensive limb swelling' occurring in 4-years old children after administration of the fifth DPT-Polio vaccine. No signals were found for alarming, special or unknown AEFI. Full report at www.lareb.nl.

Conclusion: In The Netherlands, we did not find signals for alarming vaccine safety issues.

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INTRAVENOUS IMMUNOGLOBULIN RESISTANCE IN KAWASAKI DISEASE AND ITS PREDICTION

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Objectives: The purpose of this study was to find the predictors and develop a predictive scoring system of resistance to intravenous immunoglobulin (IVIG) in patients with Kawasaki disease (KD).

Methods: We performed a retrospective review of patients with KD treated within 10 days of fever onset. To identify independent predictors of IVIG- resistance, multivariable logistic regression models were constructed using variables selected by univariable analysis. And the independent predictors were combined into a scoring system. The discriminatory capacity of the scoring system was assessed using the area under the receiver-operating-characteristics (ROC) curve.

Results: According to the logistic regression analysis, polymorphous exanthema, changes around anus, days of illness at initial treatment, percentage of white blood cells representing neutrophils (% neutrophils), CRP, albumin and total bilirubin were proved to be independent predictors of IVIG-resistance. Based on the clinical characteristics of children in our hospital, variables such as polymorphous exanthema, changes around anus, days of illness at initial treatment, % neutrophils and CRP were used to generate the new scoring system, which gave an area under the ROC curve was 0.672. Kobayashi scoring system and Eqami scoring system were tested in our study, respectively. The area under ROC curve was 0.627 for Kobayashi scoring system and 0.614 for Eqami scoring system.

Conclusions: The new scoring system including polymorphous exanthema, changes around anus, days of illness at initial treatment, % neutrophils and CRP, has much higher sensitivity for Chinese children, compared with Kobayashi scoring system and Eqami scoring system.

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A CASE OF MUCORMYCOSIS IN A CHILD WITH NEUROBLASTOMA

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Background and aims: Invasive mucormycosis is uncommon fungal infection and associated with poor prognosis in immunocompromised patients. We present a case with successful management.

Case report: An 11-year old boy on chemotherapy for recurrent neuroblastoma (NBL) presented with fever during severe neutropenia (ANC 0.1 X 10^9/lit) and was started on meropenem, amikacin and teicoplanin. Two days later periocular erythema and swelling appeared, accompanied by local sinus tenderness. Liposomal amphotericin B (LAMB) 5mg/Kg/d also was started because a fungal infection was of concern. Sinus paracentesis revealed broad aseptate hyphae, and culture of nasal discharge grew Rhizopus spp. CT scan and MRI findings showed maxilary and ethmoidal sinusitis with no evidence of orbital, or brain invasion. In view of clinical and radiological deterioration (the patient had also severe facial pain requiring morphine), LAMB was increased to 7 mg/kg/d and posaconazole 20 mg/kg/d was added three days later. Five days later, fever subsided and the patient´s condition was stabilized. Surgical removal of the infected tissue was performed followed by long period of combination and then posaconazole only therapy.

Results: The patient had complete clinical and radiological recovery and was discharged 45 days after the beginning of antifungal therapy with no apparent residual fungal infection.

Conclusions: This case illustrates the seriousness of mucormycosis in immunocompromised patients. Successful treatment in our patient was probably related to the synergistic action of antifungal agents combined with surgical resection.

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ROTAVIRUS AMONG IMMUNOCOMPROMISED PATIENTS; DISEASE BURDEN AMONG CHILDREN AND ADULTS IN A TERTIARY CARE MEDICAL CENTRE

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Background: Rotavirus (RV) is highly endemic inside and outside hospital-settings and an important potential pathogen among immunocompromised patients. Severe RV gastroenteritis (GE) has been described, but little is known on general RV disease severity and manifestations among immunocompromised patients and RV contribution as gastrointestinal pathogen before RV vaccination.

Methods: We used 5-year laboratory records from a Dutch tertiary-care hospital to identify adult and pediatric RV infections. Medical records were reviewed for immunocompromising conditions and, when present, RV disease manifestations and interventions evaluated. In addition, 3-year hospital viral and bacterial stool-testing records as surrogate for GE episodes were used to estimate RV testing rates, prevalence and underreporting among adult and pediatric GE.

Results: Among 35 and 259 confirmed RV infections in hospitalized adults and children, respectively, 20 (57%) and 35 (12%) patients were immunocompromised. Apart from GE, complicating disease manifestations among immunocompromised patients included high transaminases (46%), hypokalemia (41%), feeding intolerance (31%) and, among children, prolonged illness (28%). Common interventions included rehydration (77%), antibiotics (24%), adjusting medication including chemotherapy (31%) and parental nutrition (18%). Of 3653 and 2215 adult and pediatric GE episodes, 433 (12%) and 1493 (67%) were tested for RV, with RV confirmed in 27 (6%) and 182 (12%), respectively. An estimated 87% and 30% of RV infections in adult and pediatric GE remain unreported.

Conclusions: RVGE has significant impact on immunocompromised patients. RVGE among hospitalized adults seems substantially underestimated affecting mainly immunocompromised patients. Anticipating sustained herd-immunity of infant RV vaccination, indirect benefits could be substantial among these patients.

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FEASIBILITY OF THE COCOON STRATEGY FOR THE PREVENTION OF PERTUSSIS IN THE LOCAL HEALTH AGENCY 4 "CHIAVARESE", LIGURIA (ITALY)

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Background and aims: Among the strategies implemented to control pertussis, such as infants' vaccination, booster of preschool children and adolescents, and the periodic vaccination of adults, the "cocoon" strategy has been widely recommended (Global Pertussis Initiative, Centers of Disease Control). It consists of the indirect protection of susceptible newborns through the immunization of their close contacts (parents, other family members and healthcare workers). The aim of this study is to investigate the feasibility of the "cocoon" strategy in an Italian Local Health Agency (LHA).

Methods: Since July 2012 the following actions have been implemented by the Department of Prevention:

- Training of the "cocoon" working group: health workers, gynecologists, pediatricians, midwives.

- Distribution of a specific leaflet for families.

- Implementation of OASIS software to appropriately register the project data.

- Vaccination of hospital/healthcare staff in contact with newborns.

- Vaccination of parents prior to hospital discharge postpartum unit.

- Vaccination of family members of the newborn at the vaccination unit.

- Communication of the results to the participating staff.

Results: The total number of newborn in our LHA is 1100 each year. Between July and December 2012, 381 booster doses of diphteria-tetanus-acellular pertussis vaccines were administered. About 43% of mothers, 17% of fathers, 39 grandparents and 7 other family members have been vaccinated.

Conclusions: Despite operational difficulties, such as the involvement of a healthcare professionals multidisciplinary team, preliminary results suggest that a "cocoon" strategy is feasible at the LHA4 "Chiavarese" and should be implemented in other LHAs.

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POTENTIAL CLINICAL CONSEQUENCES OF ERADICATING MENINGOCOCCAL DISEASE

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Background and aims: With the success of meningococcal conjugate vaccine (MCV) programmes, attention has turned to Neisseria meningitidis serogroup B disease (MenB) and its prevention with MenB vaccine. In some countries where MCVs have been deployed, MenB is now the predominant serogroup. Our aim was to predict how further reductions in meningococcal disease could change clinical practice.

Methods: We drew on experience from other vaccines and from other therapeutic areas, to predict expected and unexpected changes in clinical practice arising from the deployment of MenB vaccine.

Results: Haemophilus influenzae type b (Hib) and diphtheria vaccines have resulted in a marked decrease in epiglottitis and membranous pharyngitis respectively, and a decreased clinical risk associated with examination of the upper airway. Rubella vaccination has decreased the rate of therapeutic abortion for suspected congenital rubella syndrome. Compulsory vaccination of healthcare workers against hepatitis B virus (HBV) has reduced the risk of HBV transmission to patients.

With overall reductions in bacterial meningitis brought about by Hib, pneumococcal and meningococcal vaccines, there are likely to be further reductions in:

(i) medical consultations for suspected meningitis,

(ii) the ability of practitioners to distinguish serious from non-serious infection, and

(iii) the ability of practitioners to perform a full septic work-up, as well as changes in training needs, algorithms and recommendations for antibiotics.

It is also possible that care facilities can re-focus on patients with chronic conditions.

Conclusions: Predicted changes in clinical practice arising from the deployment of new vaccines need to be factored in to pharmacoeconomic models.

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KNOWLEDGE LEVELS OF 8TH YEAR STUDENTS ABOUT TETANUS VACCINE

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Background and aims: Almost all of the reported cases of tetanus disease, which is caused by tetanus microbes, are composed of those who are either not vaccinated at all or do not receive booster shots in the ten year period after the primary tetanus vaccination. This study was descriptively conducted in order to increase awareness of the children who received tetanus vaccination about the future booster shots and to determine their knowledge level about tetanus and tetanus vaccination.

Methods: The study was conducted with 365 students who studied at the 8th class of four secondary schools located in Ordu city center. Data was collected in October-December 2012 through a questionnaire developed by the researchers. The analysis of the data was performed using percentages and Chi-square test.

Results: It was seen that mean age of the participant students was 13.59±0.54 and 51.5% of them were girls.

82.7% of the participant students considered tetanus vaccination necessary, 80.8% knew about tetanus vaccination and 51.2% of them obtained this information from their families. The question how tetanus microbe was transmitted was answered as follows: contact with rusty metal (80.8%), an open wound (52.1%). It was explored that 57.3% of students thought that protection of tetanus vaccine was between 1-5 years.

Conclusions: It may be argued that students did not have sufficient knowledge about tetanus vaccination and tetanus transmission. We were of the opinion that teaching children about tetanus at an early age and educational programs designed to this end will be helpful.

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A HIV INFECTED CASE DIAGNOSED WITH DISSEMINATED CRYPTOCCUS INFECTION

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Background: Opportunistic infections are seen in HIV infected patients especially who are at advanced stages. Cryptococcus neoformans is one of the life threatening opportunistic infections. A HIV infected female case diagnosed with disseminated C.neoformans infection with initial complaints of fever, cough, bloody mucous is presented.

Case: A six year old girl was hospitalized with fever, fatigue and lack of appetite during the last one month. On physical examination, she had 39^{o}C fever with reduced interest around, had white plaques at oral mucosa, hepatomegaly and bilateral diffuse crepitation on auscultation. We learned that her mother had HIV infection and a history of Cryptococcus meningitis. Her anti HIV test was positive too. Laboratory data revealed bisitopenia (WBC: 3170 µL, lymphocyte: 366 µL, hemoglobin: 7.80 g/dL, hematocrite: % 24), hyponatremia (132 mmol/L,), hypocalcemia (8.3 mg/dL) and elevated CRP (15.2 mg/L). Because of the disseminated infiltrations at pulmonary x-ray examination, thorax computed tomography was done and interstitial milimetric nodular infiltrations and disseminated bronchiolitis were detected. At this period, C.neoformans was reported at hemoculture and bone marrow aspiration culture. Soon after admission she developed septic shock with pancytopenia, hypoalbuminemia and metabolic acidosis. She was treated with HAART and antifungal therapy (fluconazole + amphotericin-B) for four weeks with adequate clinical and laboratory response. HIV RNA was reported as 3.442.000 copy/mL. At the first month of the therapy, she was discharged with fluconazole prophylaxis.

Conclusion: At childhood period, HIV infection was transmitted 90% from mother. Opportunistic infections diagnosed at late symptomatic periods are critically important.

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MIDWIVES' AND NURSES' OPINIONS ABOUT DRAWBACKS SEEN IN IMPLEMENTATION OF CHILDHOOD VACCINATIONS: A QUALITATIVE STUDY

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Background and aims: Projected objectives cannot be attained due to the problems seen in policies used in vaccination programs and drawbacks faced during the implementation of vaccines. The aim of the research was to increase vaccination rates by increasing awareness and by citing opinions of midwives and nurses about drawbacks seen in implementation of childhood vaccinations.

Methods: The study was conducted with ten midwives and nurses who worked at two family health centers in Yozgat on the 7th of December,2012. The study used method of focus group interviews and face-to-face in-depth interviews for qualitative studies. Data was obtained using semi-structured question form.Qualitative data were recorded and analyzed with content analysis.

Results: It was seen that midwives and nurses faced such problems as not taking babies to the family health center in time for vaccinations, delay in vaccination due to the late registration of the migrated families and due to climatic conditions. The reasons of the problems was prejudice for vaccinations, negligence of vaccination, various problems caused by the system and health care personnels. It was understood that midwives and nurses provided written and oral information to the corresponding institutions, gave parents trainings about vaccinations, sent their requests for on-job trainings and made efforts for a systemized registration system.

Conclusions: There are still various problems of vaccination caused by parents, health care personnels and system in our country. Eliminating lack of information of parents and health care personnels, increasing their awareness will contribute to the elimination of these drawbacks and thus vaccination rates.

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PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY OF STREPTOCOCCUS PNEUMONIAE NASOPHARYNGEAL CARRIAGE IN HEALTHY CHILDREN AGED 3-59 MONTHS IN MILAN: PRELIMINARY RESULTS

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Background and aims: The 13-valent pneumococcal conjugate vaccine (PCV13) has been introduced recently and few data are available on nasopharyngeal carriage (NC) of S. pneumoniae (SP) after its introduction. We evaluated the prevalence and the antimicrobial susceptibility of NC-SP in healthy children aged 3-59 months.

Methods: Nasopharyngeal specimens were obtained from 1255 healthy children presented for routine well care at 24 primary care practices in Milan between 5 Sep and 6 Dec 2011. Potential risk factors for NC-SP were assessed. SP isolates were tested for resistance to penicillin, ceftriaxone, erythromycin, trimethoprim/sulfamethoxazole, chloramphenicol, tetracycline, vancomicyn, levofloxacin and linezolid(E-Test method) using EUCAST breakpoints.

Results: 1035 children were vaccinated (82%), 798 with PCV13. The prevalence of SP-NC was 27%. At multivariable analysis, age ≥ 25 months (prevalence rate ratio [PRR] = 0.73) and use of antibiotics in last 3 months (PRR= 0.66) were protective while ≥ 1 siblings (PRR ≥ 1.78), daycare attendance (PRR = 2.32) and infection in last 3 months (PRR = 1.40) were risk factors for NC-SP. Vaccination with PCV13 was not associated with SP-NC (PRR= 0.93). The most common SP serotypes were 6C (9%) and 23A (7%). 33% of isolates had intermediate resistance to penicillin and 2% were fully resistant. 36% and 26% of isolates were resistant to erythromycin and tetracycline, respectively. Resistance to other antibiotics was uncommon.

Conclusions: The most common SP serotypes were non-vaccine serotypes; the vaccination with PCV13 was not associated with SP-NC. Our data, furthermore, support the relative rise of penicillin-resistant SP.

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IMMUNITY AGAINST POLIOMYELITIS IN THE NETHERLANDS

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Background and aims: In the Netherlands, a poliomyelitis epidemic occurred in 1956. Routine childhood vaccination using inactivated polio vaccine (IPV) was introduced in 1957. Thereafter, three outbreaks occurred that were restricted to Orthodox Protestant individuals, refusing vaccination and living in a socio-geographically closely-knit network. We estimated age-specific antibody titers against poliomyelitis in the general population (NS) and religious groups.

Methods: We used a serum bank, established in 2006-2007 to estimate seroprevalence of diseases, targeted by the National Immunisation Programme (NIP).

We used Sabin-strain viruses as challenge viruses and determined neutralizing antibodies against poliovirus types 1, 2, and 3 in the NS and religious groups refusing vaccination. Results were given as ^{2}log reciprocal titers (GMT), cut-off for seroprotection was GMT = 3.

Results: Overall seroprotection in the NS (n=6386) was 94.6% (95%CI 93.9-95.3), 91.8% (95%CI 90.9-92.6) and 84.0% (95%CI 82.9-85.1) for the three serotypes. In 0-7-month-olds, eligible for 3 IPV-doses, mean seroprevalence was ≥ 80% for all serotypes. Seroprotection reached the highest level in 5-year-olds (100%, type1 and 2) and 9-10-year-olds (96%, type3). After a completed NIP, high and long-lasting GMTs were found.

For orthodox protestant people (n=326), seroprotection was 46.4% (95%CI 29.7-63.2), 38.4% (95%CI 26.9-49.9) and 44.6% (95%CI 35.7-53.9) for the three serotypes.

Within the NS, risk factors for non-protection were less than 6 IPV-doses, adherence to orthodox protestant religion, not traveling and a Dutch ethnicity.

Conclusions: A completed NIP results in high protection against all three poliovirus-types. However, people, refusing vaccination on religious grounds, remain at risk.

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VISCERAL LEISHMANIASIS AT AN UNIVERSITARY HOSPITAL

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Background and aims: Cases of visceral leishmaniasis (VL) have been reported in 66 countries, with an estimated amount of 12 million cases worldwide. The resurgence of leishmaniasis, its emergence in newer geographical areas, besides changing the clinical profile of infected patients, has put forward newer challenges in the areas of diagnosis, treatment, and disease control. We reviewed the clinical features, diagnosis and safety and efficacy of liposomal amphotericin B treatment of visceral leishmaniasis (VL) in children.

Method: A retrospective study was conducted among patients younger than 14 years diagnosed of VL at Universitary Hospital Infanta Cristina in Badajoz (Spain) between January 2001 and December 2010.

Results: We registered 8 immunocompetent children, 6 of them with associated pathology, mean age was 20 months. Diagnostic test confirmations were bone marrow biopsy positive in 75%, and serologic studies positives in 100 % cases. The main clinic signs and symptoms were anemia (100%), splenomegaly (100%), fever (100%), thrombocytopenia (75%), and hepatomegaly (75%). Every children were treated with liposomal amphotericin B at dose 3 mg/kg/day, on days 1, 2, 3 4, 5, and there were no relapse or death. The results of treatment were fever remission (24% at 24 hours, 72% at 48 hours), hepatosplenomegaly remission (100%) in 3-4 weeks, and anemia remission (100%) in 4-5 weeks.

Conclusions: Fever, splenomegaly, pancytopenia and epidemiological data should suggest the diagnosis of VL. Short course treatment for VL with liposomal amphotericin B in immunocompetent patients was favorable in all cases in our patients.

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REVERSIBLE SPLENIAL LESION IN PEDIATRIC CEREBRAL MALARIA

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Introduction: Cerebral malaria (CM) is a severe complication of Plasmodium Falciparum (P.F.) infection. We describe the first pediatric case of reversible lesion involving the splenium of corpus callosum (RLSCC) in cerebral malaria.

Case report: An 18-month-old African child, recently been in Burkina Faso and Ghana without performing antimalarial prophylaxis, was admitted to our Hospital because of fever, vomits and diarrhoea. She was poorly reactive with neck stiffness and mild liver enlargement. Laboratory tests: WC 16310/mm3 (N63%), Hb 7.5 g/dl, MCV 71.5 fL, Plt 49.000/mm3, CRP 251 mg/l, blood smear positive for P.F. (parasitaemia at 3% level). The child presented sensory deterioration; Hb decreased to 5.9 mg/dl despite treatment with quinine and clindamycin. She was intubated and admitted to our Intensive Care Unit (PICU): she was transfused and extubated the same day. Few hours later, the patient showed episodic clonic limb movements treated with lorazepam and phenobarbital. Lumbar puncture was negative, blood and fecal cultures were positive for Salmonella. Brain magnetic resonance imaging (MRI) showed edema with supra-tentorial white matter T2 hyperintensity, sparing "U" fibres. On diffusion-weighted imaging (DWI) the involved areas appeared markedly hyperintense with reduction of apparent diffusion coefficient (ADC) values. After 2 days, the child was transferred to the Pediatric Emergency department, in good general conditions; a week later she was discharged. Follow-up Brain MRI, performed 10 days from clinical onset, was normal.

Conclusion: RLSCC can be present in pediatric cerebral malaria. It is not correlated to a poor prognosis.

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IMMUNOMODULATORS TO TREAT ATOPIC DERMATITIS AND VACCINATION: REVIEW

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Background and aims: Immunomodulators creams used to treatment of atopic dermatitis, inhibit the synthesis and release of inflammatory cytokines. Our interest is to evaluate its action on the vaccine response.

Methods: Literature review of period 2003-2013 using the keywords “vaccine” and “tacrolimus” or “pimecrolimus” in databases: CINAHL, CUIDEN, DOCUMED, EMBASE, ERIC, IBECS, IME, LILACS, MEDLINE, OvidMD, PubMed, SciELO.

Results: We found three published clinical trials:

· A 7-month, multicentre, randomised, controlled trial[i] investigated the equivalence of response to vaccination against meningococcal serogroup C disease in children (2-11 years) with moderate to severe atopic dermatitis, by applying either 0.03% tacrolimus ointment (N=21) or a hydrocortisone ointment (N=111), versus control group (N=44) non-atopic dermatitis children.

· In a open-label, noncomparative study[ii], 23 children aged 2 to 12 years with moderate to severe atopic dermatitis were treated with tacrolimus 0.03% ointment for 7 weeks, immunized with a pneumococcal polysaccharide vaccine, and had their antibody response measured before and 4 weeks after vaccination.

· A 2-years prospective study[iii] investigated whether treatment with pimecrolimus cream 1% in 91 infants with mild to severe atopic dermatitis (aged 3 to 23 months), affects the development of a normal antibody response to vaccinations againts tetanus, diphtheria, measles, and rubella.

Conclusions: Topical application of tacrolimus 0.03% ointment doesn't affect response to vaccination against neither meningococcal serogroup C nor pneumococcal.

Treatment of atopic dermatitis with pimecrolimus cream 1% in early childhood doesn't appear to interfere with the development of a normal immune response to vaccinations.

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THE NEONATAL AND PAEDIATRIC ANTIMICROBIAL POINT PREVALENCE SURVEY: ANTIMICROBIAL USAGE IN LATVIAN HOSPITALS IN 2012

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Background and aims: The Point Prevalence Survey (PPS) was conducted as part of the Antibiotic Resistance and Prescribing in European Children (ARPEC) Project. The study aimed at analyzing paediatric and neonatal antimicrobial prescribing patterns in Latvian hospitals, to identify targets for quality improvement.

Methods: A one-day PPS on antibiotic use in hospitalised children was conducted in November 2012 in 10 Latvian hospitals, using a validated and standard method. The survey included all inpatient paediatric and neonatal beds and identified all children receiving an antimicrobial treatment on the day of survey.

Results: There were 448 paediatric and 101 neonatal (< 29 days) inpatients reported. 169 (38%) paediatric patients and 23 (23%) neonates received at least one antibiotic. Overall, 8 antibiotics accounted for 75% of total paediatric use (DU75%). Paediatric top one antimicrobial was ceftriaxone (20% prescriptions). Top three classes were third-generation cephalosporins (27% prescriptions), broad-spectrum penicillins (15%), first generation cephalosporins (13%). Antibiotics were most predominantly used intravenously (78% of 207 prescriptions). Bacterial lower respiratory tract infections (LRTI) were the most common indication for antibiotic use (23% of all prescriptions). Neonatal DU75% included 5 antibiotics; top one antibiotic - benzylpenicillin (33% of 36 prescriptions). Top three classes were beta-lactamase sensitive penicillins (33%), aminoglycosides (25%), broad-spectrum penicillins (14%). LRTI were the most common indication for antibiotic use (39% of all 36 prescriptions).

Conclusion: We identified three problem areas for improvement: high use of third-generation cephalosporins for paediatric patients, prescription of antibiotic combinations with broad-spectrum antibiotics for neonates and predominant use of parenteral antibiotics.

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HIGH COVERAGE OF RECOMMENDED INFANT VACCINES IN FLANDERS (BELGIUM) CONTRASTS WITH LOW COVERAGE OF PERTUSSIS BOOSTER IN THEIR PARENTS

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Background and aims: Previous infant surveys in Flanders demonstrated a high coverage but delay in age at vaccination. A new EPI-based survey (2012) ordered by the Flemish government evaluated timeliness and incomplete vaccination in infants, and assessed uptake of the recommended pertussis-containing booster vaccine (dTpa) in their parents (cocoon strategy, since 2009).

Methods: Through a randomized cluster design 946 toddlers were selected from 105 municipalities in Flanders. After consent of the parent(s), 874 (91%) families were interviewed at home. The requested information included socio-demographic characteristics and documented vaccination history. Infants' vaccination data were updated from medical files when incomplete. We assessed coverage of poliomyelitis (mandatory), tetanus-diphtheria-pertussis, H. influenzae type b, hepatitis B, measles-mumps-rubella (MMR), pneumococcal (PnC), and meningococcal C vaccines in infants, and dTpa vaccine in their mother or father.

Results: Coverage rates at 18-24 months of age were high at 97% for MMR and PnC and 93% for all other vaccines. Though 75% of infants had received their first vaccine dose at the recommended age of 8 weeks, only 25% received the third pertussis-containing dose at the recommended age of 16 weeks. Infants who were not immunised in well-baby clinics or who had more siblings or a younger or non-working mother were more at risk for not being fully vaccinated. Only 35% of mothers and 27% of fathers remembered having received dTpa booster.

Conclusions: Though infant vaccination rates meet high standards in Flanders, timeliness of infant vaccination and parent compliance to pertussis cocoon strategy leave room for improvement.

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CASE REPORT : ARRHYTHMIA IN A CHILD TREATED WITH LIPOSOMAL AMPHOTERICIN B FOR VISCERAL LEISHMANIASIS

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Background and aims: To report a cardiac side effect of liposomal amphotericin B in a child treated for visceral leishmaniasis (VL). Liposomal amphotericin B is the drug with the highest therapeutic efficacy and the most favorable therapeutic profile for the treatment of VL. Cardiac side effects as tachycardia, bradycardia, chest pain, arrhythmia, atrial fibrillation, cardiomegaly, valvular heart disease, cardiac failure and cardiomyopathy have been rarely reported in adults treated with liposomal amphotericin B. To the best of our knowledge, there are not reports in children.

Methods: We report a previously healthy Caucasian boy of 13 years with VL who was treated with liposomal amphotericin B, 3mg/kg on days 1 - 5, 14 and 21. On day 21, before the last dose, he was found to present arrhythmia.

Results: The cardiological assessment followed (ECG, Holter) detected ventricular contractions (Ventricular Premature Beats : 12568, 12%), without couplets or triplets, monofocal, more frequent during the day, disappearing on tachycardia. The heart rate was 80/min. Arrhythmia could not be attributed to causes others than the drug. The patient was examined repeatedly with gradual improvement and the arrhythmia was eventually resolved after 2 weeks. He never received the last dose of liposomal amphotericin B. He received a total cumulative dose of 18 mg/kg.

Conclusions: It is essential for clinicians to be aware of cardiac side effects of liposomal amphotericin B whenever they use the drug although these may be rare. In our case, the arrhythmia was reversible.

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THE CONTRIBUTION OF NON-CONVENTIONAL T CELLS AND NK CELLS IN THE MYCOBACTERIAL-SPECIFIC IFNΓ RESPONSE IN BCG IMMUNISED INDIVIDUALS

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Background: BCG vaccine is given to >120 million infants each year worldwide. The key components of a protective immune response against TB remain incompletely understood. The importance of γδ T cells and natural killer (NK) cells in the mycobacterial-specific immune response has recently been recognised.

Methods: Participants in four age-groups (birth, 2 months, 10-24 months and adults) were BCG-immunised. Ten weeks later, in vitro BCG-stimulated blood was analysed for NK and T cell markers (CD3, CD4, CD8, CD56, TCRγδ) and intracellular IFNγ by flow cytometry. Total functional IFNγ response was calculated using integrated mean fluorescence intensity (iMFI).

Results: In infants and children, $CD4^+CD8^-$ and $CD4^-CD8^-$ (double negative (DN)) were the main IFNγ-expressing cells. In adults, $CD4^-CD8^+$ cells were the main IFNγ-expressing cells, followed by $CD4^+CD8^-$ and DN T cells. The iMFI was higher in DN T cells compared to CD4 T cells in all age groups; most significant differences in infants immunised at birth ($p=0.002$) or 2 months of age ($p< 0.0001$). When NK cells were included for analysis, they accounted for the majority of total IFNγ-expressing cells and, together with γδ T cells, had the highest iMFI in infants immunised at birth or 2 months of age.

Conclusion: In addition to CD4 T cells, NK cells and DN T cells including γδ T cells are the key cell populations producing IFNγ in response to BCG in infants and children. This suggests that the innate immune response and unconventional T cells play an important role in protection against TB.

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TRENDS IN ROTAVIRUS IMMUNIZATION COVERAGE OF CHILDREN AGED LESS THAN ONE YEAR FROM 2009 TO 2012 IN THE VALENCIAN COMMUNITY

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Background and aim: The rotavirus is the main etiologic agent of severe infant diarrhea world-wide. In Spain oral vaccines such as Rotateq® and Rotarix® are available and have been licensed by the European Medicines Agency since March 2006. Rotavirus vaccination is not included in the immunization program of the Valencian Community. The aim of the study was to determine rotavirus immunization coverage from 2009 to 2012 in the Valencian Community.

Methods: A retrospective descriptive study of rotavirus immunization coverage in children less than one year of age has been done. Vaccinated data were obtained from the Vaccine Immunization System(SIV). Study variables: age, coverage, vaccine, year.

Results: The mean of population aged less than 1 year is 46 189. 52 907 doses of rotavirus vaccine were administered in 2009, 27 184 (2010), 43 585 (2011), 57 702 (2012). The 55% of doses of rotavirus vaccine administered in 2009 and 2010 were Rotateq®, the percentage of this vaccine for 2011 and 2012 was 93%. Trends in rotavirus immunization coverage in children less than 1 year from 2009 to 2012 in Valencian Community are showed on table 1.

	2009	2010	2011	2012
Dose 1	48.88	25.06	38.14	44.68
Dose 2	45.58	22.43	31.78	41.82
Dose 3	20.15	11.42	24.47	38.50

[Table 1. Rotavirus immunization coverage]

Conclusions: The least rotavirus immunization coverage corresponds to 2010 year. Rotavirus immunization coverage at the Valencian Community is higher than the data published for other communities of Spain. Rotateq® was the most administered vaccine.

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GENE EXPRESSION AS MARKER FOR SEVERITY OF VIRAL RESPIRATORY TRACT INFECTIONS IN INFANTS

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Background: Respiratory viruses causing lower respiratory tract infections (LRTI's) are a major cause of hospital admissions in children. Viral LRTI can deteriorate within hours or days into respiratory failure. Therefore there is a need for biomarkers that predict the course of disease.

Methods: From children < 3 years of age attending the hospital with a viral LRTI, a nasopharyngeal wash and blood sample were obtained. Based on the level of supportive care patients were allocated into a mild (none), moderate (supplemental oxygen and/or nasogastric feeding) or severe (mechanically ventilation) group. Affymetrix micro-array analysis was performed on mononuclear cell fraction (MNC) from the blood of 26 children with RSV infections. Genes of interest were subsequently validated with qPCR in a larger cohort of 104 virally infected children < 3 years of age.

Results: Transcription profiles of MNC could discriminate between mild, moderate and severe disease. The expression of Olfactomedin 4 alone could discriminate between the severe and mild group. In the validation set this marker remained differently expressed between the severity groups ($p < 0.001$).

Conclusion: The use of transcription profiles to identify biomarkers for disease severity of LRTI revealed a novel biomarker: Olfactomedin 4. This molecule plays a role in hematopoietic cell cycle and has been described as marker for several cancer types and chronic gastro-intestinal infections. This study shows for the first time a role of Olfactomedin 4 in acute respiratory infections and its potential as biomarker for disease severity.

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LOW NUMBER OF INTERFERON-GAMMA-PRODUCING VARICELLA-ZOSTER-VIRUS (VZV)-SPECIFIC T-CELLS IN AUTOIMMUNE ARTHRITIS PATIENTS

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Background and aims: Varicella-zoster-virus (VZV) is a herpes virus that establishes a life-long latent infection with risk of reactivation (shingles) particularly in immunosuppressed and patients with autoimmune disorders. This study evaluated the humoral (IgG concentration and avidity) and the cellular immune response to VZV in patients with juvenile idiopathic arthritis(JIA), with rheumatoid arthritis(RA), healthy children(HC) and healthy adults(HA).

Methods: VZV-IgG concentrations (UI/mL) and avidities (relative avidity index:RAI) were determined by ELISA (Euroimmune). VZV-specific interferon-gamma(IFNgamma)-producing T-cells were determined by ELISPOT and expressed as spots forming units (SFU/10^6cells) in 36JIA, 39RA, 11HC and 28HA.

Results: No differences in the VZV-IgG concentrations (JIA:2732±624,RA:1473±379,HC:2803±950,HA:2315±515UI/mL) or in the avidities (RAI:JIA:79.7±1.7%,RA:77.2±1.9%,HC:77.5±1.7%,HA:77.7±1.3%) were found in all groups. The frequency of IFNgamma-producing VZV-specific T-cells was low. RA showed significantly lower SFU compared to HA (mean±sem,RA:18.6±3.1;CA:63.3±10,$p< 0.001$) and to JIA (JIA:38.2±6.9,$p< 0.05$). No significant differences were determined between JIA and HC (JIA:38.2±6.9;HC:42.3±11.3). The influence of the therapy on the frequency of IFNgamma-producing VZV-specific T-cells in RA and JIA patients was analyzed. RA with non-steroidal anti-inflammatory drugs (NSAID) showed significantly higher SFU than untreated patients (NSAID+:22.1±3.9;NSAID-:12.1±5.4,$p< 0.05$), with similar findings in JIA (NSAID+:51.9±9.2;NSAID-:22.8±9.2,$p< 0.01$). No differences were found in patients treated with glucocorticoids or methotrexate.

Conclusions: These data suggest a reduction of the cellular immune response to VZV in RA. However, NSAID treatment enhanced the number of the IFNgamma-producing VZV-specific T cells in JIA and RA, suggesting patients with less inflammation. The long-term maintenance of anti-VZV cellular immunity in patients with autoimmune conditions and immunosuppressive treatments may need further investigation to prevent VZV reactivation.

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IMPACT OF THE PNEUMOCOCCAL CONJUGATE VACCINE 13 (PCV13) IN THE INVASIVE PNEUMOCOCCAL DISEASE (IPD)

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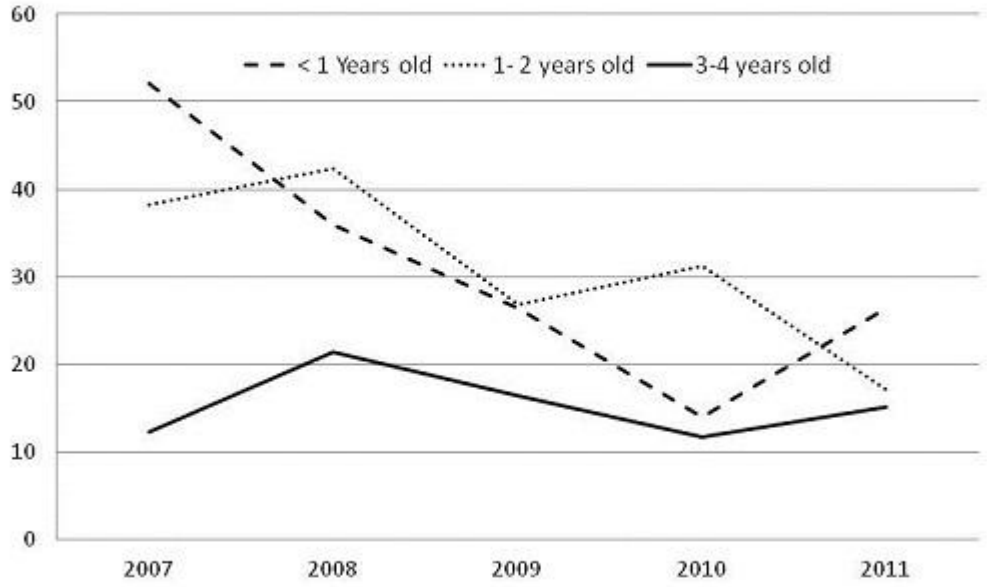
Background and aims: The strectocuccus pneumoniae (SP) is able to produce a range of infections including invasive diseases (IPD). The PCV13 can help to reduce these diseases. The epidemiological information system (AVE) and the Vaccine Information System (SIV) allow to evaluate the impact of PCV13 in the IPD. The aim of this paper is to evaluate the situation of the IPD before and after the introduction of the PCV13 in the Valencian Community (VC).

Methods: The frequency and distribution of pneumococcal serotypes was obtained from AVE. The information related with vaccination was obtained from SIV. All data correspond to the VC for the period 2007-2011.

Results: On Graph 1 it is show the IPD evolution by age.

Graphic 1.- IPD INCIDENCE (X 10^5)



[Graph 1]

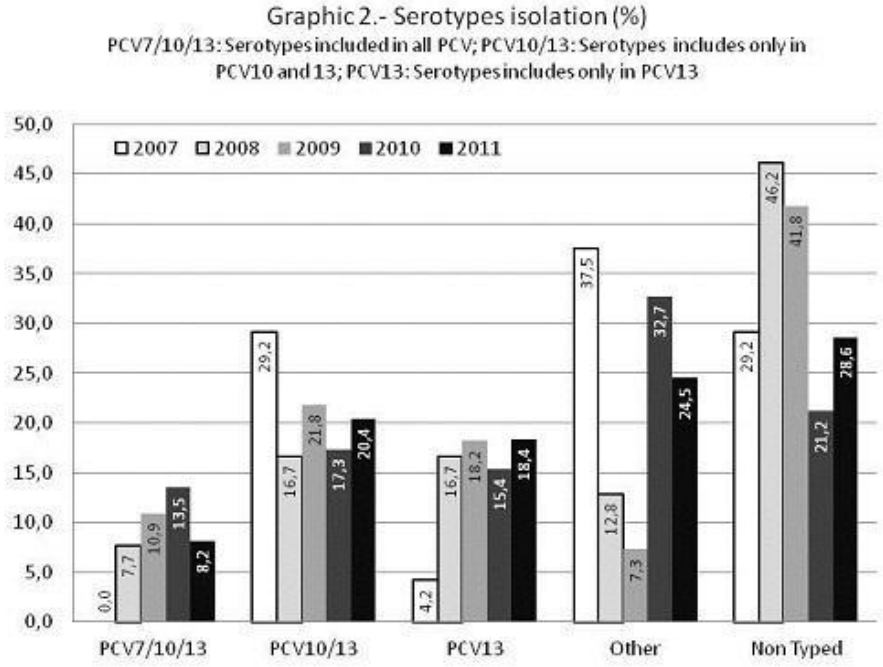
Vaccine coverage and the proportional distribution of the different types of PCV are showed on table 1.

	2007	2008	2009	2010	2011
Coverage 1 years old	45,9	52,34	57,24	65,03	70,05
Coverage 2 year old	50,99	50,73	56,06	62,8	73,32
% PCV7	97,13	98,60	99,09	40,16	0,55
% PCV10	0,05	0,05	0,70	18,78	5,07
% PCV13				40,93	94,31
% Other /unknow	2,83	1,36	0,21	0,13	0,08

Table 1.- Vaccine coverage and distribution of PCV types (%)

[Table 1. Vaccine coverage and distribution of PCV]

Graph 2 shows the evolution of serotypes isolated during the study period.



[Graph 2]

Conclusions: The incidence of IPD has been reduced to half in children less than two years, but not in older. Vaccine coverage has been increased during the study period. The PCV13 have replaced to other vaccines.

It has not already seen an impact in the isolated serotypes, although the high percentage of nontyped SP can mask the results.

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LOW FLU IMMUNIZATION OF HOSPITAL WORKERS IN HEALTH CARE INSTITUTIONS FOR AT-RISK PATIENTS

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Background and aims: Health care workers are included in the priority categories to receive seasonal influenza vaccination and have been encouraged to receive H1N1-2009 vaccination. Aim of the study was to estimate pattern and determinants of seasonal and H1N1 vaccinations in hospital workers in health-care institutions for at-risk patients.

Methods: H1N1 vaccine was provided to all hospital workers and vaccination rates were extracted from the immunization registry. A survey on seasonal influenza vaccination and attitudes towards H1N1 was administered to the personnel of three Departments (Paediatrics,Infectious Diseases, Gynecology).

Results: 492/2455 (20%) hospital workers underwent H1N1 vaccination. Vaccination rates were higher in physicians (348/1587,22%) than in nurses/paramedics (144/868,17%)($p< 0.05$). 268 hospital workers of the three enrolled Departments completed the survey on influenza. Seasonal influenza vaccination was low in all categories (43/268,16%), with the lowest rate in nurses (16/136,12%). A total of 107 (40%) hospital workers received H1N1 influenza vaccine, with the highest rate among physicians (53% versus 27% of non-medical personnel, $p< 0.05$). H1N1 vaccination was closely related to the Department, being higher in the Department of Paediatrics (46%) and Infectious Diseases (54%) than in Gynecology (2%)($p< 0.05$). Information about H1N1 vaccine was obtained predominantly from professional sources in physicians and by mass-media in other categories.

Conclusions: Despite strong recommendations, the coverage for influenza vaccination in hospital workers was poor. Understanding the determinants of influenza vaccine acceptance is essential to overcome the barrier to implementation of vaccination and improve compliance with recommendations. Compulsory policies may be considered in health institutions seeing at-risk patients.

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ASSESSMENT OF SEVERITY OF ILLNESS OF CHILDREN WITH ACUTE HEMATOGENOUS OSTEOMYELITIS: A PROPOSED SCORING SYSTEM BASED ON OBJECTIVE CLINICAL PARAMETERS

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Background and aims: Illness severity varies substantially among children with acute hematogenous osteomyelitis (AHO). Assessing severity of illness would allow greater objectivity when comparisons are made between populations separated by geography, time, or treatment methodology. Our aim is to develop a novel severity scoring system for children with AHO.

Methods: Fifty-five children with AHO who were treated in 2009 were retrospectively studied to identify objective clinical parameters pertaining to illness severity. Multiple logistic regression analysis was performed to determine parameters significantly associated with surrogates for severity (length of hospitalization, professional opinion, and Case Mix Index). Utilizing parameters present on admission (C-reactive protein, hemoglobin, and erythrocyte sedimentation rate levels, and the respiratory rate) a severity of illness score was proposed and validated.

Results: Severity of illness scores ranged from 0-10 with an average score of 4.6 (standard deviation 2.74) for the study cohort. Significant scoring differences ($p < 0.05$) occurred between children based on causative organism (MRSA - 6.4; MSSA - 4.2; and other - 3.1); and surgical intervention (multiple surgeries - 6.1; one surgery - 4.2; and no surgery - 3.1). The severity of illness score was significantly correlated with initial length of hospitalization ($p < 0.0024$); total length of stay including readmission hospitalization days ($p < 0.0005$); professional opinion ($p < 0.05$); and Case Mix Index ($p < 0.05$).

Conclusions: Severity of illness in children with AHO can be objectively assessed according to a novel scoring system. This important measure will add perspective to comparisons of populations which might differ with respect to illness severity.

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INCIDENCE OF ANTIBIOTIC-ASSOCIATED DIARRHOEA FOLLOWING ORAL PENICILLIN THERAPY IN PAEDIATRIC CLINICAL TRIALS: EFFECT OF DRUG AND FORMULATION

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Background and aims: Antibiotic-associated diarrhoea (AAD) is a well-described adverse reaction to oral penicillins. This study reviewed the literature to determine the incidence of AAD secondary to oral penicillins in paediatric clinical trials.

Methods: Using the Ovid databases an advanced search was conducted in Embase and MEDLINE for papers in any language reporting the AAD rates following oral penicillin therapy for an indicated infection in children (0-17 years). The search was limited to clinical trials. Trials were excluded if treatment related to chronic conditions, involved concomitant antimicrobials, or the dose or number of patients was not specified.

Results: 435 papers on clinical trials were identified (307 from Embase; 128 from MEDLINE). 36 papers (reporting 43 studies) were included for analysis. The indications included acute otitis media, sinusitis, pharyngitis and pneumonia. The trials reported on co-amoxiclav (n=34), amoxicillin (n=6) and phenoxymethylpenicillin (n=3).

In total, the 43 trials included 9655 children treated with oral penicillins. On average, 14.3% had AAD. The data were pooled for each penicillin: the AAD incidence was higher for co-amoxiclav (19.7%) compared to amoxicillin (3.1%) and phenoxymethylpenicillin (1.2%). For co-amoxiclav, the pooled data were analysed by formulation: the pooled-average AAD rate was 25.7% for the 4:1 formulation, 12.8% for the 7:1 formulation and 20.2% for the 14:1 formulation.

Conclusions: These results demonstrate an increased AAD incidence with co-amoxiclav compared to amoxicillin and phenoxymethylpenicillin, and varying AAD rates with different co-amoxiclav formulations. These findings warrant consideration when prescribing. Prospective AAD research is required to elucidate the underlying mechanisms.

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DYNAMIC EVALUATION´S MODEL ABOUT VACCINE´S CONDITION AGAINST HPV IN 5 COHORTS OF YOUNG PEOPLE

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In the community of Madrid, vaccine against HPV is on the systematic vaccination schedule for 14 years old girld thought primary care centers. Those who born in 1994, 1995, 1996 and 1997, should have received 3 doses of tetravalent HPV vaccine to the standard 0-2-6 months, those who born in 1998 bivalent the standard 0-1-6 months.

The vaccination coverage of each cohort is evaluated on the basis of nominal immunization registry. The data mining allows us, among other options, analyzing the evolution over time on different populations updated every year.

On December 2012 it was performed an evaluation of 5 cohorts of young people who should be vaccinated against HPV completely. In all of the analyzed coverages it was observed decrease between dose of vaccine. It was more elevated on the foreign case than the Spanish.

Those who born in 1994 ,1995 and 1996 experienced a higher decrease of the coverage achieved on the three doses, comparing the results on population of the year of vaccination with the evolution obtained about current population.

In those who born in 1997 it was observed an increase in coverage of 3 doses being the only group which populations decrease. In those born in 1998 the coverage wasn´t reached on proper time.

Results shows that the vaccination of the population incorporated after the year that it corresponds to them it is not properly done.

Coverage in the incoming cohort is low in the first year.

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INCIDENCE OF INTUSSUSCEPTION FROM A HOSPITAL-BASED RETROSPECTIVE SURVEY OVER 6-YEAR PERIOD: 2006-2011

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Background and aims: The concern about live-attenuated oral rotavirus vaccines is its possible association with intussusceptions. Thus, it is necessary to determine the baseline incidence for intussusceptions in the first year of life. Two new vaccines against rotavirus gastroenteritis were introduced in Korea in June 2007(RotaTeq) and March 2008(Rotarix).

Methods: A total of 359 intussusception-related hospitalizations were identified during the 2006 through 2011. Intussusception was confirmed by ultrasonography specialist. We reviewed a retrospective cross-sectional study of all hospitalized intussusceptions patients. The database for eligible age was under 10 year of age.

Results: During this 6-year period, 90(25%) children younger than 1 year of age were diagnosed with intussusception. 228(63.5%) cases were under 2-year of age, and 348(96.9%) cases were under 4-year age. The annual case of infant in the first 12 month of life during the study period, there was no change in its incidence. There are 18 cases in 2006, 19 cases in 2007, 12 case in 2008, 17 cases in 2009, 9 cases in 2010 and 15 case in 2011. The seasonal incidences are significant more cases occurring during summer(108/359, 30%) compare to winter(69/359, 19.2%).

Conclusions: The incidence of intussusceptions peaked under 36 month of age (304/359, 84.6%).The rotavirus vaccine does not appear to be a major cause of intussusception. And there is no increased in the incidence of intussusceptions after the introduction of rotavirus vaccine (including RotaTeq and Rotarix) in Korea.

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EPIDEMIOLOGY OF ACUTE GASTROENTERITIS IN HOSPITALIZED CHILDREN IN NW GREECE DURING A 12-YEAR PERIOD

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Background and aims: To determine the etiology of acute diarrhea in hospitalized children under 5 years of age in Northwest Greece and to improve knowledge of the etiology of gastrointestinal pathogens using conventional and molecular diagnostic techniques.

Methods: From 2001 to 2012, 7278 faecal samples from consecutive children were collected from five hospitals in NW Greece. Various common bacteria, viruses and parasites associated with diarrhea were investigated.

Results: Etiologic agents were detected in 2819 cases (38.73%). Monobacterial infections were detected in 611 (21.68%) cases (Salmonella spp. in 394, Shigella spp. in 11, Campylobacter jejuni in 186, Yersinia enterocolitica in 8, E. coli in 6, Aeromonas hydrophila in 6), while single viral infections were identified in 2112 children (74.92%). Mixed infections were found in 3.4% of positive samples. No sample was positive for parasites. Viral pathogens were identified in 2208 children (30.3%): Group A rotavirus was detected in 1559 (21.42%) cases (1493 monoinfections, 48 virus-virus coinfections and 18 virus-bacteria coinfections), adenoviruses in 246 (3.38%) cases (218 monoinfections, 22 virus-virus coinfections and 6 virus-bacteria coinfections), astroviruses in 168 cases (2.3%) (110 monoinfections, 40 virus-virus infections and 18 virus-bacteria) and noroviruses in 291 cases (3.99%) (monoinfections).

Conclusion: Eventhough Rotavirus group A was the leading cause of acute gastroenteritis with the most significant role in hospitalized children with severe diarrhea in Greece, further studies will be necessary to augment our knowledge in the aetiology of enteric infections, which will be helpful in the rational application of effective vaccines.

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PROBIOTIC ECN SUSPENSION FOR IMMUNITY IMPROVEMENT IN PRETERM NEWBORN INFANTS. FIRST RESULTS

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Background: The immature immune system is one factor responsible for the morbidity among preterm newborns. Due to its immuno-modulating properties E. coli strain Nissle (EcN) seems suitable to improve immunity in infants. Aim of the presented trial was to investigate efficacy and safety of prophylactic administration of EcN Suspension (EcN-S).

Materials and methods: 62 newborns (gestational age 35-36 weeks) were included after birth into a randomized, controlled 4-weeks-study with 2 parallel groups and a follow-up until the age of 1 year. All children of the treatment-group (30) received EcN-S orally for 3 weeks, the control-group (32) was observed only. Efficacy and safety was evaluated by incidence of acute respiratory viral infections (ARVI) and pneumonia.

Results: 10.0% of all EcN-infants suffered from an episode of ARVI. The corresponding figure within the control-group was 43.8%. No case of pneumonia was observed in the EcN-group while in the control-group the corresponding morbidity rate was 6.3%. Within the EcN-group a significant lower risk of ARVI and pneumonia was observed. Use of EcN-S resulted in relative reduction of risk of 77,2% and a number needed to treat of 3. One patient of the EcN-group and 11 of the control-group were hospitalized due to a severe infection or pneumonia during the first 4 weeks of life. There were no adverse drug reactions due to treatment with EcN-suspension.

Conclusion: Incidence of ARVI and pneumonia in preterm newborns were successfully reduced. The probiotic EcN was effective and safe for prophylaxis of acute respiratory diseases of preterm infants.

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MICROBIOLOGICAL ANALYSIS OF MIDDLE-EAR-FLUID (MEF) AND NASOPHARYNGEAL-CARRIAGE (NC) OF INFANTS WITH ACUTE OTITIS MEDIA (AOM) IN GERMANY, 4TH STUDY YEAR

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Background and aims: In Germany a general recommendation for pneumococcal conjugate vaccination was issued in 2006. In December 2009, the pneumococcal conjugate vaccine PCV13 was introduced. We analyzed the pathogens recovered from children suffering from AOM with efflux as well as their nasopharyngeal carriage in the most recent study period from Oct.2011-Oct.2012.

Methods: MEF- and NC-swabs were taken from children with spontaneously draining AOM. Serotyping of S.pneumoniae isolates was performed using Neufeld-Quellung reaction. S.pyogenes isolates were emm-typed by sequencing of the emm-gene. H.influenzae was typed using type-specific antisera.

Results: In the first three years of the study 443, 310 and 210 patients could be included. Because of this declining number of reports, the recruiting-basis was increased from 50 to 75 centers in year4 of the study. From Oct.2011 to Oct.2012, 439 children with AOM with efflux were documented. Nasopharyngeal swabs were obtained from 416 patients (96.5%).

Following pathogens were identified from 163 MEF-samples: S.pneumoniae (30/18.5%), S.pyogenes (79/48.5%), S.aureus (34/20.1%), H.influenzae (27/16.6%) and M.catarrhalis (1/0.6%). NC-rates were: S.pneumoniae 49.8%, M.catarrhalis 35.8%, H.influenzae 41.3%, S.pyogenes 21.3% and S.aureus 7.2%.

Most prevalent serotypes in MEF and NC were 3, 19A and 11A. Coverage of the PCV13 was the highest. The vaccination-rate increased to 91.7%.

Conclusions: In the 4th study year considerably more S.pyogenes were isolated from both MEF and NC. The prevalence of S.pneumoniae in MEF did not decline further in the 4th study year. Serotype 3 and 19A remain the most prevalent among AOM. The increase in 11A needs further observation.

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UNIVERSAL VARICELLA VACCINATION PROGRAMME IN TUSCANY REGION (ITALY), 2008-2011: IMPACT ON DISEASE INCIDENCE, IMMUNIZATION COVERAGE AND ADVERSE REACTIONS

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In Italy, the majority of vaccine-preventable diseases are subject to mandatory notification. Varicella is an important cause of morbidity in Italy, where 500,000 cases were notified each year. Starting from July 2008, Regional Tuscany authorities recommended universal varicella vaccination with two doses of MMRV (measles-mumps-rubella-varicella) vaccine for children aged 13 to 15 months and 5-6 years. The aim of this work is to describe the results of the adoption of universal varicella immunization during the first three years of implementation.

Mandatory notifications in subjects under 15 years, immunization coverage and adverse reactions to MMRV vaccine were obtained from the regional archives. Incidence rates were calculated by age group and a comparison between the pre-vaccine period (2005-2007) and the vaccination-period (2009-2011) was also performed, excluding the 2008 transition year from the analysis.

After three years of varicella immunization implementation the incidence rates have been halved in each age group target of the program. In the vaccination period, the notification system recorded 8,547 cases less than in the previous period, in subjects under 15 years. In 2011, immunization coverage with one dose of MMRV vaccine reached 82.2%. An overall adverse reaction reporting rate of 6/10,000 doses was registered (45 cases). Only 15 cases out of 77,938 doses were classified as severe without permanent damage.

The impact of the immunization strategy in Tuscany was very positive in terms of incidence reduction. High immunization coverage with MMRV was achieved in a very short time with a low reporting rate of adverse reactions.

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EFFICIENCY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE. SYSTEMATIC REVIEW

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Background and aims: Streptococcus pneumoniae is the major reason of bacterial pneumonia in paediatric population. Before the development of conjugate vaccines, children under 2 years were unprotected opposite to the disease. Pneumococcal conjugate vaccines have supposed a great advance in prevention of pneumococcal disease.Safety and efficacy of the vaccine have been assessed in the literature but the decision-making process requires considerations about efficiency. The aim was to review the available scientific evidence regarding economic evaluations of 13-valent pneumococcal conjugate vaccine.

Methods: Systematic review (2012) of economic evaluation studies. Databases searched were Medline, Embase, CRD, and Euronheed, with MeSH terms "conjugated pneumococcal vaccine", "costs and cost analysis", and "quality-adjusted life year". Inclusion criteria were studies of cost-effectiveness (CEA), cost-utility (CUA) and cost-benefit (CBA). The intervention considered was pneumococcal conjugate vaccination. Selected outcomes were costs per-life-year-gained (LYG), cost per quality-adjusted-life-year (QALYs) and cost-benefit ratios. Quality of articles has been measured with checklist of economic studies proposed by CASP.

Results: 44 references were found after removal duplicates, 27 of them were excluded by title and abstract. Finally 17 studies were included (11 CUAs, 3 ACEs, 3 CBAs). A wide range of values were found in terms of cost per QALY gained (980$-456,770$). The quality of the studies was good.

Conclusion: Vaccination with 13-valent pneumococcal conjugate vaccine could be considered as an efficient intervention in terms of cost per QALY in most recent studies, although the influence of the value of the parameters, and the comparator on the models would modify the decisions.

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WHOLE-BLOOD CYTOKINE RESPONSES TO QUANTIFERON PEPTIDES IN PEDIATRIC TUBERCULOSIS ACCORDING TO INFECTION STAGES AND SEVERITY

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Background and aims: The primary aim of this study was to explore cytokine/monokine responses to Mycobacterium tuberculosis (M.tb) peptides that would aid in diagnosing and staging M.tb infection. The secondary objective was identification of host immune responses to M.tb that help to contain the pathogen by comparing cytokine/monokine profiles in LTB versus non-severe Tuberculosis (TB) versus severe TB.

Methods: 15 cytokines/chemokines were quantified in a multiplexed microsphere-based assay following whole blood stimulation with M.tb antigens in 47 children (median age: 8 years). Cytokine/chemokine concentrations were compared in latent-TB infection (LTBI n=12) versus TB-disease (n=28) and in non-severe pulmonary TB (non-severe PTB, n=11) versus severe-TB (complicated PTB or disseminated TB n=17). Seven non-infected children were simultaneously analysed as controls.

Results: Beside IFNg, the most sensitive marker to diagnose M.tb infection was IP-10 with 560 pg/ml optimal sensitivity cut-off as determined by area under ROC curve (95% CI: 83%-99%). None of the 15 studied analytes could distinguish LTBI from TB disease. Finally, TB-disease severity was associated with moderately decreased M.tb antigen-induced Th1 cytokines (IL-12: p=0.09; IFNg: p=0.07) but with clearly defective Th2 cytokine levels (IL4: p=0.08; IL5: p=0.02; IL13: p=0.02). Also IL17, IL10 and MCP-1 levels appeared depressed in severe TB (p=0.08, 0.07 and 0.08 respectively).

Conclusion: This study confirms that IP-10 should aid in diagnosing M.tb infection though as the 14 other cytokines/monokines it did not allow TB staging. Severe TB-disease in children appears related to defective mixed cytokine responses but not to the presumed unbalanced Th1/Th2/regulatory cytokine network.

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MOLECULAR EPIDEMIOLOGY OF RESPIRATORY SYNCYTIAL VIRUS OVER THREE CONSECUTIVE SEASONS IN LATVIA

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Background and aims: We studied prevalence of respiratory syncytial virus (RSV) groups A and B in children with lower respiratory tract infections (LRTIs) over 3 successive epidemic seasons in Riga, Latvia.

Methods: Previously healthy children aged 2 to 24 months that were hospitalized with LRTI from July 2009 to June 2012 were included in the study. RSV was detected in nasopharygeal aspirates by RT-PCR. Groups A and B were differentiated by group specific PCR targeting the second hypervariable region of the G gene. The amplified fragments were sequenced and aligned with reference strains for phylogenetic analysis.

Results: Of the total of 207 samples, 88 (43%) tested positive for RSV. RSV activity was the highest from February to April. RSV-infected children were younger than non-RSV group (median age 6 vs. 10 months; $p< 0.001$). Groups A and B co-circulated and were identified in 53 (60%) and 35 (40%) specimens, respectively. Group A viruses were predominant in seasons 2009/2010 and 2010/2011 (65 and 74%, respectively), while group B prevailed in 2011/2012 (63%). Clinical Severity Score and length of stay in the hospital were not statistically different between the two groups. Phylogenetic analysis assigned all of the 2009/2010 strains (n=23) to a single genotype within each group - GA2 for group A and BA-IV for group B.

Conclusions: During the peak activity RSV caused up to 90% of LRTIs. Groups A and B co-circulated with changing prevalence over seasons. All of the sequenced group B isolates belonged to the globally spreading BA subgroup.

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TWO-DOSE TODDLER VACCINATION WITH INVESTIGATIONAL MENINGOCOCCAL B RECOMBINANT VACCINE - ANTIBODY PERSISTENCE AND RESPONSE TO BOOSTER AT 24 MONTHS

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Background: A two-dose catch-up immunisation with the investigational multicomponent serogroup B meningococcal vaccine, 4CMenB, was highly immunogenic in 12−15 month-old toddlers. We examined antibody persistence and response to a booster dose one year later (NCT01139021).

Methods: Participants in this extension study, who originally received two doses of 4CMenB at 12/14 or 13/15 months of age, received a booster dose 12 months after their last dose. Serum bactericidal activities with human complement (hSBA) against four serogroup B strains representative for individual vaccine antigens - factor H binding protein (fHbp), Neisserial adhesin A (NadA), Neisseria heparin binding antigen (NHBA) and New Zealand strain outer membrane vesicles (NZOMV) - were measured before, one month and six months after the booster.

Results: Of the 85 exposed subjects, 100% originally displayed seroprotective hSBA titres (≥ 5) against fHbp and NadA, 71% against NHBA and 99% against NZOMV one month after their primary immunisations. One year later the respective proportions were 71%, 96%, 37% and 15%, rising to 100%, 100%, 99% and 100% one month after a 4CMenB booster dose. GMTs after the booster were higher than after the primary series, indicating a true booster response. Six months after the booster these levels were 99%, 100%, 93% and 75%, respectively.

Conclusions: Two doses of 4CMenB, administered as a catch-up vaccination in toddlers, induced a response against all antigens in the majority of subjects. Levels remained high for 12 months against fHbp and NadA, and were boosted for all antigens by a third dose.

PATTERN AND RESISTANCE RATES OF BACTERIA ISOLATED FROM BLOODSTREAM INFECTIONS IN A TERTIARY LEVEL NICU: COMPARISON OF TWO PERIODS

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Background and aims: Knowledge of incidence and antimicrobial susceptibility patterns of bacterial pathogens is essential for empirical antimicrobial treatment in NICU.

Methods: Retrospective analysis of bacteria isolated from blood cultures of neonates hospitalized in a NICU between 2 periods (A:1/2007-12/2008 and B:1/2011-10/2012).

Results: Among 228 and 116 pathogens isolated during period A and B, Gram-positive bacteria constituted 80% and 72.4%, respectively. Coagulase-negative staphylococci (CoNS, 89.9% vs 84.5%) were the most frequent Gram-positive bacteria followed by Staphylococcus aureus (2.8%vs 2.4%), Enterococcus faecalis (2.8% vs 3.6%), E. faecium (2.8% vs 3.6%) and group B streptococci (GBS, 1.7% vs 1.2%) in both periods. 1/3 of S.aureus and >60% of CoNS were methicillin resistant whereas all staphylococci were vancomycin-sensitive. All GBS and E. faecalis isolates were susceptible to ampicillin and vancomycin. Resistance rates of E. faecium to vancomycin were 60% vs 50% in period A and B, respectively. Table 1 depicts the most frequent Gram-negative bacteria.

Susceptibility %	Amikacin		Ceftazidime		Imipenem		Ciprofloxacin	
Gram-negative bacteria (N of isolates in period A and B)	A	B	A	B	A	B	A	B
Klebsiella pneumoniae (21 vs 14)	80.6	85.7	23.8	0	100	92	100	28.5
Enterobacter cloacae (9 vs 6)	66.7	83.3	55.6	66.6	88.9	83.3	66.7	83.3
Escherichia coli (5 vs 3)	100	100	80	100	100	100	100	100
Acinetobacter baumannii (4 vs 6)	75	16.6	50	16.6	75	16.6	75	16.6

[Table 1]

Conclusion: CoNS are the most frequent bloodstream isolates demonstrating high-level resistance to beta-lactams. Resistance of E. faecium to vancomycin and of Gram-negative bacteria to third-generation cephalosporins are of concern. Emerging carbapenem resistance further limits available therapeutic options.

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NEONATAL LIVER ABSCESS ASSOCIATED WITH CANDIDEMIA IN NICU: THREE CASES REPORT

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Background: Candida infections are a major cause of morbidity and mortality in NICU. Preterm newborns are predisposed to Candida infections because of immaturity of their immune system and invasive interventions. Candida species invade virtually all tissues, including the retina, brain, heart, lung, spleen, joints and liver. Hepatic abscess is rare in the neonatal period and usually not taken into consideration in the differential diagnosis of sepsis. We evaluated three cases of Candida liver abscess,so they were analysed for demographic data, age of diagnosis, possible risk factors, clinical presentation, diagnostic methods, treatment and outcome.

Materials and methods: The fungal cultures in the examination of the tip of umbilical catheter and blood cultural examinations were positive for C. Albicans.The ultrasound scan detected liver abscess.RESULTSThe position of umbilical catheter tip into the liver could have predisposed to abscess formation, when the UVC were placed no antifungal prophylaxis was started. These patients were successfully treated with fluconazole and liposomal amphotericin B. No complications reported, include rupture of the abscess into the peritoneal cavity,metastatic septic emboli to the brain and portal cavernoma formation. Every three infants were discharged with normal laboratory tests, following with clinical and ultrasound findings.

Discussion and conclusions: Candidemia is an increasingly recognized complication in premature infants with a prolonged NICU stay. Liver abscesses are rare in newborns and their diagnosis is difficult and delayed. The prevention of Candida spp. infection, the reducing of risk factors, the clinical evaluation and the choise of antifungal treatment are the key to success in neonatal settings about Candidiasis.

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AN AGGRESSIVELY PROGRESSED CASE OF CHRONIC ACTIVE EPSTEIN-BARR VIRUS INFECTION OF T-CELL

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Background and aims: Chronic active Epstein-Barr Virus (EBV) Infection is understood as a lineage of dysregulation of EBV proliferation and can be considered as a chronic version of hemophagocytic lymophohistiocytosis, for its clinical presentation with chronic or recurrent mononucleosis-like symptoms for at least 3 to 6 months.

Methods: The authors retrospectively reviewed a case of 13 month old boy with medical record, laboratory results, and radiologic and pathologic findings.

Results: The boy was admitted for persistent fever for a week. He had cervical lymphadenopathy, abdominal distension, hepatosplenomegaly. His peripheral blood showed lymphocyte dominant leukocytosis at admission and leukocytosis with left shifted maturation a week later. EBV PCR and VCA IgM were both positive. Computerized tomography revealed multiple lymph nodes enlargement in cervical, supraclavicular, axillary, mesentery, and inguinal areas. Excisional biopsy of a left supraclavicular lymph node confirmed the diagnosis of chronic active EBV infection of T-cell: EBV-encoded RNA in situ hybridization was positive; CD3, CD5, and Bcl2, positive; Ki67, 80% positive; Bcl6 and MUM1, weakly positive; CD10, CD15, CD20, CD30, CD56, CD138, Kappa, and Lambda, negative. During the last 2 days, he had several generalized tonic-clonic seizures and CSF exam showed WBC 45 /mm^3 (lymphocyte 70%), protein 239 mg/dL, and glucose 51 mg/dL. Intravenous immunoglobulin had no effect; he expired on the 18^{th} hospital day.

Conclusion: We report a pediatric case of chronic active EBV infection of T-cell which progressed fatal less than a month after the first symptom presented.

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LONG-TERM LINEZOLID TREATMENT IN TWO CHILDREN WITH MULTIDRUG-RESISTANT TUBERCULOSIS

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Multidrug-resistant tuberculosis (MDR-TB) is a growing health challenge worldwide. The difficulty of culture-proven diagnosis, the lack of evidence-based treatment guidelines as well as limited experience with most second-line tuberculostatic drugs specifically complicates MDR-TB management in children. Linezolid is a relatively new antimicrobial drug with encouraging efficacy in the treatment of drug-resistant tuberculosis in adults. Unfortunately, drug-attributed adverse events have been documented in up to 60% of treated patients. In children, experience regarding the efficacy and safety of long-term linezolid treatment is very limited. Here, we report on two siblings of two and five years of age with pulmonary tuberculosis - both confirmed by detection of M. tuberculosis from gastric aspirates. Drug sensitivity testing revealed resistance to isoniazid, rifampicin, pyrazinamide, ethambutol as well as streptomycin. Due to limited treatment options, we initiated an off-label treatment regime containing levofloxacine, protionamide, linezolid and four months of additional intravenous amikacin. Mycobacterial clearance could be achieved rapidly and no relevant adverse events occurred during the 12-month-treatment period and a short-term follow-up over 4 months. These cases illustrate the promising potential of long-term linezolid as a treatment option for drug-resistant tuberculosis in children and encourage its systematic evaluation in future studies and clinical trials.

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IS LINEZOLID AN EFFICIENT AND SAFE ALTERNATIVE TO VANCOMYCIN IN VERY PREMATURE INFANTS WITH LATE-ONSET INFECTION?

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Background: Glycopeptide is the usual probabilist treatment in coagulase-negative staphylococcus late-onset sepsis in premature infants, but provides renal toxicity. Linezolid is effective in gram-positive cocci infection, and devoid of renal side-effects. Its efficacy and safety in premature population is unknown.

Aim: To determine whether linezolid is a possible alternative to vancomycin in very premature infants with late-onset infection.

Methods: We conducted an observationnal retrospective study including infants born before 37 weeks of gestation (WG), hospitalized in neonatal intensive care unit from January 2008 to September 2010, treated by i) linezolid in continous infusion in case of renal failure or ii) twice a day oral treatment if intravenous access was no more available.

We assessed clinical and microbiological efficacy and safety of treatment.

Results: 35 treatments were studied among 33 infants aged 27.9 +/- 3.4 WG, treated during 7.6 +/- 3 days. Bacteria were isolated mainly from blood cultures (staphylococcus epidermidis, haemolyticus…). 8 children died (25%) in context of sepsis and renal failure. Clinical and biological efficacy were observed in 78% (18/23) and 79% (27/34) cases, respectively. No renal toxicity, no anemia, but 17% thrombocytopenia and 5.7% lactic acidosis were observed.

Conclusions: Whatever the global clinical efficacy observed in this newborn population, this study reports serious concerns about possible side effects like thrombocytopenia and lactic acidosis, even if imputability seems difficult to affirm in this septic context. This underlines the need for controlled randomized studies before using linezolid safely in this high-risk population.

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COMPARISON OF INTERFERON-GAMMA RELEASE ASSAY (IGRA) AND TUBERCULIN SKIN TEST (TST) FOR DIAGNOSIS OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

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Background and aims: There is still no gold standard for diagnosis of tuberculosis. We compared IGRA (Quantiferon, QTF) with TST for diagnosis of tuberculosis in children/adolescents.

Methods: Records of children/adolescents of tuberculosis clinic for evaluation of latent/active tuberculosis from 2007 to 2012 were analyzed. The study population was tested with QTF and TST and divided in three groups based on final diagnosis: active tuberculous disease (TD), latent tuberculous infection (LTBI) and controls (CT). Mann-Whitney U test, $\chi 2$ test and kappa (κ) coefficient were used to analyze and compare QTF and TST results.

Results: 331 children/adolescents (161 male) were included with median age 7yrs (range 0.3-17); TD, LTBI and CT were recorded in 4.8%, 40.5% and 54.7%, respectively. QTF was positive in 117 (35.3%) and TST in 140 (42.3%) children. Eleven (8.2%) LTBI cases presented negative TST and positive QTF results. Overall, median IFN-gamma concentration achieved was 0.05IU/ml (range 0-79.3) with no significant difference between children (0-10yrs) and adolescents (>10yrs); in TD, median concentrations were 23.1IU/ml and 11.3IU/ml for ≤2yr-old and >2yr-old patients respectively (p=0.638). In LTBI, IFN-gamma values tended to be higher in children than adolescents (4.9 vs 0.8IU/ml, p=0.1). Median ages and IFN-gamma values but not TST sizes differed between LTBI and TD (7 vs 5.5yrs, p=0.003 and 4.5 vs 15.6IU/ml, p=0.001), respectively. TST and QTF results were concordant in 274 of cases (91%) (κ=0.639).

Conclusions: IFN-gamma values of QTF are higher in TD than LTBI and tend to be higher in younger age. QTF and TST show concordant results.

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DECLINING PREVALENCE OF TUBERCULOUS INFECTION IN CHILDREN OF CENTRAL MACEDONIA, GREECE

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Background and aims: Studies conducted in the 90's demonstrated a reduction in the prevalence of tuberculous infection in 6-7 year-old children of Thessaloniki region, Northern Greece, from 12.1/1000 in 1988 to 4.7/1000 children in 1997 (Paediatr N Gr 2001, 13:55-9). Therefore, we retrospectively investigated the trend of tuberculous infection prevalence over the following 14 years, from 1998 to 2011, in children of the same age.

Methods: Analysis of Tuberculosis Clinic records of Thessaloniki region, which performs yearly mass screening of primary school children (aged 6-7 years) with tuberculin skin test (TST) before vaccinating them with BCG; children with history of BCG vaccination at birth or tuberculosis were excluded from screening. The prevalence of tuberculous infection was calculated as the ratio of children with positive TST (induration ≥10mm) over those screened. For data smoothing and regression analysis for time trend, the method of 3-year moving averages was used.

Results: A total of 136,527 children were screened from 1998-2011. Average prevalence of tuberculous infection for the whole 14-year period was 3.37/1000. A significant decline of this prevalence during study period was found (p=0.008), ranging from 4.32/1000 (average of years 1999-2001) to 2.99/1000 (average of years 2009-2011).

Conclusions: The sustained declining of tuberculous infection prevalence among school-aged children over the last years, despite previous massive immigration to Greece, is reassuring. However, in view of recent socioeconomic changes followed by reduction in the budget and personnel of public health care services, continuous monitoring is warranted.

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SPUTUM-POSITIVE TUBERCULOSIS CASE IN A DAY CARE EMPLOYEE: MANAGEMENT AND CONSEQUENCES

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Background and aims: Sputum-positive tuberculosis is a public health care emergency, especially when children are exposed. We describe the investigations and preventive measures undertaken in a day care center following detection of sputum-positive tuberculosis in a male employee in June 2012.

Methods: Contact tracing of potentially exposed children and adults in the center was performed. Children were divided into close contacts with the source (same or neighboring classes) and non-close contacts. Tuberculin skin testing (TST) was used to detect mycobacterial infection in all children and adults; induration ≥5mm was considered positive in those with previously negative TST. Children/adults with positive TST and normal chest x-ray/physical examination were prescribed isoniazid and rifampin for 3 months. In those with negative TST, another TST was performed after 3 months; the children subgroup of close contacts with negative TST was prescribed isoniazid for 3 months until the second TST.

Results: 42% of 114 children were close contacts and 5.3% tested positive on the first TST; none had active tuberculosis. 12.9% of 108 children with negative first TST stopped attending the center by the time the second TST was due. All 94 children re-tested after 3 months had negative TST. Only 22 (46%) of close contacts received the prescribed 3-month isoniazid course. One of 23 adults with negative first TST had positive TST 3 months later.

Conclusions: Application of guidelines for containment of tuberculous infection in high-risk pediatric groups is challenging. Parental anxiety and problems of compliance may complicate management in these circumstances.

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UNUSUAL PRESENTATION OF TUBERCULOUS MENINGOENCEPHALITIS

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A 13-year-old girl, of moroccan origin, is investigated for right upper quadrant abdominal pain, vomiting, intermittent headache, fever (39°). In a second time, psychomotor regression and drowsiness appeared.

Laboratory tests are normal (inflammation, liver function, kidney function, hemogram). Lumbar puncture shows 28 leukocytes/mm3, protein 0.95g/l, normal glucose. Encephalitis is confirmed with electroencephalography and brain MRI shows cortical and Under cortical hypersignals. Treatment is initiated with acyclovir.

Evolution is bad with left VI nerve paralysis and deterioration of consciousness.

MRI performed at day 15 signs a meningo-myelo-rhombencephalitis complicated with vascularitis suggestive of tuberculous meningoencephalitis. Despite the absence of respiratory symptoms, lung CT scan shows miliary and mediastinal calcified lymphadenopathy. Sputum cultures are positive for Mycobacterium tuberculosis. LCR is sterile.

Probabilistic treatment with isoniazid, rifampicin, ethambutol, pyrazinamide associated with corticosteroid bolus is initiated at day 17. Consciousness improves in one week. Fever and behavioral disorders persist two months and a strong and prolonged cortisosteroid therapy is necessary (2-3 mg/kg/day).

Tuberculous meningoencephalitis can have an unusual presentation without neurological signs at the begining. High dose of corticosteroid is necessary to control the disease.

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INVASIVE FUNGAL INFECTIONS DUE TO MALASSEZIA PACHYDERMATIS IN THREE PREMATURE INFANTS IN NEONATAL INTENSIVE CARE UNIT

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Introduction: Malassezia pachydermatis is a lipophilic yeast rarely incriminated in human morbidity. This basidiomycete is commonly associated with canines, especially with dog's otitis externa. M.pachydermatis is distinguished by its ability to grow on complex media without supplementation with fatty acids.

Object: Describe invasive M.pachydermatis infection's features in three premature infants, in our Neonatal Intensive Care Unit.

Methods: The identification of M.pachydermatis was performed by conventional techniques, mass spectrometry Maldi-Tof and confirmed by molecular biology (sequencing ITS and D1D2 regions coding for ribosomal RNA).

Results: Two fungemia and one disseminated infection (fungal ball in the kidney and endocarditis) with M.pachydermatis were diagnosed. Patients were (median, range) 26 weeks (25-28.3) gestational age and 750 g (740-1100) birth weight. Parenteral nutrition was administered with a central venous catheter. The infection occurred at age 24 days of life (17-35). After diagnosis, fluconazole was started and catheter removed. The outcome was favourable in all three patients.

Discussion and conclusion: Similar cases have been reported in previous publications: Infection was transmitted via hand contact or by the intravenous soiled lipid solutions' perfusion. In our patients, investigations to identify the source of contamination are still in progress.

Zoonoses' prevalence in human newborn is probably underestimated and M.pachydermatis could be an emerging fungal agent. Hand washing, prohibition of jewelry and hand moisturizers by caregivers are potential strategies to limit the transmission of this type of yeast.

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A VERY UNUSUAL PRESENTATION OF DISSEMINATED TUBERCULOSIS

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A 5-year-old girl presented to our attention for a three weeks history of fever.

Physical examination was notable for vescicular and vasculitic lesions of the right foot. Laboratory test showed microcitic anaemia and elevated C-reactive protein; abdominal ultrasound, echocardiography and chest X-ray were normal. After few days the patient start to suffer from headaches, palpebral and neck myoclonous. She underwent lumbar puncture, total body CT and electroencephalography. Cytological examination of cerebrospinal fluid showed high cellularity with lymphocytic and granulocytic cells, EEG: generalized parossistic discharges simultaneous with myoclonic movements. The CT scan revealed multiple nodular lesions in the brain parenchyma. Suspecting cerebral microabscess, antibiotic therapy with linezolid and meropenem was administrated resulting in temporary disappearance of the fever, which reappeared after two days. Cranial MRI, bone marrow and skin biopsy were performed. Cranial MRI revealed leptomeningeal enhancement with pseudonodular lesions in the frontal-parietal lobe and enhancement of left middle cerebral artery. The histological examination of the skin biopsy reveale necrotizing epithelioid cells, Langhans giant cells and tubercle with acid-fast bacilli, histological examination of the bone marrow biopsy also showed an non necrotizing granuloma.

Investigations for tuberculosis were started: TST, batterioscopic exam and PCR of gastric aspiration were negative while the IGRA test results positive. Suspecting disseminated tuberculosis antitubercular therapy was started with progressive improvement in the patient's clinical condition. The diagnosis was confirmed by a positive culture for Mycobacterium Tuberculosis on gastric aspiration and cerebrospinal fluid.

After one year MRI and EEG were completely normal and antitubercular therapy was suspended.

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STREPTOCOCCUS PNEUMONIAE EPIDEMIOLOGICAL AND CLINICAL FEATURES IN HOSPITALIZED CHILDREN IN LATVIA

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Background and aims: Every year S. pneumoniae (pneumococcus) affects about 10 million children. Pneumococcal infection is one of the leading causes of mortality in young children. There are more than 90 serotypes known worldwide. A retrospective-prospective study about the S. pneumoniae serotype distribution and clinical features in hospitalized children was commenced in April, 2011, in Children Clinical University hospital.

Materials and methods: Swabs from nasopharynx and middle ear, blood and CSF cultures were collected from children with evidence of pneumonia, otitis or invasive pneumococcal disease (IPD). Identification of the isolates was confirmed by optochin sensibility test and in questionable cases with VITEK GN. Serotyping was performed by multiplex PCR.

Results: Totally 102 samples were obtained until December, 2012. S. pneumoniae was isolated in 25.5% (26) cases. Median patient age was 50.6 months. The most prevalent diagnosis were pneumonia - 27% (7), and acute otitis media - 19% (5). 1 child (3.8%) died from IPD. 1 child (3.8%) had received pneumococcal vaccination (PCV7). Cultures have been serotyped, and serotype 14 was the most common pneumococcal serotype detected - 38.5% (11), followed by 19F and 18A/18B/18C/18F - 15.4% (4) each.

Conclusions: The most common serotype isolated was serotype 14. Only 1 child (3.8%) had received pneumococcal vaccination (PCV7). Taking into account that routine anti-pneumococcal vaccination in Latvia was started only in 2010 and vaccination coverage continues to increase, further studies would be necessary.

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PREVENTING MOTHER TO CHILD TRANSMISSION OF HIV PAEDIATRIC AUDIT CYCLES BETWEEN 2004 - 2010

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Aim: This audit was undertaken firstly to look at the performance of a local regional Paediatric team over a 6 year period and secondly to estimate the impact of several service changes.

Methods: Three cycles of retrospective case note audit of all babies exposed to HIV and followed up in a large Regional Centre were performed using a near identical standard proforma.

Results:

	2004 - 2005	**2008**	**2010**
Number included	57	30	24
New Maternal Diagnosis	54%	26.7%	30%
Maternal VL < 40 copies/ml before delivery	75%	76.7%	89%
Baby's sample documented	49%	75%	96%
Care Plan filed?	26%	85%	100%
Transmission Rate *	1.7% (n=1)	0%	0%

[Audit Results]

*Two confirmed detectable DNA PCT at the age 6 weeks and 3 months

Discussion: In line with the data from NSHPC we have also seen a higher proportion of mothers diagnosed before conception and a decreasing delivery rate of babies exposed to HIV in 2010. It has been noted that most of the significant outcome measures have improved over the audit period. As the care of HIV in Pregnancy requires a multidisciplinary approach the improvements have to be attributed to the joint effort of the whole team involved. Some of the improved outcome measures are also related to the Paediatric service changes as shown in the selected outcome measures above.

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BACTERIAL ETIOLOGY AND SEROTYPES OF ACUTE OTITIS MEDIA IN TURKISH CHILDREN

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Background: Acute otitis media (AOM) is one of the most common childhood diseases requiring antimicrobial prescription in pre-school children. This study aimed to describe the bacterial etiology of pediatric cases with AOM in Turkey.

Methods: We conducted a prospective, multi-center, tympanocentesis-based epidemiological study of Turkish children three months to less than six years age.

Results: Overall, 45 % of samples were culture positive for bacterial pathogens Streptococcus pneumoniae (13.1 %) was the leading cause of bacterial AOM followed by Streptococcus pyogenes (10.5 %) and H. influenzae (7.9 %). Serotype-3 was detected in 2 of the samples and each of serotype-9V, serotype-19, and serotype-19A were isolated from one patient. S. pneumoniae was detected in 36 % (4/11) of otorrhea samples. All of the samples that were positive for H.influenzae collected by tympanocentesis. All H. influenzae isolates were identified as non-typeable. The pneumococcal serotypes covered by PCV-7, PVC-10 and PCV-13 were 20 % (1/5), 20 % (1/5), and 80 % (4/5), respectively. PHiD-CV (PCV-7 types plus 1, 5, and 7F) targets non-typeable H. influenzae, and 4 of 38 (11 %) of the pathogens caused episodes of AOM were also covered.

Conclusion: In Turkey, S. pneumoniae remains the most common pathogen in children with AOM. Both S. pneumonia and non-typable H. influenzae represent important targets for vaccination strategies to reduce AOM in Turkish children. Based on our results, conjugate pneumococcal vaccines may have potential impact to decrease the burden of AOM.

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SUSPECTED BACTERIAL INFECTION AND ANTIBIOTIC USE IN SICKLE CELL DISEASE: A RETROSPECTIVE STUDY

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Background: Bacterial infections are a major cause of morbidity and death in children with sickle cell disease(SCD). Baseline leukocytosis is common in these patients. C-reactive protein(CRP) is a biomarker of recognized value, although exact cut-offs are not defined. Procalcitonin(PCT) is a more recent marker of infection with growing interest.

Aims: Analyze patterns of antibiotic use in children with SCD according to levels of laboratorial markers of bacterial infection.

Methods: Retrospective study of admissions of children with SCD in a pediatric nursery of a secondary care hospital, during a 5-year period(2008-2012). Selected cases had fever or clinical features suggestive of bacterial infection during hospitalization.

Results: Eighty-eight cases were included. The median age of patients was 5 years (interquartile range:3.25-8). Antibiotic was started in 77 cases (CRP< 2mg/dL:7 of 12; CRP2-8mg/dL:28 of 33; CRP>8mg/dL:42 of 43). PCT was measured in 13 cases and influenced therapeutic decision in 2. Bacterial agents were identified in 7 cases: Mycoplasma pneumoniae(4), Escherichia coli(1), group D Salmonella(1) and Streptococcus viridans(1) and all of them had started antibiotic. Average length of stay of those treated with antibiotic was 5.95 days versus 4.25 for those without. In the 11 cases without antibiotic, no complications or readmissions were reported.

Conclusions: CRP level was an important criterion to guide therapeutic decision. The outcome was not adversely affected in the cases that did not start antibiotic. More specific markers of bacterial infection can be helpful but further studies in children with SCD are needed to support their use in therapeutic decision.

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SEROPREVALENCE OF HEPATITIS A, B AND C MARKERS AMONG NEWLY ARRIVED IMMIGRANT AND REFUGEE CHILDREN: A PRELIMINARY STUDY

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Background and aims: An increasing number of children migrate to Greece from countries with inadequate health care, frequently lacking immunization records. Therefore, they are asked to receive vaccines, possibly already administered or for diseases they present immunity against. Aim of our study was to evaluate seroprevalence of hepatitis A, B, and C virus (HAV, HBV, HCV) markers among immigrant (I) and refugee (R) children.

Methods: From 09/2010 through 04/2013, we examined all children, referred to an outpatient hospital clinic, within three months of their arrival. Serology for HAV, HBV and HCV was performed by ELISA.

Results: A total of 205 children, (I/R ratio:1.16; mean age: 7.27, median: 7.0, range: 1-14 yrs) were recruited, but only 25% provided vaccination records. Protective antibodies (≥10 IU/L) to HBV surface antigen were detected in 55.1% of all children (60.9% versus 48.4% among immigrants and refugees, respectively, p=0.091). No child tested positive for HBV core or surface antigen. Of forty fully vaccinated individuals, 25% remained seronegative. Seventy one (34.6%) of all children were immune against HAV, with no significant difference between immigrants and refugees. All four children fully immunized against HAV, were seropositive. Seropositivity for HAV and HBV did not differ significantly among subjects from countries of high, medium or low human development index. Finally, no child tested positive for HCV markers.

Conclusions: A large proportion of the above population remains susceptible to HAV and HBV, the latter often despite vaccination. Designing local strategies to provide optimal care to this vulnerable population is important.

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MULTIDRUG RESISTANT BACTERIA IN A TERTIARY CARE CHILDREN'S UNIVERSITY HOSPITAL

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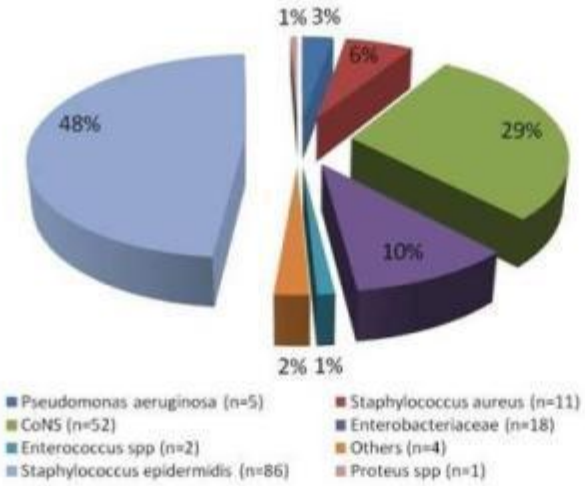
Background and aim: To describe frequency and pattern of multidrug resistant (MDR) pathogens in a tertiary care children's hospital.

Methods: All bacterial isolates of children admitted from January 1st, 2006 to December 31st, 2007 and from January 1st, 2011 to December 31st, 2011 were collected. Clinical records were retrospectively reviewed to identify children's characteristics.

Results: 1028 bacterial isolates were collected from 523 children [median age: 18.6 (2.3-88.1) months]. On the whole, 41.9% of isolates were MDR, with no significant difference during the 3-year observations. The incidence of MDR bacteria was 3.9/1,000 patient-days. On the whole MDR bacteria, 41.5% were isolated from blood (table 1), 25.3% from respiratory specimens (table 2), 24.6 from pus and wound samples (table 3) and 8.6% from invasive device. The wards with higher incidence were Neonatal Intensive Care Unit (24.8%), Intensive Care Unit (21.8%) and Haematology/Oncology ward (16.7%). 70.3% of infections caused by MDR bacteria were healthcare-associated. Antimicrobial resistance for sentinel pathogen were: Extended-spectrum β-lactamase Enterobacteriaceae: 20.9%, Vancomycin-resistant Enterococci: 9.8%, Methicillin-resistant Staphylococcus aureus: 19.9%, Carbapenem-resistant Enterobacteriaceae: 1.1%, Carbapenem-resistant Pseudomonas aeruginosa: 28.4%.

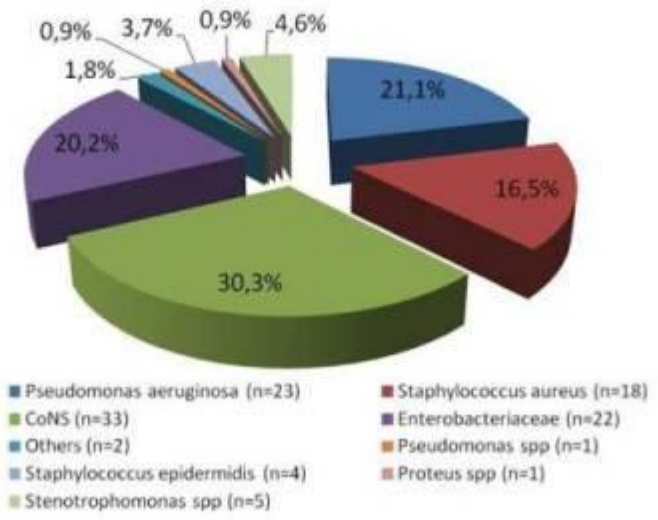
Conclusion: The high diffusion of MDR bacteria in a tertiary care children's university hospital and their elevated association to healthcare practice suggests the need of more attention in antimicrobial drugs use and preventive strategies.

Table 1: Distribution of MDR bacteria from blood (n=179)



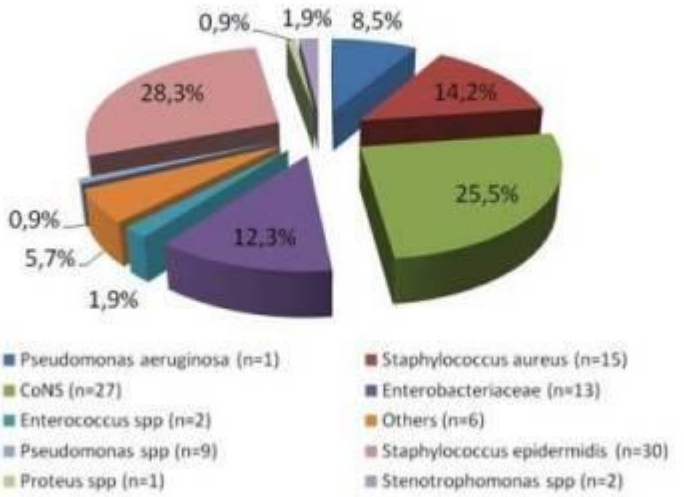
[Table 1]

Table 2: Distribution of MDR bacteria from respiratory specimens (n=109)



[Table 2]

Table 3: Distribution of MDR bacteria from pus and wound samples (n=106)



[Table 3]

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PROPHYLACTIC AND LONG TERM ANTIBIOTIC USE IN A CHILDREN'S HOSPITAL

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Introduction: Appropriate choice duration and dose of antibiotic treatment is essential in the current climate of increasing bacterial resistance. The use of antibiotics as prophylaxis for infection is controversial but there is some evidence to support use in immunocompromised children, bronchiectasis, recurrent otitis media and cystic fibrosis. Guidelines in the UK are limited and many have been drawn up on the basis of small studies. We reviewed use of prolonged courses of antibiotics in children with chronic medical conditions in a paediatric hospital.

Methods: Antibiotic, antiviral or antifungal prescriptions dispensed for more than 4 weeks treatment over a 1 month period in June 2011 were reviewed. Children where the standard treatment course of the condition (e.g. osteomyelitis) might be > 4 weeks were excluded.

Results: 138 prescriptions were dispensed for 4 weeks or more of treatment. 79/138 (57%) of prescriptions were for less than standard treatment dose. 18 different antibiotics, 3 different antivirals and 2 different antifungals were prescribed. Evidence to support many of prescribing practices could be found in the literature but formal national guidelines or BNFC dosing could be found for < 50%.

Conclusions: A wide variety of specialties used long antibiotic courses in children who appear immunologically normal and are not on immunosupression. More evidence based guidance is needed in the appropriate use of prophylactic antibiotics in medical patients.

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ROTAVIRUS EPIDEMIOLOGY AND GENOTYPES AFTER MONOVALENT VACCINE INTRODUCTION IN ARACAJU, BRAZIL (2006 - 2012)

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Background and aims: Rotavirus diarrhoea is still an important cause of children mortality worldwide. Vaccine introduction can lead to a reduction in the mortality and morbidity and in Brazil, Rotarix®, a monovalent rotavirus vaccine, was introduced since March 2006. This study describes the epidemiology of rotavirus diarrhoea after the vaccine introduction; the current incidence; age groups distribution; seasonality; predominant rotavirus genotypes and vaccine efficacy.

Methods: In a cross sectional survey, children with acute diarrhoea were enrolled prospectively from October 2006 to April 2012 at Emergency Hospital of Sergipe (HUSE), in Aracaju, Brazil. A questionnaire with clinical and epidemiological information and stool samples were obtained. ELISA tests were carried out to detect rotavirus infection and positive samples were genotyped. Descriptive statistic calculations were carried out to define rotavirus epidemiology.

Results: ELISA positive results were found in 231 of 1881 specimens. Overall incidence was 12.2% (95%CI, 10.7-13.7%). Rotavirus positive cases were more severe and in older patients (p=< 0.01). They circulated throughout the year with some increase in June and September. The most frequent genotype were G2P[4] with 167 cases (71.4%) and G1P[8] with 29 cases (12.4%). During 2006-2008 G2P[4] was predominant, during 2009-2010, G1P[8] has reappeared, and in 2012, G8 and G3 genotypes were the most frequent.

Conclusions: Rotavirus incidence in all causes diarrhoea remains low after Rotarix® introduction in Brazil, confirming the success of the programme. Nevertheless, new rotavirus strains associated to severe diarrhoea are emerging. Surveillance is needed to monitor the shifts in rotavirus epidemiology.

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BACTERIAL PATHOGENS (SHEIGELLA, SALMONELLA, COMPYLOBACTER, E COLI 0157) AND THEIR ANTIBIOTIC SUSCEPTIBILITY IN CHILDREN WITH ACUTE INFLAMMATORY DIARRHEA

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Introduction: Gastroenteritis is one of the most important diseases in childhood and has infectious and noninfectious etiology.

The aim of this research is find out the etiology of inflammatory Gastroenteritis and the most common causes of it and the ant biotical resistance of these agents.

Method: We conducted a prospective, hospital-based study. Data collected from 2009-2010. Children stool sample gathered and move to microbiology lab and examined for pathogens, blood and at the end and anti-biogram test had been done. Children from 1 month age to 14 years old entered to the research. Analyses of data was done with SPSS.

Results: The epidemiology, clinical features, nutritional status, and causative agents of diarrhea were studied in Iranian children. 566 case of diarrhea recognized in this time. 322 cases of inflammatory Gastroenteritis collected in this period. 57 of them have positive culture. Most of the cases happened in summer. 177 of these children were male. 212 of children were hospitalized. The most frequent germ was E.coli o157 (60 %), and after that were shigella with 22 cases and salmonella with 2 cases. None of the samples were positive for compilobacter. 87 % of pathogens were suspected to ciprofluxin.

Conclusion: One of the most frequent causes of inflammatory gastroenteritis in this study was E.coli.

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RISK FACTORS IN CHILDREN WITH MULTIDRUG RESISTANT BACTERIA INFECTIONS IN A THIRD CARE UNIVERSITY ITALIAN HOSPITAL

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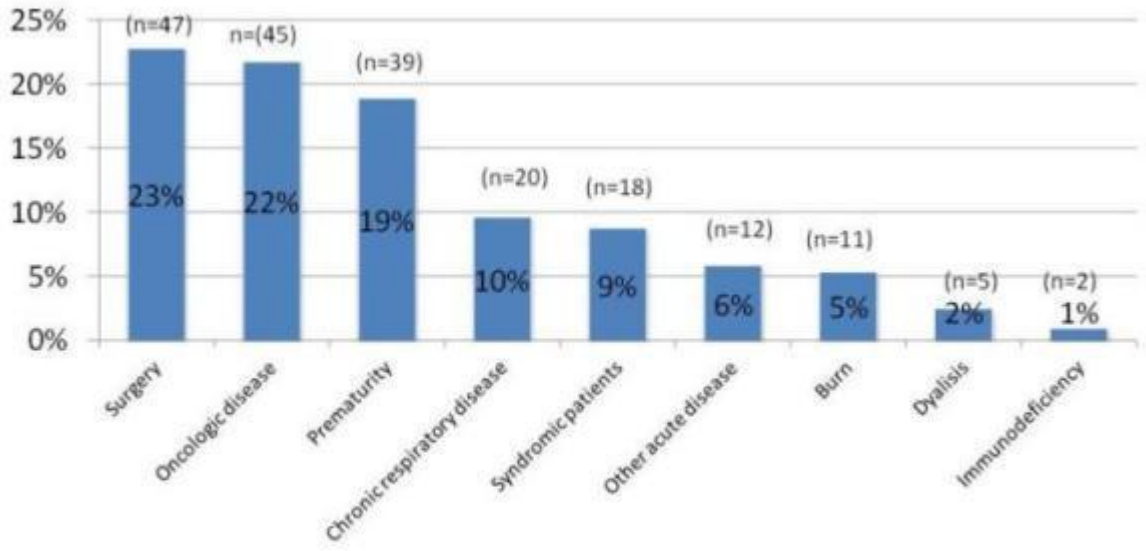
Background and aim: Multidrug resistance (MDR) is the most actual emergency among hospitalized patients, especially in children. Compared to adults, children have different risk factors linked with MDR, but studies focused on this topic haven't been published yet. Our aim was to identify the most frequent risk factors in hospitalized children with MDR bacterial infections.

Methods: All bacterial isolates of children admitted from January 1st, 2006 to December 31st, 2007 and from January 1st, 2011 to December 31st, 2011 were collected. Clinical records were retrospectively reviewed to identify children's characteristics. Multidrug-resistant bacteria were identified with the more recent CDC and ECDC definitions.

Results: 1028 bacterial isolates were collected from 523 children [median age: 18.6 (2.3-88.1) months]. On the whole, 41.9% of isolates were MDR, with no significant difference during the 3-year observations. The 88.3% of all the hospitalized children with MDR infection presented at least one risk factor, and the most common found were recent surgery (22.8%), oncologic disease (21.8%) and prematurity (18.9%) (Table 1). The 67.9% had at least one invasive device: the 77.1% of blood samples MDR positive were found in children with implanted CVC, and 75.2% of MDR isolated from bronchial aspirate were obtained in ventilated patients.

Conclusion: With the spread of MDR bacteria in hospitalized children, identification of main risk factors in pediatric patients is now becoming increasingly urgent.



[Risk factors in hospitalized children with MDR.]

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MENINGITIS CAUSED BY NEISSERIA MENINGITIDIS, HAEMOPHILUS INFLUENZAE TYPE B AND STREPTOCOCCUS PNEUMONIAE DURING 2005-2011 IN TURKEY: A MULTICENTER PROSPECTIVE STUDY

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Background and aims: Bacterial meningitis, caused by Neisseria meningitidis, Haemophilus influenzae type b (Hib) and Streptococcus pneumonia, is an important cause of childhood morbidity and mortality. Etiologic agents of bacterial meningitis in Turkey were evaluated.

Methods: This prospective observational study was performed during 2005-2011 in persons < 16 years-old hospitalized for suspected meningitis at 12 hospitals and universities that provide healthcare to ~32% of the population. All isolates were cultured and serogrouped by PCR.

Results: During 2005-2011, 619 cases of bacterial meningitis were diagnosed (186, pneumococcal; 116, Hib; and 317, meningococcal). Pneumococcal and Hib meningitis accounted for 22.5% and 20.5% (2005-2006); 36.8% and 22.8% (2007-2008); 31.8% and 6.1% (2009-2010); and 27.9% and 2.3% (2011) of cases, respectively. Among meningococcal meningitis, cases of serogroup A, B and W-135 were 0.7%, 31.5%, and 42.7% (2005-2006); 8.3%, 35.1%, and 17.6% (2007-2008); 36.6%, 7.3%, and 56.1% (2009-2010); and 3.3%, 3.3%, and 60% (2011), respectively. No serogroup C or Y cases were detected.

Conclusion: Despite available vaccines there was no prominent decrease in pneumococcal meningitis incidence, but Hib meningitis has decreased since 2006. Meningococcal serogroups demonstrated considerable variation. Serogroup W-135 was most common in 2005-2006, due to transmission from returning Hajj pilgrims; decreased in 2007-2008; but increased in 2010-2011. Serogroup B was common in 2005-2008 and decreased prominently in 2010-2011. Serogroup A cases increased recently (2009-2010). A quadrivalent meningococcal conjugate vaccine and meningococcal B vaccine are needed in Turkey.

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SEVERITY OF ACUTE ROTAVIRUS GASTROENTERITIS IN PRESCHOOL CHILDREN - A CASE CONTROL STUDY ON HOSPITALIZED PATIENTS

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Background: In Bucharest the rotavirus positive acute gastroenteritis is currently the main cause of acute diarrheal disease with known etiology, in preschool children.

Objective: The aim of the study was to identify the characteristics of acute gastroenteritis (AGE) rotavirus-positive cases, suggestive for clinical severity.

Methods: Retrospective matched 1:1 case-control study upon hospitalized AGE cases rotavirus positive (cases) and negative (controls) respectively; matching criteria - age, gender and calendar month of hospitalization.

Results: Enrolment criteria allowed assembling of 202 case-control sets. After the univariate analysis of 10 characteristics, the unconditional logistic regression identified 4 of them as being independently and significantly associated ($p < 0.05$) with AGE rotavirus-positive: dehydration [Odds Ratio (OR): 4.93; 95% Confidence Interval (CI_{95}): 2.14-11.25)], hypoglycemia (OR: 2.65; CI_{95}: 1.18-5.98), hospitalization longer then 6 days (OR: 4.24; CI_{95}: 2.01-8.96) and clinical relapse (OR: 2.92; CI_{95}: 1.35-6.34).

Discussions: The characteristics validated through this study as being highly specific for the severity of AGE rotavirus-positive represents consistent evidences that might support integration of universal rotavirus vaccination in the routine of schedule vaccination of infants in Bucharest.

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MEASLES VACCINE COVERAGE RATES OF FRENCH CHILDREN AND TEEN-AGERS IN 2011

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Background and aims: France has faced a major measles epidemic last years, and accounts for more than half of all European cases in 2011. This reflects an insufficient level of immunity in the population: in adults, SeroInf study showed that 9% of 20 to 29 y.o adults were seronegative in 2010. The objective of our study was to assess vaccination coverage in children and teen-agers.

Methods: A representative sample of 4,250 mothers was surveyed from September 16th to November 27th. They filled in an internet questionnaire with their children's vaccinations records. Mothers were sorted according to their children's age: 1,000 from 12 to 23 months, 1,000 from 24 to 35 months, and 2,250 from 14 to 16 years.

Results: Vaccination coverage rates for the full schedule (2 doses) were respectively 27.3% in the 12-23 months age group, 81% in the 24-35 months age group, and 88.8% in the 14-16 years age group. For the first dose, 96.7% of infants 24-35 months and 95.8% of 14-16 y.o were vaccinated, but only 88.5% between 12-23 months.

Comments: In order to achieve measles elimination, a very high coverage (> 95%) with 2 doses is needed. Despite a progression in all age groups compared to previous data, none of the age groups reached this target.

Conclusion: Efforts should be pursued to fully vaccinate all targeted population. Special attention should be given for the second dose catch-up at all ages, and especially teenagers and young adults, as they have a risk of more severe disease.

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VISCERAL LEISHMANIASIS PRESENTING AS LYMPHOPROLIFERATIVE DISORDER

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Background: Paraproteinuria is an uncommon finding in childhood. It is typically associated with monoclonal gammopathies in adults. Here we report a 14 year old boy who presented with paraproteinuria and imaging results suggestive for a lymphoproliferative disorder.

Case report: An otherwise healthy 14 year old German boy presented with a history of dysuria. Urinalysis revealed microhaematuria and paraproteinuria. He also reported significant weight loss, night sweats but no fever, and residency in Spain for several years.

Results: Ultrasound evaluation showed generalized lymphadenopathy and hepatosplenomegaly. Whole body MRI and PET-CT imaging were compatible with a lymphoproliferative disorder. A lymph node biopsy failed to reveal a malignant lymphoma. Serum chemistry showed polyclonal rather than monoclonal gammopathy suggestive of an inflammatory or infectious process. Microbiological workup, including EBV, CMV, TB, Bartonella, toxoplasmosis, HIV and hepatitis viruses, was negative. Bone marrow aspirates were normal. The findings of hepatosplenomegaly and hypergammaglobulinemia coupled with previous residency in Spain ultimately led us to investigate the differential diagnosis of visceral leishmaniasis. Serology by IFA indeed showed a high IgG antibody titer of 1:20.000, and PCR in blood was positive for the L.donovani/infantum complex. A five-days course of liposomal amphotericin was given and led to complete clinical response, conversion of the PCR to negative, and successively decreasing antibody titers.

Conclusion: The differentiation between monoclonal gammopathy (paraproteinaemia) and polyclonal gammopathy is critical for differentiation between multiple myeloma or other diseases associated with hypergammaglobulinemia. A microbiological workup is essential in these patients to differentiate between lymphoproliferative and infectious diseases.

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A STUDY OF BACILLUS CALMETTE-GUÉRIN (BCG) RELATED LYMPHADENITIS OCCURRENCE AND MANAGEMENT IN THE PAEDIATRIC POPULATION OF CORK UNIVERSITY HOSPITAL

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Background and aims: A universal neonatal BCG vaccination program was re-introduced to the Cork region in October 2008. Consequently, BCG related adverse reactions are presenting to the paediatric service at Cork University Hospital, Ireland. The optimum treatment for local BCG disease is poorly defined and controversial.

Methods: A combination of a retrospective review of cases from 2008 to 2010 and a prospective study of cases presenting to the hospital's paediatric services during 2011. All children with suppurative and simple lymphadenitis were included.

Results: 23 patients presented at a median of 16.3 weeks post-vaccination: 11 with simple lymphadenitis and 12 with suppurative lymphadenitis. Age distribution was atypical, with a peak between 0 and 8 months. The overall complication rate for neonates was 1 case per 1089 vaccinees (0.092%). 52.2% of patients underwent some form of treatment, with 83% of those (n=10) undergoing a surgical intervention. 92% of those treated received at least one antibacterial agent. 33% of the surgical interventions were retrospectively considered potentially unnecessary. Simple lymphadenitis was more likely to heal faster.

Conclusions: The incidence of BCG lymphadenitis is consistent with other reports in the literature nationally, and lower than expected when compared internationally. The analysis of the management of each patient showed a variety of approaches. There was a high level of inappropriate antibacterial prescribing, in addition to a number of inappropriate surgical procedures performed. The development of a local, evidenced-based, management protocol would help to standardise best practice.

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SHORT COURSE OF ANTIBIOTHERAPY FOR OSTEOARTICULAR INFECTIONS IN MONTPELLIER UNIVERSITY HOSPITAL, A RETROSPECTIVE STUDY

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Introduction: Recent studies have shown the efficiency of 15 to 21 days of antibiotherapy in osteoarthritis and osteomyelitis in children.

Methodology: We evaluated this short-term protocol of antibiotherapy in these cases in the University Hospital of Montpellier by a retrospective study. We excluded spondilodiscitis, nosocomial infections, osteoarthritis with surgical implanted material, children that received recent antibiotherapy and children over 15 years. Two to 4 days intravenous antibiotherapy was administered followed by oral antibiotics depending on the clinical and biological (CRP and fibrinogen) monitoring. The total duration of treatment was 15 to 21 one days. Bacterial diagnosis was made by culture and molecular biology (ARNr 16S and specific Kingella kingae PCR).

Results: Seventy six cases of osteoarticular infections were included in this study (24 osteomyelitis and 52 osteoarthritis). Forty six out of 76 patients have bacterial identification: 14 Staphylococcus aureus (all methicillin-susceptible), 12 Kingella kingae, 6 Streptococcus pyogenes and 6 others. The mean duration of antibiotherapy was 17.7 days for osteoarthritis and 15.5 days for osteomyelitis. Prognosis in all cases was good even though five children had more than 3 weeks of antibiotherapy, and 8 necessitated a new surgical intervention. Only six children required insertin of central venous catheters.

Conclusions: Our retrospective study suggests that a short-term antibiotherapy is possible with similar complication rate and prognosis than long-term antibiotherapy protocols. There is a need for a prospective study in these cases.

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INCREASING RATES OF COMMUNITY ASSOCIATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS IN CHILDREN WITH ACUTE PYOGENIC ARTHRITIS OR OSTEOMYELITIS

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Background: This study was conducted to measure the prevalence of community associated methicillin-resistant Staphylococcus aureus (CA-MRSA) in children with acute pyogenic arthritis or osteomyelitis.

Methods: We retrospectively reviewed the medical records of children (younger than 18 years) with culture proved acute pyogenic arthritis or osteomyelitis from January 2001 to December 2012. S. aureus cultures from 2001-2006 and 2007-2012 were compared for methicillin-resistant pattern.

Results: Forty-nine cases of acute pyogenic arthritis or osteomyelitis were identified. Of these, 34 cases (69%) were culture-proved. CA-MRSA accounted for none of the 14 cases from 2001 through 2006 and 7 of the 20 cases from 2007 through 2012 (P = 0.026).

Conclusions: The data from a single children's hospital suggest that methicillin resistance rate of S. aureus from acute pyogenic arthritis or osteomyelitis has increased over a 12 year period in Korea.

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AN OPEN-LABEL RANDOMISED CONTROLLED STUDY ASSESSING THE IMMUNE RESPONSE TO ROUTINE INFANT IMMUNISATIONS ADMINISTERED IN CONSISTENT VERSUS ALTERNATING LIMBS

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[1]Oxford Vaccine Group, Department of Paediatrics, University of Oxford, and the NIHR Oxford Biomedical Research Centre, Oxford, UK, [2]Department of Paediatrics, Mater Dei Hospital, Msida, Malta, [3]NIHR Oxford Biomedical Research Centre, University of Oxford, Centre for Statistics in Medicine, Oxford, [4]University Children`s Hospital Bristol NHS Foundation Trust, Bristol Children's Vaccine Centre and NIHR Medicines for Children Research Network, South West, Bristol, [5]University Hospital Southampton NHS Foundation Trust, University of Southampton and Southampton NIHR Wellcome Trust Clinical Research Facility, Southampton, [6]Vaccine Institute, St Georges, University of London, London, [7]Health Protection Agency, Public Health Laboratory, Manchester, UK

Background and aims: Sequential doses of a rabies vaccine have been shown to result in reduced immunogenicity if administered in alternating limbs rather than in the same (consistent) limb. This study was conducted to test whether this also occurs with routine infant immunisations.

Methods: Participants were randomised to receive DTaP-IPV-Hib at 2,3 and 4 months of age and 13-valent pneumococcal conjugate vaccine (PCV 13) at 2,4 and 12 months, all in the right leg (´Consistent Limb Group´ (CL), n= 254); or DTaP-IPV-Hib in the left leg at 2 months and right leg at 3 and 4 months and PCV13 in left leg at 2 months, right leg at 4 months and left arm at 12 months (´Alternating Limb Group´ (AL), n =255). Serum IgG geometric mean concentrations (GMC) against Hib, tetanus-toxoid (TT) and PCV13 serotypes were compared at 5, 12 and 13 months.

Results: A significant difference in Hib IgG GMCs between both groups was seen at 5 months: 0.43 µg/ml (95%CI 0.33-0.57) (CL) vs. 0.66 µg /ml (0.49-0.87) (AL) (p=0.04) and at 12 months: 0.35µg/ml (0.28-0.43 ;) (CL) vs. 0.49µg/ml (0.40-0.61) (AL) [p=0.04], but not at 13 months [p=0.19]; and in TT IgG GMCs at 13 months: 1.66IU/ml (1.43-1.93) (CL) vs. 2.20 IU/ml (1.91-2.54) (AL) [p=0.009] but not at 5 or 12 months [p=0.77 and 0.13]. No difference was seen with twelve of pneumococcal serotype.

Conclusion: The immunogenicity of infant vaccines is not hindered, and may even be enhanced, by sequential immunisation in alternating rather than consistent limbs.

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IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINES ON ACUTE OTITIS MEDIA AMONG CHILDREN IN GERMANY

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Background: Routine infant immunization with the pneumococcal conjugate vaccine PCV7 started in Germany in 2007. Although substantial decline of invasive pneumococcal diseases has been observed, the effect of PCVs on non-invasive disease is unknown so far. Therefore, we assessed in these analyses the impact of PCVs on otitis media (OM) in children in Germany.

Methods: Data from IMS-Health-VIP® were used for uninterrupted time series analyses that used ICD-10 diagnosis rates as main outcomes (H66=suppurative OM, H65=non suppurative OM). The pre-vaccine period 2003-2006 provided baseline values and was compared to the single years 2007-2011 characterized by a rapidly growing vaccination rate with 7-valent and higher-valent PCVs in children < 2 years of age. Percentaged reduction rates were adjusted to the size of the corresponding age cohorts; the Poisson model was used for statistical analysis.

Results: During baseline period an average of 1,403,497/391,828 episodes of suppurative/non-suppurative OM occurred annually in children aged 0-4 years. In 2011, the episodes had reduced significantly by 19.3%/25,9% (p-value for both < 0.0001) for suppurative/non-suppurative OM representing a reduction of 270,875/101,483 cases in 2011 compared to baseline. During the 5 years from 2007 to 2011 the cumulated numbers of reduced episodes were 833,677/346,483 for suppurative/non-suppurative OM. Analysis among children aged 5-10 years showed similar trends.

Conclusion: A significant reduction in otitis media diagnoses among children in Germany after introduction of PCVs was demonstrated. Our results contribute to the growing body of evidence supporting the beneficial impact of pneumococcal conjugate vaccines in children also in non-invasive disease.

998

ANTIBIOTICS PRESCRIPTIONS ARE TOO OFTEN INAPPROPRIATE IN PEDIATRIC PRACTICE: ANALYSIS OF THE PRESCRIPTIONS IN AN EMERGENCY ROOM DEPARTMENT

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Background and aims: Misuse of antibiotics is largely responsible for the emergence of the bacterial resistance which becomes a major public health concern in France. Because of the frequency of fever and infections in childhood, antibiotics are often abusively used in pediatric practice. The main objective of our study was to assess the frequency of inappropriate antibiotics prescriptions in children admitted in emergency room.

Methods: We conducted a prospective study from July 2011 to November 2012 including children aged from 0 to 15 years-old, receiving antibiotics and admitted at the emergency room (ER) in Nantes University Hospital. Antibiotics prescriptions were analyzed by two independent experts to state on the conformity to the current national recommendations.

Results: 88 prescriptions were analyzed, the median age of included children was 2,8 years [IQR :1,1-5,3]. Fifty-nine percent (n=67) of the antibiotics prescriptions concerned an upper respiratory tract infection. Seventy-six percents of the analyzed prescriptions were considered as inappropriate by the experts with a good inter-rater agreement (kappa=0.79, p< 0.001). The major reason of inappropriateness of the prescriptions (some had more than 1 reason) were: use of a too large spectrum (3rd generation cephalosporin or association amoxicillin/clavulanate instead of amoxicillin) in 72%, absence of indication in 31%, absence of justification of antibiotic by a rapid diagnostic test in 30%.

Conclusions: Antibiotics prescriptions in pediatric practice remained often inappropriate. Real efforts have still to be made to educate physicians and parents to the reasonable use of antibiotics in order to protect their efficacy.

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IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINES ON PNEUMONIA AMONG CHILDREN IN GERMANY

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Background: Routine infant immunization with the pneumococcal conjugate vaccine PCV7 started in Germany in 2007. Although substantial decline of invasive pneumococcal diseases has been observed, the effect of PCV on non-invasive disease is unknown so far. Therefore, we assessed in these analyses the impact of PCVs on pneumonia in children in Germany.

Methods: Data from IMS-Health-VIP® were used for uninterrupted time series analyses that used ICD-10 diagnosis rates as main outcomes (J18=pneumonia, J18.1=lobar pneumonia). The pre-vaccine period 2003-2006 provided baseline values and was compared to the single years 2007-2011 characterized by a rapidly growing vaccination rate with 7-valent and higher-valent PCVs in children < 2 years of age. Percentaged reduction rates were adjusted to the size of the corresponding age cohorts; Poisson model was used for statistical analysis.

Results: Episodes of pneumonia decreased by up to 17.0% in 2008 in children aged 0-4 years, showed a re-increase in the following years and a final significant reduction of 10.3% in 2011 ($p < 0.0001$). More extremely, episodes of lobar-pneumonia (sub-diagnosis) decreased by 87.6% in 2008, increased again and the reduction from baseline in 2011 added up to 42.4% ($p < 0.0001$). During the 5 years from 2007-2011, the cumulated number of reduced pneumonia-episodes was 111.133. Analysis among children aged 5-10 years showed similar trends.

Conclusion: Significant reduction in pneumonia diagnoses among children in Germany after introduction of PCVs was demonstrated. Our results contribute to the growing body of evidence supporting the beneficial impact of pneumococcal conjugate vaccines in children also in non-invasive disease.

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DAPTOMYCIN LOCK-THERAPY TO TREAT COAGULASE-NEGATIVE STAPHYLOCOCCUS CATHETER-RELATED INFECTION : ABOUT 2 CASES

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Background and aims: To remove catheter is often questioning in case of pediatric catheter-related infection particularly in those who absolutely require venous access. Daptomycin was shown to have a good efficacy against biofilm and some clinical observations in adults related a good efficacy to treat catheter-related infection when used in lock therapy. We reported the case of a successful use of daptomycin lock-therapy in 2 children.

Methods: Daptomycin was prescribed as daily infusion of 10mg/kg/day associated to daptomycin lock in two children (18 and 3 months old) after failures of treatments with vancomycin and linezolid. Catheter-related infections were documented with at least 4 positive blood cultures with Staphylococcus epidermidis. Daptomycin lock consisted in the placement of a solution of 5mg/ml of daptomycin reconstituted in Ringer's solution plus heparin. This solution was placed once a day when catheter could be locked (at least 30 min) during 2 to 7 days. One child (with Porth-a-Cath) was under chemotherapy for neuroblastoma and the other (with femoral catheter) received parenteral nutrition after diaphragmatic hernia surgical cure. Hemodynamic situations of the patients were stable and search for infection dissemination was negative.

Results: Blood cultures remained negative after 48 hours of treatment for both cases. Catheter was finally removed after completion of chemotherapy for one child and culture was negative. We didn't observe any muscular pain or elevation of creatine kinase under therapy.

Conclusion: Use of daptomycin lock could be a rescue therapy in some situation of coagulase-negative staphylococcus catheter related infection.

1001

ANTIMICROBIAL TREATMENTS FOR ESBL PRODUCING-ENTEROBACTERIACEAE RELATED URINARY TRACT INFECTIONS: RESULTS OF A FRENCH NATIONAL SURVEY

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The emergence of ESBL producing-enterobacteriaceae (ESBL-PE) is an increasing problem.

Aim: to evaluate the medical practices in French institutions when an ESBL-PE related urinary tract infection (UTI) is identified.

Methods: A survey that should involve 26 paediatric hospitals has been performed. The last five cases of ESBL-PE/centre and the answers to two simulated clinical cases of ESBL-PE related non septic pyelonephritis (7 months-old girl without underlying diseases) and cystitis (30 months-old girl) should be collected.

Results: 83 cases of ESBL-PE related UTI (E. coli 90%, K. pneumoniae 8%) in 21 participating centres have been collected. Antimicrobial susceptibility was 100% for penems, 88% for amikacine, 52% for fluoroquinolone and 41% for trimethoprim. For acute pyelonephritis (n=53, mean age: 29 months, M/F sex ratio=0.33), ESBL adapted antibiotic treatment was intravenous in 81% of cases with 55% bi-therapy. Penems were used in 53% and aminosides in 36% of cases. For cystitis (n=26, mean age: 61 months, sex ratio=0.33), 22 were treated with antibiotics. An intravenous treatment was used in 3 (penems=2).

For the simulated clinical cases (85 answers), the pyelonephritis would have been treated with penems (76%) and/or aminosides (80%). A bi-therapy would have been used in 71% of cases. Intravenous antibiotic treatment would have been used in 29% of the cystitis case with 8% bitherapy including 16% penems and 11% aminoside prescriptions.

Conclusion: This survey highlights the heterogeneity of antimicrobial treatments in ESBL-PE related UTI and the overuse of penems. There is an urgent need of specific guidelines for ESBL related infections.

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CASPASE 3/7 ACTIVITIES MEASUREMENT OVER A RANGE OF CYAA TOXINS CONCENTRATIONS ON DIFFERENT CELLS

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Introduction: Adenylate cyclase toxin (CyaA) toxin is an important virulence factor of Bordetella pertussis, the causative agent of whooping cough, and a potential component of acellular pertussis vaccine.

Materials and methods: The work involved the production of three purified forms of CyaA with different enzymic and invasive properties. These were: the native enzymatically-active, invasive toxin (CyaA), an invasive derivative lacking AC enzymic activity (CyaA*) and a non-acylated, non-invasive form of CyaA (proCyaA). These were expressed in E. coli BL21/DE3 as recombinant proteins. After purification by a combination of chromatographic methods (Q-and Butyl-Sepharose) their properties were investigated by several assays.

Results: The AC enzymic activity was assayed by a conductimetric method. CyaA and pro-CyaA had a high level of enzymic activity but that of CyaA* was very low. Caspase 3/7 activities were measured over a range of toxin concentrations. At these concentrations, neither urea buffer alone nor CyaA* induced any significant increase in caspase 3/7 from different mammalian cells. The greatest effect of CyaA was observed on J774.2 and RBL-2H3 cells where increasing concentration of toxin gave increasing activity.

Coclusions: regard to the results of this the study showed that both enzymatic and invasive functions are required for the cytotoxic effects of adenylate cyclase toxin.

1003

HERPES SIMPLEX ENCEPHALITIS IN NEONATES RESISTANT TO ACYCLOVIR-TREATMENT

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Despite available antiviral therapy viral encephalitis is a life-threatining disease with significant morbidity and mortality. The most common cause of sporadic fatal encephalitis worldwide is herpes simplex virus (HSV) type 1. But herpes encephalitis may be caused by either HSV type 1 or HSV type 2 in neonates. Treatment with acyclovir is highly effective in these diseases. Here in, we report two neonates with clinically acyclovir-resistant HSV encephalitis those were treated with foscarnet sodium**.** Twenty-four-day-old and twenty-one-day-old two babies were admitted to the hospital because of neonatal sepsis. The acyclovir therapy was given when they were diagnosed as herpes simplex virus type-1 and type-2 encephalitis. But during the course of acyclovir therapy HSV was not cleared from CSF. Under the assumption of infections with acyclovir-resistant HSV-1 and HSV-2 encephalitis, foscarnet therapy was given to both two patients. After the initiation of foscarnet, HSV was cleared from CSF. In conclusion, we describe the emergence of clinically significant acyclovir-resistant HSV-1 and HSV-2 encephalitis in two neonates. Acyclovir-resistant HSV mutants can develop in the course of therapy. The antiviral drug resistance should be considered in infants who not respond appropriately to acyclovir therapy .

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BCG ADVERSE EVENTS: OUTCOME WITH ISONIAZID TREATMENT

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Background and aims: There is no consensus regarding the best treatment for BCG adverse events (BCG-AE). Herein we describe clinical characteristics and outcome of BCG-AE in São Paulo city, Brazil.

Methods: From January 2009 to December 2011, patients identified from the surveillance data or spontaneous demand to the Immunization Reference Center were evaluated, treated and follow-up monthly until 3mo after lesion involution. All individuals were immunized with BCG Moreau-Rio de Janeiro strain. Treatment was performed mainly with isoniazid in accordance with the Brazilian guidelines.

Results: Among the 163 patients evaluated, 31 had normal reaction, 130, locoregional adverse events and 2, other diagnoses. None of the children had HIV-seropositive mothers. No cases of BCG dissemination were identified. Six patients had more than one clinical manifestation. Clinical presentations of the 136 locoregional BCG-AE were: suppurative lymphadenitis,52.2%; injection-site abscess,26.5%; ulcer>1cm,2.9%; lymph nodes>3cm,3.8%; BCG-induced lupus vulgaris,0.7%; infected wound,0.7%; warts-like lesion,5.1%; BCG scar reactivation,5.9%; vasomotor phenomenon,0.7%, and other skin lesions,1.5%. Isoniazid was used in 96 patients and multiple drug treatment, in 3. Median period of treatment was similar between the two most common types of BCG-AE (injection-site abscess: 2.8mo, suppurative lymphadenitis: 3.2mo, p=0.450). Most warts-like lesions and BCG reactivation had spontaneous regression. Regarding the outcome, 93.9% patients had healing, 4.5% were lost for follow-up, 2 died of causes not related to BCG-AE and 3 patients are still on follow-up.

Conclusion: BCG-AE following BCG Moreau-Rio de Janeiro strain has usually favourable outcome. In cases of treatment failure, other differential diagnosis or antimicrobial resistance should be considered.

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AETIOLOGICAL DIAGNOSIS OF BLOODSTREAM INFECTIONS THROUGH A MULTIPLEX REAL-TIME POLYMERASE CHAIN REACTION TEST IN PAEDIATRIC AGE: PRELIMINARY RESULTS

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Background and aims: Outcome of bloodstream infections (BSIs) is strongly related to microbiological diagnosis. Molecular methods may be useful in children as they can speed up pathogen identification and require smaller blood amounts than blood cultures (BC).

Methods: Medical records of patients who underwent a multiplex real-time Polymerase Chain Reaction (PCR) test (Septifast test - SF - Roche Diagnostics) in the tertiary Regina Margherita Children's Hospital (Turin, Italy) from September 2009 to September 2011 were retrospectively revised. Results of SF were compared with BC (automated Bact/Alert 3D, BioMérieux) closely collected.

Results: 307 SF were collected from 166 patients: 112 males, median age 9.11 years (range 0-26.8). 109 had immunodeficiency and 16 were newborns. Clinical and laboratory data led to a BSI diagnosis in 174 cases (57%). At the time of sampling, all patients were receiving empirical chemotherapy. SF resulted positive in 34 cases, 3 interpreted as contaminants. Aetiological definition was achieved simultaneously by SF and BC in 17 cases: 15 were monomicrobial and 2 polymicrobial infections. BC failed microbiological identification in 11 cases (with SF identifying more than one pathogen in 2), and was not performed in 3. Conversely, BC alone resulted positive in 18 septic episodes, although 3 isolates were not included in the SF master list (Fusarium, Ralstonia mannitolytica, Sphingomonas paucimobilis). A 31% increasing of bacteria identification chances due to SF was documented.

Conclusions: PCR methods can't replace BC, but they are a valuable adjunctive diagnostic tool for aetiological BSIs definition, especially in children receiving empirical chemotherapy.

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PREDICTIVE VALUE OF INTUSSUSCEPTION ICD-9 CODE FOR POST-LICENSURE SURVEILLANCE OF ROTAVIRUS VACCINES IN SPAIN

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Background and aims: Post-licensure vaccine safety can be assessed using computerized medical databases if diagnostic codes adequately predict the outcome of interest. Recently, intussusception has been observed in temporal association with one of the new rotavirus vaccines.

Our aim was to assess the positive predictive value of the ICD-9-CM code for intussusception in the Spanish hospital discharge database (CMBD).

Methods: Retrospective study conducted in the Valencian Region, Spain, over a five-year period (2007-2011) in infants under 10 months of age at the time of the diagnosis of intussusception, that were admitted to a public hospital.

Cases were identified using the ICD-9-CM code for intussusception (560.0). All cases had a review of their medical charts and were classified as Level 1, Level 2, Level 3, insufficient evidence or non-evidence following the Brighton Collaboration definition. Positive predictive values for the ICD-9-CM code using medical records as gold standard were calculated.

Results: There were 160 cases of intussusception, of them 137 (85.6%) were classified as Level 1, 12 (7.5%) as Level 2, 2 (1.3%) as Level 3, 8 (5%) as insufficient evidence and 1 (0.5%) as non-evidence.

The PPV for the Level 1 was 85.6% (95%CI:79.4-90.2)%, taking into account Level 1 and Level 2, 93.1% (95%CI: 88.1-96.1)%, and 94.4% (95%CI: 89.7-97.0)% for the three levels together.

Conclusion: Specific hospital discharge code for intussusception could be a useful tool for post-licensure surveillance of rotavirus vaccines in Spain.

1007

NT-PROBNP AS A PREDICTIVE INDICATOR OF INITIAL INTRAVENOUS IMMUNOGLOBULIN TREATMENT FAILURE IN CHILDREN WITH KAWASAKI DISEASE : A RETROSPECTIVE STUDY

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Background: Intravenous immunoglobulin (IVIG) in the acute stage of Kawasaki disease (KD) is the standard therapy. Failure of initial treatment with IVIG remains the most consistent risk factor for coronary artery lesions (CALs). However, there are few reports on non-responders to initial IVIG therapy in KD. The goal of this study was to investigate the risk factors for initial IVIG treatment failure and to predict non-responders to initial IVIG therapy in KD.

Methods and Results: A total of 135 patients diagnosed with KD admitted for IVIG treatment were retrospectively enrolled for analysis. Of these, 22 patients were non-responders who received additional rescue therapy because they had an elevated body temperature at 36 hours after completion of initial IVIG treatment. NT-proBNP concentration was significantly higher in non-responders than in responders (2465.36 ± 3293.24 vs 942.38 ± 1293.48 pg/mL; $p < 0.05$). The optimal cutoff point of sensitivity and specificity for predicted non-responders was ≥1093.00 pg/mL. The sensitivity and specificity for prediction of IVIG response was 70.0% and 76.5%, respectively.

Conclusions: We have discovered a biomarker able to identify KD patients at high risk of complications who did not respond to initial IVIG treatment. We suggest that patients who have a NT-proBNP level of ≥1093.00 pg/dL are likely to fail initial IVIG and may require further rescue therapy.

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ACUTE CHOLECYSTITIS AND LIVER ABSCESSES IN CROHN´S BOWEL DISEASE TREATED WITH INFLIXIMAB

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Background and aims: Liver abscesses is a rare complication of treatment with infliximab. We present a patient with Crohn´s disease, treated with infliximab, with acute cholecystitis and liver abscesses.

Case report: A 13 years old boy was diagnosed of Crohn´s disease and received enteral nutrition therapy, azathioprine and methotrexate. An azathioprine-related pancreatitis resolved with withdrawl. At 14 years he had a flare of the disease. Infliximab (IFX) was started (5 mg/kg/dose) at 0- 2 and 6 weeks and then every 8 weeks. Following fifth dose, he had fever, abdominal pain, hepatomegaly and elevated acute phase reactants. Abdominal ultrasound showed an acalculous cholecystitis. Amoxicilin-clavulanate (A-C) IV was started, without obtaining remission of fever, and this was replaced with piperacilin-tazobactam. He experienced complete laboratory, clinical and ultrasonographical recovery. After 15 days, the antibiotic therapy was discontinued. The patient remained assymptomatic. An abdominal ultrasound control revealed multiple, peripheral, hypoechoic, focal images (1 cm diameter) suggestive of liver abscesses. MRI showed similar lesions and ruled out the presence of enterohepatic fistula. Blood cultures and cultures and PCR of the exudate of a microabscess were negative. Two more weeks of piperacilin-tazobactam were completed. Therapy with oral A-C and ciprofloxacin for 4 weeks was added. MRI performed 2 weeks after stopping antibiotics was normal. IFX was resumed and 8 months after the patient continues asyntomatic.

Conclusion: Liver abscesses are rare in IFX therapy and Crohn´s disease, but acalculous cholecystitis complicated with liver abscess has not been previously reported. These injuries can be managed only with antibiotics.

1009

BRAIN ABSCESSES IN CHILDREN: THE EXPERIENCE OF AN ITALIAN PAEDIATRIC CENTER

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Background and aims: Brain abscess (BA) is an uncommon but potentially life threatening infection in paediatric population. The objective of this case series is to describe management and outcomes of BAs in a single Paediatric Tertiary Referral Center.

Methods: We retrospectively reviewed medical records of children with BA admitted to Regina Margherita Children's Hospital, Turin, Italy, from 1998 to 2012.

Results: Eighteen children (12 M, 6 F) were included. Age ranged from 2 weeks to 16.5 years (mean 8.1 ± 5.6 years). Contiguous infections, especially otitis, were the most frequent predisposing factors (10/18 patients). At presentation, 9 patients had headache and 8 fever. Seizures occurred in 6 children. Neuroimaging consisted in CT in 14 patients and MRI for 4. Fourteen children had a single BA;16 abscesses were located in the cerebral hemispheres and 2 in the cerebellum.

Antimicrobial therapy was administered for a mean of 53.2 days (range 13-117 days). Ceftriaxone plus metronidazole and meropenem plus vancomycin were the most frequent combinations. Fourteen patients underwent surgery and consequent microbiologic examination. Gram positive bacteria, in particular Streptococcus intermedius, were the predominant isolated pathogens; four cultures were sterile. No death was recorded. Six children presented neurological sequelae, including motor deficits (3), hydrocephalous (2), visual impairment (1).

Conclusions: Despite the advances in surgical and diagnostic techniques, and the availability of new antimicrobials, BA in children remains associated with a high morbidity rate and may cause relevant neurological damage. Along with an appropriate antimicrobial treatment, neurosurgical intervention is often crucial in BAs' management.

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PATTERNS OF DRUG RESISTANCE IN VERTICALLY HIV INFECTED CHILDREN AND ADOLESCENTS

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Background and aims: Long term highly active antiretroviral therapy (HAART) of vertically HIV infected children is affected by a variable burden of viral drug resistance in adolescence and early adulthood. We aimed at investigating the factors associated with such phenomenon.

Methods: We retrospectively evaluated the clinical records of children with HIV infection referred to our tertiary care center for infectious diseases in Southern Italy.

Results: Forty-three vertically HIV infected children(< 13 years; n=14) and adolescents (≥13; n=29) (median age 176 months, range 8-267; 19 boys) were included, whose HAART mean duration was 138.8±68 months. Of them, 25.6% and 55.8% had prolonged inadequate adherence to HAART and suboptimal viral suppression, respectively, and 44.8% had drug resistance according to genetic testing. Drug resistance was significantly associated with inadequate adherence (81% vs 37.5%, P< .05), and was more frequent in orphans (60% vs 23%P< .05) and adopted children (68% vs 33.3%, P< .05).

There was a significant relationship between HAART duration and total number of resistance mutations (r^2=0.135, P< .05) as well as with the number of therapeutic changes due to resistance (r^2=0.098, P< .05).

Conclusions: The pattern of drug resistance in HIV infected children is influenced by adherence to HAART, which is in turn more adequate in families with natural parents, probably because of the presence of other family members on antiretroviral treatment. Adherence monitoring during childhood is essential to maintain sufficient therapeutic options in adult life.

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RISK OF MISMANAGEMENT OF TUBERCULOSIS IN IMMIGRANTS AND IN FAMILIES WITH LOW SOCIAL AND CULTURAL BACKGROUND

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Background and aims: Childhood tuberculosis (TB) is becoming a worrying problem in public health in Europe. An increasing number of cases occur in immigrants or in social minorities, with related cultural, social and economic issues. We aimed at identifying socioeconomic factors affecting the management of pediatric TB.

Methods: We retrospectively evaluated the clinical records of children with tuberculosis disease (TBD) and latent tuberculosis infection (LTBI) referred to our tertiary care center for pediatric infectious diseases in the years 2010-2012.

Results: Forty-eight children (median age 5.2 yrs, range 0.1-15.9; 25 M) were included, 23% had LTBI and 77% TBD (86.5% with pulmonary disease). Forty-two% of them were immigrants, 29% from Eastern Europe. Immigrants had a younger age at diagnosis (4.5±4 vs 7.5±4 yrs, P< .05), a higher percentage of multi-drug resistant TBD (20% vs 0%, P< .05) and a longer hospital stay (11.3±20 vs 3.2±4 days, P< .05) than Italian children. Case tracking was positive in 46% low income vs 25% medium/high income families (P< .05). In low cultural background, adherence to therapy was lower and “no shows” at scheduled follow-up more frequent (61% 2.1±2 missed days, respectively) with regard to families with higher education (100%, P< .05; 0.9±1, P< .05). More treatment failures/relapses (13% vs 3.5%) were observed in immigrants.

Conclusions: Mismanagement of TB is present in families at social and cultural risk and it is associated with poorer clinical outcome. Early risk identification could prompt the application of specific prevention and follow up mechanisms in childhood TB care.

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JUVENIL PARKINSONISM DUE TO ENTEROVIRUS: REPORT OF A CASE

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Introduction: Juvenile Parkinsonism, a particular type of Parkinson Disease (PD), is a very rare entity in childhood. Viral infections may have a role in the etiology of the secondary juvenile parkinsonism.

Case report: Sixteen year old girl admitted to our hospital with complaints of fever, diminished speech, echolalia and difficulty in walking. A week before, a fever raising up to 40°C, vomiting and non-bloody, non-mucous diarrhea had started. Her family denied any previous illness. Her body temperature was 36° C, with a general condition being moderate; she was looking apathic, uncooperated and disoriented. After clinical assessment and ordinary laboratory investigations, meningoencephalitis with brainstem encephalitis was diagnosed. Enterovirus has been shown as a causative agent by multiplex polymerase chain reaction from the cerebrospinal fluid. On the 11^{th} day of follow up; spasticity, visual hallucinations, peripheric facial paralysis, difficulty in starting a movement, weakness on the right side and tremors were observed. JP was diagnosed. Substantia nigra involvement on magnetic resonance imaging (MRI) related to enterovirus was documented. She was treated with L-dopa as advised as the first line symptomatic treatment of PD with no obvious complication.

Conclusion: This report is aimed to suggest physicians to take into consideration of the high level of neurotrophism due to enteroviruses with not only classical clinical pictures, but also with nadir complications like PD.

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POSTPARTUM EVOLUTION OF NEWBORNS TO MOTHERS ADDICTED TO "NEW DRUGS" AND RECENTLY DIAGNOSED WITH HIV INFECTION

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Background and aims: In 2011 and 2012 Romania registered a significant increase in the number of IDUs along with a change in the use pattern, namely the replacement of heroin among users with the so called "new drugs". These are mostly synthetic cannabinoids and cathiones. Within this context, the share of new IDU-HIV cases expanded from, 3% in 2010 to 29% in 2012.

Our objective was to observe the evolution of 30 newborns to mothers recently diagnosed with HIV infection, who were also "new drugs" consumers.

Methodology: During 1 January 2011-31 December 2012 we assessed 30 newborns exposed to HIV and "new drugs" by clinical and biological screenings. Relevant data were recorded: gender, age, moment of diagnosis, ART prophylaxis, type of birth, type of nourishment, CD4 count, VL, ultrasound evaluation. For mothers we focused on age, time of HIV diagnosis, treatment/prophylaxis, type of birth, type of consumed drugs.

Results: The number of newborns perintally exposed to HIV/HVB/HCV/drugs and new drugs augmented in 2011-2012 compared to previous years. They presented several neo-natal problems of adaption especially a severe withdrawal syndrome from the very first hours of life with life threatening risks.

Conclusions: Most of these pregnant women do not access routine check-ups, this explaining their absence from records as drug users; also, if they are diagnosed with HIV during pregnancy they refuse to take specific treatment.

From the social perspective these women are either very poor or come from dysfunctional families, who are reluctant in providing them the proper support.

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ANTIBIOTIC PRESCRIBING GUIDELINES FOR URINARY TRACT INFECTION IN CHILDREN: WHAT ARE WE CURRENTLY RECOMMENDING IN EUROPEAN HOSPITALS?

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Background and aims: Urinary tract infection (UTI) is on of the most common indications for antibiotic use in children. The aim of our study was to assess the prevalence and recommendations of guidelines for the treatment of UTI in European paediatric hospitals.

Methods: This was an ARPEC study initiative which is a European Union funded project. A web-based preformed questionnaire was used to document availability of guidelines, choice of first line antibiotics and treatment duration for UTI in infants >3 months old and children in European hospitals between September 2011 and November 2012.

Results: Seventy three hospitals from 18 European countries responded of which 52 (71%) reported the existence of UTI guidelines. Monotherapy was recommended in 90% of hospitals with guidelines. For monotherapy, 49% of guidelines recommended a cephalosporin of which 61% were of 3rd generation agents. Other antibiotics recommended as monotherapy included gentamicin (17%), trimethoprim (15%) and co-amoxiclav (12.5%). Combination therapy with a beta-lactam plus aminoglycoside was recommended by guidelines at 5 (10%) hospitals. The recommended duration of therapy ranged between 5 and 14 days (mean 9 days).

Conclusions: We found significant variability in recommendations for antibiotic prescribing for children with UTI in European hospitals. The majority of guidelines recommended broad spectrum antibiotics, such as 3rd generation cephalosporins, as first line agents. Identifying conditions like UTI for which there are both frequent and variable antibiotic use enables the prioritization of high-impact targets for antimicrobial stewardship interventions. These interventions should be informed by evidence and local antibiotic resistance patterns.

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KERION - A DIAGNOSIS TO REMEMBER

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Introduction: Kerion is a fungal inflammatory infection of the scalp, hair follicles and surrounding skin, with regional lymphadenopathy. It's caused by zoophilic and geophilic fungi, and characterized by a suppurative painful plaque, caused by an intense inflammatory reaction. There is hair loss and possibly a permanent cicatricial alopecia.

Clinical case: Female child, 5 years old, presenting an exuberant erythematous inflammatory plaque, painful and suppurative lesions, areas of crust and alopecia, evolving for three months.

Initially diagnosed and treated (oral flucloxacillin 50mg/kg/day), in the local health services, for an impetigo. For lack of improvement, mycological examination was performed, isolating Tricofitum spp and began treatment with oral terbinafine 7mg/kg/day and ketoconazole shampoo for two months. She inhabited a low social class with poor adherence to treatment.

For surveillance and to ensure treatment, was admitted under therapy with oral flucloxacillin 60mg/kg/day (7days), oral terbinafine 7mg/kg/dia (13days), topical bacitracin (4days), topical betamethasone (3days), acetaminophen 15mg/kg (SOS), petroleum jelly in crusts, ketoconazole shampoo.

Presented favorable evolution with the fall of crusts and decreased granulation tissue, keeping areas of alopecia.

Discharge at day 13 treated with oral griseofulvin 250mg and topical bacitracin (20days).

One year after the onset presented with large areas of cicatricial alopecia, a situation which persisted 2 years later.

Discussion: The diagnosis of Kerion in children presenting suppurative plaques of the scalp should be considered. It's important to differentiate this disease from bacterial infections since the specific treatment is imperative and a late diagnosis of fungal infection can cause cicatricial alopecia.

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CLIMATIC EFFECTS ON THE SEASONALITY OF RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN HOSPITALISED WITH LOWER RESPIRATORY TRACT INFECTIONS IN MALTA

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Background and aims: Respiratory Syncytial virus (RSV) is a major cause of hospitalisation in small children. We aimed to study the influence of meteorological factors on the onset of RSV related hospitalisations in children < 2 years old.

Methods: A prospective study was performed from October 2009 to September 2011. RSV was cultured from nasopharyngeal swabs. Daily readings of temperature, relative humidity, rainfall and wind speed and direction were recorded. Spearman correlation was used to analyse any relation with meteorological factors whilst climatic differences were analysed using Student t-test.

Results: The first season lasted from February till May 2010, during which 30 of 134 children admitted with bronchiolitis (22%) had RSV infection. The subsequent season started in December 2010 and ended in March 2011 during which 49 of 144 children (34%) had positive RSV cultures.

RSV hospitalisations were negatively correlated with a decreasing wind chill index

(p=< 0.01). Comparison of the climatic factors only revealed significant differences in relative humidity. January 2010 (weeks 1-5) was significantly less humid during the day (72.87% vs 82.48%;p=0.0001) and night (76.16% vs 88.07%;p=0.0001) compared to January 2011. Similarly, November 2010 (weeks 46-47) was significantly less humid during the day (70.67% vs 79.87%; p=0.0009) and night (74.33% vs 87.87%;p=0.0001) than November 2009. These periods preceded exactly the onset of the RSV seasons.

Conclusion: Relatively lower humidity, on a background of cold temperature, was conducive to the different onset of the RSV seasons possibly from its effect on the stability and transmissibility of RSV.

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VISCERAL LEISHMANIASIS IN CHILDREN HOSPITALIZED FOR HEPATOSPLENOMEGALY

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Background: Visceral leishmaniasis, also known as kala-azar, is a vector borne disease caused by the protozoan parasite, L. donovani. It is endemic in areas bordering the Mediterranean Sea. Untreated visceral leishmaniasis has fatal course. Therefore, early diagnosis and specific therapy with pentavalent antimony drugs are mandatory.

The aim of this study was to analyze patients hospitalized for investigation of hepatosplenomegaly that turned out to be visceral leishmaniasis.

Material and methods: This retrospective study was carried out at University Children's Hospital Skopje, Macedonia - Department of Gastroenterohepatology in 2011-2012. Data were analyzed for age, gender, place of residence, clinical symptoms, investigations, treatment and outcome.

Results: During 2 years period 4 patients were included. Mean age was 17,5 months (range 6 months to 2,5 years), 75% were female. The main clinical signs and symptoms of the patients were hepatosplenomegaly (100%), abdominal distension (75%) and fever (50 %). Anemia was the most frequent hematological abnormality found in all patients, mean hemoglobin value 86.2 ± 17.3 g/l. Trombocytopenia was present in half of the patients. Elevated liver enzymes were present in 75%, AST 181,0 ± 190,1U/l , ALT 106,2 ± 106,0 U/l and hypergamaglobulinemia in 50% of the patients. The diagnosis was made by detecting leishmainias in bone marrow aspirate associated with positive serology. All patients were treated with meglumine antimonate (glucantime), achieving rapid clinical and laboratory response.

Conclusion: Visceral leishmaniasis is an existing infection among children in Macedonia. It should be considered in differential diagnosis of hepatosplenomegaly with or without fever.

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SENTINEL HOSPITAL SURVEILLANCE FOR ROTAVIRUS IN SÃO PAULO STATE, BRAZIL, AFTER INTRODUCTION OF VACCINE ROTARIX®

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Aims: Rotavirus (RV) infections are recognized as a major cause of severe gastroenteritis in infants and young children worldwide. In March 2006, Brazil introduced a monovalent G1P[8] human RV vaccine (Rotarix®) into its national Expanded Program for Immunization. The aim of this study was to assess the impact of immunization on the incidence of severe RV acute gastroenteritis and to determine the genotypes after introduction of vaccine.

Methods: Surveillance of diarrhea was conducted involving 975 children < 5 years of age who were admitted for treatment of diarrhea at 3 sentinel hospitals in São Paulo State**,** from January 2010 to December 2012.

Results: RV was detected in 23.8% of the fecal specimens. Of all episodes of RV diarrhea, 81.0% occurred during the first 2 years of life. RV isolates were characterized by RT-PCR to determine G and P genotypes. G2 (30.2%) was the most prevalent serotype followed by G3 (25.4%), G9 (23.7%), G12 (7.3%) and G1 (5.2%). P[8] was the most common genotype of RV. The most common G-P association identified was G2P[4], G9P[8], G3P[8] and G12P[8].

Conclusion: Preliminary data obtained from hospitals in São Paulo State and information concerning the program of Acute Diarrheic Diseases Monitoring show that hospitalization for diarrhea in children under 5 years had a significant reduction after the introduction of RV vaccine. Sentinel hospital-based surveillance is essential to monitor changes in the epidemiology of RV disease and the impact of vaccination after introduction, considering change in frequency, severity of disease, and circulating RV types.

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ONYCHOMADESIS DURING THE COURSE OF HAND-FOOT-MOUTH DISEASE

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Background - aim: Hand-foot-mouth disease (HFMD) is an acute viral infection, very common in childhood. Main strains causing HFMD are Coxsackie A virus and Enterovirus 71. Onychomadesis (idiopathic shedding of the nails) is a rare complication of HFMD. We present cases with onychomadesis because of the rarity of it.

Methods: The period October to December 2012 there was a HFMD outbreak in our area. During this outbreak we observed some cases with onychomadesis, in a private clinic. This is an analysis of them.

Results: There were 5 cases, 3 males, 2 females. The age of them was 21 months to 4 years old. All patients had a picture of typical HFMD with fever and vesicles on the hands, feet, and mouth. No patient took any medication for HFMD. The course of the disease was mild and all patients were cured. However, two (1 patient) to four weeks (4 patients) after the disappearace of all symptoms and signs of HFMD, onychomadesis appeared in the nails of the fingers that had the typical eruption and skin lesion of HFMD. The nail changes were temporary with spontaneous normal regrowth.

Comments: Onychomadesis is an acute, painless, noninflammatory disease that affects the nail matrix, with unknown mechanism. The fact that it is observed in fingers with skin eruption perhaps means that there is a direct inflammation which inhibit nail matrix proliferation.

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EPIDEMIOLOGY, SEROTYPE DISTRIBUTION, AND ANTIMICROBIAL RESISTANCE OF STREPTOCOCCUS PNEUMONIAE IN KUWAIT: AN 8-YEAR STUDY OF PNEUMOCOCCAL CONJUGATE VACCINE IMPACT

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Background: The 7-valent polysaccharide-protein conjugate pneumococcal vaccine (PCV7) was introduced in Kuwait in August 2006, and the PCV13 in August 2010, for children aged < 2 years.

Objectives: To evaluate the impact of PCV7 and PCV13 on epidemiology, serotype distribution and antimicrobial resistance of both invasive and non invasive S.pneumoniae isolates, and to estimate the vaccine coverage rate in all age groups.

Methods: The study included all cases of invasive and non-invasive pneumococcal disease in children and adults from January 2004 to December 2011. Serotyping and susceptibility to penicillin were done using Quellung reaction antisera and Etest method, respectively.

Results: 645 pneumococcal isolates were studied. From January 2004 till July 2006; there were 250 isolates (22% were invasive isolates and 27% were from children ≤5years) and from August 2006 till December 2011, there were 390 isolates (32% were invasive isolates and 35% were from children ≤5years). The predominant invasive serotypes from 2004-2006 were 19F, 23F, 9V and 14, while from 2006-2011 they were 19F, 8, 6A, 9V, 14, 3, 1, 19A, 5 and 15B. The percentage serotype coverage by PCV7 in children < 2 years dropped from 75.0% in the first period to 34.6% in the second period. A positive impact of PCV7 on the incidence of IPD was demonstrated in both children < 5 years and adults > 50 years. There was a significant drop in antibiotic resistance.

Conclusions: With the appearance of non-PCV7 pneumococcal serotypes, broader serotype coverage vaccines are needed for the prevention of IPD in children.

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RAPID IDENTIFICATION OF MYCOBACTERIA USING PCR RESTRICTION FRAGMENT LENGTH POLYMORPHISM ANALYSIS (PRA) METHOD

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Background: Aytipical Mycobacteria cause various infections and some of them lead to Tuberculosis-like disease. Treatment of atypical mycobacteria is different from tuberculosis so identification of mycobacterial species is important for better control of tuberculosis. PRA is a more rapid and accurate method in comparison with phenotypic ones. During the present study using 3 restriction enzymes for digestion of 644 bp PCR product of hsp65 gene, identification of 50 mycobacterial isolates were accomplished.

Methods: Fifty different atypical mycobacterial isolates from patients referred to the Pasteur Institute of Iran over 89-90 years were tested for PRA. A 644 bp fragment of hsp65 gene was amplified by PCR. Subsequently,PCR products were digested with AvaII, HphI and HpaII enzymes. Digested fragments were compared with standard algorithm and identified with GelcomparII software.

Results: Forty nine of 50 atypical Mycobacteria were identified in to 13 groups including 15 M.fortuitum,12 M.simiae، 6 M.kansasii، 3 M.szulgai, 2 M.triviale ، 2.M.gordonae، 2 M.aichiense، 2 M.gallinarum.1 M.hassiacum،1 M.malmoense،1 M.aurum، 1 M.marinum،1 M.abscessus and one unknown species.

Conclusion: The results showed PRA using AvaII، HphI وHpaII is a simple,fast and accurate for identification of atypical mycobacteral isolates into species or sub species level. Rapid and exact identification of atypical mycobacteria from Mycobacterium tuberculosis is essential for effectiveness of TB surveillance programs.

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INVESTIGATION OF GENETIC DIVERSITY AMONG CIPROFLOXACIN RESISTANT ENTEROCOCCUS FAECALIS ISOLATED FROM CLINICAL SPECIMENS WITH PULSED-FIELD GEL ELECTROPHORESIS (PFGE) METHOD

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Resistance to ciprofloxacin among Enterococcus faecalis (E.f) isolates especially in UTI makes difficulties for treatment. In this study, the genetic diversity using PFGE method and detection of resistance genes including parC, gyrA , gyrB and parE among ciprofloxacin resistant E.f isolated from clinical specimens, are determined.

Methods: A total of 384 entreococcal isolates were collected from 6 hospitals and 3 private laboratories in Tehran and 50 ciprofloxacin resistant E.f isolates were obtained. Identification of species and resistance genes were done by PCR method. Antimicrobial and minimum inhibitory concentration (MICs) tests were assayed with standard methods and finally genotyping was accomplished using PFGE method.

Results: The range of ciprofloxacin MICs was 16 to 512 µg/ml. All of these isolates contained parC, 98 % gyrA , gyrB and 80 % parE genes. PFGE analysis, grouped 50 strains in 11 common types and 7 single types. The P4, P9 and P10 genotypes were shared between hospital and community isolates.

Discussion: According to these results the E.f isolates showed high clonal diversity. Because of the ciprofloxacin high MICs level among common pulsotypes we concluded that thy have various distribution which maybe due to highly transmission of resistant genes among enterococci. Indeed the colonized patients with these resistant isolates are reservoir for releasing of the resistant genes to community which requires more surveillance programs.

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MOLECULAR CHARACTERIZATION OF ROTAVIRUS IN CHILDREN ADMITTED TO THE WARSAW DEPARTMENT OF PEDIATRICS IN 2011 - INITIAL REPORT (*)

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Background and aims: The rotavirus gastroenteritis is a significant cause of morbidity and hospitalization in developed countries. The G1P[8] strains are considered predominant. Prospective surveillance is needed to monitor and characterize rotavirus infections and to allow the identification of potentially epidemic and emerging strains.

Methods: In 2011, we reviewed 551 cases with acute gastroenteritis admitted to the hospital. Rotaviruses, as the most common cause of diarrhea, were detected in 244 (44.3%) samples. They were randomly selected to determine their genotype by a reverse transcription-polymerase chain reaction, according to their protein capsids VP6, VP4, VP7.

Results: The genotyping of 50 rotaviruses showed a predominance of the G9- 34.7%, followed by the G2 -8.2%, the G4- 6.1%, the G1- 4.1%, and a high coexistence of strains- 32.7%, including the emerging G12- 4.1%. Most strains were associated with the P[6]- 62%, followed by the P[8]- 14% and the P[6]P[8] coexistence- 14%. The rotavirus group A (human) was found in 71.4% samples, while 20.4% of the gastroenteritis was caused by zoonotic reassortants. Also, a clear seasonal variation of the predominant strains was found. In autumn/winter the G9P[6] strains were dominant, while in spring/summer mostly co-infections were observed.

Conclusions: The most common rotavirus strain was the G9P[6], not included in the current rotavirus vaccines. However, mixed and zoonotic infections were also frequently discovered. Monitoring should be maintained to document the strain diversity and circulation, and to evaluate the emergence of new reassortants that may not respond to the present rotavirus vaccines.

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NOCARDIA ASTEROIDES PERITONEAL DIALYSIS-RELATED PERITONITIS; FIRST CASE IN PEDIATRICS, TREATED WITH PROTRACTED LINIZOLID. CASE REPORT AND LITRATURE REVIEW

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Background and aims: Peritonitis is a common problem in patients undergoing continuous ambulatory peritoneal dialysis (CAPD).Fungi and higher bacteria such as Nocardia asteroides as etiological agents have been infrequent in children undergoing CAPD.The predisposing factors,treatment protocol,and whether to treat with or without catheter in situ are unanswered questions in Nocardia peritonitis.

Material and methods: 13 years old female diagnosed with end stage renal failure on CAPD since 3 years.She presented with history of high grade fever leaking from the exit site of the peritoneal catheter,abdominal pain.On admission,patient started imprically on intraperitoneal (IP) Vancomycin,Ciprofloxacin.Initial peritoneal fluid examination was turbid appearance with white sediment and high WBC.Amphotricin-B was added after 4 days to cover for suspected fungal peritonitis.Peritoneal culture grew Candida Alberta and Nocardia after 12 days.Child went into cardiac arrest and septic shock.Catheter was removed.Child was managed in PICU with CVVH,ventilation and inotropic support.Case was complicated with peritoneal abscess that was evacuated by ultrasound guided aspiration.Jeujonal adhesions with some feeding intolerance were treated conservatively.

Results: Linizolid was given IV for 3 months in hospital then orally for 5 months with monitoring of side effects.Patient discharged home after 3 month on haemodialysis.

Conclusions: Nocardia peritonitis not reported before in pediatrics.It generally present as infection unresponsive to empirical treatment and initially an apparent 'culture-negative' peritonitis.Diagnosis and management can be problematic due to the slow growth and difficult identification.Duration of treatment for Nocardia peritonitis is not known.Linizolid can be used for prolonged period in trimethoprim-sulphamethoxazole resistant cases with close monitoring of side effect.

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CONCURRENT INTRACEREBRAL AND SPINAL INTRAMEDULLARY TUBERCULOMAS IN A YOUNG CHILD: A CASE REPORT

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Background: Co-occurrence of spinal intramedullary and intracerebral tuberculoma is an extremely rare presentation of central nervous tuberculosis in children.

Case report: An 18month old immunized girl with no history of tubercular contact presented with progressive weakness of both lower limbs and inability to walk for 1 month. There was no history of seizures, alteration of sensorium, cranial nerve or upper limb involvement and no systemic symptoms (fever, cough or weight loss). On examination she had flaccid paraparesis of bilateral lower limbs with exaggerated deep tendon jerks and upgoing plantars. There was no sensory level and anal tone was weak. Spine was grossly normal with no external swelling. Rest of general, nervous and systemic examination was within normal limits.

MRI spine showed a focal relatively well defined smoothly marginated intramedullary space occupying lesion at D1-3 with peripheral ring enhancement and central necrotic foci s/o intramedullary tuberculoma. CT scans revealed two ring enhancing lesions in right frontal and left cerebellar hemispheres suggestive of intracranial tuberculomas and multiple conglomerate necrotic peripherally enhancing mediastinal lymph nodes in the chest with no parenchymal lesions. Work-up for tuberculosis revealed positive Mantoux with normal chest Xray and 3 negative gastric aspirates for acid fast bacilli. Patient was started on antitubercular therapy and showed significant clinical and radiological improvement on follow up.

Conclusion: Spinal intramedullary tuberculoma is a rare differential diagnosis of spinal space occupying lesion causing paraparesis and should be promptly diagnosed and evaluated as it is amenable to cure by early medical or surgical treatment.

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THE CHALLENGE: PCT VS CRP PREDICTING INVASIVE BACTERIAL INFECTIONS IN YOUNG FEBRILE INFANTS

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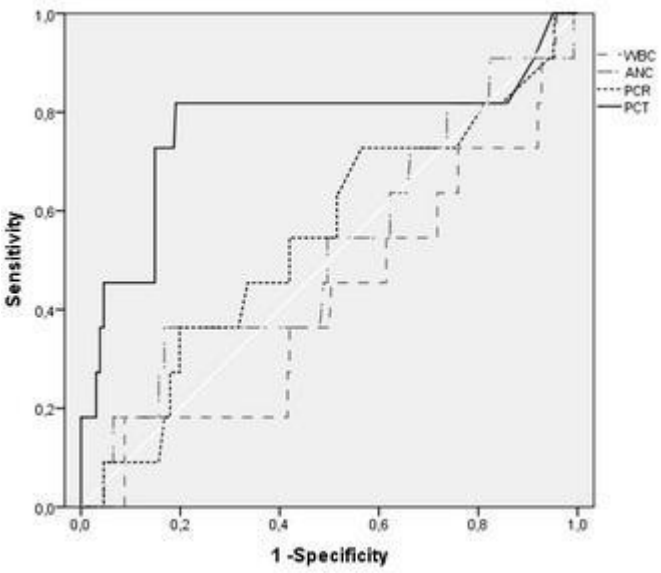
Fever without source (FWS) is one of the most common presenting complaints to pediatric ED. The aim of this study was to determine the accuracy of C-reactive protein (CRP) and procalcitonin (PCT) to rule out invasive bacterial infections (IBI) in these children.

We conducted a retrospective study among children < 90 days of age with FWS admitted to our ED during July/2008-January/2012 with at least one blood culture and RCP/PCT determination. IBI was defined as the isolation of a bacterial pathogen from the blood or cerebrospinal fluid (CSF).

During the study period 454 children were evaluated and 176 did not met inclusion criteria. Potentially severe bacterial infection was documented in 75 patients (27%): 64 UTI and 11 bacteremias (2 Pneumococcus, 5 GBS, 2 E.faecalis, 1 S.mitis and 1 E.coli).

PCT showed larger area in the ROC curves (0,767 (0.573-096)) than CRP (0,544 (0.36-0.72)) to detect IBI.



[ROC FWS]

Positive likelihood ratios for PCT (>0.5 ng/ml) and CRP (>3 mg/dl) were 4.8 (95% CI: 3-7.7) and 1,1 (95% CI: 0.27-3.36), respectively. Negative likelihood ratios for PCT and CRP were 0.32 (95% CI: 0.12-0.84) and 0.97 (95% CI: 0.76-1.3) respectively. Clinical appearance presented higher positive LR and lower negative LR than CRP in IBI detection.

Conclusions: PCT is a better marker than CRP for identifying children with IBI. CRP showed low sensitivity in young febrile infants. We should not underestimate other markers as clinical appearance in children with FWS.

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PERTUSSIS VACCINE COVERAGE OF PARENTS: CURRENT SITUATION IN MATERNITY UNITS IN NORTH-WEST FRANCE AND IMPACT OF COCOONING STRATEGIES

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Background and aims: Transmission of pertussis from parents to children is still a major problem in France. Despite the recommendations issued in 2004 on 'cocooning' vaccination strategies, which were to include parents, the vaccine coverage rate remains low. The purpose of this study was to assess the rate of vaccine coverage against pertussis among young parents and to assess the impact of having a protocol based on a cocooning strategy in place in the maternity hospital.

Methods: The study was based on the main study entitled Neocord, which covered 8,968 healthy newborns and compared two umbilical cord care strategies. A telephone survey was carried out one month after discharge from the maternity unit. The questionnaire also had questions of a general nature, including some on the parents' pertussis immunisation status.

Results: The overall vaccine coverage rate was 42.8% among mothers and 36.0% among fathers. Three of the six maternity units participating in the study had a protocol in place based on a cocooning strategy. Of the parents connected with these units, 55.4% of mothers and 46.4% of fathers were vaccinated, as opposed to 25.6% of mothers ($p< 0.01$) and 22.0% of fathers ($p< 0.01$) from units with no protocol.

Conclusions: This study shows the significant impact on the pertussis vaccine coverage rate among young parents achieved by effective cocooning strategy in maternity units.

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SPINAL EPIDURAL ABSCESS IN CHILDREN

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Background and aim: Spinal epidural abscesses (SEA) are rare but serious infections that require prompt diagnosis and treatment to avoid complications.

Methods: Retrospective review of all cases of SEA admitted to a tertiary paediatric hospital in the last 6 years.

Results: A 43-day-old girl was admitted with a 2-day history of low-grade fever and irritability. A dorsal spinal mass was noticed. WCC=29560/µL and CRP=90mg/L. Spinal MRI showed posterior SEA from T6-T11. Surgical drainage was performed and vancomycin and cefotaxime started, later switched to flucoxacillin when MSSA was isolated. A 4-year-old boy, one day after minor facial trauma, presented with high fever, abdominal pain and meningeal signs. WCC=15470/µL, CRP=380mg/L and ESR=78mm/h. Abdominal and heart ultrasounds and CSF were normal. Three days later a scarlatiniform rash and worsening back pain were noted. Bone cintigraphy scan was normal. Spinal MRI showed SEA from C7-T10. Ampicillin+clindamycin were started. S. pyogenes was isolated in the blood culture. A 14-year-old girl presented with an 8-day history of worsening back pain, with an episode of bladder dysfunction and lower limbs paresthesia. WCC=24580/µL, CRP=512mg/L and ESR=103mm/h. Spinal CT was normal. Ceftriaxone and flucloxacillin were started. Spinal MRI showed SEA from C7-L5, with subcutaneous infiltration. Surgical aspiration of the subcutaneous collection grew MSSA. All responded well to treatment and repeat MRI showed residual collection.

Conclusions: The initial clinical manifestations were nonspecific, leading to a delayed diagnosis in 2 cases. Spinal MRI was the best imaging tool. A conservative approach was adopted in 2 patients with good outcome.

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IS BREASTFEEDING A PROTECTIVE FACTOR AGAINST BRONCHIOLITIS IN HEALTHY INFANTS?

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Background and aims: Relationship between bronchiolitis and breastfeeding in developed countries has been mainly researched in hospitalized and risk patients. The objective of this study was to ascertain if exclusive and prolonged breastfeeding provides protection against bronchiolitis to healthy term newborns.

Methods: Retrospective cohort study. 200 healthy infants born between 10/01/08 and 12/31/09 registered at a Basic Health Unit were included. Preterm or weighed less than 2500 grams newborns and patients with chronic diseases were excluded. Type of feeding and duration, sociodemographic characteristics, seasonality of birth and morbidity due to bronchiolitis in their first year of life were recorded. Logistic regression adjusted for confounding factors.

Results: Rates of exclusive breastfeeding at 4 and 6 months of life were 41.0% and 30.0% respectively. Bronchiolitis incidence was 49.0% annually. Exclusive breastfeeding was a protective factor, with a risk reduction of bronchiolitis of 59.1% (OR 0.409, p0.026) if it lasted less than 4 months or it was mixed with formula milk; 66.4% (OR 0.336, p0.002) if infants were fully breastfed for 4 months or more, and 66.5% (OR 0.335, p0.007) if exclusive breastfeeding lasted for 6 months. Childcare attendance and exposure to cigarette smoke resulted risk factors of bronchiolitis (OR 2.045, p0.025 and OR 4.474, p0.031 respectively).

Conclusions: Bronchiolitis is a significant morbidity cause in healthy infants in our environment and breastfeeding is a protective factor, even more if it is exclusive and lengthy. By contrast, childcare attendance and familial smoking habits increase risk of bronchiolitis in the first year of life.

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CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO): THE IMPORTANCE OF DIFFERENTIAL DIAGNOSIS WITH INFECTIOUS OSTEOMYELITIS

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Background: CRMO is an uncommon noninfectious inflammatory bone disease of unknown etiology. There are not internationally accepted criteria for diagnosis, and rheumatic diseases, histiocytosis, bone tumors and bacterial osteomyelitis are the main differential diagnoses.

Methods: Case report.

Results: A 7-year-old caucasian girl presented a 7-day history of pain in the right thigh and mild fever. On her medical family history highlighted a grandfather with psoriasis. The previous year she had presented two self-limited episodes of pain in the right hip and left shoulder, without associated symptoms. Hip radiographs and blood count were normal. ESR was raised (62 mm/h). A presumptive diagnosis of osteomyelitis was made, and parental cloxacillin was initiated. Clinical response was not satisfactory and started pain in her left shoulder. RMI detected an osteolytic lesion surrounded by sclerosis in the coracoid process of the scapula. Ultrasound showed swelling and fragmentation of the left clavicle. Dual tracer scintigraphy suggested inflammatory etiology. The histologic findings in clavicular biopsies were a predominant lymphoplasmocytary infiltrate with some polymorphonuclear leucocytes and osteoclastic bone resorption. Aerobic, anaerobic, fungal, and acid-fast bacilli cultures and extended serologies were negative. Attending to these findings patient was diagnosed of CRMO and received empirical treatment with NSAIDs, reaching clinical remission within six months.

Conclusion: CRMO is an uncommon disease, but it is important to consider it in the differential diagnosis of bone lesions mainly at scholar age in order to avoid unnecessary antimicrobial treatments. The diagnosis of disease is complex and it often requires assessing the clinical course.

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ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) ASSOCIATED WITH MILIARY TUBERCULOSIS IN AN IMMUNOCOMPETENT CHILD: A CASE REPORT

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Background: ARDS is a rare but severe complication of miliary tuberculosis, and is associated with very high mortality.

Case report: A 14year old previously healthy immunized girl presented with fever for 7 days and acute onset progressively increasing breathlessness for 2 days. There was no history of cough, expectoration, flu like illness, chest pain or pedal edema. Her father died 6 months back following a chronic febrile illness.

On examination patient was sick looking, febrile, with marked tachycardia and tachypnea (respiratory rate >80/min) and cyanosis on room air. Cardiovascular and pulmonary system examination was normal. Chest X-ray showed bilateral fluffy infiltrates and a diagnosis of ARDS was made on clinical and blood gas analysis. Patient was managed with mechanical ventilation but had persistent fever. Sepsis workup including influenza was negative. Further workup including Mantoux, sputum for AFB and HIV serology was also negative. Ophthalmologic examination showed bilateral choroid tubercles. CECT chest showed bilateral miliary nodules with right pretracheal and hilar caseating lymphadenopathy. A diagnosis of miliary TB was made and confirmed by AFB seen in bronchoalveolar lavage fluid. Patient was managed with first line antitubercular drugs and steroids. Significant clinical improvement was seen and patient was discharged after 15 days of treatment.

Conclusion: Miliary Tuberculosis is an unusual cause of ARDS even in countries endemic to Tuberculosis. A strong clinical suspicion on the basis of history and a suggestive X-ray / CT scan can help in early diagnosis and institution of definitive therapy to improve the prognosis in these patients.

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ACUTE BRONCHIOLITIS: WHAT HAS CHANGED OVER THE YEARS? A RETROSPECTIVE STUDY

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Background: Bronchiolitis is a common cause of illness in infants. Management consists of supportive measures to maintain oxygenation and hydration.

Aims: Characterize children hospitalized in a secondary care hospital with the diagnosis of bronchiolitis. Describe the use of diagnostic tests, treatment, length of hospitalization and morbidity/mortality, over the years.

Methods: Descriptive**,** retrospective study of children hospitalized with bronchiolitis in 1997, 2004 and 2011.

Results: In 1997, 100 patients were hospitalized with bronchiolitis, 129 in 2004 and 88 in 2011. There was a predominance of male sex and infants under 6 months. The most common risk factor was prematurity. Chest X-rays were obtained in 88% patients in 1997, 97% in 2004 and 56% in 2011. Blood tests were obtained in 69% patients in 1997, 58% in 2004 and 51% in 2011. Respiratory syncytial virus was the most common etiological agent identified. In 2011 enteral feeding was more used than intravenous hydration. Chest physiotherapy was done in 97% patients in 1997 and in 14% in 2011. The same decrease was noted for bronchodilator therapy (93% in 1997; 35% in 2011). The median length of hospitalization was similar in the three years. Complications were less observed in 2011. There were no deaths.

Conclusions: Management of acute bronchiolitis has changed over the years. In this study there was a decrease in the use of diagnostic tests and institution of chest physiotherapy and bronchodilators. There was no increase in complications and median length of hospitalization.

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INVASIVE STREPTOCOCCUS PYOGENES DISEASE IN THE PEDIATRIC DEPARTMENT OF A PORTUGUESE TERTIARY HOSPITAL, 2002-2012

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Introduction: Invasive Streptococcus pyogenes (iGAS) disease is associated with high mortality and morbidity. It has been documented a rise in its incidence.

Aims: Evaluate the epidemiology, diagnostic procedures, therapeutics and risk factors of iGAS disease in the Pediatric Department of a Portuguese tertiary hospital.

Material and methods: Retrospective analyses of the medical records of children admitted from January2002 to June2012.

Results: There were 26 cases, ages between 2 months and 9 years, 62% were boys and the majority of them occurred in the Winter-Spring months(65%), with a maximum of five cases/year. There was an 88% increase in the frequency of the disease in the last evaluated years. The most common signs and symptoms at admission were fever(88%), rash(50%), respiratory symptoms(50%) and articular pain(31%). The diagnoses were sepsis(7); necrotizing fasciitis(5); septic arthritis(5); otomastoiditis(3, 1 with meningitis and venous sinus thrombosis); toxic shock syndrome(2); periorbital cellulitis(2); bacteriemia(4) and a case each of septal pyohematoma, piomiositis, subperiosteal abscess, necrotizing pneumonia and osteomyelitis. Risk factors were identified in 15 cases: infected wounds(7), varicella(6, 1 with the consumption of NSAIDs) and viral infection(RSV/H1N1)(2). In 54%GAS was isolated from blood. A 3rd generation cephalosporin was the initial therapeutic choice in 20patients, and an association including clindamycin was the choice in 7(with cephalosporin/penicillin). Surgery was required in 14patients. There were no recorded deaths.

Conclusion: The number of cases is small but demonstrates the wide variety and severity of iGAS disease. We evidenced a significant increase in the frequency of the disease in the last evaluated years.

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TRENDS IN INCIDENCE AND ANTIMICROBIAL RESISTANCE OF LATE-ONSET SEPSIS: 5 YEARS OF EXPERIENCE

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Background and aims: Late-onset sepsis (LOS) continues to be a challenging complication, especially in very low birth weight infants, increasing morbidity, mortality and medical costs. **Aim:** to evaluate clinical data of newborns with LOS and trends in causative microorganisms and their antimicrobial susceptibility.

Methods: Retrospective analysis of medical records and microbiological data of all newborns with LOS, defined by signs/symptoms compatible with positive blood culture or with laboratory studies suggestive of infection (WBC>30.000/µL or < 5.000/µL, platelet count< 100.000/µL, CRP>2mg/dL), after 72hours of life. Study period: January08-December12.

Results: Among a total of 14950 live births (LB), we identified 76 newborns with LOS (5,1 per 1000LBs), with median gestational age 28weeks (99% preterm, 11%>32 weeks) and median birth weight 975g. Fifty-five had positive blood cultures (3,7 per 1000 LBs). Forty-four percent started symptoms in the 2nd week of life, with respiratory distress being the major sign identified. Necrotizing enterocolitis was associated in 7 cases, meningitis in 2 and pneumonia in 1.Coagulase-negative staphylococci (CoNS) predominated (33; 2.2 per 1000LBs) followed by E. coli (6; 0.4 per 1000LBs). Among major pathogens identified, CoNS showed no resistance to vancomycin as well as E. coli to gentamicin. Methicillin resistant Staphylococcus aureus was isolated in just 1 case (5 S. aureus in total).Vancomycin and 3rdgeneration cephalosporins were the main antibiotics used. Lethality occurred in 7 cases.

Conclusions: CoNS remain the leading cause of LOS, as described in previous studies. In vitro susceptibility test of isolates showed low levels of resistance to commonly used antibiotics.

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IMPORTED CUTANEOUS LEISHMANIASIS OUTBREAK CAUSED BY LEISHMANIA MAJOR IN SOUTHEASTERN SPAIN

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Background and aims: Cutaneous leishmaniasis (CL) is a worldwide public health problem caused by different Leishmania species widespread in 88 countries. Currently, this condition appears to be underestimated and on the rise. Southeastern Spain is an endemic area of L.infantum. Early recognition and diagnosis of disease are important to detect imported infections by travellers from other areas.

Methods: Outbreak report.

Results: Between December 2009 and February 2010 10 patients (one infant, 6 children, 3 adults) from 4 unrelated families were visited in Dermatology and/or Pediatrics Services due to skin lesions. All of them lived in the same neighborhood in Almería (Spain). Furthermore, all were native from Errachidia (Morocco), and had travelled there on the previous summer season. They all presented multiple rounded crusty ulcers with raised, erythematous borders, varying in diameter from 2 to 5 cm in face or limbs that had evolved within two months. Lymphatic or mucosal involvement was not present. Travel history and unusual clinical features led to suspect an imported CL outbreak. L.major, endemic in Northern Africa, was demonstrated by PCR, instead of L.infantum, causative leishmaniasis species in our environment. Seven patients were treated: three received intramuscular meglumine antimoniate for 20 days, two received fluconazole for 6 weeks, and cryotherapy was performed in two; all with satisfactory progress.

Conclusions: A geographically influenced infectious disease as leishmaniasis may be modified by migration in an increasingly globalized world. Diagnosis of different clinical patterns is essential in returning travellers to assess imported species and to avoid further outbreaks.

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POTENTIAL IMPACT OF TEMPORARY WITHDRAWAL OF ROTAVIRUS VACCINES IN ACUTE GASTROENTERITIS HOSPITALIZATIONS IN NORTH-WEST SPAIN (GALICIA)

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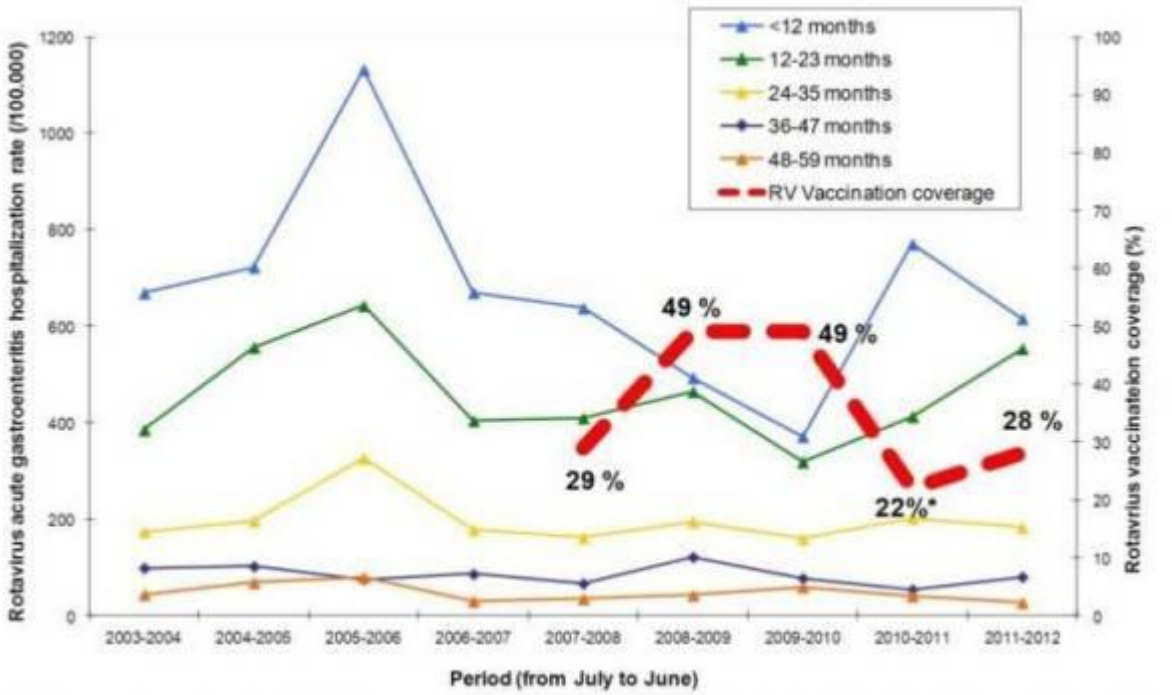
Aims: In 2010, rotavirus vaccination (RV) was held in Spain during 5 months June, due to a quality problem identified in the vaccine manufacture. Our study aims to evaluate the impact of this RV cease on rotavirus acute gastroenteritis (RAGE) hospitalizations in children< 5 years.

Methods: The annual hospitalization rates of RAGE were calculated by using the official surveillance system for hospital data for the Autonomous Region of Galicia (CMBD) and the population census (INE). Rotavirus vaccination coverage was estimated using sales data provided by IMS Health.

Results: In the 5-yearly periods pre-vaccination, the median RAGE hospitalization rate was of 696.2/100.000 children ≤1 years. Hospitalization rates in post-vaccination period July 2009-June 2010 decreased by 47% (371.3/100.000). Rates in the period just after vaccination cease -i.e., July 2010-June 2011- increased by 11% (771.1/100.000). In the period July 2011-June 2012, with rotavirus vaccination resumed, RAGE hospitalization rate decreased by 12% (615.5/100.000) as compared to the median AGE-rotavirus rate for the pre-vaccination period. A similar pattern was found on all-cause AGE hospitalization rates, correlating well again with vaccine coverage variation.



(*) 22% is the mean RV vaccine coverage for that period. However, for 5 months within that period, no new batches of vaccine were released onto the market, and the coverage estimated for those months was 0-5%.

[Rotavirus hospitalization rate]

Conclusions: A rebound increase in the rates of hospitalization for rotavirus AGE just after vaccination cease has been observed in Galicia. This increase is more pronounced in children for whom the vaccine was indicated (< 12 months). Although other factors might contribute to explain this variation in rotavirus incidence, our data points out changes in vaccination coverage as a main determinant.

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MULTIPLE ERYTHEMA MIGRANS AS A MANIFESTATION OF EARLY STAGE LYME BORRELIOSIS IN CHILDREN

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Background: Multiple Erythema Migrans is rare in early stage of Lyme borreliosis in European children.

Patients and methods: During 2011 we have diagnosed and cured 34 children with Erythema Migrans. Demografic,clinical,ECG and borrelial serum ELISSA antibody titers were obtained.Patients were followed up clinically and serologically one year after a tick bite.

Results: All patients developed Erythema Migrans 7-10 days after a tick bite.Multiple EM occured in 94% of patients. Skin lesions were more frequently presented with a ring -like lesion (94%) than mixt lesions (6%).

All patients had normal ECG.Systemic symptoms were reported by two patients (6%);local symptoms were reported by 41% of patients. Four weeks after a tick bite 97% of patients were borellial serum ELISSA antibody titers positive.

All patients had a good response to antibiotic therapy.Clinical and serological findings were normal in all one year after a tick bite.

Conclusion: Analysis of our group of children showed that the predominant skin lesion was Multiple EM which is not characteristic of early stage of the disease. Response to antibiotic therapy was good similarly solitary EM.

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INVESTIGATION OF GENETIC DIVERSITY AMONG MYCOBACTERIUM TUBERCULOSIS ISOLATES WITH PULSED FIELD GEL ELECTROPHORESIS METHOD(PFGE) IN IRAN

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Introduction: Tuberculosis is a considerable public health problem especially in developing countries. According to the WHO there is the emergence of multi-drug resistant M. tuberculosis and the association of TB with HIV has led to TB being declared. Molecular genotyping methods are important in detecting the dominance of transmission or reinfection in a population. During one year study genotyping of 100 of M. tuberculosis (M.t.) isolates from patients referred to Pasteur Institute of Iran were accomplished with PFGE method.

Methods: After identification of M.t. isolates and performing of antibiotic susceptibility test using standard methods, melted Incert agarose and lysozyme were mixed with bacterial suspension to prepare PFGE plaques and digested with XbaI restriction enzyme. Finally the digested DNA fragments on 1% agarose with PFGE method were analyzed with GelcomparII software.

Results: Dendrogram of genetic diversity were obtained and revealed two common types. Pulsotype A with 71 isolates and just one MDR and pulsotype B included 29 isolates and 3 MDR cases. No correlation between antibiotypes and pulsotypes were observed.

Conclusion: It is very important to know about the existence of any clonal expansion of special M.t. genotypes with resistant strains. Our research shows 3 MDR isolates into the low incidence pulsotype B which could be an alarm for more accurate MDR-TB surveillance program. Probably such observed limited polymorphism may be due to conservation of restriction sites of XbaI enzyme. In order to investigate the genetic relatedness of isolates using other restriction enzymes and different molecular typing methods simultaneously were recommended.

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FEBRILE URINARY TRACT INFECTIONS IN CHILDREN: EPIDIMEOLOGICAL STUDY

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Background and aims: Urinary tract infections (UTI) are common in childhood. We, epidemiologically, studied 162 children with febrile UTI who were hospitalized in our departments during 2011.

Methods: The incidents were studied based on the cause, sex, age, and clinical presentation. The urine was obtained aseptically and the cultures were evaluated on the basis of the diagnostic criteria for UTI. The pathogens were recorded and the imaging findings from kidney- ureter - bladder ultrasound, voiding cystourethrogram (VCUG) and DMSA scan were analyzed.

Results: Among the 162 patients, 62.3% were female and 57% infants. Clinical findings - by frequency: fever, anorexia / poor appetite, fuzzy, diarrhea ,

vomiting, failure to thrive. Responsible microorganisms: E.coli 83.3% (n = 135), Proteus mirabilis 6.8% (n = 11), Klebsiella pneumoniae 4.3% (n = 7), Pseudomonas aeruginosa 3.7% (n = 6), Enterococcus faecalis 1.9% (n = 3). Abnormal imaging findings were found in 67 children (41.4%). Dilation of the renal pelvis and calyces was found in 49 children (73.1%). 67.3% of them had I-II grade VUR, 24.5% III-IV - in which chemoprophylaxis and follow-up were established and 8.2% IV-V grade VUR (and went surgery because of recurrence). 13 (19.4%) children had renal stones. 5 (7.5%) had another type of anatomical abnormality (hydronephrosis, neurogenic bladder, polycystic kidney, solitary kidney).

Conclusions: Febrile UTI is more common in infancy (with a clear predominance of girls) with VUR existence in 30.2% of cases.

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IN VITRO EXPRESSION OF CANDIDA ALBICANS SAP1-10 GENES IN THE INTESTINAL CANDIDIASIS MODEL

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Background and aims: The production of secreted aspartyl proteinases (Saps encoded by SAP1-10 gene family) is considered as key virulence factor of Candida albicans. The aim of the study was to investigate the contribution of aspartic proteases secreted by C. albicans for the invasion of in vitro model of intestinal candidiasis.

Methods: Quantitative reverse transcription-PCR assay of the C. albicans SC5314 SAP1-10 genes during different stages of the invasion of human enterocytes in vitro (cell line Caco-2 ATCC, HTB 27) was performed using QuantiTect Probe PCR Kit (Qiagen). TaqMan primer and probe (5' FAM, 3' TAMRA) sets were designed based on unique sequence regions of each individual SAP1-10 gene. Moreover, expression of tested genes was normalized to the ACT1 housekeeping gene and analyzed using $\Delta\Delta C_t$ method.

Results: SAP10 was the most highly expressed gene at the very early stages of the interaction (up to 2 h of infection) and became dominant at later stages (from 3 h of infection). SAP1-2 were activated at early stages, whereas SAP4-6 expression was detected at later stages of infection. Furthermore, SAP7, SAP8 and SAP9 were induced in both early and later stages of the invasion of intestinal cells.

Conclusions: Our data suggested that the intestinal cell layers do not apparently influence SAP expression in C. albicans cells attached to their surface. Our future studies testing endoprotease Kex2 will shed further light on Sap function in C. albicans virulence.

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OSELTAMIVIR USAGE IN PRETERM INFANTS DURING THE INFLUENZA OUTBREAK IN NEONATAL INTENSIVE CARE UNIT

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There is little data an influenza treatment and oseltamivir prophylaxis in the newborn infants, in particularly premature infants. In this study, we present prophylactic oseltamivir use in the newborn during influenza outbreak in a tertiary neonatal intensive care unit (NICU). Initially, influenza was detected in 3 preterm infants and one term infant by indirect immunofluorescence assay (IFA). After detecting influenza in these four babies, newborns in the NICU were screened for influenza and influenza was detected additionally in 8 newborns. Twelve newborns received oseltamivir treatment while oseltamivir prophylaxis was given remaining 5 newborns whose influenza IFA was negative. Two doctors working in NICU was found to be influenza IFA positive. No prophylaxis was given to health care workers. Mean age of onset of oseltamivir (treatment/prophylaxis) was 19.5 days. Mean birth weight was 1724 gr (range; 685-4665 gr) and mean weight was 1951 gr. Mean oseltamivir dose was 1.95 /mg/kg/dose (range:2-6mg/kg/day). there was no mortality due to influenza infection and related complications. Necrotizing enterocolitis (NEC) developed in two patients who were given oseltamivir prophylaxis on the ninth day of prophylaxis for one baby and on the first day for the other baby. This study shows oseltamivir is highly effective for the treatment of influenza and should be considered for prophylaxis of influenza outbreaks in premature infants however further studies are needed to determine the safety profile of the drug in particularly preterms.

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HPV-VACCINATION IN FLANDERS (BELGIUM): RESULTS OF THE FIRST TWO YEARS OF THE VACCINATION PROGRAMME

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Background and aims: In September 2010 HPV-vaccination was added to the vaccination programme of Flanders. Girls in the first year of secondary school are the target group for vaccination. All vaccinators can obtain the vaccines free of charge. They are asked to register vaccinations in the vaccination registry Vaccinnet. We want to estimate HPV-vaccination coverage for the first two years of this vaccination programme.

Methods: We estimate the vaccination coverage based upon registrations in Vaccinnet. To evaluate the accuracy of these estimates, we compare them with the results of a vaccination coverage study performed in 2012 regarding HPV-vaccinations in girls born in 1998.

Results: Analysis of the registered vaccination data for the first two school years shows a participation degree of over 86%. Registered vaccination coverage with three doses was 80% and 82%. About 95% of vaccinations are registered by school health services (SHS). The vaccination coverage study performed in 2012 showed documented full vaccination in 83% of girls born in 1998, which suggests that about 4% of vaccinations aren't registered in Vaccinnet yet.

Conclusions: For the first two years of the vaccination programme a real participation degree is estimated at about 87% with a vaccination coverage of 83% for full vaccination. Vaccinating SHS are of upmost importance to reach a high vaccination coverage in school aged children. Analysis of registered HPV-vaccinations in Vaccinnet gives a good estimate of vaccination coverage compared with the results of a vaccination coverage study.

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IMPACT OF RECURRENT RESPIRATORY TRACT INFECTIONS ON CHILDREN WITH DEVELOPMENTAL DISABILITIES

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Objective: Parents and professionals believe that recurrent respiratory infections have impact on process of development.

We studied relation between parent-reported RRTI and impact on developmental progress in children with developmental disabilities

Method: During a 1-year period, 125 children with DD (developmental disabilities) were recruited for this observational study. Mean age was 62 month. Parents were asked to fill in the Child Behavior Checklist. A developmental assistant was administrated as Denver II assessment tool and PIK-17 parent's questioner. The children were divided into a group with presence of RRTI and a group without RRTI, on the basis of parental report. Linear regression analyses were performed to assess the effect of RRTI.

Results: Compared with RRTI children (n = 56), RRTI children (n = 79) showed decreased mental and motor development more behavioral problems and lower scores on most scales ($P < 0.05$). Moreover, school enrolment is less favorable in RRTI (+) children.

Conclusion: In 62 month olds with DD, the children with parent-reported RRTI show more delayed development, more behavioral problems and lower DQ compared with the children without RRTI. Although this association does not prove a causal relationship, further studies should focus on this, because RRTI are potentially preventable.

1044

EFFECTIVENESS OF ICE CUBE AS TOPICAL ANESTHETIC IN REDUCING THE PAIN OF INTRAMUSCULAR INJECTION AMONG 4-6 YEAR OLD CHILDREN

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Introduction: Intramuscular injection is often viewed as a frightening medical procedure among children that can lead to needle phobia. Minimizing the pain during injection can help prevent their anxiety and reduce their distress.

Objective: To determine the effectiveness of ice cube as topical anesthetic in reducing the pain of intramuscular injection specifically Diphtheria-Pertussis-Tetanus vaccine booster among 4-6 year old children.

Research design: Randomized Controlled Trial

Methods: Thirty-seven subjects were randomly assigned to group A, where ice was applied prior to intramuscular injections and Thirty-four subjects to group B, where no ice was applied. After injection, each subject were asked to choose the face that best described how they felt during the injection, using the Wong-Baker Faces pain scale.

Results: The study showed that at 95% confidence limit, Group A experienced less pain during intramuscular injection with an average pain level of 5.14, compared to group B where the average pain level was significantly higher at 7.18. The result showed that age and gender were not determinants in determining the different pain levels.

Conclusion: This study showed that ice cube is an effective topical anesthetic in reducing the pain of intramuscular injection. In a country where standard of living is low, ice cube can be a good alternative as anesthetic in reducing the pain in vaccination.

1045

FAMILIAL AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME (ALPS)

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Background: Autoimmune lymphoproliferative syndrome (ALPS) is a rare genetic disorder of immune regulation caused by defective Fas-mediated apoptosis and characterized by chronic non-malign lymphoproliferation and autoimmunity, i.e. cytopenias.

Case reports: 11-year-old girl with recurrent febrile syndromes without evidence of an infectious cause, chronic splenomegaly and cervical lymphadenopathy without B symptoms, persistent neutropenia and thrombocytopenia, the later responding to IVIG administration. Family history of NHL of paternal grandmother. Negative blood cultures, bacterial and viral serology, bone narrow aspirate without pathology, biopsy of LN reactive and ultrasound homogeneus hepatoesplenomegaly. Screening for auto-inflammatory syndromes, anti-neutrophil antibodies and ANAs was negative. Persistent neutropenia (500-1500/mm3), elevated IgG (4930 mg/dL) and vitaminB12 (1930 pg/ml) serum levels.

The father, aged 38 years, had a history of abdominal discomfort and a abdominal imaging revealed marked retroperitoneal adenopathy; biopsy showed lymphoid hyperplasia.

Screening for ALPS in daughter and father was positive demonstrating raised alpha/beta TCR+CD4-/CD8- ("double negative") T-lymphocytes, elevated sFasL, vitamin B12 and IL-10 serum levels as well as impaired apoptosis assays. Genetic studies confirmed a germ-line mutation in exon 9 of the gene encoding FASprotein (CD95) in both father and daughter. Treatment was initiated with prednisolone (1mg/kg/12h), followed by Mycophenolate (600mg/m^2/12h) for 6 months and due to incomplete response (persistent neutropenia in the daughter and adenopathy in the father) changed to Sirolimus (2mg/m^2/d).

Conclusions: ALPS is a likely under-diagnosed immunopathology, and should be included as differential diagnosis in patients with chronic non-malign lymphoproliferation, organomegaly and autoimmune cytopenias.

1046

FACTORS WITH IMPACT ON ASTHMA PREVALENCE IN CHILDREN AFTER RESPIRATORY SYNCITIAL VIRUS INFECTION IN INFANCY

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Background: There is an increasing body of evidence in supporting the association of higher prevalence of asthma in paediatric population with previous exposure to respiratory syncytial virus (RSV) infection in infancy. Nevertheless, to date this association remains controversial.

Objective: To identify factors with impact on asthma prevalence in children with RSV infection during pregnancy.

Methods: One hundred and eight children (age=6,7 +/-1,9 yrs., 61 boys) hospitalised during the first year of life with the diagnosis of acute bronchiolitis with RSV were retrospectively evaluated. Multivariate regression analysis was used to identify possible risk factors.

Results: Asthma diagnosis was confirmed in 39% of the children in the studied group, significantly more than both the non-hospitalized comparisons (12%) and the general prevalence of asthma in Romanian children of this age group (7,2%). Independent variables statistically significant were maternal asthma (OR: 6,4; 95% CI: 1,9-14,2; p = 0,002), clinical allergic sensitization (OR: 3,7; 95% CI: 1,3-8,5; p = 0,011), and children attending day care (OR: 1,8; 95% CI: 1,04-3,1; p = 0,037).

Conclusion: Data collected during this study show a three-fold higher risk for diagnosed asthma at school age in children with RSV bronchiolitis during infancy, and underline the existence of specific risk factors, thus supporting other observation in the field.

1047

S. PNEUMONIAE CARRIAGE IN CHILDREN IMMUNIZED AGAINST PNEUMOCOCCI USING CONJUGATE 13-VALENT VACCINE IN COMPARISON WITH NON-VACCINATED CHILDREN IN POLAND

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Introduction: Streptococcus pneumoniae (SP) gains entry into the host by colonizing the nasopharynx. Surveillance of pneumococcal resistance among nasopharyngeal isolates from children has been found to be a useful way of estimating the prevalence of resistant isolates in the community.

Aim: The study was conducted to assess the influence of vaccination with a conjugate 13-valent vaccine (PCV13) on the nasopharyngeal carriage in terms of antibiotic resistance in pediatric population in Poland.

Methods: A randomized, prospective epidemiological study was conducted to determine the prevalence of SP carriage among 750 children aged 17 months-60 months of age divided into two groups. The first group consisted of 359 fully, age appropriately immunized against pneumococci children, by using PCV13 within the official vaccination program in the city of Kielce (schedule - at 3,5,14 months of life). The second group consisted of 391 children living in the city of Ostrowiec, in the same region, not vaccinated against pneumococci. Nasopharyngeal swabs were obtained by trained medical personnel, cultured in certified laboratory, SP isolates were tested on antibiotic resistance according to standard microbiological procedures.

Results: In both groups, the prevalence of pneumococcal carriage was similar with 28,4% in non-vaccinated children and 27,6% in immunized group. Among 106 carriers in vaccinated group, only 7 were colonized by penicillin-resistant SP strains in comparison with 55 in 111 carriers in non-immunized children (6,5% vs 50,5%, $p< 0,0001$).

Conclusions: Mass vaccination has no impact on the general prevalence of SP carriage, however strongly reduces the carriage of penicillin-resistant strains.

1048

PERSISTENT EPSTEIN-BARR VIRUS DNA DETECTION IN CHILDREN WITH INFECTIOUS MONONUCLEOSIS AND COINFECTION BY CYTOMEGALOVIRUS AND HUMAN HERPESVIRUS-6

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Background and aims: Infectious mononucleosis (IM) is a clinical syndrome caused by primary infection with Epstein-Barr virus (EBV). We evaluated the possible role of coinfections by cytomegalovirus (CMV) and/or human herpesvirus 6 (HHV6) as enhancing factors of persistent EBV DNA detection.

Methods: Forty-seven children (27 males) aged 0.8 to 15.3 years (mean: 5.8) were admitted with typical IM signs. All were examined for antibodies and specific DNA detection in saliva blood and/or urine on admission and every 3 to 9 months; follow-up was 1.1-12 years (mean: 5.4). Based on the detection of different viral DNA detected on admission, the patients were grouped in: 1)EBV only; 2)EBV+HHV6; 3)EBV+CMV; 4)EBV+CMV+HHV6.

Results: Thirty-five children (74%) had coinfections. Mean persistence of EBV DNA occurred for 8 months (range 2-14) in children with only EBV, 26.7 months (4-87) in EBV-HHV6 group, 31.1 months (7-89) in EBV-CMV group, 47.2 months (13-120) in children with EBV-CMV-HHV6 coinfections. A statistically longer persistence of EBV DNA occurred in coinfected children than in only EBV infected (EBV vs EBV-HHV6 p=0.016, EBV vs EBV-CMV p=0.007, EBV vs EBV-CMV-HHV6 p=0.001). No statistical difference was observed among the groups of coinfected children.

Conclusions: In our hospital-based study, the great majority of children admitted with IM had a herpesvirus coinfection, which enhanced EBV replication and persistence of EBV DNA, presumably by transacting genes.

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REFRACTORY DISSEMINATED FUSARIOSIS IN A PATIENT WITH RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA: A CASE REPORT

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Fusarium species are among the leading fungal pathogens to cause invasive mould infections in patients with hematopoietic malignancy. Disseminated fusarial infections occur mostly in patients with hematologic malignancies with myelosuppressive chemotherapy or in patients with severe immunodeficiency. Although more frequent than Aspergillus fungemia, Fusarium fungemia remains a rare event. Herein, we report the case of a 14-year-old boy with Philadelphia-positive with relapsed acute lymphoblastic leukemia who developed multiple maculopapular and vesicular skin lesions on their legs and arms during chemotherapy treatment. Then it turned into a vesicle lesions frequently with central necrosis giving the lesions an ecthyma gangrenosum-like appearance. The diagnosis of Fusarium infection was made by blood culture. He received treatment with systemic antifungal using both liposomal amphotericin B and voriconazole as well as granulocyte colony-stimulting factor and granulocyte suspension. Despite these treatments persistent fungemia caused by Fusarium spp continued and finally the patient died. Disseminated fusarial infection and prolonged fungemia depent on profound, persistent granulocytopenia. This case highlights the poor outcome of an invasive fungal disease caused by Fusarium in the setting of profound, persistent granulocytopenia. Early diagnosis and treatment is very important to improve the prognosis, because these infections in immunodepressed hosts have a high mortality rate.

1050

LONG-TERM POSACONAZOLE SALVAGE THERAPY IN CHILDREN

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Posaconazole is an extended spectrum triazole with in-vivo and in-vitro activity against Aspergillus species. Here in, we presented 3 children with invasive Aspergillus infection that was unresponsive to first-line antifungal agents but treated with long term posaconazole salvage therapy for at least 16 months without major complications. Case 1, a 5 year old male with chronic granulomatous disease who was unresponsive to combination antifungal therapy with voriconazole and amphotericin B for invasive pulmonary aspergillosis. Upon treatment failure, he underwent pulmonary surgery followed by a switched antifungal treatment to posaconazole at a dose of 4x200mg/day. He currently receives this for the last 30 months without any complications. Case 2, an 18 year-old female with Hyper-IgE syndrome and invasive pulmonary aspergillosis that was unresponsive to voriconazole. Posaconazole salvage therapy at a dose of 4x200mg/day was given but due to nausea and vomiting dosage changed to 2x400mg/day, she has been receiving this regimen for the last 16 months with no complaints. Case 3, a 13 year-old female with Hyper-IgE syndrome and invasive pulmonary aspergillosis unresponsive to amhotericin B, untolerant to voriconazole and caspofungin was ordered posaconazole in 200 mg 4 times daily dosage but changed to 200 mg 3 times daily due to abdominal pain and nausea. She has been receiving posaconazole for 24 months without any side effect and disease progression. We conclude that posaconazole is safe and effective for a long-term salvage therapy in children who is refractory to other antifungal agents.

1051

AN UNEXPECTED PARASITOSIS IN ITALY

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Background: Amoebiasis is a common disease in tropical areas, such as Africa, Central and South America and India, most related with crowded living conditions and poor sanitation.

Methods: A 11-year-old Italian female was admitted in another hospital for persistent fever, unresponsive to beta-lactam antibiotic treatment, after a brief holiday in Sardinia. Patient showed no diarrhea and vomiting. Routine examinations, serology for EBV, CMV, Toxoplasmosis, Salmonella, Brucella, Mycoplasma, Bartonella, Rickettsia as well as protein chain reaction (PCR) for meningococcus, pneumococcus, Adenovirus, Heamophilus influenzae were negative. Tick and thin blood films for malaria and bacterial cultures resulted negative, too. No evidence of Leishmaniasis in bone marrow aspirate was found. Chest radiography and cardiac ultrasonography showed no abnormalities. An abdomen ultrasonography showed celiac and hepatic lymphadenopathies and two hypoechoic lesions, suggestive of liver microabscesses. Patient was admitted to the Infectious Disease Unit at our Pediatric Department. Serology for Ecchinococcus, Schistosoma were negative. Amoeba Indirect Hemagglutination (IHA) resulted highly positive (128 L/tit). A treatment with metronidazole for 10 days was performed and followed by paromomycin for other 10 days, with progressively decreasing antibodies titre until reaching a negative value after 1 month. Moreover, several follow-up abdomen ultrasonographies showed a progressive reduction of hepatic lesions until complete resolution after 3 months.

Conclusion: Amebiasis is a tropical disease caused by Entamoeba histolytica. Our case was unusual in its presentation, since patient had no intestinal symptoms and no epidemiological data were suggestive of this parasitosis. Ultrasonography of abdomen was essential for considering the diagnosis.

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ACUTE NON-SEPTIC MONOARTHRITIS IN CHILDHOOD IS FREQUENTLY ASSOCIATED WITH STREPTOCOCCAL OR EPSTEIN-BARR VIRUS INFECTIONS

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Background and aims: Acute monoarthritis in childhood is a relatively common rheumatic disease of frequently unknown origin. Since viruses are common and have a wide spectrum of diseases, we performed a prospective serologic and virologic study, in addition to bacteriologic examinations, to investigate on a possible correlation between infections and acute monoarthritis.

Methods: Prospective bacteriologic, serologic and virologic studies, including culture or detection of specific DNA and specific antibodies in children consecutivey admitted with acute monoarthritis.

Results: Among 32 children meeting the diagnostic criteria of acute monoarthritis, 26 (81.2%) had concomitant infections, and the most frequently implicated agents were group A β-hemolytic Streptococcus (GAS) (17 children: 53.1%) and Epstein-Barr virus (EBV) (12 children: 37.5%). Of these, 5 children (15.6%) had a coinfection by GAS and EBV, and one child had GAS concomitantly with CMV (3.1%). Two single cytomegalovirus (CMV) infections (6.2%) also occurred. Totally, a viral involvement was found in 15 children (46.9%). The most frequently involved joints were hip (15 children: 46.9%), and ankle (10: 31.2%).

Conclusions: Our study showed that acute monoarthritis in children may be frequently associated with streptococcal or EBV infections, and searching for EBV-specific antibodies and DNA, in addition to GAS infection, could allow for an accurate etiological diagnosis and prognosis.

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CLINICAL CHARACTERISTICS OF RSV INFECTION: A COMPARISON OF 2 WINTER SEASONS IN ONE CENTRE

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Background: Respiratory syncytial virus (RSV) infection is a leading cause of hospitalisation in infants and young children. RSV infections seem to be more severe and affect younger children in 2012 compared to 2011.

Methods: We retrospectively compared the clinical characteristics of children, hospitalised in our centre for RSV infection in the periods October-December 2011 and 2012.

Results: 154 children were hospitalised with RSV infection, 71 in 2011 and 83 in 2012. 52% were males. Median age ad admission was 2.6 months (1.5weeks-43.8months,2011), and 3.1 months (1week-55.5months,2012) (P=0.7). 22.5% (2011) and 19.3% had an underlying medical condition, prematurity being most prevalent. Length of hospital stay (5.6±3.8 days vs. 6.5±3.9 days,P=0.16), need for oxygen supplementation (59.2% vs. 61.4%,P=0.87) and for tube feeding (34% vs. 31.3%,P=0.86) were comparable. Duration of tube feeding was longer in 2012 (3.5±2.1 days vs. 5.1±2.5 days,P< 0.05). There was no significant difference in the need for intensive care unit admission (11.3% vs. 15.7%,P=0.5) or mechanical ventilation (2.8% vs. 6%,P=0.45). All children were cured. In 2012, the dominant subtype was RSV A (epidemiologic study WIV-ISP, ongoing); the dominant subtype for 2011 in Belgium is unknown.

Conclusion: Despite the subjective impression that RSV infections were more severe in 2012, we conclude that severity in 2012 was comparable to 2011, although a prolonged need for oral supplementation was observed. RSV remains an important cause of morbidity, especially in infants and young children. Seasonal variation in clinical presentation and severity are poorly documented in the literature, as is the relationship with RSV subtype.

1054

THE EVOLVING EPIDEMIOLOGY OF PERTUSSIS IN THE LAST TWO DECADES

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Background: The introduction of pertussis vaccine to the routine immunization program in Israel (1957) resulted in a 100-fold incidence decline (1960s-1970s) with a stable 1-2/100,000 annual incidence rate for 40 years. Since 1998 the incidence increased to 23/100,000 (2004). Due to pertussis resurgence, Israel implemented 2 booster-vaccine doses in schoolchildren, in 2005 a 5th-dose for second-graders (7-8y), and in 2008 a dose for eight-graders (13-14y).

Methods: Population-based epidemiologic study in the Jerusalem district.

Results: 2520 pertussis cases were reported during 1990-10/2012. Most cases (74.4%) were < 20 years (median 11y). Incidence rates increased from 2.6/100000 (1990) to 28.8/100000 (2006). Following the vaccination schedule modification, incidence rates declined: 21.7/100000 (2007), 15/100000 (2009), 13/100000 (2010). The two age-groups showing significant decline were children aged 5-9 years (61.5% reduction) and 10-14 years (73.9% reduction). However, in 2011, a rise to 30/100000 occurred, specifically among infants. Incidence rates in infants increased from 61 to 190/100000). Infants < 1 year (12.5% of cases) had the highest rates specifically those < 6 months (84.3% of cases < 1 year). The vaccination status was: unvaccinated -19.2%, partially vaccinated - 7.6%, fully vaccinated - 73.2%. The hospitalization rate was overall- 5.4%; infants < 6 months 45%, < 3 months 70%. Household transmission occurred in 16.1%. Laboratory confirmation was available in 89%. Low birthweight and increasing birth order were identified as risk markers.

Conclusions: While additional pertussis vaccine doses in children and adolescents were followed by morbidity decline in these groups, pertussis burden is still noteworthy among infants.

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MEASLES OUTBREAKS IN POPULATION GROUPS WITH SUBOPTIMAL IMMUNIZATIONS COVERAGE

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Background: A-two dose measles vaccination schedule is used in Israel since 1994 with good overall coverage (94-95%). However, in 2003, 2004 and 2007/8 measles outbreaks occurred in Jerusalem´s ultra-orthodox communities.

Methods: An epidemiologic investigation, case-control study and vaccination coverage study.

Results: In 2003 the index case was a 2 year-old unvaccinated child from Switzerland. Within 5 months, 107 cases emerged in three crowded neighborhoods. The 2004 outbreak started in a kindergarten and in 5 months, 117 cases occurred (one fatality). In August 2007 a tourist from London attended a wedding in Jerusalem and two days later diagnosed with measles. The subsequent outbreak lasted ten months, 1527 cases nationally, 992 (65%) in the Jerusalem district. Most cases (72.6%) were under 15 years, 42.9% under five years, 12.8% infants under one year. The peak incidence rate in 2007-2008 was among 6-12 month-old infants (916.2/100000) - a significant shift from 2003-2004, where the peak was in1-4 year-olds.

In a case-control study (74 cases/148 controls) children with measles were less likely to be registered in a well-baby clinic and had lower overall vaccination coverage. The differences for registration, DTaP3 and MMR1 coverage were 35.1%, 48.6% and 80.8%, respectively (all $p< 0.001$). Increasing birth order of cases and their siblings was associated with non-registration and non-compliance with MMR immunization.

Vaccination coverage among 2-years old children was lower in outbreak vs. non-outbreak neighbourhoods (88.3% vs. 90.3%, $p=0.001$).

Conclusions: These outbreaks hinder the goal of measles elimination.

The increased susceptibility of young infants should be noted.

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NO EVIDENCE FOR SELECTED ANIMAL RETROVIRUSES ENV SEQUENCES IN SAMPLES FROM JUVENILE IDIOPATHIC DISEASES AND OTHER IDIOPATHIC PEDIATRIC DISEASES

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Mammalian retroviruses cause a variety of diseases in their hosts including hematological, neurological, and immunodeficiency disorders that develop through neoplastic, lytic or inflammatory mechanisms. Both human retroviruses are the results of zoonotic transmission events and since cross-species transmissions from animal to humans are not so rare, we investigated if other retroviruses could be involved in some pediatric idiopathic infectious diseases whose symptoms suggest retroviral infections.A total of 73 samples were obtained from 44 children who exhibited either of the following hematological, neurological or inflammatory pathologies: autoimmune hemolytic anemia, aregenerative anemia, thrombocytosis, idiopathic thrombocytopenic purpura, neutropenia, idiopathic aplasia, leucosis, encephalitis, Henoch-Schönlein syndrome, dermatomyositis, and juvenile idiopathic arthritis (JIA). Samples were selected and collected within the last two years in Montpellier hospitals. DNA samples were extracted from blood (44 samples) or synovial fluid cells (JIA, 29 samples).Samples were first tested for RT activity using a C-type retrovirus RT activity (Cavidi). Then, samples were screened by nested PCR with primers able to amplify the receptor binding domain (RBD) of the SU env gene for delta retroviruses such as PTLV (primates) and BLV (cattle) ;beta retroviruses such as MMTV (mice) and MPMV (primates) and gamma retroviruses such as FeLV (cats) and PERV (pigs).Both reverse transcriptase activity and PCR were negative for blood and synovial fluid samples in all patients indicating that it's unlikely that these viruses are the cause of these pediatric diseases. However, we cannot exclude that divergent retroviruses may be implicated.

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INFANTILE HYPERTROPHIC PYLOR STENOSIS IN A PRETERM TREATED WITH ERYTHROMYCIN FOR FEEDING INTOLERANCE

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Background and aims: Infantile hypertrophic pyloric stenosis is a disease of infancy which increased work of the smooth muscles leading to pylorus hypertrophy results in gastric outlet obstruction. The etiology is still unclear. Genetic predisposition and environmental factors are the accepted explanations. Erythromycin, commonly used for pertussis and chlamidial infections, is also a prokinetic agent as being a motilin receptor agonist inducing gastric and pyloric bulb contractions and resulting in pylorus hypertrophy.

Methods: We would like to present our case of a preterm with pylor stenosis. He was a 1610 g male delivered at 31-weeks of gestation age to a 30-year-old woman via c-section. After several prematurity related problems we started erythromycin (5mg/kg) on 7th day to induce gastrointestinal motility with an indication for abdominal distention and treated him for 21 days. On day 59, he started vomiting. Concomitant UTI treated appropriately but symptoms continued. On day 67 we performed an abdominal ultrasonography showing 11mm for pyloric diameter and 18mm for the length.

Results: After a succesful pyloromyotomy our case rapidly tolerated enteral feedings and discharged from hospital with full recovery in a week.

Conclusions: By this time, several studies has revelaed that exposure to erythromycin in the first 2 week of life is significantly associated with infantile hypertrophic pyloric stenosis (IHPS). The risk is nearly eight-fold increased. Our case is a rare one as we used erythromycin for feeding intolerance and the time period between treatment and diagnosis is quite long. Reports of new cases are still needed.

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IMPORTED MALARIA IN AN ITALIAN PAEDIATRIC DEPARTMENT, 1996-2012

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Imported malaria is progressively increasing in Italy in the last two decades. A significant number of malaria cases is registered every year in North-eastern Italy due to the high immigration rate. Most cases are non - immune African children born in Italy and visiting friends and relatives (VFR) in endemic areas without proper chemioprophylaxis.

We described 65 paediatric cases of imported malaria (age range: 7 mo-15 yrs),admitted to our Paediatric Department during the period 1996-2012. 39 (60%) were long-term immigrants VFR, 24 (38%) were new immigrants arriving in Italy for the first time, 1 was Indian adopted child and 1 an Italian child visiting Africa with parents for tourism. 64 children came back from Sub-Saharan Africa, while only one child came from Asia. Non-appropriate prophylaxis was reported in all cases.

Up to 2009 Plasmodium falciparum was the only isolated parasite while, during the last 3 years, 7 cases of mixed malaria (P. falciparum, P. ovale, P. malariae and P. vivax) were observed.

All the cases were treated with quinine and since 2011 with Artemisinin derivatives, according to WHO Guidelines.

All patients survived, nobody reported neurological sequelae. We emphasize a case of severe malaria complicated with rhabdomyolysis and acute renal failure due to delayed diagnosis.

These epidemiological data demonstrate how important should be the information about chemoprophylaxis in long-term immigrants in order to prevent imported malaria.

Early diagnosis of malaria reduces severe complications: we recommend physicians to suspect this infection in all febrile children coming from malaria endemic areas.

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RHABDOMYOLYSIS AND PLASMODIUM FALCIPARUM MALARIA: A CASE REPORT

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Introduction: Rhabdomyolysis in Plasmodium falciparum malaria is reported occasionally in the literature;the pathogenetic mechanism is not clearly understood.A determinat role in skeletal muscle damage is played by red cells sequestration in muscle capillaries and parasite's toxins.

Case report: We describe a case of severe malaria complicated with rhabdomyolysis in a 6-year old girl, born in Italy, who presented fever 6 weeks after visiting her relatives in Cameroun.

She was transferred from another Hospital to our Paediatric Department with a 6 days history of fever(max 39.2°C),vomiting, olyguria, hypotension, calves and feet edema, generalized muscle pain, weakness and red urine.

Blood samples revealed: serum hemoglobin 8.5g/dL, White Blood Cell count 18200/mmc, Platelet count 49000/mmc, C-Reactive Protein 10.75mg/dL, CPK 8178U/L and Creatinine levels 1.51mg/dL. Urine myoglobin was 1884ng/mL; no hemoglobinuria was present.

The suspect of myoglobinuria due to Plasmodium falciparum malaria was confirmed by blood smear examination showing low parasitemia. The final diagnosis was acute renal failure induced by rhabdomyolysis. The treatment with Artemisinin derivatives obtained rapid resolution of parasitemia. CPK reached values greater than 25.000 IU. The renal failure and rhabdomyolysis resolved with proper hydration.

In the same period her 7-year-old brother and her mother were admitted to the Hospital with malaria infection but they did not present rhabdomyolysis or other important malaria complications.

Conclusion: Rhabdomyolysis is an unfrequent malaria complication. Its origin is unclear. Severe myalgia, darkened urine, swelling soft tissues are paradigmatic synthoms of rhabdomyolysis.In our young patient the delayed diagnosis could have influenced the severity of this rare complications of the disease.

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MALARIA AND SALMONELLA INFECTION: RELATIONSHIP OR CASUALITY?

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Introduction: In Sub-Saharan Africa, non-Typhoid Salmonella (NTS) bacteriemia is a common and often fatal complication of Plasmodium falciparum malaria. Thus WHO protocols recommend to treat children with severe malaria also with broad-spectrum antibiotics.

Case report: We describe the case of a four year old boy, born in Italy, admitted to our Department for severe Plasmodium falciparum malaria after visiting relatives in Burkina Faso. The child presented high fever, diarrhea and vomiting. Intravenous quinine therapy was promptly administrated with improvement of the conditions and decrease of fever after 24 hours. During the third day of hospitalization the temperature abruptly raised and child's conditions worsened. Laboratory testing showed increased CRP level (280 mg/L) and decreased total White Blood Cells count (6940/mm3). Blood smear examination was negative for Plasmodia while blood culture resulted positive for Salmonella enteritidis. The patient was treated with parenteral ceftriaxone for 10 days and oral quinine for one week with a complete recovery.

Discussion: Recent studies in mice (Cunnington et al.,2012) showed that the increased risk for developing NTS bacteriemia during malaria is caused by the hemolysis of red cells infected by Plasmodium. Intravascular hemolysis releases heme which induces heme oxigenase-1 leading to reduced macrophage antimicrobial activity and consequently impaired resistance to NTS with increased bacterial replication.

Conclusion: Concurrent malaria and salmonella infections are frequently described in endemic areas. This vulnerability to NTS in malaria infection is being assessed in literature. In Medicine coexisting pathologies are rarely explained by casuality.

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ON HOW THE SEASON SHAPES MIXING PATTERNS IN FRANCE: SOCIAL CONTACT DATA RELEVANT FOR THE SPREAD OF INFECTIOUS DISEASES

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Background and aims: Mathematical modeling of infectious diseases helps guiding Public Health policy by providing information on the spread of infectious diseases. Mixing patterns between individuals have proven to be valuable to inform such models. Here, we report on a recently conducted contact survey in France where people reported on their contacts during Winter and Spring.

Methods: Recruiting of participants was made by telephone to obtain defined quotas of age, with an emphasis on children. Participants had to fill in a paper diary of all contacts during two consecutive days, with a mix of mix of week day, week end and holidays. Diaries included information on each contact including age of the contact, gender, location, duration, frequency and touching. Participants were recruited in 2 waves (Winter/Spring).

Results: Among the 24250 persons called, 3977 were recruited, 2033 effectively participated and 278 participants were common to the 2 waves. Children represented 39.1% of all participants (< 3 yr: 9.2%; 3-5 yr: 8.3%; 6-9 yr: 10.4%; 10-17 yr 11.2%). Coding error and missing data involved 0.17% and 0.4% of data (10% of diaries were checked), respectively. Participants reported 38881 contacts on 2 days, resulting in a mean number of contacts (without professional contacts) of 9.56 per day. Differences in the number of contact were found according to the wave, day of week, holidays, age of participants and household size.

Conclusions: It is the first population based survey conducted in France, and the first to consider 2 consecutive days on 2 different waves.

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MILIAR TUBERCOLOSIS: AN UNUSUAL CLINICAL ONSET

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Female 13 years old. Since 2 months weakness and fever. Refer to us for lower gastrointestinal bleeding, paleness and lipotimia. She was suffering, pale, tachycardic, TC 37,5° C. Laboratory findings: Hb 7,6 g/dl; WBC 4100/mm^3; RCP 1,18 mg/dl (< 0,5). She performed 99Tsc, bloodcolture, mantoux test, chest Xray, tumoral markers all negative; colonscopy and explorative laparotomy with intestinal biopsy: non-specific granulomatous inflammation with multinuclear giant cell. She began empiric broad-spectrum antibiotics. On day 11^{th} because of unrensponsive fever and worsing general condition she performed a TB CT scan which showed a reticulo-micronodular interstitial lung infiltrate, a nodule in the inferior lobe of the right lung, one in the inferior extremity of the right kidney, small areas of bone rarefaction in the thoracic spine, not brain lesion. Bronchoscopy with biopsy showed epiteliod granulomas. On BAL PCR detected mycobacterium tubercolosis DNA, cultural examination was positive, bacterioscopic exsamination negative. BK on urine sample: negative PCR and positive colture. She began multidrug therapy with isoniazid, rifampicin, pyrazinamid, streptomycin. At ocular examination micronodular lesions in the retina; at NeuroMRI microtubercles with surrounding edema so she practiced steroids for 4 weeks.

Miliar tubercolosis may begin as a fever of unknown origin; the diversity of the clinical presentation and the non specific nature of most symptoms complicate the diagnosis. Puberty is a risk factor for progression. Recent studies have demonstrated that underlying molecular defects of interferon g-dependent pathway of macrophage activation, IFN-g receptor 1, interleukin-12, IL-12 receptor b1 may have a role in disease evolution.

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TIME TRENDS IN PEDIATRIC HOSPITAL ADMISSIONS FOR HEPATITIS A POST UNIVERSAL VACCINATION IMPLEMENTATION

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Background and aim: Hepatitis A vaccine was recently introduced in the Greek National Immunization Program. Time trends were examined in pediatric hospital admissions for hepatitis A at the Infectious Diseases department of a Greek Tertiary Pediatric Hospital during 1999-2011.

Methods: Pediatric hepatitis A admissions were expressed as frequencies and rate of annual departmental hospital admissions. Time trends were assessed with time series analysis (ARIMA modeling procedure). Interrupted time series analysis assessed the vaccination impact. Changes among age groups and ethnicity were examined by Fischer´s exact test. Analyses were undertaken with the SAS 9.0, using a $p< 0.05$ as the criterion of significance.

Results: Among all admissions (n=9,647), the hepatitis A admissions rate was 44.13/1000 children and decreased by almost 50% during the study period (77.3 to 36.9/1000 admissions). ARIMA analysis revealed a periodicity every 3 years ($p< 0.007$) and a trend of reduction on hepatitis A admission rates across years ($p=0.0135$). However, interrupted time series analysis revealed no significant effect of vaccine introduction ($p=0.319$). When pre (1999-2007) and post (2008-2011) vaccination periods were compared, the admission rates of Greek children (71.5% to 63.4%, $p=0.037$) and children < 6 years old (59.3% to 47.6%, $p=0.033$) were significantly decreased.

Conclusions: The hospitalization rate of children with hepatitis A decreased. However, the vaccination effect is still unclear mainly due to the periodicity of the disease incidence. A significant decrease of the hospitalization rate of young children and those of Greek origin is observed, implying a need to increase coverage rates among immigrant children.

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ACUTE BACTERIAL GASTROENTERITIS (ABG) IN A PAEDIATRIC EMERGENCY SERVICE (PES): EPIDEMIOLOGICAL CHANGES IN THE LAST 6 YEARS

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Background and aims: Diarrhoea is an important cause of morbidity in developed countries. Our aim was to assess local epidemiology of ambulatory intestinal bacterial infection.

Material: Retrospective analysis of stool cultures from children admitted to a PES between 2006-2011.

Results: 3435 stool cultures were requested, of which 703 (20%) were positive (range: 10% in 2010, 36% in 2007). Mean age was 3.1Y (1M-16Y). The most frequent bacteria were: C. jejuni (45%), S. enteritidis (32%), S. typhimurium (17%) and Y. enterocolitica (5%). In children 0-6 months and 7-12 months C. jejuni prevailed (59 and 66%, respectively); 1-5 years C. jejuni (44%) and S. enteritidis (33%); 5-10 years S. enteritidis (54%) and >10 years S. enteritidis (47%). Throughout the years a decline in the proportion of S. enteritidis (average 5.8%, 2011—2.4%) and raise in C. jejuni (average 9.3%; 2011—15.8%) was noticed. C. jejuni had no significant variation in its monthly distribution. S. enteritidis was more frequent in the Summer. S. enteritidis resistance to ampicillin remains low (average 8.9%; 2011—0%) and to cotrimoxazol has risen (average 14.5%; 2011—25%). S. typhimurium resistance to ampicillin remains high (average 66%) and to cotrimoxazol low (average 12.5%, 2011—0%). Y. enterocolitica remains fully resistant to ampicillin and susceptible to cotrimoxazol.

Conclusions: C. jejuni and S. enteritidis were the most frequent bacteria identified in children with ABG. Similarly to northern European countries, a rise in C. jejuni was noticed, distributed throughout the year and mainly infecting children in their first years of life.

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CHILDREN´S MILIARY TUBERCULOSIS

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Background and aims: Miliary tuberculosis (TB) usually occurs as a complication of primary infection. It is more frequently in malnourished and immunocompromised infants and young children.

Methods: We present the case of a 10-months-old girl with TB contact and measles convalescent, who was hospitalized in Children's Hospital, Timisoara. The patient had productive cough, fever (38.6-40.3˚C), loss of appetite and weight loss. She received antibiotherapy at home for one week without illness improvement. During hospital admission, her evolution was unfavorable with persistent symptoms. She was transferred to TB Clinic.

Clinical examination: fever, intense pallor of skin, generalized lymphadenopathy, hepatosplenomegaly, without scar after antituberculosis vaccination.

Biological tests revealed leukocytosis (23340/mm3) with neutrophilia (70%), inflammatory syndrome, a positive QuantiFERON, iron deficiency anemia, thrombocytosis, hypercholesterolemia, hypertriglyceridemia and a negative tuberculin skin test.

Direct smear	Negative for bacillus Koch
Culture	Positive for bacillus Koch

[Sputum obtained by gastric lavage]

Chest radiography: disseminated small nodules on both lung areas.

No pathological changes on cardiology and ophthalmological exams, abdominal ultrasound or bone marrow biopsy.

Results: Based on the epidemiological context, clinical examination and characteristic chest X-ray, the patient was diagnosed with miliary TB. Emergency tuberculostatic therapy (Isoniazid,Rifampin, Pyrazinamide, and Ethambutol) was initiated with slow favorable evolution. Sputum culture confirmed the diagnosis.

Conclusions: Miliary TB diagnosis is difficult, requiring primarily clinical presumption. Epidemiological context was useful for diagnostic orientation and the immunosuppression played an important role in the pathogenesis of this disease. The recovery is slow,but possible under appropriate therapy.

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IMPORTED TYPHOID AND PARATYPHOID FEVER IN CHILDREN: A CASE SERIES OF 45 PATIENTS IN A TERTIARY CARE CENTRE

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Enteric fever is rare in France and has become a predominantly travel-associated disease. Paediatric data are scarce and mainly provided by field studies in endemic countries.

In this retrospective study, we reviewed all cases of typhoid and paratyphoid fever treated in a tertiary care centre from 1993 through 2011.

Among the 45 cases, 80% were travel-associated. Sixty-three percent of the children had travelled to Africa and 34% to the Indian subcontinent for a median duration of 8 weeks (IQ 5.6-8.9). Eighty-six percent were visiting friends and relatives. Ninety-five percent of the patients had fever associated with gastrointestinal symptoms, 70% had elevated liver enzymes and 89% had an abnormal CRP. Blood cultures were positive in 89% of cases and S. typhi and S. paratyphi were isolated in 40 cases (89%) and 5 cases (11%) respectively. Ten strains were resistant, 9 of which were acquired in the Indian subcontinent. Eight had decreased susceptibility to Ciprofloxacin and one was resistant to Ciprofloxacin. Patients infected with these strains were indistinguishable both clinically and biologically from those infected by non resistant strains. Ceftriaxone was administered to 41 patients for a median duration of 6 days (IQ 4-8.5). Complications occurred in eight children and all 45 patients recovered.

Enteric fever is mainly observed in patients returning from a prolonged stay in an endemic area. Clinical and biological presentations are poorly specific and these infections can be severe in children. Drug resistance reflects the situation in endemic countries and is a major concern.

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INVASIVE PNEUMOCOCCAL DISEASE IN PICU PATIENTS BEFORE AND AFTER INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN THE NETHERLANDS

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Background: Invasive Pneumococcal Disease (IPD) continues to be a major cause of morbidity and mortality worldwide, especially in children under 5 years of age. The 7-valent pneumococcal conjugate vaccine (PCV7) was included in the national immunization program in the Netherlands in 2006. We compared patient and disease characteristics in patients with IPD admitted to the Paediatric Intensive Care Unit (PICU) before and after PCV7 introduction.

Methods: IPD patients admitted to the PICU of the Radboud University Medical Centre (1991-2010) were identified via electronic hospital registries. Clinical and laboratory findings of patients were collected by retrospective chart review. Differences were analyzed by Fisher's exact test.

Results: A total of 52 patients was included (36 patients diagnosed in the pre-vaccination era). The percentage of PCV-7 serotypes in IPD patients decreased following introduction of PCV7 (62,1% vs 10,0% ; $p< 0.05$)). No significant changes were observed in the percentage of patients older than 5 years (22.2% vs 18,8%), mortality (33.3% vs. 25.0%), or the percentage of patients with an IPD predisposition (36,1% vs. 31,3%).

Conclusions: National infant PCV-7 vaccination in the Netherlands caused a decrease in the percentage PCV-7 serotype strain related IPD in patients admitted to PICU. This decrease in PCV serotype strains related IPD was not associated with a decrease in percentage mortality. Most IPD cases requiring PICU admission are < 5 year of ages. One third of IPD PICU patients occurs in patients with a predisposition for IPD.

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3-YEAR OBSERVATION OF MINERALIZATION DISORDERS AND VITAMIN D3 LEVELS IN VERTICALLY HIV-INFECTED CHILDREN

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Background and aims: To assess prevalence of densitometric disorders and vitamin D3 deficiency in HIV-infected children treated with antiretroviral therapy and to estimate efficiency of vitamin-calcium supplementation.

Methods: Threefold (0-1-2years) densitometric measurements with simultaneous vitamin D3 level evaluation were performed in 50 vertically HIV-infected children aged 4-16 years, receiving cART. All children with impaired DEXA results and those with lower range were given supplementation of calcium and vitamin D3 (31/50). Age at DEXA measurements, cART duration, level of vitamin D3 in group with impaired DEXA result, administered supplementation and its influence on DEXA result were recorded. Regardless of DEXA results, cART was not modified.

Results: 25/50 (50%) children presented impaired 1st DEXA result of lumbar spine, among which 13 had incorrect results in total spine. Vitamin D3 level was low in 19/25 (76%), of which 4 had extremely low level. Measurements performed after 1 year showed DEXA improvement in 3 children (with supplementation) and deterioration in 3 children with previously correct DEXA (without supplementation). Results after the next year showed that 7 children with primarily impaired results improved to have no abnormalities, none subject worsened previous result. Level of 25OHD3 increased in consecutive years. Children with and without supplementation presented improvement and stability, respectively.

Conclusions: Impaired results of densitometry and 25OHD3 level were observed in significant percentage of vertically HIV-infected children receiving cART. Introducing supplementation of vitamin D3 and calcium improves bone mineralization and increase vitamin D3 level.

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ORAL BACTERIA POTENTIALLY PATHOGEN IN HIV+/AIDS CHILDREN

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Background and aims: The information about the presence and prevalence of potentially pathogen oral bacteria of HIV+/AIDS children is scarce. Therefore the principal objective was to establish the prevalence of several potentially pathogen bacteria in the oral cavity of HIV+/AIDS children.

Methods: 30 HIV+/AIDS children ≥ 3 years old (15 boys and 15 girls; age mean 7.7; ±7.7) perinatally infected under antiretroviral treatment coming from Hospital General, Tijuana, Baja California, Mexico were included. From medical record gender, age, antiretroviral therapy, CD4 lymphocyte count/mL and viral load were obtained. The patients were immunological and virological classified according to CDC-WHO. A total sample of oral mucosa was taken with a sterile hisopus and seeded in selective chromogenic mediums (HardyCHROM HUrBI®, HardyCHROM Staph®, HardyCHROM MRSA®). The distribution of frequencies of bacterial species in regard gender, immunologic and virologic status was obtained. For statistical purposes the chi square test was used ($p < 0.05_{IC\ 95\%}$).

Results: 90% of the children had positive cultures, girls showed high prevalence than boys: 100% vs 80% ($p<0.05$). The most prevalent bacterial species were: Streptococcus spp (73.3%), Staphylococcus spp (73.3%) and Enterococcus (70%). 6 cultures of methicillin-resistant Staphylococcus aureus were observed. The girls showed high prevalence of enterococci (p 0.04) while no statistical association of bacterial species with immunological or virological status were observed. The children undergoing double non-nucleoside analogue therapy had high prevalence of Pseudomona spp ($p < 0.05$).

Conclusions: The oral cavity of HIV+/AIDS children should be considered as an ecologic reservoir of potentially pathogen bacteria.

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THE VARIABILITY IN THE COURSE OF HEPATITIS B IN CHILDREN AFTER MOTHER-TO-CHILD TRANSMISSION AS A REASON TO ADJUST TREATMENT

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Background and aims: In Poland currently, despite obligatory hepatitis B vaccination we expect the occurrence of mother-to-child infection. We present 3 different courses of the HBV mother-to-child infections as a basis to differentiation of the therapeutic models .

Methods: We investigated history of 3 children infected with HBV by their mothers HBsAg(+) HBeAg(+) during pregnancy or perinatal period. After delivery 2 children was vaccinated against hepatitis B (two and and three times respectively) without HBIG. The 3rd child received HIBG with the first dose of vaccine.

Results: Hepatitis B virus infection in 2 children was revealed in the 3rd year of life. Acute hepatitis with the Gianotti- Crosti syndrome was diagnosed in 1 child in the 6th month of life. Subsequently, all children were diagnosed with chronic hepatitis B and the course of the disease was different in each case. In the first child aged 1, the activity of alanine aminotransferase decreased to nearly normal level with the seroconversion of HBe antigen to antibodies anti-HBe. The second child in the fourth year of life had high level of HBV viral load and moderate activity of ALT. We observed a failure of the interferon treatment. The third child (12 years old) had an exacerbation of disease after failure of treatment (lamivudine, interferon twice).

Conclusions: 1. A different course of hepatitis B, in one case typical for an adult, has been observed in children after mother-to child transmission. 2. Despite a passive-active prophylaxis HBV in neonate, vertical transmission is still possible.

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MOLECULAR SURVEILLANCE OF ROTAVIRUS INFECTIONS IN FRENCH INFANTS: TOWARDS THE EMERGENCE OF G12P[8] EPIDEMIC STRAINS?

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Background and aims: Rotaviruses are the major cause of acute gastroenteritis in young children worldwide, and require careful surveillance, especially in the context of vaccination programs (current vaccination coverage is under 10% in France) to characterize circulating rotaviruses and detect the emergence of potentially epidemic strains.

Methods: From 2005 to 2012, stool samples were collected from 5080 children under 5 years old with acute diarrhea admitted to the pediatric emergency units of 15 French large public hospitals. Rotaviruses were detected, then genotyped by RT-PCR for G (VP7) and P (VP4) types.

Results: The genotyping of 4643 rotaviruses showed that G1P[8] strains (62.1% [53.0-75.0]) were predominant, G9P[8] (17.0% [7.3-25.1]) still had a high circulation although declining, G2P[4] (7.9% [0.9-17.9]) were very variable, and G3P[8] (5.1% [1.7-15.1]) and G4P[8] (2.8% [0.9-5.6]) were mostly circulating locally. G12P[8] were progressively increasing over time from 0.4% to 3.3% in the last season. Most strains were associated with P[8] (87.5% [76.3-94.1]). Overall, 96 uncommon strains or possible zoonotic reassortants (2.1% [0.7-4.5]) were also detected such as G8 and P[6] strains.

Conclusions: The relative stability of rotavirus genotypes may ensure vaccine effectiveness in the short and medium terms in France. But, the recent increase in G12P[8] strains circulation might prefigure their emergence during the next seasons. Finally, the unusual strains should be monitored during ongoing and future vaccination programs, especially as all genotypes can cause severe infections. Special attention should be paid to the emergence of new rotavirus reassortants not included in current rotavirus vaccines.

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FATAL CEREBRAL ASPERGILLOSIS IN A CHILD TREATED FOR AUTOIMMUNE HEPATITIS

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Cerebral aspergillosis (CA) is a rare and often lethal condition in immunocopromised patients. We report the case of an 8-year-old girl who was treated with Methylprednisolone and Azathioprin for a presumed autoimmune hepatitis with acute liver failure and fluctuant hepatic encephalopathy. One month after beginning of immunosuppressive therapy, she developed right lower lobe pneumonia while liver function remained altered. Despite broad-spectrum antibiotics (Piperacillin-Tazobactam, Trimethoprim-Sulfamethoxazole, Azithromycin) her condition did not improve with occurrence of a pleural effusion and supplemental oxygen requirements. Bronchoalveolar lavage (BAL) and pleural tap were done day 6 after her hospital admission. After anesthesia she went into a coma (GCS 8/15). A brain MRI showed multiple disseminated hemorrhagic nodes compatible with abscesses. BAL and pleural fluid specimen grew for Aspergillus fumigatus. Galactomannan antigen was strongly positive in both BAL and serum. Liposomal amphotericin B was initiated but the patient demised the same day. This case highlights the challenge of diagnosing cerebral aspergillosis and underscores the importance of prevention, early diagnosis and treatment of this condition, also in hepatic patients.

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MARKEDLY DECREASED ANTIBODY TITERS AGAINST HEPATITIS B IN PREVIOUSLY IMMUNIZED CHILDREN PRESENTING WITH JUVENILE IDIOPATHIC ARTHRITIS

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Hepatitis B is a vaccine preventable disease with intermediate endemicity in Greece. Patients with Juvenile Idiopathic Arthritis on immunomodulating therapy are prone to infection or reactivation of HBV. The aim of this study is to define the immune status against HBV in children newly diagnosed with JIA.

Methods: Case-control prospective study including 89 JIA patients and 89 controls matched for age and gender. Sera were tested for hepatitis B surface antigen, hepatitis B core antibody, and anti-HBs. Patients with anti-HBs titers ≥10 IU/L were considered immune. Data were analyzed with SPSS 18.0 version.

Results: Eighty nine JIA patients were included in the study (22 males), with a mean age of 6.7 years. In the JIA group 55% were HBV immune (anti-HBs level ≥10 IU/L) while in the control group 92% were immune against HBV ($p< 0.001$). Antibody levels in the patient group were significantly lower compared to the control group. The mean concentration of anti-HBs levels in JIA patients was 18.3 IU/L versus 82.6 IU/L in the control group ($p< 0.001$).

Conclusion: Results suggested that antibody titers against HBV in fully vaccinated JIA patients due to start treatment are significantly lower compared to matchedhealthy children. Diagnosis of JIA , older age and single versus hexavalent vaccination were associated with the absence of protective antibodies. Although there is no evidence to support the introduction of a booster HBV dose in healthy children who mount low antibody response following immunization, further studies are required to address this question in patients with JIA.

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LIFE-THREATENING KINGELLA KINGAE ENDOCARDITIS IN A 13-MONTH-OLD HEALTHY BOY

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Introduction: Kingella Kingae (Kk) is increasingly reported in childhood. It is a common etiology of osteoarticular infections in young children. However this germ can be responsible of more aggressive clinical picture.

Clinical case: We report the case of a 13-month-old boy admitted for fever, vomiting, photophobia and deterioration of the general state. The diagnosis of aseptic meningitis was done, based on laboratory findings and lumbar puncture. A treatment with cefotaxime and aciclovir was initiated with improvement of the patient´s general condition and resolution of the fever over 24hrs. However, on day 2, blood culture grew for Kk. An echocardiogram showed the presence of a wide vegetation (10x9 mm) on the posterior mitral valve leaflet with moderate regurgitation. A cerebral scan showed a right-frontal hypodense lesion. The diagnosis of bacterial endocarditis with frontal septic embolization and reactive meningitis was made.

A mitral plasty was complicated by an embolization in the LAD coronary artery with myocardial ischemia. The patient needed ECMO during 4 days. Eventually, the cardiac function improved dramatically and the final evolution was excellent with IV ampicilline continued for 6 weeks.

Conclusion: Kingella Kingae is included in the HACEK group that causes 5% of the endocarditis, even on healthy heart. Some authors recommend an echocardiogram in case of bacteremia.

Our case demonstrates that endocarditis can be associated with infected material embolizations, including in the cerebral and coronary territories. Amazingly, this case also shows the impressive recovery potential of children after an acute ischemic event in a peripheral circulation.

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DIAGNOSTIC VALUE OF PROCALCITONIN IN PREDICTING INVASIVE BACTERIAL INFECTIONS IN NEONATES WITH FEVER WITHOUT SOURCE

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Background and aims: Procalcitonin (PCT) value in management of neonates with fever without source (FWS) is still lacking. Our aim is to assess the diagnostic accuracy of PCT in detecting invasive bacterial infections (IBI) in neonates with FWS.

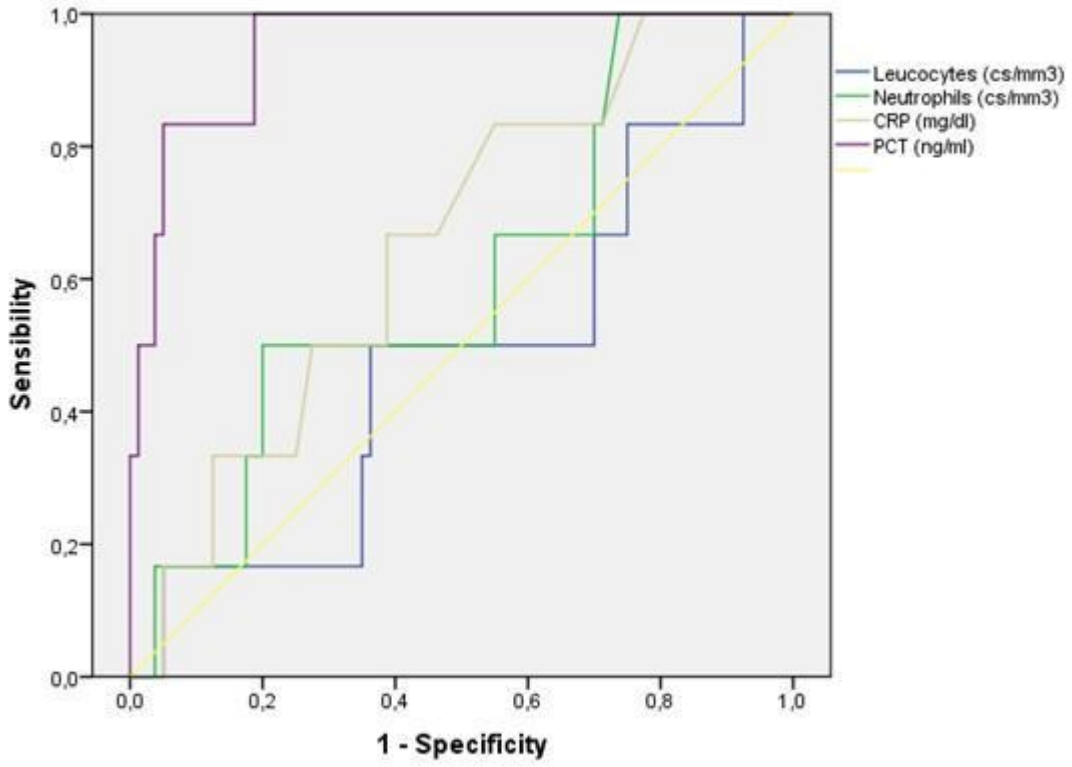
Methods: A retrospective study was conducted on previously healthy neonates with FWS admitted to a tertiary care Pediatric Emergency Department between August 2008 and August 2012. Children born preterm, with underlying diseases or without available blood culture, c-reactive protein value (PCR) and PCT value were excluded. An IBI was defined by isolation of a bacterial pathogen in blood or cerebrospinal fluid culture.

Results: 129 neonates were admitted during the study period and 88 children met the study inclusion criteria. IBI was diagnosed in 6 children (6.8%). Negative likelihood ratio (LR-) for IBI and PCT 0.5 ng/mL was 0 (IC95% 1.35-3.07). Positive likelihood ratio (LR+) for IBI and PCT 2 ng/mL was 11.38 (IC95% 4.87-26.62) (Table1). AUC for PCT, CRP, neutrophils and leucocytes were 0.952 (0-1), 0.654 (0.453-0.855), 0.602 (0.374-0.830) and 0.477 (0.231-0.723) respectively (Graphic1).

Conclusions: PCT is an accurate marker of IBI in healthy neonates with FWS. It´s better test than CRP for ruling out or suspect IBI in newborns.

	Sensitivity	Specificity	LR +	LR -
IBI PCR 3 mg/dl	16.67% (3-56.35)	89,02%(80,44-94,12)	1.51(0.22-10.07)	0.94(0.64-1.34)
IBI PCT 0.5 ng/ml	100% (60.97-100)	81,71%(71.99-88.59)	5.45(3.45-8.63)	0(1.35-3.07)
IBI PCT 2 ng/ml	83.33%(53.51-100)	92.68%(87.04-98.31)	11,38(4.87-26.62)	0,17(0.03-1.07)

[Table 1]


Sensibility
1 - Specificity
0,0
0,2
0,4
0,6
0,8
1,0
Leucocytes (cs/mm3)
Neutrophils (cs/mm3)
CRP (mg/dl)
PCT (ng/ml)

[Graphic1]

1076

PNEUMOCOCCAL SUPURATIVE ACUTE OTITIS MEDIA (PSAOM) IN AN AREA WITH UNIVERSAL PENUMOCOCCAL VACCINATION

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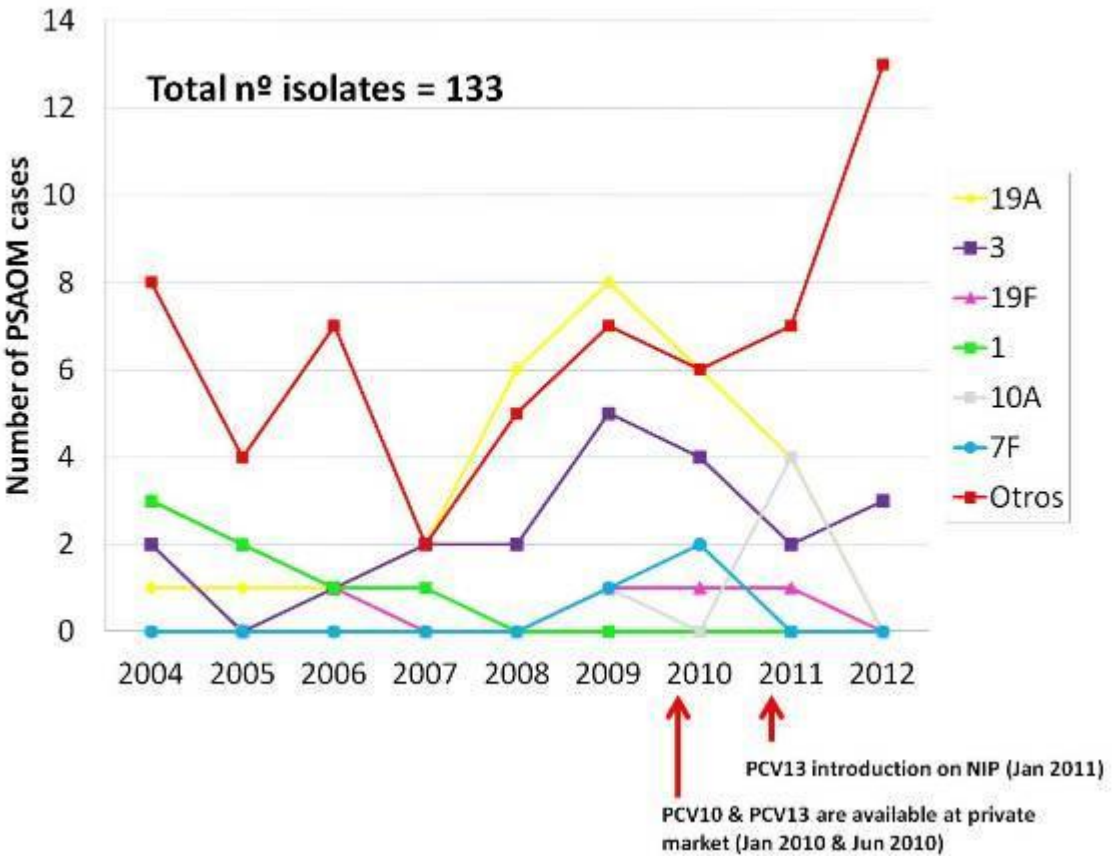
[1]Hospital da Costa, Lugo, [2]Pediatrics, Hospital Clínico Universitario de Santiago, [3]Genetics, Vaccines, Infecctions and Pediatric Research Group (GENVIP), Healthcare Research Institute of Santiago, [4]Microbiology, Hospital Clínico Universitario de Santiago, Santiago de Compostela, [5]Microbiology, Hospital Arquitecto Marcide de Ferrol, La Coruña, Spain

Aims: In January 2011 the PCV13 was included in the immunization program of Galicia (north-west Spain). We aimed to assess the serotype distribution and eventual impact of PCV13 in children with pneumococcal supurative acute otitis media (PSAOM).

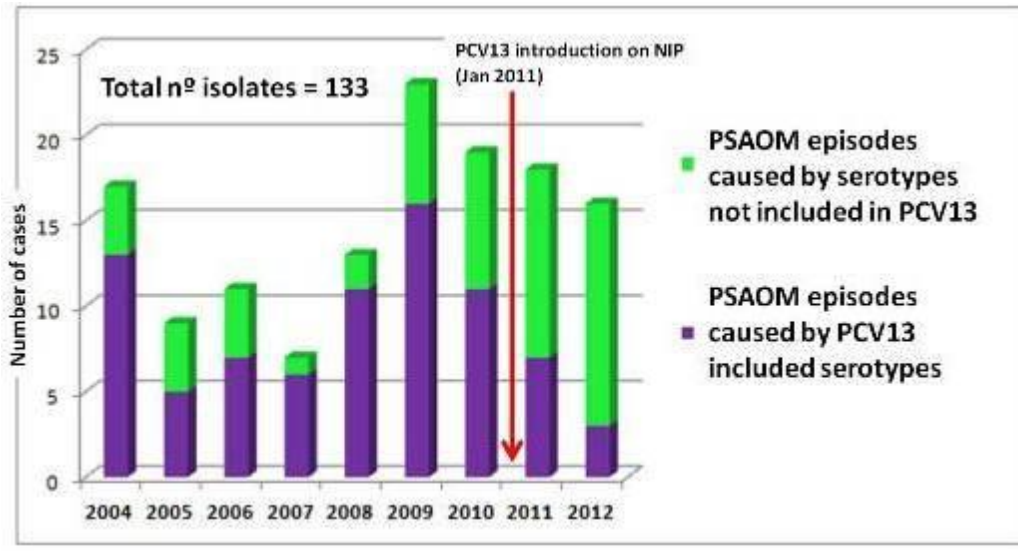
Methods: All PSAOM isolates of children < 15 yo collected from jan-2004 to dec-2012 in our hospital were included and serotyped.

Results: 133 PSAOM cases with a mean age of 3.6 (3) yo were included: 19A (22%) and 3 (16%) were the more prevalent isolates.



[SEROTYPE DISTRIBUTION]

Since the PCV10/PCV13 availability in 2010, an outstanding decrease in the isolation of vaccine serotypes in PSAOM has been detected, with no 19A cases during the last season, and only 3 cases of PSAOM caused by PCV13 serotypes, all of them by serotype 3.



[SEROTYPE COVERAGE]

Regarding to antibiotic resistance, we have observed a decrease of both amoxicillin resistant strains (from 10% to 3.8%) and erythromycin resistant strains (from 34% to 25%) in the last two years as compared to previous period, without any further changes.

Conclusions: Despite the obvious limitations of our study, it seems that the introduction of PCV13 in the NIP has led to the almost disappearance of isolates of PCV13 serotypes in SPAOM. Active surveillance remains essential.

1077

THE IMPACT OF INCLUDING PRODUCTIVITY COST ON THE COST-EFFECTIVENESS OF 10- VERSUS 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN DENMARK AND SWEDEN

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Background and aims: Recently a study concerning the cost-effectiveness of 10- versus 13-valent Pneumococcal conjugate vaccine in Denmark and Sweden, only focusing on direct medical cost, was published. The aim of this study was to investigate the impact of including productivity cost.

Methods: A decision-analytic model was used to estimate the impact of PCV10 and PCV13 on reducing cases of invasive pneumococcal disease (IPD), pneumonia (PNE), and acute otitis media (AOM). Direct medical costs were based on the cases prevented and associated direct medical costs for treatment. For productivity costs lost days of work for either care-givers (in pediatric cases) or patients (adult cases) were estimated and associated costs were based on hourly wages in Denmark and Sweden.

Results: PCV13 is expected to save 280.7 (97.1 % due to indirect effect) million DKK in Denmark and 288.2 (94.8 % due to indirect effect) Million SEK in Sweden in direct medical costs compared to a vaccination program with PCV10. In productivity costs PCV13 is expected to save an additional 497.6 (97.6% due to indirect effect) million DKK in Denmark and 388.1 (96.5 % due to indirect effect) million SEK in Sweden compared to a vaccination program with PCV10. In both countries, the results indicate that, compared to PCV10, PCV13 will have a greater impact on cases of IPD, PNE, AOM and deaths avoided.

Conclusions: This analysis shows that including productivity costs greatly improves the cost-effectiveness of PCV13 compared to PCV10 when used in a NIP in Denmark and Sweden.

1078

CHRONIC COUGH FOLLOWING ACUTE RESPIRATORY ILLNESS IN CHILDREN

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Introduction: Despite chronic cough being a substantial cause of childhood morbidity and associated costs, data on its prevalence following acute respiratory illness (ARI) in children are scarce.

Aim: To determine the prevalence and predictors of chronic cough (>4 weeks duration) amongst children following presentation to a tertiary paediatric emergency department (ED) with ARI.

Methods: A cohort study of children aged < 15 years attending the Royal Children's Hospital ED, Brisbane, Australia with cough as a symptom. Children participate for 28 (±3) days following enrolment. Demographic, epidemiological, risk factor, microbiological and clinical data are collected at enrolment. Daily diary cards and weekly contacts are used to ascertain cough persistence. Children with persistent cough at day 28 are reviewed by a paediatric respiratory physician.

Results: We report preliminary data on 248 children (median age 30.3 months, range 1.02 months - 13.9 years, male: 62.1%) enrolled between December 2011 and August 2012, contributing a total of 5663 child-days of follow-up. The prevalence of chronic cough at day 28 was 20% (95% CI 14.8, 24.7); wet cough (37%), dry cough (22%), variable cough (18%), unsure (22%). At baseline, 41.6% of all children were virus positive on nasal swab, 81% bacteria positive and 36% both virus and bacteria positive.

Conclusions: The prevalence of chronic cough in these children following ARI is the highest yet reported. Our ongoing study will comprehensively describe the natural history, aetiology and outcomes of cough during and after ARI.

Acknowledgements: Funded by NHMRC Australia and QLD Children´s Health Foundation

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SHOULD HANTAVIRUS INFECTIONS BE INCLUDED IN THE DIFFERENTIAL DIAGNOSIS OF ACUTE UNDIFFERENTIATED FVER IN PEDIATRIC PATIENTS? A PRELIMINARY REPORT

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Background and aims: Worldwide, hantavirus infections in children are rare. We here investigate hantavirus etiology among pediatric patients presenting with acute undifferentiated fever (AUF) in secondary community hospitals in India.

Methods: In a prospective observational study, sera samples of adult (n=363) and pediatric (n=43) AUF patients > 5 days onset of fever, from secondary hospitals in three regions in India, were screened for anti-hantavirus IgM.

Patients were from Tamil Nadu, South India (adults, n=190; pediatric, n= 29), Western India, Maharashtra (adults, n = 45) and North East, Assam (adults, n=171; pediatric, n=14). The mean age of pediatric patients included in the study was 7.9 (SD 2.5) years.

Serum samples were tested for anti-hantavirus IgM antibodies by an in-house indirect ELISA. Recombinant truncated nucleocapsid protein (NP) was used as antigen. Cut-off OD, 0.2 was calculated using 50 healthy donor samples. Samples with OD above cut-off were considered positive.

Results: Of the 406 samples tested, 36 (8.8 %) had serological evidence of acute hantavirus infection. Among pediatric patients, four were hantavirus IgM positive; all these four were negative by diagnostic tests for malaria, dengue, chikungunya, leptospira and brucellosis. All pediatric hantavirus positives had no localizing signs and symptoms for fever and were from Tamil Nadu. Mean age of pediatric hantavirus positives was 8.5 (SD 2.98) years.

Conclusion: Our study based on serology provides preliminary evidence of pediatric hantavirus infections manifesting as AUF. It is important to consider hantavirus infection as a differential diagnosis of AUF in children.

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SEROCONVERSION AFTER QUADRIVALENT HUMAN PAPILLOMAVIRUS VACCINE IN HIV-INFECTED GIRLS

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Background and aims: HIV-infected women have an increased prevalence of human papillomavirus (HPV) infections and a higher risk of cervical cancer. The quadrivalent HPV (QHPV) vaccine is effective in preventing genital precancerous lesions and warts in immunocompetent people. We aim to describe the immunogenicity of the QHPV vaccine in HIV-infected girls.

Methods: Cross-sectional study in a series of 27 HIV-infected girls who received a complete QHPV (types 6, 11, 16 and 18) vaccination series. Serum antibodies against QHPV antigens in the first 6 months after the third vaccine dose were measured by an enzyme immunoassay (DRG Diagnostics, Germany). Seropositivity was defined as an anti-HPV index > 1.00 and results were analyzed according to different clinical and immunovirological variables.

Results: Twenty-seven girls were included (median age: 15 years; 26 and 16 vertically-infected and with AIDS, respectively). Only one remained antiretroviral naive, 10 (37%) had received HAART as first treatment (median number of regimens: 3.5), and 13 (48%) had interrupted HAART at least once for a median time of 26 months.At the time of vaccination and assessment all patients were symptom-free, none of them presented with severe immunosuppression and viral load was undetectable in 19 (70%) and 16 (59%), respectively. Seroconversion occurred in 25 (93%) vaccinees with no differences based on clinical and immunovirological variables.

Conclusions: QHPV was highly immunogenic in this series of HIV-infected adolescent girls. Long term antibody levels need to be mesured to assess the durability of the protection.

1081

ORBITAL TUBERCULOSIS. A CASE REPORT.

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Background: Orbital tuberculosis is extremely rare and potentially devastating. It results from haematogenous spread or direct invasion of adjacent areas. Diagnosis is difficult and based on Interferon-gamma release assays (IGRA)/tuberculin-skin test, histopathology, radiology and response to empiric antituberculous treatment.

Case: Previously healthy 3-year old boy, Indian background, born in the UK, with unremarkable family history, fully vaccinated (including BCG), presented with a four-month history of progressive right orbital swelling and proptosis. There was no fever, rash or lymphadenopathy. Investigations were normal including FBC, inflammatory markers and chest X-ray. A four-week course of IV ceftriaxone and metronidazole was given for presumed cellulitis without clinical improvement. CT-imaging showed a mass involving the right maxilla, with bony destruction of the superior lateral wall of the orbit. Biopsy showed non-caseating granuloma, Langhans-giant cells, without AAFBs or features of malignancy. Immunological and vasculitis screening (including NBT and ACE) were unremarkable. In view of positive IGRA, rifampicin, ciprofloxacin, ethambutol and amikacin were started to cover mycobacterial infection with dramatic improvement in the ensuing seven days and complete clinical and radiological resolution of the orbital tumor within two months. A total 12-month course of isoniazid, ethambutol and rifampicin was completed, without subsequent relapse or recurrence of orbital swelling after 24-month of follow-up.

Commentary: Ocular tuberculosis is uncommon, but should be considered in any patient with unilateral proptosis, invasive bone involvement, that does not respond to empiric antibiotics and in whom malignancies and rheumatologic disorders have been excluded. Early diagnosis and treatment may prevent unnecessary treatment and sequelea.

1082

EBV ASSOCIATED LYMPHOMA IN A BOY WITH PURINE NUCLEOSIDE PHOSPHORYLASE DEFICIENCY

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Purine Nucleoside Phosphorylase (PNPase) deficiency is an autosomal recessive disorder affecting purine degradation and salvage pathways. Clinically, patients typically present with severe immunodeficiency, neurological dysfunction, and autoimmunity. Biochemically, may be suspected in the presence of hypouricemia. Viral infections like Ebstein-Barr virus lead to lymphoma in these patients and cause mortality. A 28-month-old boy, born of a first degree consanguineous marriage was referred to our hospital with recurrent lower respiratory tract infections, developmental delay fever continuing about three weeks and cervical lymphadenopathy. Serum uric acid level was 0.04 mg/dl. Serum immunglobulin levels were elevated but $CD3^+$ T cell and $CD19^+$ B cell levels were low. With these findings, the patient was diagnosed as T^-, B^-, NK^+ severe combined immun deficiency. We thought PNPase deficiency in this patient with hypouricemia, neurological dysfunction and severe combined immun deficiency findings. Mutation analysis confirmed the PNPase deficiency with a homozygous nonsense mutation c.700C>T in exon 6 leading premature termination of protein at residue 234 (R234X). Parents are carriers for this mutation and it was not a novel mutation. Cervical lymph node biopsy was performed to rule out any possible malignancy. Biopsy showed EBV positive diffuse B cell lymphoma. Staging protocole showed pathological abdominal and thoracal lympadenopathy without CNS involvement. Cranial MRI revealed cerebral atrophy. With this result, rituximab, prednisolone, cyclophosphamide, adriamycine and vincristine (R-COP protocole) were initiated. Serum EBV viral load was found to be 56000 copy/ml and acyclovir treatment was initiated. He died because of pancytopenia and sepsis.

1083

IMMUNITY OF NURSING STUDENTS TO MEASLES, MUMPS RUBELLA AND VARICELLA

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[1]Infectious Diseases and Clinical Microbiology, Bozok University, Faculty of Medicine, [2]Bozok University, School of Health, [3]Biochemistry, Bozok University, Faculty of Medicine, Yozgat, Turkey

Background and aims: Nursing students are at risk of acquiring and transmitting vaccine-preventable diseases such as measles, mumps, rubella and varicella, especially in pediatric and infectious diseases departments. The aim of this study was to determine the vaccination history of nursing students and their serologic immunity against these diseases.

Methods: The immunity was assessed by determining specific antibody titer by ELISA and a self-recorded questionnaire was filled including their disease and vaccination history.

Results: The antibody titers to measles, rubella, mumps and varicella viruses were measured in 90 nursing students (67 women, 23 men, the average age 18.7 +/- 1.1 years old). Immunity rates to measles, mumps, rubella and varicella were 69 (76.7%), 75 (83.3%), 89 (98.9%) and 90 (100%) respectively. The immunity to measles, rubella, mumps and varicella viruses in were similar in males and females ($p>0.05$). Of the study group, 35.5% (n=32) was not immune at least one of these viruses, and 17 (18.9%) students were not immune against measles alone. The history of infection and vaccination were evaluated by self-recorded questionnaires. The students who declared that they have received all their childhood vaccines (n=54, 60%), only 68.5% had protective antibody titers against measles. Although all of the students were immune to varicella, 34.4% of them had not neither infection nor vaccination history.

Conclusions: Self-reported disease or vaccination history is not a reliable indicator for assesing immunity. It is necessary to determine immune status against measles, rubella, mumps and varicella in nursing students.

1084

A NATIONWIDE POINT PREVALENCE SURVEY FOR ASSESSING VARIATIONS IN ANTIBIOTIC USE AMONG NEONATAL AND PAEDIATRIC PATIENTS IN GREECE

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[1]Second Department of Paediatrics, National and Kapodistrian University of Athens School of Medicine, [2]Collaborative Center for Clinical Epidemiology and Outcomes Research (CLEO), 1st and 2nd Depts. of Paediatrics, University of Athens School of Medicine, Athens, [3]Third Department of Paediatrics, Aristotle University School of Medicine, Thessaloniki, [4]Department of Paediatrics, University Hospital of Patras, Patras, [5]Department of Paediatrics, University Hospital of Heraklion, Heraklion, Greece, [6]University of Antwerp - CDE, Faculty of Medicine and Health Science, Laboratory of Medical Microbiology, Vaccine & Infectious Disease Institute, Antwerp, Belgium, [7]Department of Paediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA, USA

Background and aims: Within Europe, Greece has among the highest rates of drug resistant organisms and antibiotic consumption. However, the majority of data on antibiotic utilization is derived from adult hospitalized patients. The objective of the study was to determine antibiotic utilization patterns among hospitalized children in Greece.

Methods: A point prevalence survey (PPS) of antibiotic use was conducted in November 2012 in hospitalized children in Greece within the context of the broader ARPEC study. The study sites included the paediatric and neonatal units at the 5 largest paediatric hospitals in Greece. A standardized, web-based data collection form was utilized.

Results: A total of 701 patients were included in the survey, 556 (79.3%) paediatric and 145 (20.7%) neonatal patients. Overall, 53.2% (n=296) paediatric and 46.2% (n=67) neonatal patients received ≥1 antibiotic. The most common indication for antibiotic use was systemic infection (n=102; 16.1%) followed by surgical prophylaxis (n=97; 15.3%). The most frequently prescribed antibiotics in children were third- and second-generation cephalosporins (n=72, 14.3% and n=64, 12.7%, respectively), and aminoglycosides (n=42; 7.3%). Among neonates aminoglycosides (n=32; 24.9%), third-generation cephalosporins (n=21; 16.3%), and ampicillin (n=21; 16.3%) were most often prescribed. Combinations of ≥2 antibiotics were administered to the majority (80.0%) of neonates with systemic infections (n=30).

Conclusion: We found high rates and broad spectrum antibiotic use in hospitalized children in Greece. Compared to previously reported ARPEC data, the rates of use are among the highest in Europe. Antimicrobial stewardship strategies including evidence-based guidelines should be adopted in order to improve prescribing practices.

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PEDIATRIC PROFILE OF FIRST HUMAN TRICHINELLOSIS OUTBREAK IN INDIA

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Background: Trichinella infection is extremely uncommon in India with the diagnosis being even more difficult because of the non specific symptoms of the disease. We report an outbreak of human Trichinellosis in India.

Methods: Two children, belonging to the same community, presented as acute onset fever with generalized myalgia and eosinophilia, after consumption of uncooked pork in a common gathering. Trichinellosis was suspected in both index cases and was confirmed on muscle biopsy. A detailed epidemiological survey was carried out in the affected community and 54 people including 8 children, who participated in the gathering, were subjected to Proforma based assessment and blood investigations after informed consent.

Results: Out of 8 children, 1 had consumed pork in uncooked form, 4 in open fire roasted form and 3 in fried form. Clinical symptoms were found only in children who consumed pork in uncooked or open fire roasted form (n=5). These included fever with chills(100%), myalgia(100%) and periorbital edema(80%). One child developed dysphagia and breathing difficulty. Laboratory parameters studied in both symptomatic and asymptomatic patients showed eosinophilia in 75%(n=6), raised ESR in 50%(n=4), and an elevated creatinine phosphokinase enzyme levels in 37.5%(n=3). The analysis revealed milder severity of symptoms in children as compared to the adult population of the community. All symptomatic patients were treated with a short course of oral steroids and albendazole therapy.

Conclusion: In areas with high prevalence of raw meat consumption, infection due to Trichinella should be suspected in children presenting with eosinophilia myalgia syndrome.

1086

CLINICAL IMPACT OF INTRODUCING VENTILATION WITH HIGH FLOW OXYGEN IN THE TREATMENT OF BRONCHIOLITIS IN A PAEDIATRIC WARD

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Objective: To analyze the safety and efficacy of high-flow oxygen therapy for treatment of moderate to severe bronchiolitis in children admitted to the pediatric hospital wards.

Methods: We performed a prospective observational study of children < 18 months of age with bronchiolitis admitted to the pediatric ward of a tertiary-care teaching hospital. Children were treated with high-flow ventilation system (Fisher & Paykel). Clinical and cardio-respiratory parameters were evaluated every hour for the duration of therapy.

Results: We included 32 patients, with a median age of 2 months (rank 0,4-10 months) during the 2011-12 respiratory season, and November and December of 2012. 71% were RSV positive. Indications for high-flow therapy included: progressive respiratory distress (Wood-Downes ≥ 8) (87.5%), apnea (12,5%) Median duration of therapy was 4 days (rank 3-7 days), with a median of 10 days of total hospitalization (rank 8-12 days). High flow therapy was associated with a significant decrease of cardio-respiratory parameters: heart rate, respiratory rate, which resulted in significant improvement of the Wood-Downes Score (from 10.5±1,37 to 3±0,77, p=0,001). No adverse effects were observed. Eight patients (25%) were admitted to Pediatric Intensive Care Unit (PICU), wich represents an 75% reduction of PICU admissions compared with historic data of previous years.

Conclusions: High-flow ventilation therapy achieved a significant improvement in heart rate, respiratory rate and scale of severity in patients with bronchiolitis. This novel therapeutic strategy allows safe management of bronchiolitis patients in the regular ward, reducing admissions to the PICU.

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EXTERNAL VALIDATION OF THE REFINED LAB-SCORE, FOR IDENTIFICATION OF SEVERE BACTERIAL INFECTION IN FEBRILE CHILDREN UNDER THREE MONTHS

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[1]Epidemiology, Biostatistics and Bio-informatics Department, Nîmes Hospital, Nimes, [2]EA2415, Montpellier 2 University, Montpellier, France, [3]Cruces University Hospital, Bilbao, Spain, [4]Ca'Foncello Hospital, Treviso, Italy, [5]12 de Octubre University Hospital, Madrid, [6]Donostia University Hospital, Donastia, [7]Jesús Children's University Hospital, Madrid, [8]Navarra Hospital Complex, Pamplona, Spain, [9]University of Padova, Padova, Italy, [10]Basurto University Hospital, Bilbao, Spain

Background: The identification of severe bacterial infection (SBI) in children with fever without source (FWS) remains a diagnostic problem. A risk index score, the Lab-score, associating CRP, procalcitonin and urinary dipstick (UD) to predict SBI was derived and recently refined and re-validated, providing a 94% [90-100] sensitivity and 70% [66-74] specificity. We aimed to validate it on the particular and problematic population of children ≤3-months of age.

Methods: Data from multicentre cohort study of children with FWS. The refined Lab-Score was calculated for each children.

Results: 1098 children (28% SBI) were included. The refined Lab-Score yielded a 0.86 [0.82-0.89] AUC ROC, significantly higher than the one of all biomarkers (CRP, Procalcitonin, neutrophil count - $p < 0.0001$), as well as the Lab-Score one ($p=0.0007$). According to a decision curve analysis, the refined Lab-Score performed better than biomarkers and the original Lab-Score in children ≤3-months of age, for all thresholds. The cut-offs previously chosen offered 77% [72-82] sensitivity, with 87% [84-89] specificity. The second threshold identified led to 67% [62-72] sensitivity, and 92% [90-94] specificity. Both sensitivities were lower than the original ones (98% and 94% respectively); however specificities were higher (53% and 70% respectively). A new threshold yielded a 80% [75-84] sensitivity, with 81% [78-84] specificity.

Conclusion: The refined Lab-score demonstrated higher specificities in children ≤3-months of age, but with decreased sensitivities. This could be problematic given that clinicians would not accept to misdiagnose SBI in this particular population of infants, and specific thresholds for this age were warranted.

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FEVER RISK FOLLOWING TRIVALENT INFLUENZA VACCINATION IN CHILDREN 6 TO < 36 MONTHS: COMPARISON OF PUBLISHED AND UNPUBLISHED STUDIES

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Background: In Australia, annual influenza vaccination is recommended for children aged ≥6 months. During 2010, high rates of febrile reactions and convulsions occurred in young children following administration of a specific brand of seasonal trivalent influenza vaccine (TIV).

We sought to define a baseline risk for febrile reactions following TIV in children aged 6 to < 36 months.

Methods: We conducted a review using published and unpublished literature (PubMed/Google Scholar & Clinicaltrials.gov respectively). Identified studies were screened and duplicates removed. Data were extracted in duplicate using a standard template, with discrepancies resolved by consensus. We compared the febrile reaction prevalence reported in published and unpublished studies.

Results: After screening 515 published articles and 50 unpublished clinical trials, 6 published articles and 12 clinical trials were included in the review. Studies varied by vaccine manufacturer, method, timeframe and location.

Following influenza vaccination, the median prevalence of 'mild-moderate' febrile reactions (37.0° to < 39.0°C) among children aged 6 to < 36 months was 11.0% in published studies (range 0-25.0%) and 13.8% in unpublished clinical trials (range 0-37.1%). For 'severe' febrile reactions (≥39.0°C), the median prevalence was lower in both groups: 2.1% in published studies (range 0-4.6%) and 0% in unpublished clinical trials (range 0-6.1%). Two clinical trials each reported one febrile convulsion.

Conclusion: Severe febrile reactions (≥39.0ºC) following TIV are more prevalent among children < 36 months in published studies compared with unpublished results. Whilst potentially incomplete, published data can be used to provide baseline values for adverse events following immunisation.

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THREE-WAY COMPARISON OF THE PERFORMANCE OF THE TUBERCULOSIS SKIN TEST AND INTERFERON-GAMMA ASSAYS FOR DETECTING TUBERCULOSIS INFECTION AMONG CHILDREN

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Background and aims: Limited evidence exists regarding the comparative performance of interferon gamma release assays (IGRAs) for detecting TB infection in children. We compared the performance of the tuberculosis skin test (TST) with the QuantiFERON-TB Gold-In-Tube (QFT-IT) and TSPOT-TB assays for detecting TB infection in children.

Methods: A cross-sectional study was conducted among 153 children evaluated for active TB disease (n=63) and for latent tuberculosis infection (LTBI; n=90) (mean age±SD:7.8±4.7 years). Participants were assessed with the TST, QFT-IT and TSPOT-TB concomitantly. Comparisons of tests were evaluated with the kappa statistic.

Results: Among children with active TB disease, TST was positive in 95.2% (n=60), while QFT-IT and TSPOT-TB were positive in 84.1% (n=53) and 74.6% (n=47), respectively. The concordance between tests was highest between TST and QFT-IT (82.5%) and lowest between TST and TSPOT-TB (73.0%). Moreover, the concordance between QFT-IT and TSPOT-TB was 77.8% (κ=0.33). In contrast, in children evaluated for LTBI, TST was positive in 64.4% (n=58) while QFT-IT and TSPOT-TB were positive among 51.1% (n=46) and 45.6% (n=41), respectively. In this group the agreement between QFT-IT and TSPOT-TB was good (κ=0.62; concordance:81.1%), while it was limited to moderate between TST and TSPOT-TB (κ=0.50; concordance:74.4%).

Conclusions: A lower proportion of positive results were obtained with IGRAs as compared to TST in children with either active TB or LTBI. Agreement between the TST and QFT-IT exceeds that with TSPOT-TB among children with active TB disease. In contrast, good agreement between the QFT-IT and TSPOT-TB was observed among children with LTBI.

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CLINICAL FEATURES OF TOXOCARIASIS AMONG CHILDREN IN BULGARIA

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The classical clinical symptoms described in children by Beaver (1952) were connected with hepatomegaly, eosinophilia and bronchospasm. Later were described several forms of the disease from which visceral and ocular syndromes were leading. Now more often for toxocariasis are serologically tested children with different forms of allergy or other non-specific symptoms, often without eosinophilia. In Bulgaria, the spread of toxocariasis is currently under study and particularly this relates to children. Mainly the research for toxocariasis is conducted at NCIPD and for the period 2008-2012 serologically for this parasitosis were tested 95 children aged from 1 to 18 years old. Clinical symptoms for which the suspected children were referred for serological toxocara testing regarding toxocariasis were: skin lesions (28), eosinophilia (25), bronchospasm, cough and pneumonia (8), lymphadenopathy (4), hepatomegaly (1) and alopecia (1). Significant is the number of the children (16) without prior diagnosis or other symptoms. Suspected for ocular toxocariasis were 12 children with uveitis, pars planitis or chorioretinitis.

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PEDIATRIC HERPES ZOSTER HOSPITALIZATION RATES REMAIN UNCHANGED DURING THE FIRST DECADE POST INTRODUCTION OF THE VARICELLA VACCINE IN GREECE

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Background and aims: The varicella vaccine was introduced in the Greek National Immunization Program (NIP) in 2004. Toddler vaccination and catch-up of susceptible older children, adolescents, and adults was implemented. The study examined time trends in pediatric herpes zoster (HZ) hospitalizations following vaccine implementation.

Methods: A retrospective study was conducted among all pediatric HZ patients hospitalized at a pediatric referral hospital in Greece during 1999-2011. Time trends in the occurrence of pediatric HZ cases were evaluated with ARIMA modeling. HZ hospitalization rates prior and following the introduction of the varicella vaccine in the NIP were compared with the Rao-Scott test.

Results: During the study period, 9647 pediatric patients were admitted to the study site, while 134 (1.4%) patients were hospitalized for HZ. The rate of HZ hospital admissions increased from 1999 (12.67 cases/1000 admissions) to 2011 (17.12 cases/1000 admissions). However, no significant increase in the rate of HZ cases was detected over time (p=0.673). Moreover, no significant decrease in the rate of HZ admission prior to and following the introduction of the varicella vaccine in the NIP was identified (p=0.680). However, the mean age of study participants increased significantly during the study period (2.53±1.8 years in 1999 to 14.00±0.01 years in 2011; p=0.006).

Conclusions: The rate of hospitalized pediatric HZ patients remains unchanged following the introduction of the varicella vaccine in the Greek NIP. The present evidence may serve as a baseline to detect future changes in HZ hospitalization rates. Ongoing surveillance of HZ hospitalization rates is deemed necessary.

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VACCINATION COVERAGE OF ADOLESCENTS

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Aim: Investigation of our region's adolescents' vaccination status.

Methods: The study included adolescents aged 13-18 years (middle age 15 years) that visited our institution's outpatient clinic during 2011. 127health books were studied. Vaccination coverage was recorded for:

1) MMR (complete immunization: 2 doses, incomplete ≤ 1),

2) Hepatitis B (complete immunization: 3 doses, incomplete ≤ 2),

3) Hepatitis A (complete immunization: 2 doses, incomplete ≤ 1),

4) VZV (complete immunization: 2 doses, incomplete ≤1),

5) DTP-IPV (complete immunization: 5doses for ages ≤ 15 and 6doses for >15, incomplete ≤ 4 or 5doses respectively)

6) Meningitidococcus C.

Results: Fully covered with MMR were 112 patients (88, 2%), 12 (9,5 %) non fully, 3 (2,4%) unvaccinated. For HBV fully covered were 120 patients (94,5%), non fully 5 (3, 9%), unvaccinated 2(1,6%). For HAV: fully covered 63 patients (50%), non fully 21 (17%), unvaccinated 42(33%). Regarding VZV, 15were fully vaccinated and 58 mentioned illness, making a total of 57,5% for immunized adolescents- 10(9,2%) underwent 1dose and 43 (33,4%) were unvaccinated and mentioned no illness. DTP-IPV adequate vaccination had 106 adolescents (83,5 %) - inadequate 19 (15%), while 2 (1,6 %) were unvaccinated. 43(33,9%) patients were vaccinated against Meningitidococcus C.

Conclusions:

1. The percentages of incomplete immunization are not negligible.

2. Parents and children should not forget that vaccination continues at puberty.

3. Taking for granted the difficulty of patients' compliance as well as their demanding programme during puberty, makes it important for the pediatrician to have completed the greater part of immunization by the age of 14.

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CLINICO- LABORATORY PROFILE OF CHILDREN WITH NEUROBRUCELLOSIS IN BIKANER, NORTHWEST INDIA

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Background and aims: Neurological manifestations of Brucellosis are rare. The aim of this observational study is to establish the evidence of neurobrucellosis in children in Bikaner.

Methods: The study is related to patients with brucellosis whose principal presenting features were neurological symptoms (headache, vertigo, dizziness, vomiting, seizure, altered sensorium and encepalopathy) along with fever. The diagnosis of active brucellosis was confirmed by raised brucella agglutination titre of 1:320 or more in the serum and confirmation of neurobrucellosis was done by raised brucella agglutination titre of 1:640 or more in the cerebrospinal fluid.

Results: This study included 11 children out of 68 having active brucellosis. The median age was 5 years. Median duration of fever was 15 days. Fever with seizures was the most common presentation (100%). Other associated neurological manifestations included irritability (88.9%), headache (77.8%), neck rigidity (77.8%), vomiting (66.7%), upper motor neuron signs (44.4%) and impaired consciousness (33.3%) with median GCS scale 9 (range 2-15). Hepatosplenomegaly and joint pain were found in 88.9% and 33.3% children respectively. CSF lymphocytosis was observed in seven (77.8%) cases. CSF Culture and staining was negative in all the cases. The response to treatment started within 10-15 days and all the children became symptom-free at the end of six weeks.

Conclusions: Neurobrucellosis is an uncommon but serious manifestation affecting central and peripheral nervous system. Treatment combination of cotrimoxazole, rifampicin and doxycyclin showed marked clinical and radiological improvement. All children were completely disease-free at the end of one year follow up.

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A CASE WITH CANDIDA ARTHRITIS

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A 10-month-old male infant presented with increasing swelling, redness, hotness and limited extension on his right knee. His physical examination showed growth retardation and multiple anomalies. There was no organomegaly. His fever was high. He had received oral antibiotic(which is not known) due to nasopharingeal infection 2 weeks before. His past medical history was remarkable. He was born at 35 gestational weeks, 1200 gr as twin boys. His brother was in good health. He was put in intensive care unit at 2 months of age and performed cardiac surgery with the diagnosis of Fallot tetralogy 30 days later. Genetic studies were normal.

His inflammatory response to infection were all positive. His IgG and IgM were high. His lymphocyte count, flow-cytometric analysis, NBT test were normal. We performed a puncture into the knee joint and harvested material for the microbiological diagnosis. Scan of knee did not revealed osteomyelitis.

Vancomycin and cephotaxim therapy were chosen considering infection with a strain of staphylococcus since the majority of septic arthritis are due to this agent in childhood. However, we were not able to overcome the inflammation until the result of microbiological studies. Five days later Candida Albicans was yielded. So, Amphotericin B was added to the therapy, course was uneventful and he improved without any complications.

In conclusion, considering his normal immunity, representing any genetic syndrome and without trauma, candida artritis was not expected. Reviewing data from the literature there are no case available like this so we decided to present the case.

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BACTEREMIA ASSOCIATED COMPLICATIONS AND MORBIDITIES IN NEONATES: THE CHARACTERISTICS, INCIDENCE AND RISK FACTORS

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Background: Few data are available on the clinical characteristics and morbidities of neonates who had complications after bacteremia, understood as any newly infectious focus or organ dysfunction directly related to bacteremia but not occur concurrently.

Methods: All neonates hospitalized in our neonatal intensive care unit (NICU) with bacteremia between 2004 and 2011 were reviewed, and those who developed bacteremia associated complication (BAC) were analyzed to identify the clinical characteristics and outcomes. Logistic regression was used to identify independent risk factors for BAC.

Results: Of 975 episodes of bacteremia, 101 (10.4%) in 93 neonates were followed by BACs with a median interval of 3 days (range, 0-17 days) after onset of bacteremia. The major BACs consisted of newly infectious focuses (n=40, 39.6%), major organ dysfunctions after septic shock (n=36, 35.6%), and neurological complications after meningitis or septic shock (n=34, 33.7%). All patients with BACs after bacteremia suffered from various morbidities, including 30 (32.3%) neonates finally died, 4 (4.3%) discharged with family requested cessation of all treatment, 17 (18.3%) with persistent sequelae, and 42 (45.2%) were stable. Independent risk factors for BACs included initial inappropriate antibiotics (odds ratio [OR], 5.7; 95% CI, 3.49-9.32), bacteremia with septic shock (OR, 5.35; 95% CI, 3.23-8.86), meningitis (OR, 8.9; 95% CI, 4.18-18.95), and group B streptococcus sepsis (OR, 3.1; 95% CI, 1.12-8.13).

Conclusions: A worth noting percentage of neonates with bacteremia suffered from sequelae or died of infections complications. Further studies regarding avoidance of infectious complications and better treatment strategies to optimize outcome are worth consideration.

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AN OUTBREAK OF PERTUSSIS IN KURDISTAN; DO WE NEED CHANGING VACCINATION POLICY

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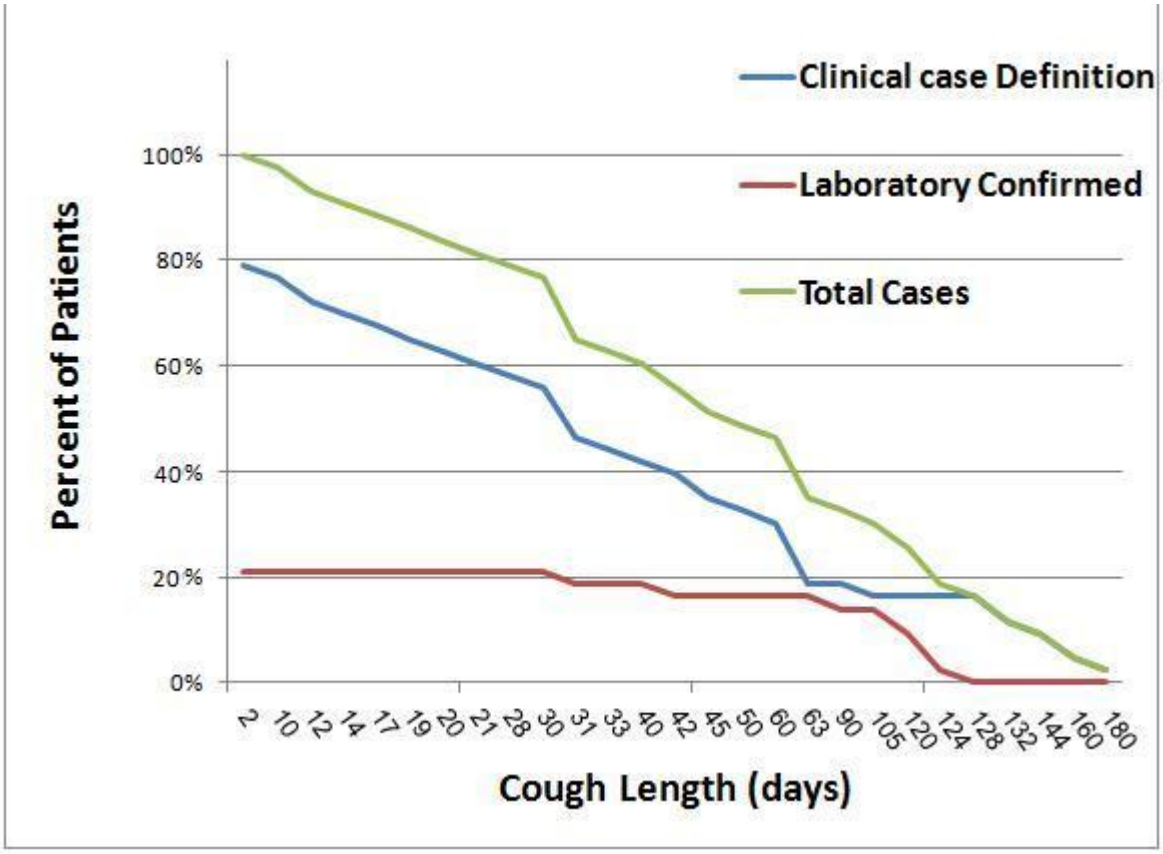
Background and aims: Pertussis is a major cause of childhood morbidity and mortality. We report a community pertussis outbreak that occurred in Sanandaj, west of Iran during May-December 2012.

Methods: All patients referred to Besat Hospital in sanandaj with symptoms and signs suggesting Pertussis were investigated. Nasopharyngeal swabs for all suspected cases were sent to Pasteur Institute in Tehran for bacterial culture and Real time PCR.

Results: A total of 96 cases were investigated because of symptoms and signs suggesting pertussis. Based on clinical findings, 52 patients fulfilled WHO clinical case definitions for Pertussis. Culture of nasopharyngeal specimens were negative in all patients, however Real time PCR were reported positive in 10 cases to date including 4 cases with cough duration of less than 2 weeks. These cases classified as "Laboratory confirmed" based on WHO case classification. Twenty nine cases (55.8) occurred in infants aged < 6 months. Cough duration in 48 (90.7%) patients were longer than 2 weeks. In all cases (100%) cough was paroxysmal that followed by cyanosis in 40 patients (76.9%). Posttussive vomiting was present in 31 (59.6%) cases as well as whooping in 13 (25%) patients.



[Figure 1- Duration of Cough in Pertussis Patients]

Conclusions: Weaning of immunity due to vaccine failure may be the cause of pertussis outbreaks. Attention should be paid to start DTP1 at earlier ages and vaccination of adolescents to protect newborn infants due to the higher incidence and mortality rate in this age group.

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MENINGOCCAL C CONJUGATE VACCINE COVERAGE IN VALENCIA. SPAIN. ESTIMATION BY A MULTIPLE IMPUTATION ANALYSIS

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Background and aims: Meningococcal C conjugate vaccination (MCCV) is very effective in controlling the disease, and shows herd immunity when high vaccine coverage is reached in adolescents and young adults.

MCCV schedule is expected to be changed in the near future to provide higher protection to the adolescents. Before that, it is then important to have reliable data on vaccine coverage.

The Valencian Vaccine Information System (VIS) is a population-based computerised system set in place in 2001. Its sensibility and specificity have increased over the years. Multiple imputation, a technique for analyzing data sets with missing values, can be applied to improve precision of vaccination coverage.

Methods: Vaccination status of 1880 subjects taking part in a seroprevalence study was assessed reviewing the VIS. Cases with no information about the vaccine could be either vaccinated and not recorded in the system or not vaccinated. As we are unable to know their actual vaccine status, they were imputed to two groups: vaccinated and non-vaccinated, according to the percentage of seroprotection at every age group. A Bayesian mixture model with two populations was carried out to know the percentage of vaccinated in those without registry.

Results:

AGE GROUP (YEARS)	VACCINE COVERAGE OF THE SAMPLE IN THE VACCINE REGISTRY % (95% CI)	VACCINE COVERAGE OF THE POPULATION IN THE VACCINE REGISTRY % (95% CI)	VACCINE COVERAGE ASSESSED BY MULTIPLE IMPUTATION % (95% CI)
3-4	99,4 (98,4-1,00)	85,6 (85,4-85,7)	99,1 (97,8-99,8)
5-6	93,6 (89,0-98,2)	90,1 (89,9-90,3)	93,9 (88,9-97,3)
7-8	90,3 (85,1-95,5)	89,2 (89,0-89,4)	92,1 (86,8-96,0)
9-11	74,3 (68,4-80,2)	80,3 (80,1-80,5)	83,6 (77,3-89,6)
12-13	77,9 (71,5-84,3)	94,7 (94,6-94,9)	87,7 (82,0-92,8)
14-16	80,1 (73,9-86,4)	93,2 (93,1-93,4)	87,4 (81,6-92,4)
17-19	70,7 (64,8-76,6)	76,4 (76,1-76,6)	89,3 (83,5-94,2)
20-21	64,4 (54,3-74,4)	59,7 (59,3-60,0)	88,5 (80,5- 95.3)
22-29	24,4 (17,6-31,1)	20,3 (20,2-20,4)	67,6 (54,0- 80,4)

[Vaccine coverage by multiple imputation]

Conclusion: Vaccine coverage is higher than the figure given by the VIS, especially in the age groups targeted for the catch up, that took place in the years 2000-2004.

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ANTI-INTERLEUKIN-6 AND ANTI-TNF-ALPHA TREATMENTS DO NOT HAVE A NEGATIVE IMPACT ON THE CYTOMEGALOVIRUS-SPECIFIC INTERFERON-GAMMA RESPONSE IN JIA PATIENTS IN VITRO

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Previous studies showed lower proportions of CD28+ T-cells in Cytomegalovirus (CMV)-seropositive healthy donors (HD), which could not be shown in patients with Juvenile Idiopathic Arthritis (JIA), a T-cell-mediated autoimmune disease in children and adolescents. However, data on CMV-specific immune responses in JIA patients on anti-cytokine-treatments are missing.

This study determined the CMV-specific immune response in patients with JIA and age-matched HD using in vitro blockade of Interleukin-6(IL-6) and tumour-necrosis-factor-alpha(TNFalpha).

Peripheral blood mononuclear cells (PBMCs) and serum samples were obtained from 5 JIA patients in clinical remission on medication with non-steroidal anti-rheumatic drugs and 4 HD. CMV-specific IFNgamma-production was determined by ELISPOT following stimulation with CMV-antigens (CMVpp65,CMV-IE) in combination with monoclonal antibodies against IL-6 and TNFalpha. Results were expressed in spot forming units (SFU)/1000000 cells.

CMV-seropositive JIA patients showed a significant higher number of IFNgamma-producing effector T-cells (CD4+CD45RA-CD28-) (39.03±6.54%) than CMV-seronegative JIA (16.55±2.44%) . No differences were found in the IFNgamma-production by CMV-specific T-cells between HD and JIA in the presence of anti-TNFalpha (JIA:27.8% vs. HD:27.3%), but a trend to lower IFNgamma-production by anti-IL-6 (JIA:13.3% vs. HD:35.0%). Furthermore, the IFNgammma production following CMVpp65 stimulation was not affected in the presence of anti-IL-6 (CMVpp65:25.56±13.82% vs CMVpp65+anti-IL-6:13.33±10.32%,p=0.138) or anti-TNFalpha (CMVpp65:25.56±13.82% vs CMVpp65+anti-TNFalpha:27.78±13.17%,p=0.686) in JIA patients.

Our preliminary findings did not reveal a significantly altered immune response in JIA patients against CMV in vitro. However, long-term aspects of chronic stimulation of the T-cell immune system by CMV as known from healthy elderly persons resulting in exhaustion of CD28- T-cells may follow in older age.

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CLINICO DEMOGRAPHIC PROFILE OF DENGUE AMONG ADOLESCENT PATIENTS ADMITTED AT A TERTIARY HOSPITAL IN QUEZON CITY JANUARY´07 - DECEMBER´11

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Background: Dengue Fever and Dengue Hemorrhagic Fever has emerged as the most important mosquito - borne human viral disease in the Philippines. Ever since the first outbreak of Dengue Hemorrhagic Fever (DHF) in 1956, similar epidemics have occurred in the country at approximately five - year intervals with increasing numbers of cases until 2001.

Aims: To describe the Clinico - Demographic Profile of Dengue Among Adolescent Patients 10 - 18 years old Admitted At A Tertiary Hospital in Quezon City from January 2007 - December 2011.

Method: It is a descriptive study among adolescent patients 10 - 18 years old diagnosed with Dengue Fever and Dengue Hemorrhagic Fever from 2007 - 2011.

Results: The highest percentage of Dengue Fever and Dengue Hemorrhagic Fever among adolescent patients admitted at a tertiary hospital was seen in the year 2009 (27.91%) and the lowest was in 2011 (10.46%). Majority of the cases among adolescent patient belonged to ages 10 - 13 years old (early adolescence) accounting for 41%. The mean age was 12 years.

Conclusion: Year 2009 had the highest percentage of admission and 2011 had the lowest percentage of admission. Researchers recommend further studies on admission criteria of Dengue Fever and Dengue Hemorrhagic Fever, complete data base, comparison studies on survival and prevalence of the disease with other hospitals and case - control study to identify independent variables for mortality.

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EFFICACY OF ANTIMICROBIAL PROPHYLAXIS IN CHILDREN WITH UTI OR VUR: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Antibiotic prophylaxis is though as one of the few useful interventions to prevent infectious recurrence in children after UTI and/or with VUR. Although this recommendation has been applied for many years, several recent randomized trials comparing antimicrobial prophylaxis vs. placebo failed to demonstrate benefits to prevent recurrent symptomatic UTI. However, meta-analyses results remained conflicting. We aimed to update systematic reviews to study whether antibiotic prophylaxis was effective to reduce recurrent UTI in children after UTI and/or with VUR.

Methods: A systematic review identified all relevant randomized trials.

Results: From the 536 relevant articles, 10 were included, representing 1756 children; 3 (30%) were placebo controlled trial, co-trimoxazol was the antibiotic used as prophylaxis in most of studies and the follow-up ranged from 1 to 4 years. Antibiotic prophylaxis was significantly associated to infectious recurrence reduction (pooled RR: 0.7 [0.6-0.8]) when pooling all trials, as well as when pooling only data from trials that had included children UTI regardless VUR (pooled RR: 0.7 [0.5-0.9]). However the association turned non significant in the sub-group of patients with VUR (whatever UTI): pooled RR: 0.8 [0.6-1.0]. There was no evidence of heterogeneity ($p > 0.1$).

Conclusions: We found conflicting results between the global analysis and the sub-group analysis of patients with VUR: meta-analysis on individual data be warranted to better characterize in which patients prophylaxis may prevent from infectious recurrences, or not. Lastly, none of the included trials were equivalence trials whereas such design are required to draw a conclusion on non therapeutic efficacy.

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EFFICACY OF ANTIBIOPROPHYLAXIS FOR CHILDREN WITH UTI AND/OR VUR: A SYSTEMATIC METHODOLOGICAL REVIEW OF THE PUBLISHED META-ANALYSES

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Background: Antibiotic prophylaxis is though to be a useful intervention to prevent children with UTI and/or VUR from infectious recurrence and scaring. However, this recommendation is nowadays debated because trials found contradictory conclusions, and meta-analyses (MAs) of them also demonstrated conflicting results. We aimed to perform a systematic review (SR) of SRs published to clarify their strengths and weaknesses and tempt to draw a conclusion.

Methods: All SRs on antibiotic prophylaxis in children with UTI and/or VUR were systematically identified.

Results: From the 116 abstracts identified, 2 SRs and 7 MAs were included, all published since 2000. This represented 15 original trials published since 1968, and 6240 children. Two MAs included children with VUR, 5 included children with UTI whatever VUR. MAs included 6 to 11 trials mostly because on different inclusion criteria (UTI or VUR only). The SR methodological quality was good, however the MAs methods quality was intermediate: 86% searched for heterogeneity but without further explorations; 43% searched for publication bias. All MAs found non-significant RR for recurrent UTI or renal scarring, 2 MA showed significant RR for recurrent positive urine culture. Their conclusions varied between antibiotics efficacy (1), non-significant results (4), and evidence of no efficacy (2), resulting in confusion between efficacy and equivalence trials.

Conclusions: MA experimented difficulties to draw conclusions about antimicrobial prophylaxis because of varied inclusion criteria, and variability. MA on individual patients data would help in analyzing data regarding VUR grade, and other patients' characteristics to make definitive conclusion for some patients' groups.

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IMPACT OF VARICELLA VACCINES IN CASTILLA Y LEON (SPAIN)

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Background and aims: The varicella vaccine was included in the Public Health Childhood Vaccination Program of Castilla y Leon (Spain) in 2005 for susceptible aged 11 years. It is also recommended by pediatricians individually in aged 12-15 month. The aim of this study is to estimate the compliance of both recommendations and the potential impact on the incidence of varicella in Castilla y Leon.

Methods: Varicella is a notifiable disease. Since 2007 it is also an individualized notifiable. Annual incidence rates per 100.000 persons during study period (1999-2012) and aged-specific incidence rates (2008-2012) were calculated. We compared the annual average incidence rate between two periods: pre-introduction (1999-2005) and post-introduction vaccine (2006-2012). Aged 11 years and 12-15 month varicella vaccine coverage came from Regional Vaccine Program (2011- 2012).

Results: There was a significant decline of 48,5% (95%CI 0,66-0,70; p< 0,05) between annual average incidence before and after vaccine use (437 vs 225). Nevertheless, in 2012 we have found a rise of 36% with respect to 2011. Concerning age-specific rates, we have detected a significant increased in aged < 1 year (19,3%) and in aged 5-9 years (40,8%) .The monitoring vaccine coverage has reached 13-18% of the whole cohort aged 11 years and 44-60% aged 12-15 month in 2011- 2012.

Conclusions: The incidence of varicella has moderately decreased after introduction of vaccine. However an increased on the incidence and a change on the presentation age pattern have been observed in 2012. The inappropriate vaccine coverage could be contributed to these results.

1103

INTRACRANIAL ANEURYSM FROM HIV ASSOCIATED VASCULOPATHY IN A PAEDIATRIC PATIENT

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Objective: Cerebral vasculopathy is a rare complication of HIV infection. Surgical treatment options can be limited because of complexity and risk. Optimal control of HIV infection and regular monitoring can improve outcome.

Methods: Case review of a 9 year old boy HIV infected with right terminal ICA and MCA aneurysm that is suggestive of HIV associated vasculopathy.

Results: A 9 year old boy with a 5 month history of recurrent tonsillitis and weight loss was admitted one month post tonsillectomy with throat pain, abdominal pain, pallor and dehydration. He also had an episode of rectal bleeding, oral thrush and lymphopenia. The HIV antibody screen was positive with a high HIV viral load and low CD count thus antiretroviral therapy was commenced. Whilst on treatment he developed a fever which did not improve on antibiotics or empiric antimycobacterial therapy. Investigations included a head CT, which revealed a right terminal ICA and MCA aneurysm. He was also found to have a HHV6 viraemia. Following ART, the clinical symptoms have improved, with an undetectable viral load and a rapid increase in CD4 counts. Following treatment, he remains asymptomatic, but there has been a slow increase in the size of the aneurysm, possibly secondary to immune reconstitution inflammatory syndrome. This is being closely monitored jointly by medical and neurovascular teams. Currently, surgical intervention is considered high risk.

Conclusion: HIV associated vasculopathy needs to de considered in all HIV positive patients. Optimal management is at present unclear but will involve both medical and surgical approaches.

1104

THE FIRST REPORT OF OROPHARYNGEAL CARRIAGE OF NEISSERIA MENINGITIDIS IN PORTUGAL: DATA FROM 600 UNIVERSITY STUDENTS IN 2012

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Background and aims: Portugal introduced conjugate meningococcal C vaccines (MenC) into their national universal schedule (3,5&15M) and conducted a catch up programme (age up to 18Y, 80-90% coverage) in 2006. In January 2012, the 3&5M doses were discontinued. MenC disease incidence has fallen but there are no data on carriage.

Methods: Oropharyngeal (OP) swab samples, demographic and clinical data were collected from healthy University of Coimbra students between 21 & 25th May 2012. Swabs in STGG broth, frozen at -80^{0}C within 3h were batch cultured using standard techniques (Oxidase, Gram stain and API-NH tests) for Neisserial spp. Analysis, using Stata 12.1, included logistic regression to assess predictors for carriage. Serogrouping is ongoing.

Results: Neisseria meningitidis was cultured from 13.6% (n=76/557) OP swabs (27.5% male, mean age 20.7Y, range 18-32). Neisseria lactamica and other Neisserial species were cultured from 2.9% (n=16). In univariate analysis, the number of people in the house (p=0.005) and antibiotic use in the previous month (OR 0.12 95% CI 0.02-0.84 p=0.002) were associated with carriage and remained important in multivariable analysis. Antibiotic use at the time of swabbing (2.9%), smoking (9.2%), smoking in the household (2.5%), gender, living in student residences (21.2%), rhinitis score and presence of and duration of cough were not significantly associated with carriage prevalence.

Conclusions: OP carriage rates are concordant with studies in other European countries. There was no suggestion of respiratory symptoms in association with carriage. Data on carriage by serogroup will inform future meningococcal immunisation policy.

1105

THE DISTRIBUTION OF RESPIRATORY VIRUSES IN CHILDREN WITH ACUTE RESPIRATORY ILLNESSES. REPORT FROM ROYAL COLLEGE GENERAL PRACTITIONERS SENTINEL SURVEILLANCE NETWORK

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Background and aims: The Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) operates a sentinel swabbing scheme during the winter season across England. Swabs are taken from patients with acute respiratory illness. This study aims to describe the contribution of respiratory pathogens from 2003/04 to 2011/12 in children of age groups < 1, 1-4 and 5-14.

Methods: The proportion of positive virological samples was analysed by virus type and age group. These viruses included influenza H1, H3, B, RSV and HMPV.

Results: During 5 season RSV has been the highest contributor to virus positive samples in the < 1 age group, in 2 seasons RSV was the joint highest contributor with either influenza H1 or H3. During 4 seasons in the 1-4 age group RSV has been the highest contributor to virus positive samples, 3 seasons influenza H3 was the highest contributor and for 2 seasons (pandemic seasons) influenza H1 was the highest contributor. During the past 9 season, in the 5-14 age group, 5 were to influenza H3, 2 were to influenza H1 and 2 were to influenza B.

Conclusions: During the past 9 seasons RSV has had the highest contribution to positive virology samples in the < 1 and 1-4 age groups; influenza H3 has had the highest contribution to positive virology samples in the 5-14 age group.

1106

WATCH OUT - HLH CAN CATCH YOU OUT!

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Background: Haemophagocytic lymphohistiocytosis (HLH) is rare but increasingly recognised. Secondary HLH follows immunolgical activation. The exact aetiology is seldom identified. Diagnostic difficulties arise as both clinical and laboratory criteria often overlap with severe sepsis which is conmmon in PICU.

Methods: We conducted a retrospective study of our experience over a one year period of four children diagnosed with HLH. More than 1,000 children are admitted annually, approximately 85% of these being intubated.

Results: Patient details and diagnostic criteria are illustrated in table 1 shown below. Probable causation was established in all four patients. Survival (75%) was favourable in this small series. Nevertheless, these patients had considerable morbidity. One patient had seven re-admissions to PICU within one year. Another had a protracted hospital stay of eleven months.

Case	Age and Gender	Probable Cause. On-going Symptoms	Initial Ferritin Level (mcg/l)	Time to Diagnosis of HLH	Status
1	Male age 2 years	Meningococcus. MSOF Fever Hepatomegaly	1021.4 mcg/l Peaked at 11,262	28 days Bone marrow+ve	Died
2	Female age 18 months	Meningococcus. Persistent fever CNS features	2,170.5 mcg/l Peaked 5,502	22 days Bone marrow+ve	Alive
3	Female 14 years	Streptococcus Persistent fever, rash.	51,105 mcg/l peaked at diagnosis	28 days Bone marrow+ve	Alive
4	Male 8 months	Cardiopulmonary by-pass. Rash abnormal haemodynamics	373 mcg/l Peaked at 18,373	23 days Bone marrow+ve	Alive

[Table 1]

Conclusions: Diagnosing HLH in already critically ill patients on PICU remains challenging and can easily be confused with nosocomial infection. Diagnostic criteria may be masked by treatment modalities such as haemofiltration which reduces fever. Repeated reassessment is necessary as some criteria may be absent initially but subsequently fulfilled.

We would suggest relentlessly considering the diagnosis of HLH in children with multiorgan dysfunction who do not respond to maximal medical therapy.

1107

ESTIMATING THE PNEUMOCOCCAL VACCINE COVERAGE AND VACCINE SCHEDULE ADHERENCE IN 5 EUROPEAN COUNTRIES

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Introduction: Pneumococcal conjugate vaccine (PCV) is part of national immunization program (NIP) in children in most European countries since 2006-2008 with 2+1 or 3+1 schedules. The aim of this study was to describe the pneumococcal vaccination coverage and schedule adherence in 5 European countries.

Methods: Web-based survey was conducted in September - October 2012 to mothers having at least one child of 9 to 30 months of age with available vaccination booklet in France, Germany, Spain (excepting Madrid and Galicia regions) and Switzerland and face to face interview survey in Portugal.

Results: In children 9-18 months of age, total of 57 to 85% received at least one dose of PCV. Among those children, 54 to 98% had completed the full primary series according to country recommended schedule (Table). Regarding other childhood vaccine DTP, 94 to 97% of children received at least one dose. In children 19-30 months of age with completed full primary series, only 43 to 92% had received the booster dose.

Conclusions: Pneumococcal vaccination coverage of pneumococcal vaccination is considerably low compared to that of other childhood vaccine, DTP. The adherence to full primary series and booster administration is suboptimal. In general, the vaccine coverage and schedule adherence is higher in countries where PCV was in NIP with 2 + 1 schedule. Adherence to recommended vaccine schedule should be a public health priority.

	France 2+1 (NIP)	Switzerland 2+1 (NIP)	Germany 3+1 (NIP)	Spain 3+1	Portugal 3+1
9-18 months of age					
≥ 1 dose of PCV*	85 % N=232	69% N=95	73% N=199	78% N=212	57% N=157
Full PCV series**	90% N=143	98% N=74	66% N=132	54% N=114	68% N=107
≥ 1 dose of DTP	97% N=265	94% N=130	95% N=259	95% N=258	94% N=259
19-30 months of age					
1 booster dose***	81% N=150	92% N=89	66% N=121	63% N=112	43% N=68

[The adherence to pneumococcal vaccination schedule]

1108

INFECTIONS FOLLOWING KIDNEY TRANSPLANT IN CHILDREN

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Introduction: Infections after kidney transplantation (KT) remain an important cause of morbidity and mortality.

Aim and methods: A retrospective study of all children undergoing KT in our department from 2006 to 2011 was performed to characterize the infections occurred during the first 6 months post-transplant.

Results: Thirty two children were submitted to KT; 20 were male with a mean age at transplant of 11,5 years. The most common causes of chronic renal disease were urologic (20). Twenty eight (87,5%) presented infections during this period (2,4 infections/patient) with a predominance of UTI (21 - 1,56 UTI/patient). UTI were more frequent in children with a history of previous recurrent UTI ($p < 0.05$). Klebsiella (20) and Escherichia coli (16) were the commonest organisms. Seventeen (53,1%) had the first infection during the first month (14 UTI and 3 related to the surgery). Viral infection occurred in 19 (59,4%); Cytomegalovirus was the commonest (11) and was more frequent ($p < 0.05$) in donor (+)/ recipient (-) cases. A polyomavirus disease with meningitis was registered. No invasive fungal infections occurred. The majority were of mild or moderate severity. No deaths occurred. Acute reversible graft dysfunction was presumed to be associated with infection in 7 cases (21.9%).

Conclusions: A great number of patients presented an infection after KT, mainly UTI, which was significantly associated with recurrent infections before KT. No permanent allograft dysfunction occurred. The prevention of infections and adequate early treatment are critical to the success of KT.

1109

POPULATION PHARMACOKINETICS AND DOSING OPTIMIZATION OF VANCOMYCIN IN CHILDREN WITH MALIGNANT HEMATOLOGICAL DISEASE

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Background: Vancomycin is widely used for the treatment of moderate to severe infections that are caused by vancomycin susceptible bacteria, and primarily coagulase-negative Staphylococci and methicillin-resistant Staphylococcus aureus species. Its systemic clearance was reported to be higher in adults with malignant hematological disease compared with non-oncology adults and an increased dosing regimen has been proposed in these patients. In the absence of data, an optimal dosing regimen is not available in children. The aim of this work was to evaluate the population pharmacokinetics of vancomycin in children with malignant hematological disease and to optimize vancomycin therapy.

Methods: Vancomycin therapeutic drug monitoring (TDM) concentrations were collected prospectively in children with malignant hematological diseases. Population pharmacokinetic analysis was performed to optimize dosing using NONMEM software.

Results: One hundred and two serum vancomycin concentrations from 70 children were analyzed. The concentrations ranged from 2.3 to 36.4 mg/L using empirical dosing regimen (40-60 mg/kg/d). A one-compartment pharmacokinetic model was developed. Body weight and creatinine clearance were identified as significant covariates. Vancomycin clearance was higher in children with malignant haematological disease than that in non-oncology children. Model-based optimized dosing was tested in simulated clinical trials, which achieved the adequate pharmacokinetic-pharmacodynamics breakpoint ($AUC_{0\text{-}24}$/MIC ratio).

Conclusion: An optimized dosing regimen, taking into account bodyweight, creatinine clearance and susceptibility of the pathogens involved, could be used in routine to individualize vancomycin therapy in children with malignant haematological disease. A prospective study is warranted to evaluate its potential clinical benefits and safety.

1110

OROPHARYNGEAL SWABS FOR NEISSERIA MENINGITIDIS (NM) TAKEN INTO ENRICHMENT BROTH, STORED FROZEN AND BATCH CULTURED SHOW LITTLE LOSS OF SENSITIVITY

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Background and aims: It is currently recommended that oropharyngeal swabs obtained in investigation of meningococcal carriage should be plated onto agar immediately or, if taken into transport medium, plated within 5 hours. This makes such studies expensive and logistically complex. It would be useful if swabs could be frozen and batch processed in a single laboratory later.

Methods: Oropharyngeal (OP) swab samples collected from healthy school students, were plated immediately onto agar plates and then placed into vials of STGG broth, held at 4°C for up to 3 hours, vortexed and frozen at -80°C. Subsequently 100µl of broth from all vials holding swabs identified to be Neisseria sp. on immediate plating were plated and cultured using the same standard methods employed for the direct plates.

Results: Of 1069 swabs collected, immediate plating yielded 107 Nm isolates. Of these 107 samples, 96 frozen swab-in-broth were also positive for Nm (sensitivity 90% vs. gold standard). A subset of these isolates were genotyped and where the genotype was resolved were found to be the same isolates identified by direct plating. Corresponding results for N. lactamica were 30/35 (86%).

Conclusions: Meningococcal carriage studies are important because conjugate meningococcal vaccines' effectiveness can be enhanced by their impact on transmission; the impact of newer protein-based meningococcal vaccines on carriage therefore needs to be investigated. The scientific, logistic and economic gains resulting from rapid sampling and batch processing may outweigh the losses resulting from 10% reduction in sensitivity particularly for populations where carriage rates are high.

1111

THE EFFECTIVENESS OF SEASONAL INFLUENZA VACCINE IN CHILDREN: 2012 ISTANBUL

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Background and aims: Influenza vaccine is not frequently preferred in Turkish children because of some uncertain ideas on the effectiveness of vaccine. Aim of the study was confirmation of the effectiveness of seasonal influenza vaccine in children living in Istanbul.

Methods: This retrospective study was conducted with evaluation of the patients charts. All medical data was stored in computer system. All cases was admitted to hospital between September 2011 and June 2012. Some of patients was vaccinated by Fluarix GSK September and December 2011. Influenza case was defined as a patient with symtoms of influenza and positive influenza rapid test in nasal swabs.

Results: In study period, totally 560 patients were clinically suspected as influenza in ambulatory setting. Influenza rapid test was positive 117 cases (20,9%). Among 560 cases 16 of them was vaccinated with Fluarix GSK. All of the vaccinated group influenza rapid test was negative. Any of confrimed influenza case was in vaccinated group. All influenza confirmed cases were in unvaccinated ($p< 0.01$). The effectiveness of influenza vaccine was estimated as 100%. Among 560 cases, 197 cases were hospitalized (35.1%). Hospitalization rate was two fold higher in unvaccinated group than vaccinated group (18,7% vs 35,6%).

Conclusion: Seasonal influenza vaccine in 2012 is strongly protective and effective for influenza in children living in Istanbul.

1112

RENAL ASPERGILLOSIS IN A SIX-YEAR-OLD BOY WITH BURKITT'S LYMPHOMA

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Background and aim: Invasive aspergillosis is usually observed after allogenic hematopoietic stem cell transplantation (HSCT) and in patients treated with high doses of chemotherapy, remaining neutropenic for long periods. We aim to describe an unusual case of renal abscess due to Aspergillus in a child with Burkitt's Lymphoma (BL).

Case report: A 6-year-old boy was diagnosed with BL in January, 2011. He was treated with standard chemotherapy until 05/2011. Two months after discontinuation of chemotherapy he relapsed as an isolated mediastinal mass. He was treated with chemotherapy and rituximab. In January, 2012, he was diagnosed with a nodular lesion in the right kidney, biopsied to rule out another relapse. Histopathology revealed hyphae infiltration and the RT-PCR was positive for Aspergillus fumigatus. Aspergillosis had never been diagnosed in this patient and chest CT and sinus MRI were normal. Despite the use of voriconazole for 21 days, the lesion increased, and was surgically removed. The culture grew Aspergillus fumigatus complex. Two months after, the patient underwent autologous HSCT (bussulfan/cyclophosphamide). On D+4, while on voriconazole, he had a recrudescence of the fungal lesion in the same kidney. Nephrectomy was performed for infection control, and culture grew the same agent. Galactomannan was always negative.

Conclusions: Renal abscess is an extremely rare form of invasive aspergillosis and may be included in the differencial diagnosis in immunocompromised patients. Combined medical and surgical therapy may be necessary.

1113

STREPTOCOCCUS PNEUMONIAE: SEROTYPE PREVALENCE IN NASOPHARYNGEAL CARRIAGE IN CHILDREN WITH NEPHROTIC SYNDROME AND CLINICAL IMPLICATIONS

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Background and aims: Nephrotic syndrome (NS) is common in children. Infection is a common complication and Streptococcocus pneumonia is one of the most common pathogen. The aim was to determine the carriage rate, serotypes and antibiograms of Streptococcus pneumoniae in nasopharynx of children with NS.

Methods: A Prospective study, 60 children up to 12 years of age, clinically diagnosed as NS and 60 healthy children (control) were enrolled. Nasopharyngeal swabs were cultured and morphologically suggestive colonies were identified using standard methods. Serotyping was done using group & type specific antisera. Antibiograms of oxacillin, chloramphenicol, vancomycin and cotrimoxazole were determined by Disk Diffusion test. MICs of penicillin, azithromycin, ceftriaxone and ofloxacin were obtained by E-Test.

Results: 55.5% of NS children were vaccinated with PPV23 pneumococcal vaccine. Carriage rate of pneumococcus in patients with NS was 18.3%, (Relapses-54.5%, Steroid dependent-27.3%, 1st episode-18.2%) and 11.6% in healthy children. Only 36.6 % of the NS patients with pneumococcal carriage were vaccinated. Among NS patient's serotype 19 was the most common (45.5%), followed by non-typable (36.4%), and non vaccine type-H group (18.2%). However strains isolated from vaccinated NS children were non typable and non-vaccine type H -stains. In contrast in healthy children non-vaccine type H (57%) was the predominant serotype. All strains were susceptible to all tested antibiotics, except cotrimoxazole (100% resistant).

Conclusion: Penicillin remains drug of choice for suspected pneumococcal infections. Serotype 19 is the most commonly isolated from NS patients however continuous surveillance to monitor “serotype switching” is essential to effective vaccination.

1114

HYPERLEUKOCYTOSIS AND NEUTROPHILIA IN INFANTS AND SMALL CHILDREN TUBERCULOSIS

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Background: We discuss the presence of hyperleukocytosis associated with left deviation on the leukocytary formula (until myelocyte or metamyielocyte) at the onset of tuberculosis in infants and small children. This intense granulocytic reaction associated with positive acute phase reactants can be incorrectly interpreted as a severe, unspecified bacterial infection and treated as such, without the expected outcome. This delay of diagnosis can bring serious damages, like miliary or meningitis.

Material and method: We discuss cases diagnosed with tuberculosis in infants and small children diagnosed at a Tertiary Pediatric Clinic from Craiova, Romania, between 2002-2011.

Results: We found 15 cases diagnosed with tuberculosis; 2 cases evolved until meningitis and 3 where diagnosed with miliary tuberculosis. The remaining cases were diagnosed as primary pulmonary tuberculosis. We registered a delay of tuberculosis diagnosis between 8 days and 3 weeks, patients being treated for various respiratory infections, associated with prolonged fever syndrome, dystrophy. Hyperleukocytosis varied from 10000-15000/mmc until 39200/mmc. The majority of cases presented over 70% of neutrophils on the leukocytary formula and 2 cases had a severe left deviation until metamyielocyte. The patients presented also elevated acute phase reactants, like ESR and thrombocytosis.

Conclusion: It is known that neutrophils, like the macrophages, accumulate in the early stages at the site of tuberculosis infection, but there are incapable to destroy the bacilli. We can deduce that the stimulation of the hematogenous bone marrow has an echo in the periphery that can be interpreted as an alarm sign for the diagnosis of tuberculosis.

1115

SPECTRUM OF CARDIOVASCULAR MANIFESTATIONS OF SEVERE MALARIA IN CHILDREN IN BIKANER (NORTHWESTERN INDIA)

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Background and aims: A little attention has been paid for cardiac involvement in malaria especially in pediatric age group. This study evaluates the relationship of various cardiovascular attributes to the morbidity, clinical outcome and mortality in children with severe malaria.

Methods: This prospective study was conducted on 104 admitted children with severe malaria from 2010 to 2012. They were divided in two groups depending on presence of cardiovascular manifestations and then compared in terms of demographic, clinical, electrocardiographic (ECG) and echo-cardiographic (ECHO) parameters.

Results: The prevalence of cardiovascular manifestation in severe malaria cases was 16.3% (more common with P.falciparum malaria). In cardiac group, mean left ventricular end diastolic diameter (LVEDD) (X^2-3.84, p=0.0001) and mean left ventricular end systolic diameter (LVESD) (X^2-5.18, p=0.0001) were significantly greater than the non-cardiac group. The impairment in mean left ventricular ejection fraction (EF) (X^2-2.82, p=0.005) was also significant in the cardiac group but diastolic functions were not much differing in both the groups. The abnormal ECG findings like nonspecific ST-T changes and low voltage QRS complexes were also significantly more frequent in the cardiac group (X^2-7.17, p=0.007). Mean duration of hospital stay (8±2.3 days) was significantly longer in the cardiac group (X^2-4.54, p=0.0001). The mortality risk (35.2%) was significantly greater in the cardiac group (X^2-21.80, p=0.0001). No long term cardiovascular abnormalities were seen in survived children.

Conclusions: We should always look for cardiovascular manifestation in children with severe malaria so that early diagnosis and timely intervention can be done to reduce morbidity and mortality.

1116

OUTBREAK OF HAND-FOOT-AND MOUTH DISEASE IN NORTHERN GREECE

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Background and aim: Hand-foot-mouth disease (HFMD) is a benign febrile exanthematous disease of childhood caused by human enteroviruses. Aim of this study was to determine the clinical and epidemiological characteristics of HFMD in a recent outbreak in Northern Greece.

Methods: Data of all children who were examined between October and December 2012 in the outpatient clinic of our department, and diagnosed as having HFMD, were collected and analysed. In all cases, the diagnosis of HFMD was clinical and based on strictly typical characteristics of the disease. During the above period, a total of 230 children were examined (study group).

Results: Most of cases (52,6%) occurred in November. There was a clear predominance of boys: 147 males (64%), 83 females (36%) (ratio 1,8:1). The mean age was 3,5 years old (3,5 months to 16 years). The majority of cases were younger than 5 years old (78.7%), and the 49,6% was 12 months to 3 years old. The course of the disease was mild, without complications. All children had a clinical appearance of tender macules or vesicles on an erythematous base mainly on the hands and feet, as well as oral ulcers with enanthema in the hard palate. Only few patients presented fever. One girl developed aseptic meningitis. No patient received any medication and all patients were cured.

Conclusions: In this seasonal outbreak, HFMD was mild and self-limited. Males below 5 years old were predominantly affected. Since the disease is highly contagious, good hygiene practices can help to reduce it.

1117

APPROACHES TO THE DIAGNOSIS OF CHILDHOOD TUBERCULOSIS IN A UNIVERSITY HOSPITAL OF NORTH ITALY

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Objective: In the present study we reviewed the diagnostic approach to TB among children attending a university clinic of North Italy.

Methods: Children under 16 years of age attending the out-patient clinic of IITD from 1999 to 2012 were eligible for inclusion in the study. Diagnosis of probable TB was based on epidemiological and clinical findings suggestive of TB. Definite diagnosis of TB was based on the finding of a positive culture for Mycobacterium tuberculosis (MTB) on liquid culture.

Results: A total of 146 children were evaluated for mycobacterial disease; 67 had Non tuberculous mycobacteria lymphadenitis; TB was diagnosed in 79 children (54%).TB cases had a mean age of 8.4 years (SD± 5.1), 51% were males and 81% were foreign-born. Fifty-three (67%) had pulmonary involvement; lymphadenitis was the most frequent extrapulmonary manifestation (28/79; 35%). Twenty-six percent (20/77) informed a recent contact with a TB patient, 91% (60/66) had a positive tuberculin skin test and 86% (12/14) were Quantiferon positive. Twenty-five cases (32%) were classified as probable TB and 54 (68%) as definitive TB. The most frequent sites of MTB isolation were lymph nodes (by needle aspiration or surgical biopsy; 43%) and gastric aspirate (21%). A total of 51 drug sensitivity test were performed: 1 strain resistant to isoniazid and 4 resistant to streptomycin were identified; there was no case of resistance to rifampicin.

Conclusion: The support of a good microbiology laboratory and the attitude in pursuing microbiological confirmation resulted in a high yield of MTB isolation in children with TB.

1118

LONG-TERM EXTENSION STUDY OF GARDASIL® IN ADOLESCENTS; RESULTS THROUGH YEAR 8

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Objective: We describe the second interim effectiveness data for a long-term immunogenicity, safety, and effectiveness study of the quadrivalent HPV vaccine (qHPV) GARDASIL® among adolescents.

Methods: 1781 sexually naïve boys and girls were assigned (2:1) to qHPV or saline placebo at day 1 and months 2 and 6. At the end of the base study (month 30), the placebo group received qHPV following the same regimen. Those vaccinated with qHPV in the base study are the early vaccination group (EVG). Effectiveness was assessed by calculating the incidence of HPV6/11/16/18 persistent infection or related disease. The median follow-up time for effectiveness was 6.8 years. The current analysis was done at 8 years.

Results: Vaccination-induced anti-HPV responses persisted long-term. Depending on HPV type, 64%-97% remained seropositive through year 8. The assay-dependent anti-HPV 18 response over time is consistent with that observed in other GARDASIL® clinical trials. No cases of HPV 6/11/16/18-related disease were observed. There were 2 girls and 2 boys with 6-month persistent infection due to HPV types 6 or 16. One serious adverse event was reported between months 72-96 (tonic-clonic movements) and was deemed not related to vaccine.

Conclusion: Vaccine-type anti-HPV 6/11/16/18 responses generated through administration of GARDASIL® among preadolescents and adolescents persist over the long-term, in accordance with expectations from previous GARDASIL® studies. The rate of persistent infection is similar to that seen in vaccinated populations studied in Phase II/III. No breakthrough cases of disease have been observed. GARDASIL® remains generally safe in adolescent populations.

1119

EPIDEMIOLOGICAL AND CLINICAL FEATURES OF ASEPTIC MENINGITIS: A CASE SERIES OF 20 CHILDREN

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Background and aims: Aseptic meningitis is the most common CNS infection and is mainly associated with enteroviruses. Our aim was to describe the epidemiological and clinical features of an aseptic meninigitis outbreak.

Patients and methods: Files of **c**hildren hospitalized in our department from May till August 2012 with meningitis symptoms, cerebrospinal fluid (CSF) pleocytosis and negative CSF bacteriological culture, were analysed. A total of 20 patients of this period was included. Nine CSF samples were examined with PCR for HSV, EBV, Cytomegavirus and West Nile Virus and with RT- nested- PCR for enteroviruses.

Results: The mean age of patients was 10 years. The male to female ratio was 13:7. The majority of children presented with retrovulvar headache (90%), vomiting (90%) and fever (85%). Neck stiffness was reported in 80% of children, whereas positive Kernig or Brudzinski signs were less frequent (20%). The mean CSF cell count was 209 cells/microl(45-529cells/microl) and lymphocyte cells were slightly predominant in 55% of cases. Molecular analysis with RT-nested-PCR was positive for enterovirus in 5/9 patients. Further analysis with sequencing revealed Echovirus30. All patients were treated with intravenous hydration and analgesics. The average hospital stay was 3 days and outcome was favorable in all cases.

Conclucions: This is a viral meningitis outbreak in Northern Greece most likely due to Echovirus30 with a benign clinical course and excellent prognosis. Due to lack of specificity of clinical features and laboratory findings of Enterovirus meningitis, RT-nested-PCR has proven to be an effective method for the diagnosis.

1120

DURATION OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY REGIMENS IN HIV-1 VERTICALLY-INFECTED PAEDIATRIC PATIENTS

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Background and aims: The duration of initial Highly Active Antiretroviral Therapy (HAART) regimens for antiretroviral-naïve children has not been reported in a multicentre survey. We sought to evaluate risk factors associated to short first-line HAART regimen in these patients.

Methods: Multicentre longitudinal survey of antiretroviral-naïve patients of the HIV Paediatric Cohort of the Comunidad Autónoma de Madrid. Demographics, socio-economic, clinical, immunovirological and antiretrovirals data were gathered longitudinally until December 2012.

Results: Ninety-four patients with a follow-up of 100.3 months (51.5-140.1) used a mean number of 1.6 regimens. Seventeen patients were lost to follow-up. At baseline, CD4+ count was 769 (20%) cells/ml (268-1,554) and VL was 110,000 copies/ml. Girls were less likely to discontinue first-line than boys (33% vs. 48%, respectively; P=0.011). The median duration of the first-line, second-line and third-line regimen was 39.4, 44.8 and 39.4 months, respectively. First-line was mainly based on protease inhibitors (74%). First-line regimen discontinuation was associated to poor/intermediate adherence (AHR: 5.36; 95%CI: 2.28-12.6; P< 0.001) and CD4+ count >350 cell/mm^3 (AHR: 2.63; 95%CI: 1.14-6.03; P=0.023). Despite adherence to first-line HAART, all patients achieved VL< 400copies/ml, the 75% within the first year of therapy.

Conclusions: The duration of the first-line HAART regimen observed for the children included in this study was longer than that reported for adults. Our results suggest that non-adherence remains a major concern for the duration of the first-line HAART regimen, thus it is important to identify patients at high risk for non-adherence to give special care and support to those children.

1121

CRYPTOCOCCUS NEOFORMANS - A RARE CAUSE OF CENTRAL NERVOUS SYSTEM INFECTION

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Background: Cryptococcus neoformans is an encapsulated yeast that can live in both plants and animals. Human infection is acquired by inhalation, usually occurs in immunosuppressed individuals and is rare in those with fully functioning immune system. The lung is the usual portal of entry and symptoms range from asymptomatic colonization to severe pneumonia. Depending on host factors, inoculum and virulence, the organism may disseminate either acutely or after a period of latency to extrapulmonary sites, with particular predilection for the brain.

Case report: Female with 34 months and no relevant past history was brought to the emergency department with irritability, headache, prostration with 15 days duration associated with ataxia and strabismus in the previous days. Further study revealed a normal cerebral CT scan, 6 cells/uL and low levels of glucose and proteins in cerebral spinal fluid. Yeasts were visualized by direct examination of the cerebral spinal fluid, stained by India Ink, and positive cultures for Cryptococcus neoformans confirmed the diagnosis. The immunological tests were normal. She was admitted in Pediatric Intensive Care Unit for neurological monitoring and treated with amphotericin B, flucytosine and fluconazole. She was discharged 1 month and 3 weeks later and currently she is asymptomatic without neurological deficits.

Conclusions: Cryptococcus neoformans' infection in healthy children can be associated with the contact with pigeon excrements' contaminated soil. The authors highlight the importance of epidemiological context and the early diagnosis for a prompt treatment.

1122

EXTREMELY LOW BIRTH WEIGH PREMATURE NEWBORNS AND NEONATAL INFECTION

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Introduction: Premature with extremely low birth weight represents a premature with birth weight< 1000g.

Objectives: Authors demonstrate the increased incidence of infections at a lot of premature newborns with extremely low birth weight and existing risk factors.

Material and method: The study was done in the Premature and Neonatology, on 98 premature newborns with extremely low birth weight hospitalized on a period of four years.

Results and discussions: At the studied lot we found 86(87,75%) cases with different forms of infections.

Out of these - 45(52,32%) presented early onset in the first 3 days of life and 41(47,67%) presented infection with late onset.

Among the risk factors of neonatal early sepsis maternal infection is decisive (45,70%). For late neonatal sepsis factors risk are: immaturity of the means against existing infections at premature, usage of invasive care techniques, long hospitalization. Depending of hemoculture results we split systemic infection in 3 groups:

1) Septicemia with germ identified in the hemoculture with present clinical and biological context, 33 cases(38,37 %);

2) Septicemia with germ unidentified in the hemoculture or in septic origins where the clinical and biological context is obvious:34 cases(39,53 %);

3) Septicemia with germ identified in other origins where clinical and

biological aspects are present, hemoculture negative, 19 cases(22,09 %).

Conclusions: Infection is an important factor of morbidity and mortality at the newborn with extreme low birth weight and incidence is high due to long hospitalization and intensive care maneuvers.

1123

DIVERSITY OF ROTAVIRUS GENOTYPES CIRCULATING IN GREECE DURING THE POST VACCINATION ERA (2008-12)

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Background and aims: Rotavirus (RV) genotypes present natural seasonal and geographical fluctuations. Aim was to describe the diversity of RV genotypes circulating in Greece and evaluate the impact of limited vaccine uptake (coverage 20-30%) in the natural fluctuation of the virus.

Methods: Faecal samples from children < 5 years of age who visited emergency units of 19 Pediatric Hospitals with acute gastroenteritis between September 2008-August 2012 were tested for RV Group A antigen with immunochromatography. Positive samples were G and P typed through RT-PCR and sequencing using specific primers for the VP7 and VP4 genes respectively.

Results: A total of 1471 samples were genotyped; 76% belong to children ≤3 years old. Mean age of children was significantly raised in the season 2010/12 compared to 2008/10 (26.06 vs 19.62 months, p< 0,001). Seasonal peak of RV infection was during the winter months in all seasons except for the first season 2008/09 that was late in the spring. The most predominant types were G4P[8] (42%), G1P[8] (30%), G2P[4] (16%), G3P[8] (2,9%) and G9P[8] (2,1%). Significant increase of G1P[8] (75,4%) and G2P[4] (30,5%) was observed in the seasons 2010/11 and 2011/12 respectively. Uncommon or mixed infections were account for 7%, including G12P[8] which caused localized outbreaks (3.3%). High geographical diversity was found (p< 0,001), 21 children (1,2%) had received at least one vaccine dose.

Conclusions: Continuous post-vaccine surveillance is essential for monitoring the current molecular epidemiology of RV and assessing the possible genetic evolution of RV strains as an effect of vaccine implementation.

1124

TENOFOVIR- RELATED FANCONI´S SYNDROME AND OSTEOMALACIA IN A TEENAGER WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV)

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Decreased bone mineral density with TDF use in HIV-infected populations, particularly pre-pubertal and young adolescents is a known adverse effect of TDF - especially when used with a boosted protease inhibitor. We describe a 17 year old boy who developed Fanconi syndrome and osteomalacia whilst taking anti-retroviral therapy (ART) which included TDF.

An Indigenous teenager with vertically acquired human immune deficiency (HIV) presented with bone pain of six months duration. His antiretroviral therapy (ART) consisted of tenofovir disoproxil fumarate (TDF) and ritonavir-boosted liponavir. A dual emission x-ray absorptiometry (DEXA) scan revealed osteomalacia. Plain x-rays showed stress fractures of metatarsals bilaterally.

Raised serum creatinine, hypophosphataemia, glycosuria and metabolic acidosis supported a diagnosis of Fanconi syndrome. Serum vitamin D levels were low also. Discontinuation of TDF led to significant improvement in renal function and complete resolution of bone pain.

This case uniquely features renal and skeletal toxicities with resultant stress fractures of metatarsals bilaterally.

While relatively uncommon and for the most part reversible, early recognition of mild proximal tubulopathy should be screened for at each clinic visit, with particular emphasis on renal function, bone profile, vitamin D levels and urinalysis with measurement of urinary phosphate excretion.

1125

PERFORMANCE OF VACCINATION PROGRAMME IN CHILDREN WITH CHRONIC DISORDERS IN A SINGLE PRIMARY CARE SETTING IN POLAND

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Background: Polish national immunization programme consists of mandatory (free of charge) and recommended (full paid) vaccinations. Mandatory vaccination coverage rates remain on high levels (94-98%). However children with chronic disorders often have delayed immunisations.

The aim of the study was to evaluate performance of vaccinations in children with chronic disorders.

Material and methods: We analysed medical charts of 861 paediatric patients in a single primary care setting in Warsaw. Sixty children (7%) had chronic disorders (prematurity, neurological problems, asthma, food allergy, heart defects, haemolytic anaemia and neoplastic disease).

Results: The mandatory immunization programme was complete and up-to-date in 37/60(62%) children with chronic disorders. The vast majority of children with chronic disorders (57/58) were vaccinated with acellular pertussis vaccine (DTpa) instead of whole-cell (DTPw) vaccine, universally used in Poland. Recommended immunisations against Streptococcus pneumoniae and varicella were given to 18/60 and 8/60 patients with chronic disorders respectively. Delays were observed most often in polio (25/60), mumps, measles and rubella (25/60), pertussis (24/60) and H. influenzae b vaccinations (22/60), less often in tetanus/diphtheria (9/60) and hepatitis B vaccinations (8/60).

Conclusions: The performance of vaccination programme in children with chronic disorders is suboptimal and needs improvement. General practitioners are reluctant to immunize children with chronic disorders and should be more familiar with true contraindications to vaccination.

1126

ESTIMATING THE INCIDENCE OF COMMUNITY-ONSET, SERIOUS INVASIVE BACTERIAL INFECTIONS IN PREVIOUSLY HEALTHY CHILDREN IN SOUTH WEST LONDON

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Aims: The study aimed to estimate the incidence of culture-confirmed significant bacterial infections (SBI) in previously healthy children residing in South-West London (SWL).

Methods: A web-based questionnaire was completed for all children aged 1 month to 15 years who were admitted to any of the five SWL or Surrey hospitals with a positive blood or cerebrospinal fluid (CSF) culture during 2009-11. A positive blood/CSF culture was considered significant if the child received intravenous antibiotic therapy directed specifically towards that pathogen. Hospital acquired infection (HAI) was defined as a significant pathogen isolated in blood/CSF culture taken >48 hours after hospital admission.

Results: During 2009-11, 44,118 children had 46,039 admissions in SWL, equivalent to 25.8 admissions per 1,000 children. An organism was isolated in 1,530 of 20,578 (7.4%) blood/CSF cultures taken and 571 (37.3%) were significant. A third of the SBI (208/571, 36.4%), however, were hospital-acquired and, of the community-acquired infections, more than two-thirds (252/363, 69.4%) occurred in children with significant underlying co-morbidities, many of whom will have had previous hospital admissions and could, therefore, have acquired their infection during a recent hospital admission. The incidence of community-onset SBI in previously healthy children in SWL was, therefore, only 6.2/100,000 childhood population, with the highest incidence among 1-11 month-olds (33.9/100,000), followed by 1-4 year-olds (6.5/100,000) and 5-15 year-olds (3.2/100,000).

Conclusions: SBI in previously healthy children is rare. Improved targeting of children at very low risk of a SBI at presentation will facilitate increased management of unwell children in the home.

1127

EFFECT OF NUTRITIONAL STATUS ON CLINICAL SPECTRUM OF SEVERE MALARIA IN CHILDREN

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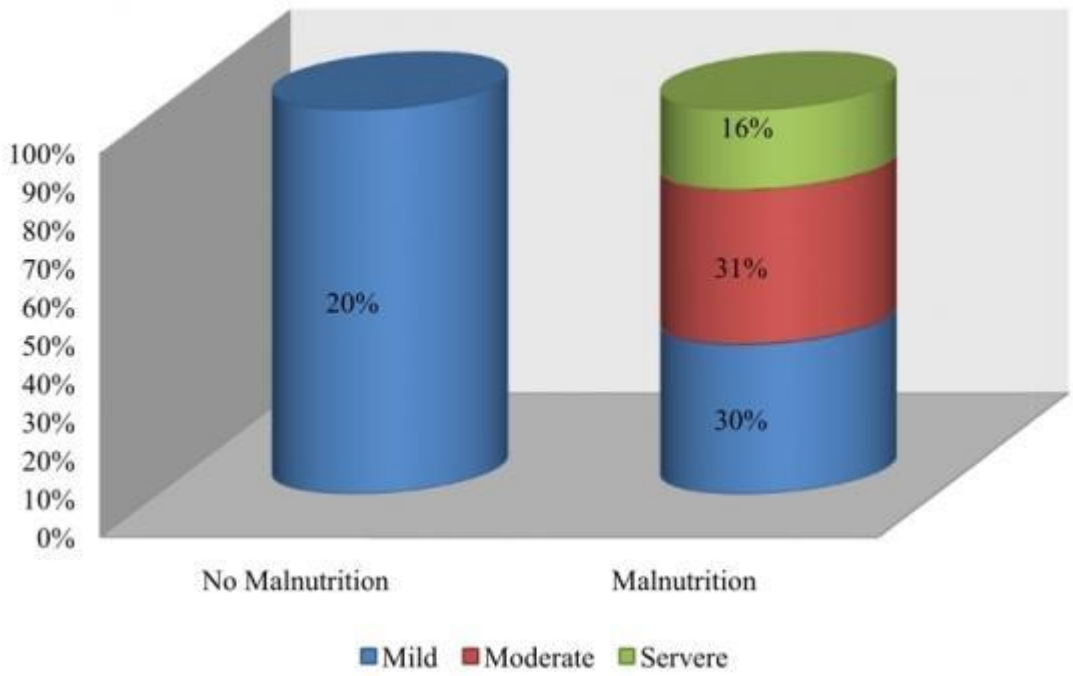
Background and aims: Malnutrition may play important role in various systemic complications observed in severe malaria. This clinico-observational study describes the effect of nutritional status on clinical spectrum of severe malaria in children.

Methods: This study was conducted on 95 admitted children with malaria in department of pediatrics, S.P.Medical College, Bikaner from January 2012 to December 2012. The species diagnosis was done by peripheral blood smear and rapid diagnostic test. Severe malaria was defined as per WHO criteria for Severe Malaria (2000). The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently. Children were grouped according to their nutritional status based on WHO/UNICEF classification.

Results: Majority of cases of severe malaria (80%) had malnutrition (figure 1).

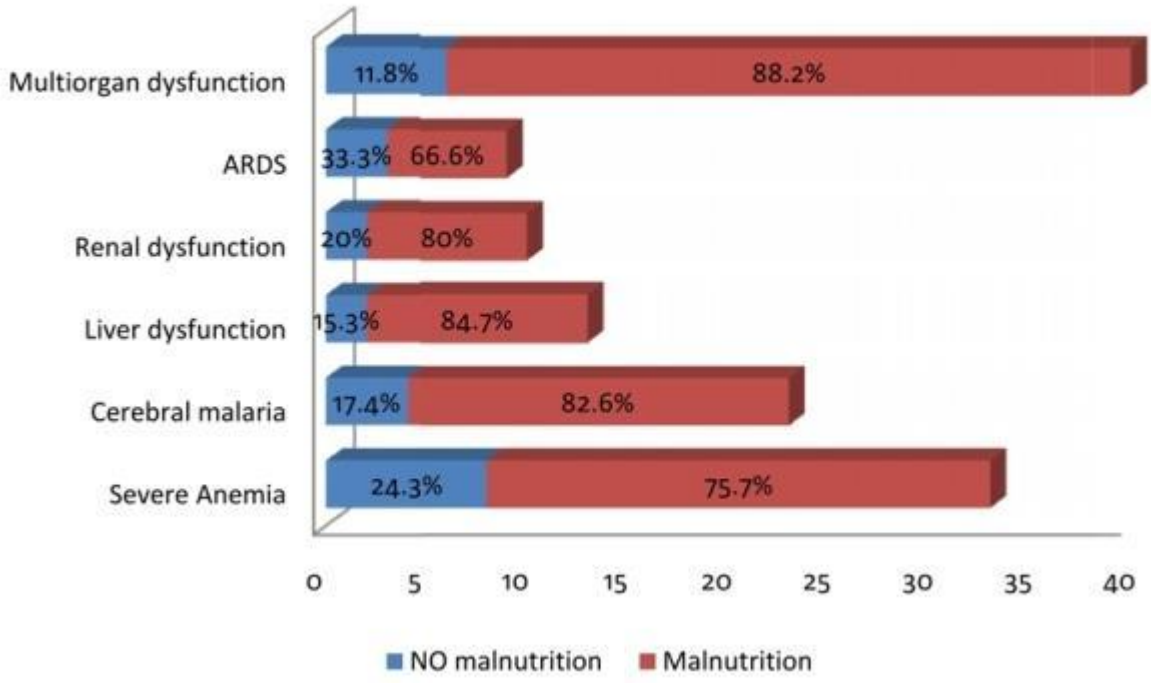
Figure 1: Incidence of severe malaria in association with nutritional status



[Figure 1: Incidence of severe malaria in associati]

Severe anemia (34.7%) was the most common severe manifestation followed by cerebral malaria (24.2%), hepatic dysfunction (13.6%), renal dysfunction (10.5%), acute respiratory distress syndrome (9%) and multiorgan dysfunction (42.1%) (figure 2).

Figure 2: Manifestations of severe malaria in association with malnutrition



[Figure 2 Manifestations of severe malaria in assoc]

Conclusions: This study affirms the association of malnutrition with severe malaria.

1128

PATHOGENS CAUSING COMMUNITY-ONSET SERIOUS INVASIVE BACTERIAL INFECTIONS IN CHILDREN WITH AND WITHOUT CO-MORBIDITIES IN SOUTH WEST LONDON AND SURREY

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Aims: This study aimed to compare risk factors and pathogens causing community-onset serious bacterial infections (SBI) in previously-healthy children and those with co-morbidities.

Methods: A web-based questionnaire was completed for children aged 1month to 15 years with a positive blood or cerebrospinal fluid culture (CSF) during 2009-11. A positive blood/CSF culture was considered significant if the child received intravenous antibiotic-therapy directed towards that pathogen. Hospital-acquired SBI was defined as a significant pathogen isolated in blood/CSF culture taken < 48 hours after hospital admission.

Results: During 2009-11, 571 SBI were identified in 450 children, including 411 (72.0%) infections with community-onset in 361 children. Co-morbidities were present in 52.9 % (n=238); those in 1-11 month-olds related mainly to neonatal complications (26/82, 31.1%), while haematological malignancies were the main comorbidities in 1-4 and 5-16 year-olds (77.6% and 75.2%, respectively). In children with co-morbidities, 200/238 (84%) children had a central-line and 197/346 (56.9%) of all SBI were line-related, mainly due to CONS (151/346 organisms, 43.6%). In the remaining 195 cases, E. coli was more prevalent in 1-11 month-olds, S. aureus in 1-4 year-olds and K. pneumoniae in 5-15 year-olds. In previously healthy children, E, coli predominated in infants (14/56, 25% infections) while S. typhi (18/169, 10.7%), S. aureus (16/169, 9.5%) and S. pneumoniae (14/169, 8.3%) were the main pathogens in older children.

Conclusions: Children with comorbidities contributed significantly to community-onset SBI and over half had central line-related infections. Interventions to reduce line-related-infections could have a significant impact in reducing the burden of childhood SBI.

1129

EFAVIRENZ AT PREGNANCY

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Objectives: To evaluate the Efavirenz (EFV)-induced fetal effects.

Methods: A prospective cohort study mother-child pair was performed since 2000 to 2009 at 9 Spanish hospitals. Children were followed up until 3 years of life.

Results: 803 mothers were included, 102 with EFV before pregnant and 41 during pregnancy and 29 during 1st trimester (median exposure: 2,87 months (SD:2,4).

Median age (n:41): 38 years (37-38); 87,8% caucasian; more frequently CDC category (19,5%): C3. C-hepatitis co infection: 46.3%. Mode of infection: heterosexual: 56,1 %, intravenous drug abuse: 46,34%. Mean viral load at 3th trimester: 323,82 cop/ml (SD:7,28,51); CD4: 457,5 cell/mm3 (SD:282).Caesarea 60,9%; twins: 5%. Mean gestational age: 37,6 weeks (SD:1,59) and newborn weight: 2900 g (SD:467,76).

Among the 803 children were detected 117 birth defects in 106 newborns: 32 heart, 23 renal-genital , 2 auricular appendix, 26 musculoskeletal, 4 skin, 2 chromosomal abnormalities (Down syndrome), 9 digestive; 13 neurological, 1 ophthalmological. There were 26 intrauterine growth retardation (IUGR) and 66 preterm. Among EFV group (n:41)there were 7 defects: 2 pyelic dilation, 1 facial palsy, 1 persistent foramen ovale, 1TGA, 1 craniosynostosis, 1 inguinal hernia; and 1 IUGR and 4 preterm.

The rate of total congenital defects was 13,2%, at EFV-group was 17% with 6,22% (50/803) and 4,87% (2/41) rate of mayor malformations, respectitively. RR was 1.35 (IC 95%: 0.61-2,97).

Conclusions: In our cohort the rate of malformations in patients exposure to EFV in pregnant is higher than general population but there were no statistical differences between EFV group and all cohort.

1130

CHILDHOOD GIARDIASIS IN MALAYSIAN ABORIGINAL COMMUNITIES: PREVALENCE AND DYNAMIC OF TRANSMISSION

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This is a cross-sectional study, conducted among Orang Asli (aborigine) children in Peninsular Malaysia to determine prevalence and dynamic of transmission of giardiasis. A total of 484 faecal samples were collected from children and examined microscopically with subsequent molecular analysis for the positive cases. The overall prevalence of Giardia duodenalis was 16%. Children with low household income, living in houses without toilet and did not cut nails in the last seven days had higher infection rate of giardiasis. No significant association was found between contact with animals and Giardia infection. Drinking piped water was a significant factor associated with Giardia infection (OR = 1.9, 95% CI (1.14-3.09), p = 0.013). Genotyping and subtyping analysis identified assemblages A(AII) and B. Mixed infection with assemblages A and B was observed in 64% of the positive cases. Univariate analysis showed that children whose mothers do not have formal education are at four times higher risk of getting Giardia infection with mixed assemblages A and B (OR= 3.6, 95%CI (1.13 - 11.37), p= 0.027). Children living in houses without toilet were at 7 times higher risk of harboring mixed assemblages A and B. The study indicates that giardiasis is still a childhood health problem in Orang Asli communities with human-to-human transmission being the most possible route of transmission.

1131

TWO CASES OF VISCERAL LEISHMANIASIS IN PREVIOUSLY HEALTHY CHILDREN IN SOUTH GREECE, CRETE

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Background and aims: Leishmaniases are vector borne diseases. Dogs constitute the reservoir for the disease. Crete is endemic for L. infantum (incidence: 7/100.000) which causes both visceral (VL) and cutaneous leishmaniasis.

Methods: Two cases of VL are presented.

Results: An 8,5-year-old-boy, presented with three-month intermittent 39^{o}C-fever, pronounced splenomegaly, lymphadenopathy, weight-loss, maculopapular rash of the trunk and extremities, pancytopenia, transaminasemia, hypergammaglobulinemia and mildly elevated infectious markers. VL was diagnosed on the basis of serology (antibodies detected with immunofluorescence and ELISA) and the visualization of parasites on bone-marrow-smear. Other causes of FUO were excluded. Intravenous liposomal-AmphotericinB, 3mg/kg/day, was given for 5days and repeated on day 10. Fever remitted by the 3rd day of treatment. Spleen-size, CBC, liver-function-tests and infectious markers normalized by day 20. One month later, a 3-year-old-boy presented with 21-day 40^{o}C-fever, splenomegaly, lymphadenopathy, tonsillitis, anemia, lymphocytosis, transaminasemia and hypergammaglobulinemia. Infectious mononucleosis was initially suspected. However, the prolonged ill-appearance, the enlarged spleen, and the inhabitance in the same rural area as the former child raised the suspicion of VL early. High titers of anti-leishmanial-antibodies confirmed the diagnosis, although no parasites were detected in bone-marrow-smear. Two-day treatment with 10mg/kg/day liposomal-Amphotericin was provided. By the 2nd day he was afebrile. Blood-tests and spleen-size normalized by day 20. Six months later both children were in perfect health. Anti-leishmanial-antibodies were undetectable.

Conclusions: In endemic areas VL should be suspected in children with FUO even in the presence of symptoms suggestive of more common diseases. The two-day-treatment appears optimal, leading earlier to symptoms remission.

1132

ASSOCIATION OF HEPATIC AND RENAL DYSFUNCTION IN SEVERE MALARIA IN CHILDREN IN BIKANER (NORTHWESTERN INDIA)

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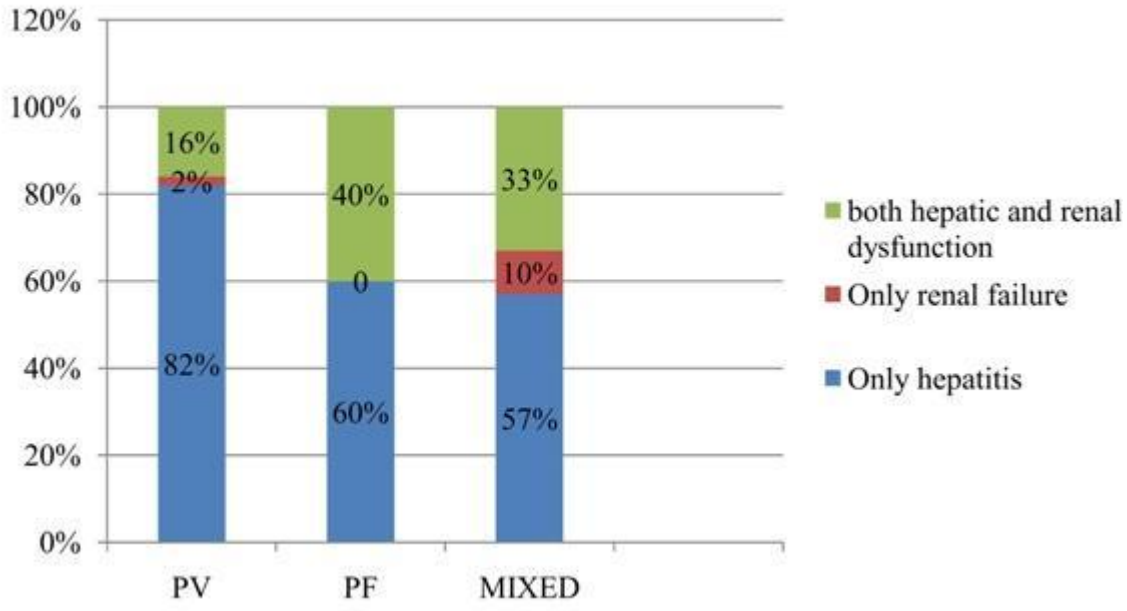
Background and aims: There are various reports regarding association of jaundice with renal failure in severe malaria. The aim of this prospective clinico-observational study is to evaluate the correlation between hepatic and renal dysfunction in severe malaria.

Methods: This study was conducted on 79 admitted children of malaria from January 2011 to November 2012. The species diagnosis was done by peripheral blood smear and rapid diagnostic test. Malarial hepatic and renal dysfunction is defined as children having derangements in either the liver or renal function tests or both at the time of presentation according to WHO criteria (2000). The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently.

Results: Incidence of renal failure in malaria patients with hepatic dysfunction was found to be 26%. Association between hepatic dysfunction (serum bilirubin > 3mg/dl) and renal dysfunction was significant in children having P.falciparum malaria (40%) in comparision to children having P.vivax malaria (16%) (figure1).

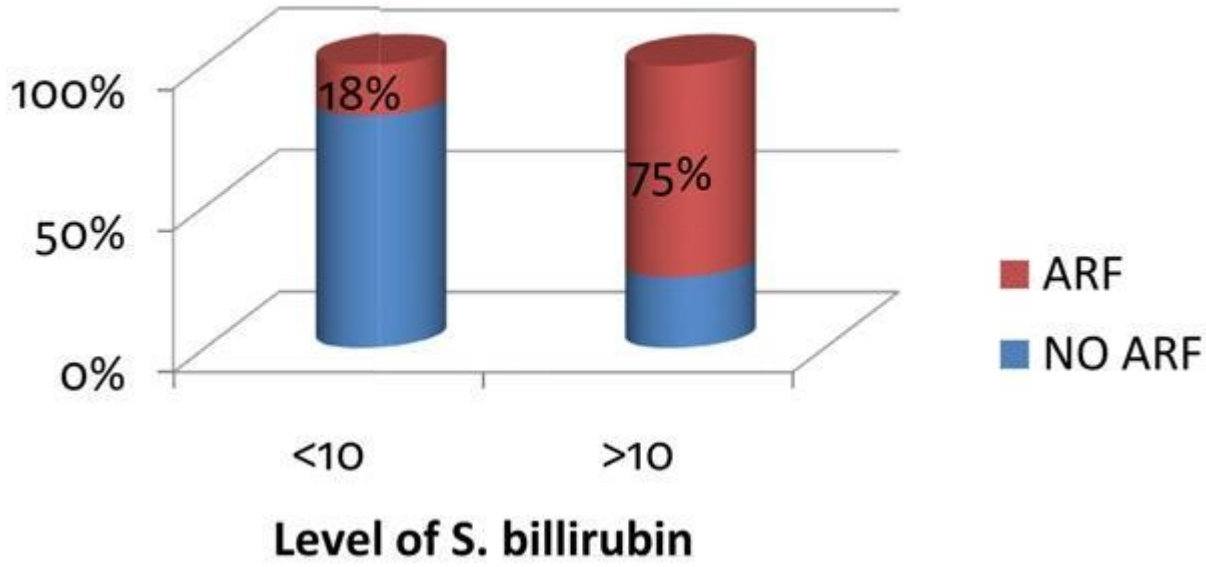
Figure 1: Association of hepatic and renal dysfunction in malaria



[Figure 1: Association of hepatic and renal dysfunc]

Association of renal failure was stronger with serum bilirubin level >10mg/dl (75%; p=0.001) (figure 2).

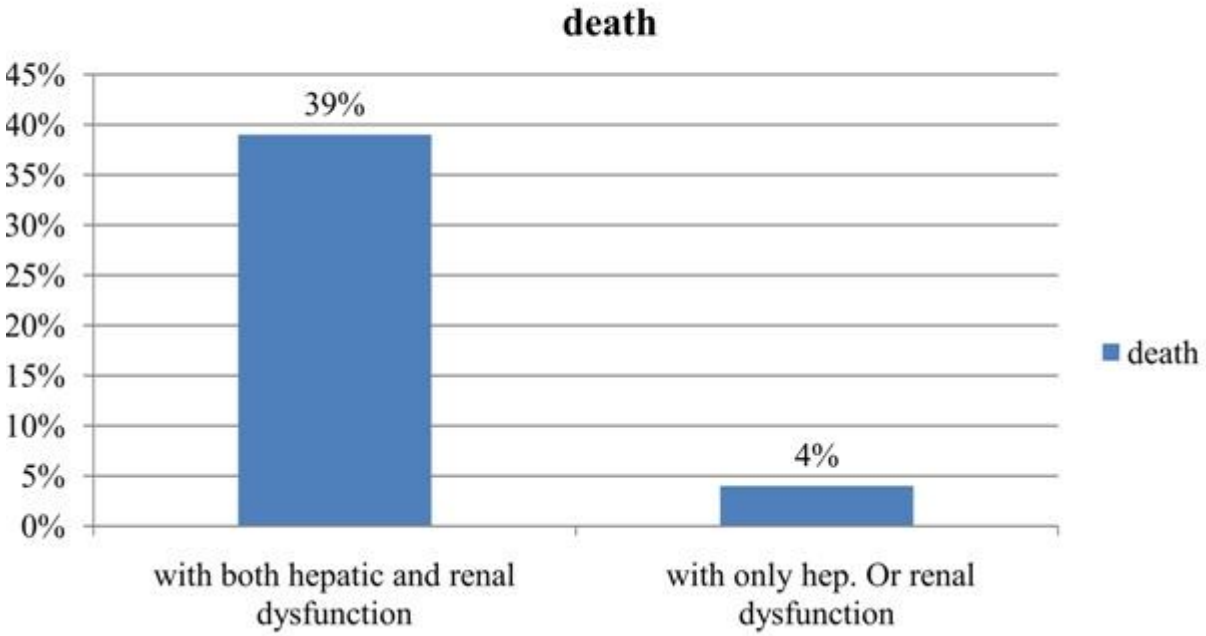
Figure 2: Association of renal failure with level of serum bilirubin



[Figure 2: Association of renal failure with level]

Mortality was significantly associated with both hepatic and renal dysfunction (39%) in comparison to only hepatic or renal dysfunction (4%; p< 0.001) (figure 3).

Figure 3: Association of mortality with multi-organ dysfunction



[Figure 3: Association of mortality with multi-orga]

Conclusions: This study affirms the association of renal dysfunction with hepatic dysfunction in children in Bikaner.

1133

SEROTYPE EVOLUTION AND ANTIMICROBIAL SUSCEPTIBILITY OF STREPTOCOCCUS PNEUMONIAE 2 YEARS POST INTRODUCTION OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN GREECE

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Background: The aim was to examine the evolving serotype epidemiology and antimicrobial susceptibility of Streptococcus pneumoniae isolates causing invasive pneumococcal disease (IPD) or acute otitis media (AOM) in children ≤14 y.o. following introduction of PCV13 to the Greek NIP in 2010.

Methods: Data from the 4th year of a prospective study initiated in September 2008 in 15 pediatric hospitals are presented. Serotyping was performed by latex agglutination and Quellung reaction using anti-sera (SSI, Denmark). Antimicrobial susceptibility was determined by E-test; isolates with MIC ≥2 μg/mL were considered resistant to penicillin.

Results: Among 94 isolates collected (37.2% ≤2 y.o.; IPD:11, AOM: 24) between November 2011-October 2012, the commonest serotypes for IPD were 19A (25.8%), 7F (25.8%) and 24F (9.7%) while for AOM 19A (17.5%), 3 (12.7%) and 11A (11.1%). A 43.9% reduction was noted in IPD cases in children ≤2 y.o. after PCV13 implementation (23 in 2010-2012 vs. 41 in 2008-2010). Theoretical coverage for PCV7, PCV10 and PCV13 in children 0-2 y.o. with IPD was 0.0%, 27.3% and 63.6% respectively whereas for AOM was12.5%, 12.5% and 29.2%. Resistance to penicillin exhibited 3.2% of IPD and 19.4% of AOM isolates, while rates for erythromycin resistance reached 25.8% and 38.7% respectively. The most prevalent resistant serotypes to penicillin and erythromycin were 19A and 19F.

Conclusions: Two years post PCV13 introduction, IPD cases in children ≤2 y.o have decreased but vaccine serotypes 19A and 7F remain the major cause for IPD in children ≤5 y.o, while non-vaccine serotypes are predominant in AOM cases.

1134

CAN ABNORMAL IMAGING FINDINGS IN CHILDREN AFTER FIRST URINARY TRACT INFECTION (UTI) PREDICT RECURRENCE OF UTI? A 4-YEAR FOLLOW-UP

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Background/aim: The aim of this study was to examine the association of imaging findings after the first episode of UTI with the risk of recurrent UTI.

Methods: We retrospectively examined the imaging findings regarding ultrasound(US), voiding cystourethrography (VCUG) and DMSA of 357 children who admitted at 'Aghia Sophia' Children's hospital with a first episode of UTI during 2008. A four-year follow-up took place for 259 children and analysis regarding risks for recurrent UTI was performed.

Results: Positive findings in US, VCUG and DMSA were found in 32/320 (10%), 93/330 (30.8%) and 18/163 (11%) respectively. In 152 children who had undergone all 3 exams, US was abnormal in 18 (11.8%), VCUG in 63 (41.2%) and DMSA in 15 (9.9%). 52/152 children were detected with severe Vesicoureteral reflux (VUR) (grade III-V) and 10 of them had abnormal US (positive predictive value (PPV) (55.6%). Of 15/152 children with renal scarring, 1 had abnormal ultrasound (PPV:5.6%) and 8 had VUR in VCUG (PPV:12.7%). Recurrent UTI during follow-up had 45/259 (17.4%) and 23 (51%) experienced it in the first 12 months. Abnormal US, renal scarring, VUR and chemoprophylaxis after first UTI episode were not associated with risk of recurrence ($p>0.05$).

In line with recent guidelines, if VCUG had not been performed to children with normal ultrasound, in 63/74 (85.1%) VUR would have not been detected and 11/63 (17.4%) children had recurrent UTI.

Conclusion: Data of our study indicate that neither initial radiographic findings nor chemoprophylaxis can be associated with the risk for UTI recurrence.

1135

HELICOBACTER PYLORI INFECTION IN DIGESTIVE ENDOSCOPY: PREVALENCE TREND AND CLINICAL PROFILE

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Background: Decreasing prevalence of H. pylori (Hp) infection has been reported worldwide, in parallel with the improvement in sociodemographic conditions. So far there are no prevalence studies concerning symptomatic Portuguese children submitted to digestive endoscopy.

Aims: To evaluate the prevalence of Hp infection in a 10-year period in a sample of symptomatic children/adolescents submitted to upper digestive endoscopy; To describe clinical features associated with Hp infection in the same population sample.

Methods: Descriptive, analytical and retrospective study; review of 359 diagnostic endoscopy records performed in 2002, 2006 and 2011 in a Lisbon tertiary Gastroenterology care center, age ≤18-year-old; Hp status was considered (+) if histology and/or culture were positive; Hp(-) if both histology and culture were negative. Statistics: Chi-square test, Fishers exact test; significance $p< 0,05$.

Results: 175 (48,7%) children/adolescents presented with Hp infection and distributed as follows: 11,4% ≤5years, 48% 5≤11years, 40,6% 11≤18years. Mean annual prevalence was 57,1% in 2002, 55,5% in 2006 and 41,3% in 2011 ($p=0,02$ in the interval 2006-2011). Endoscopic features associated with Hp(+) were normal esophagus ($p=0,032$), nodularity in the antrum and corpus ($p< 0,001$) and duodenal ulcer ($p=0,013$). Histological features associated with Hp(+) included moderate inflammation, moderate activity ($p< 0,001$) and the presence of lymphoid aggregates/follicles ($p< 0,005$).

Conclusions: Differently from data concerning other populations at similar settings, our study has shown a yet high Hp prevalence, although suggesting a recent decrease trend. These results emphasize the clinical relevance of Hp infection in symptomatic pediatric population and the need of cost-effective management strategies.

1136

CO-INFECTION WITH HEPATITIS B AND C VIRUSES AMONG HIV-INFECTED CHILDREN

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Background and aims: There is insufficient data concerning HBV/HCV infection among HIV+ children. We report the experience of a portuguese paediatric HIV-Centre.

Methods: HBV and HCV co-infected patients were sorted from HIV+ children enrolled in our Centre. Charts were reviewed concerning diagnosis, clinical and laboratorial parameters at presentation and treatment response.

Results: Seventy-five HIV-infected children are followed in our Unit. Three (4%) have HIV1-HBV (group-I) and 2 (2.7%) have HIV1-HCV (group-II) co-infection.

Group-I: Table 1. All started antiretroviral treatment (ART) with tenofovir, emtricitabine, efavirenz.

	Initial				**After 6m ART**		
	HBV Genotype	**HBV-VL (copies/mL)**	**HIV-VL (copies/mL)**	**ALT/GGT (U/L)**	**HBV-VL (copies/mL)**	**HIV-VL (copies/mL)**	**ALT/GGT (U/L)**
9y female	A	>170.000.000	56.527	37/15	399	<40	56/33
14y male	Not available	4.002	101.792	53/37	<20	<40	35/44
9y male	E	155.301	165.545	645/201 (acute hepatitis)	HBs Antibody + (3m)	57 (3m)	22/24

[Table 1]

Group-II: One was diagnosed through newborn screening, presenting at age 23 months (m) undetectable HIV-VL (with ART), HCV-VL $\log_{10}$-6.63 and ALT 2x-normal (improving). The other patient was diagnosed with HIV-infection at 17m and HCV at 10 years (y). At age 16y she presents poor adherence to ART, HIV-VL $\log_{10}$-3.86; HCV-VL $\log_{10}$-5.14; ALT 3x-normal; no liver-fibrosis. None was treated for HCV-infection.

Conclusions: Our results confirm the need for HBV and HCV screening in pregnant women and HIV-infected patients. ART in HIV/HBV co-infected children should include tenofovir and emtricitabine (or lamivudine). This association showed good results in both chronic and acute HBV-HIV co-infection. There is a need for prospective studies and recommendations on HCV treatment in children.

1137

CHANGES IN CIRCULATION OF NEISSERIA MENINGITIDIS SEROGROUP W135 IN SOUTH AMERICA

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Background: Meningococcal Disease (MD) is present in Latin America (LatAm) as sporadic cases, outbreaks or endemic-epidemic patterns. Increased circulation of Neisseria meningitidis serogroup W135 (NmW135) has been observed in recent years in some Southern Cone countries.

Methods: Data review of NmW135 circulation from SIREVA II (PAHO) and Ministry of Health websites was undertaken from 2002 to 2011.

Results:

Argentina: Incidence rate is 0.6 cases per 100,000. NmW135 was responsible for 5.8% of cases in 2006, 2 % in 2007, 24% in 2008, 41% in 2009 and 49% in 2010. Multi-locus Sequence Typing (MLST) showed that NmW135 presented the ST-11 clonal complex (ST-11).

Brazil: Reported an hyper-endemic epidemiological pattern of 2 cases/100,000. NmW135 increased from 1.5% of MD cases in 2002, to 5.5% of cases in 2008, and to 5.6% in 2011. Rio Grande do Sul showed NmW135 increased from 3.2% of MD cases during the period 1995-2002 to 17.8% during 2003-2005. MLST also showed ST-11.

Chile: Incidence rate is 0.5 cases per 100,000. NmW135 was responsible for 2% of MD cases in 2009, 10% in 2010, 32% in 2011 and 50% in 2012. During 2012, 60 NmW135 MD cases were confirmed, almost 3 times greater than what was observed in 2011 (21 cases), with a fatality rate of 25%. MLST also showed ST-11.

Conclusions: In the last ten years, there has been a steady increase of ST-11 NmW135 circulation in LatAm Southern Cone countries. This ST-11 (Hajj related) has been responsible for some epidemiological changes and high fatality rates observed.

1138

OUTBREAK OF ECHOVIRUS 11 FULMINANT NEONATAL HEPATITIS IN BELGIUM DURING SPRING 2012

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Nonpolio enterovirus infections are common during summer and fall. Among neonates clinical presentation varies from asymptomatic viral shedding and non-specific febrile illness to sepsis-like syndrome and severe liver, cardiac or cerebral diseases. Echovirus 11 is the most frequent cause of serious neonatal morbidity and mortality, often presented as fulminant hepatitis. Mortality rates are greater for infections that appear during the first week of life, probably through vertical transmission.

We report four cases of echovirus 11 neonatal infections between April and June 2012. All children were admitted during the first week of life, day 4 to 6, with sepsis-like syndrome. All the cases were biologically characterized by marked transaminase elevation (GOT >> GPT), hemolytic anemia, thrombocytopenia, and severe coagulopathy. Diagnosis was confirmed by positive polymerase chain reaction on blood, stool or cerebro-spinal fluid samples. Among them three were born by vaginal delivery and one deceased. All were treated by intravenous immunoglobulins (IVIG) within 7 days of admission (1 to 2g/kg). Contact history was only documented in the patient delivered by caesarian. Portal blood flow inversion was found in three of the reported cases, which is a marker of portal hypertension commonly reported in fulminant hepatitis.

This study shows that outbreak of enterovirus is still associated with severe infection and fulminant hepatitis in newborns. Clinical presentation is aspecific although early diagnosis and rapid treatment is mandatory to avoid fatal evolution. There was rational to administer IVIG, and positive outcome in 3 patients out of 4 might have been favored by this treatment.

1139

CONSEQUENCES OF HIV INFECTION ON MALARIA CLINICAL COURSE AND THERAPEUTIC IMPLICATIONS IN A POPULATION OF MOZAMBIQUE

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Introduction: It has been demostrated that cotrimoxazol and the protease inhibitors(PI) reduce parasitaemia and improve clinical outcome.

Aim: To compare the clinical severity of malaria in HIV-patients with the treatment administrated.

Methods: In a prospective, cross-sectional study, clinical and laboratory data were registered consecutively for all adults and children HIV-positive admitted to a medical ward in the Carmelo Hospital of Chokwe, Mozambique, during a period of two months (October-November 2012). HIV-positive patients with malaria diagnoses based in positive malaria blood slides were included.

Results: 41 patients were studied. Median age was 30,85±16.69 years, 63,4% male. Average CD4 was 326±316 and viral load 90,431±21,916. There were 5 complications: 4 severe anemia and 1 cerebral malaria. Three relapses were detected. Sixty six patients were treated with artemether-lumefrantina and the remained with quinine. 100% patients treated with cotrimoxazole had a parasitemia grade I-II and an average of days with clinical 2.57±0.97vs3,79±2.64 (95% CI 0.024 to 2.42) compared with not treated ($p< 0,05$ in both). No relapses were reported in them. HIV treated with PI had this laboratory parameters in comparison with not treated: haemoglobin (g/dl): 9,1±4,19vs7,9±3,56 (p=0,07), leukocytes (µ/L): 5968±5813vs4099±3293 (p=0,89), Lymphocytes (µ/L): 1627±1786vs1338±885 (p=0,59), Platelets ($x10^3$ µ/L): 280±193vs236±143 (p=0,42). No complication was registered in these patients.

Conclusions: The use of cotrimoxazole prophylaxis decreases the level of parasitemia and the duration of symptoms and prevents the relapses. Patients treated with PI had no complication and tended to maintain higher levels of hemoglobin, leukocytes, lymphocytes and platelets, although the values were no significative.

1140

POSITIVE BLOOD CULTURES AT BRISTOL ROYAL HOSPITAL FOR CHILDREN, UK: EVOLUTION AND ANTIMICROBIAL RESISTANCE PATTERNS OVER A FIVE YEAR PERIOD

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Background: The surveillance of paediatric positive blood cultures (BC) is central to monitoring changing epidemiology, which guides the choice of empirical therapy.

Aims: To determine trends in the aetiology of bacteraemia in children over a 5-year period and to assess antimicrobial resistance patterns.

Methods: We included all positive BC from children aged< 18 years isolated at Bristol Royal Hospital for Children between 2007 and 2011.

Results: A total of 1923 positive BC were reported. 75% of cases occurred in children aged < 5 years. There was 31% reduction in the incidence of positive blood cultures during the study period. Most commonly isolated organisms were CoNS (44%) followed by S. aureus (6%), enterococcus (5%) and E. coli (4%). Incidence of MRSA decreased during the study (23% of MRSA in 2007; no isolates in 2011). There were one case of penicillin and two cases of erythromycin resistant pneumococci. The most common pneumococcal serotypes were 7F and 19A. The incidence of meningococcal B infection remained low and there were no cases of N. meningitidis group C. There were high rates of resistance of enterococci to amoxicillin (30%) and vancomycin (19%). Of the 70 isolates of E. coli, 31% were resistant to co-amoxiclav and 10% to cefotaxime. Piperacillin-tazobactam resistance was not uncommon in P. aeruginosa (15%), Klebsiella spp (16%) and Enterobacter spp (17%). All Klebsiella and Enterobacter isolates were sensitive to meropenem.

Conclusions: This study identifies the commonest agents isolated from blood cultures in our centre and highlights shifts and trends observed over time.

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VIRAL ETIOLOGY AND CLINICAL CHARACTERISTICS OF ACUTE LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN LESS THAN 2 YEARS

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Background and aims: Viral lower respiratory tract infections (LRTI) are an important cause of morbidity and mortality in children. The aetiological background of these infections frequently remains undetermined. The aim of the present study was to investigate the aetiology of acute LRTIs in children in Cyprus.

Methods: Between November 2011 and January 2013 children less than 2 years, admitted to Archbishop Makarios Hospital in Nicosia, Cyprus, with LRTI were recruited in a prospective study. Nasopharyngeal swabs were tested for the presence of RSV, Rhinovirus, Influenza A and B, Parainfluenza 1, 2, 3 and 4, Adenovirus, Bocavirus, Metapneumovirus, Coronaviruses type 229E, NL63 and OC43, and Enterovirus using Real-time RT-PCR. Demographic and clinical data for patients were also recorded.

Results: 96 children were recruited in the study. Median age was 5 months with 57 children (59%) being male. RSV was detected in 56 samples (58.3%), Rhinovirus in 24 (25%), Metapneumovirus and Adenovirus in 5(5.2%) patients each, Influenza A and Bocavirus in 4 (4.2%), respectively. Double infections occurred in 20 cases, mainly between RSV and Rhinovirus. 41% of children had respiratory distress on admission requiring administration of O_2.

Conclusions: Real-time PCR technology allows for quick and effective determination of the aetiology of viral respiratory infections. RSV and Rhinovirus were the most predominant pathogens in younger children with acute LRTIs, but recently discovered viruses such as Bocavirus or Metapneumovirus were detected in substantial proportion of patients. Further studies are needed to explore the clinical significance of mixed infection with viruses in patients with LRTI.

1142

CONGENITAL TOXOPLASMOSIS

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Objectives: The study analysed symptoms and therapy in children with congenital toxoplasmosis.

Methods: Of 67 children born from 66 mothers managed in our department for an acute maternal infection between January 1997 and December 2012. 23 newborns were eligible in our study.They had proven congenital toxoplasmosis and had been followed up for at least today.

Results: 44 children were asymptomatic.5 infants had only eye lesion. In 18 children except ocular involvement in the form of chorioretinitis is evident neurological sequels.

Conclusions: Prenatal screening and treatment to the pregnant mother failed to prevent transmission of Toxoplasma gondii from mother to the child.Some children were infected also due to insuficcient treatment of their mothers during pregnancy.

natal

1143

EVALUATION OF EFFICACY OF INTERFERON INDUCER IN PREVENTION OF THE NOSOCOMIAL GASTROINTESTINAL INFECTIONS IN CHILDREN

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Background: It is known that nosocomial infections (NIs) are common hospitalized children.

Aim: To evaluate the opportunities of use of interferon inducer (IFN-inducer) containing release active antibodies to interferon-γ (RAAB IFN-γ) in prevention of the nosocomial gastrointestinal infections in children.

Methods: A randomized, double-blind placebo-controlled trial of RAAB IFN-γ (IFN-inducer "Anaferon for children") efficacy in treatment of a 86 children of 1 month - 3 years hospitalized with acute gastroenteritis. 46 patients of the group 1 obtained RAAB IFN-γ and 42 patients of the group 2 - placebo. Proportion of subjects in which clinical cure were evaluated. Fecal PCR was performed on days 1 and 5 of the treatment. Evaluated the proportion of patients who had negative PCR stool.

Results: The proportion of children with the normalization of the clinical status was significantly greater in group 1. On the first day PCR revealed rotavirus in 85% and 83% in groups 1 and 2, respectively. After the treatment rotavirus isolation persisted in 39% subjects of group 1 and 74 % subjects of group 2. In 7% of the children of the second group of PCR on the first day showed a mixture of rotavirus and Salmonella. On day 5 the proportion of children in group 2 with viral and bacterial infections rose to 17%. Children in Group 1 the mixed infection was not defined in any one of any five days of observation.

Conclusions: Therapeutic administration of RAAB IFN-γ may prevent cross-contamination of nosocomial gastrointestinal infections in children.

1144

VERTICAL TRANSMISSION OF HIV: REVIEW AND REPRESENTATIVE CASES IN CENTRAL TUNISIA

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Background: Mother-to-child transmission (MTCT) is by far the largest source of HIV infection in children below the age of 15 years. Tunisia is a low HIV-endemic country (prevalence < 0.1%). Since 1987, National Program against AIDS was set up. Prevention of MTCT is one of the main purposes of this program. Fewer than 3% of total HIV positive population are children below 15 years old.

Material and results: In this study, we report some representative cases of MTCT in central Tunisia.

Five children born from HIV positive mothers are monitored in Sousse and Monastir University hospitals. Transmission during delivery occurred before 2009. Two mothers had unknown HIV status during pregnancy. The discovery of their infection followed children's complications of HIV infection.

Other infants, of which HIV positive mothers were managed during pregnancy, have no HIV infection and are regularly seen in health points. All infected children are treated by HAART.

Despite the low prevalence of MTCT (4-5 cases/year), a national strategy has been developed. The effective implementation of this strategy began in 2009 with the availability of rapid testing and training of health professionals on the importance of screening pregnant women and prevention of MTCT strategy.

Conclusion: This work represents a preliminary assessment of monitoring MTCT of HIV in Tunisia. Only pregnant women with risk factors are tested for HIV infection. Increased expansion of screening program in pregnancy to peripheral health units and strengthening HIV prevention are needed to reduce MTCT of HIV at rates below 2%.

1145

ABSCESS IN THE THIGH - A CLINICAL CASE

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Introduction: The BCG vaccine is a live attenuated vaccine of Mycobacterium Bovis. In Portugal this vaccine is inoculated intradermally, on the left arm, of all newborns in nursery at the same time that the anti-HBV is administrated in the right thigh.

Case report: 6 months old infant, male, caucasian race, with irrelevant personal background that came to the Emergency Room presenting a swelling in the right thigh, since 1 month and a half, which has gradually increased, had scarce local inflammatory signs and with no significant changes in the overall state. Performed an ultrasound which showed a "massive collection in the topography of the rectus femoris with about 6x3,5x2cm." About 20cc of purulent content were drained, whose microbiological study revealed "several acid-fast bacilli resistant", and the polymerase chain reaction for Mycobacterium tuberculosis complex tested positive. No signs of systemic disease were found nor any deficiency in the Immunological status. Taking into account the good general health of the infant, the location and progress of the lesion, it was concluded that the abscess resulted from accidental inoculation of the BCG vaccine, intramuscularly, in the thigh, probably by switch with anti B Hepatitis vaccine. He began treatment with Isoniazid and Rifampicin with total recovery.

Conclusion: The BCG vaccine is tested to be inoculated intradermally and in the arm. The inoculation at any other location may arise complications. We want to stress the need to bee rigorous in the technique of BCG vaccination.

1146

CEREBRAL TOXOPLASMOSIS IN A SEVERELY IMMUNOCOMPROMISED CHILD

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Background: Neurotoxoplasmosis is a major cause of morbidity and mortality in immunocompromised patients with CD4 T-lymphocyte counts < 50/mm3.

Case report: We report a case of a 12-year-old boy who presented to us with a 4-week history of frontal headache, fever, epistaxis, constitutional syndrome and a 5-day history of vomiting. He was born in Equatorial Guinea and moved to Spain aged 9 years. There was a history of malaria and pneumonia aged 5 and 8 years. Weight at admission 22kg (0.3^{th}%), distended abdomen, marked hepatomegaly, no CNS signs. FBC showed anaemia (Hb 7g/dl), mild lymphopenia ($1.2x10^3$/µL), eosinophilia ($0.4x10^3$/µL) and platelets of $186×10^3$/µL. Liver enzymes were elevated (AST 204 IU/l) as was ESR (56mm/h). HIV serology was positive and PCR HIV viral load (VL) 177.000copies/ml, initial CD4 count 2/mm^3(0.2%), 15% naive CD4+CD45RA, 40% memory CD4+CD45RO; estimated 12-month risks of death being 26%. Neuroimaging revealed a ring-enhancing lesion in the left frontal area with marked oedema causing a mass effect. PCR in CSF/blood positive for T.gondiiand treatment was continued with sulphadiazine, pyrimethamine and dexamethasone whilst maintainingP.Jirovecii prophylaxis. HIV resistance profile was negative and HAART was initiated with lopinavir/ritonavir, lamivudine and abacavir (HLAB57 negative). Due to persistent neutropenia anti-toxoplasmosis therapy was changed to clindamycin and maintained for 12 months until CD4 count >200/mm^3/>15%. The patient improved continuously clinically (current weight 32kg; 25^{th}%) as well as his blood parameters (latest CD4 count 337/mm^3 with persistent undetectable HIV VL).

Conclusion: Neurotoxoplasmosis is an important differential diagnosis in severely immunocompromised patients with clinical neurological signs.

1147

FACTORS ASSOCIATED WITH HOSPITALIZATION OF CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA (CAP). A MULTI CENTER TWO-YEAR STUDY

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Background: Hospitalization criteria for children with CAP are not well defined. The objective of this study was to identify demographic, clinical and laboratory risk factors for admission of children with CAP.

Methods: In a prospective multi-center study, children with radiologically confirmed CAP, visiting emergency rooms in 7 different countries (Greece, Italy, Israel, Lithuania, Portugal, Romania and Spain) during two seasons: 2010-2011 and 2011-2012 were enrolled. Demographic, clinical and laboratory data were captured by standarized questionnaires. Statistics: Univariate and logistic regression models were calculated to adjust for variables $p< 0.05$ with hospitalization in the bivariant test.

Results: During the study period 261/1339 (19.5%) children required hospitalization. Admitted children were slightly younger 29.0, vs 33.3± ($p= 0.09$). Gender, gestational age, birth weight, passive smoking, past medical history related to recent consumption of antibiotics or chronic treatment had no effect on the decision of hospitalization. However, breastfed children were more often hospitalized (aOR: 1.79 95%CI: 1.30-2.50). The objective clinical symptoms associated with hospitalization were increased respiratory rate (47 vs. 40 /min; aOR 1,03; 95%CI: 1,01-1,04) and lower oxygen saturation (94.7% vs 96.1%; aOR: 0,79; 95%CI: 0,72-0,86). Clinically hospitalized children had more rhinorrea [aOR: 1,48 (1,09-2,0)] and cough [aOR: 1,64 (1,13-2,37)].

Conclusions: The main factors influencing the decision for admission of children with CAP are related to respiratory distress: increased respiratory rate and lower O2 saturation. Laboratory or Chest XR findings did not influence such decision.

1148

THE OUTCOME IN CHILDREN WITH CONGENITAL CYTOMEGALOVIRUS INFECTION

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Objectives: In this report, the authors have presented clinical picture, course and therapy used in 23 infants with congenital CMV, hospitalised at the Department of Child Infectious Diseases in Faculy Hospital Brno within January 1998 - December 2012.

Methods: The diagnosis of congenital infection was established on the base of typical symptoms of congenitally acquired disease, in a part of infants even from personal anamnesis (mother´s disease during pregnancy) and verified by PCR CMV DNA and by serological examinations.

Result: In the set of 23 newborns with confirmed congenital CMV infection, 14 of them have permanent neurological sequel. 5 of them suffer from sensoric affection (4 x disturbance up to loss of hearing, 1x eye lesion).

Conclusions: As most maternal infections are asymptomatic, repeated serological screening of all suscetible seronegative woman would be required throught pregnancy. There is no established treatment for congenital CMV infection, although ganciclovir have been suggested for use to inhibit disease progression.

1149

A COMPARISON OF NEONATAL ONSET OF SEPSIS BETWEEN VERY LOW-BIRTHWEIGHT AND LOW/NORMAL-BIRTHWEIGHT INFANTS

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Background and aims: Neonatal sepsis is a major cause of morbidity and mortality worldwide. The onset time of sepsis can reflect either maternal or prolonged hospitalization's risk factors. Aim of this single-centre study was to identify the overall incidence of sepsis and pathogen distributions.

Methods: All neonates admitted to the NICU of Papageorgiou Hospital, Thessaloniki, between 01/2007-12/2010 were included.

Sepsis was defined by positive blood culture in association to clinical signs; two subgroups were identified regarding birtweight: very low-birthweight (VLBW) (< 1500g) and low/normal-birthweight infants (L/NBW) (≥1500g).

Sepsis incidents were classified into Early (EOS) (1-7th day of age) or Late Onset Sepsis (LOS) (7-90th day of age) and pathogen distribution was analyzed between the groups.

Results: A total of 408 and 1754 infants with BW< 1500g and ≥1500g respectively admitted. 110 episodes of sepsis were identified in VLBW group versus 42 in L/NBW group. Birthweight and gestational age were inversely related to rate of sepsis (26% of VLBW infants versus 2% of L/NBW infants).

The majority of infections (67% in VLBW infants and 59% in L/NBW) were caused by CoNS (56% vs 45%), followed by Klebsiella Pneumoniae (13% vs 21%).

EOS occurred in 14% vs 35%, whereas LOS occurred in 86% vs 65% in VLBW vs L/NBW infant group respectively. No differences regarding the pathogens were noted between the two sepsis categories.

Conclusions: The high prevalence of neonatal sepsis particularly among VLBW infants is documented. EOS remains a serious problem among V/NLBW infants, whereas LOS in VLBW infants.

1150

EUROPEAN SURVEY EVALUATING USE OF AZITHROMYCIN IN NEONATES

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Background: The role of Ureaplasma Urealyticum (UU) colonisation of the lungs remains controversial in the occurrence of bronchopulmonarydysplasia (BPD) of prematurity. The present European survey was conducted between April and July 2012, as part of the FP7-TINN2-project (Treat Infections in Neonates 2, www.tinn2-project.org).

Aims and methods: It aimed to evaluate the position of neonatologists regarding the role of UU as a risk factor for BPD, use of azithromycin (AZY) for the prevention of BPD and factors that influence this practice in European neonatal intensive care units (NICUs). It was conducted using an online questionnaire of 64 questions.

Results: 167 questionnaires from twenty-eight European countries were analyzed. All responders confirmed that the two major risk factors for BPD were prematurity ≤28weeks and high oxygen requirements. Various macrolides are used in Europe to treat or prevent Ureaplasma colonisation. Among them, AZY has antibacterial, anti-inflammatory and immuno-modulating properties, is employed throughout Europe (27% NICUs in 12countries), usually administered at a starting dose of 10mg/kg (60% of NICUs), followed by a maintenance dose of 5mg/kg/day (43% of NICUs). For 10 days.

78% of the NICUs were interested in the TINN2-project to evaluate the efficacy and safety of AZY versus placebo in reducing the risk of BPD in premature babies. For most neonatologists, newborns between 23 and 28weeks gestational age would be the best group of premature babies to be included in the trial.

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CHILDREN WITH DIARRHEA HAVING COMPLICATIONS OF HYPOKALEMIA ADMITTED IN ACCIDENT AND EMERGENCY DEPARTMENT OF THE CHILDREN'S HOSPITAL, LAHORE

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Aim: To observe children with diarrhea having complications of Hypokalemia

Material and method: An observational study conducted in children's hospital and institute of child health Lahore from 1st May 2012 to 31st August 2012. Patients were divided into five groups. **Group 1** potassium level < 1.5 to 1.5mEq/l,**Group 2** 1.5 -2.0mEq/L, **Group 3** 2.0 to 2.5mEq/L, **Group 4** 2.5-3.0mEq/L **Group V** l 3.0- 3.5mEq/L Children with chronic renal diseases, congenital heart disease and on diuretics were excluded.A predesigned Pro forma was filled; Informed consent was taken . 3ml of blood taken on admission with ECG.

Results: 400 patients included in the study with diarrhea age 1 month - 5 year. During this period 14874 admitted in diarrhea section. Children having serum potassium level < 3.5 mEq/L were enrolled. 12.0%(48) were 2months - 1 year,24.25%(97) of 1 - 2 year,32.25%(129) of 2-3 year ,9%(76) of 3-4 year and 12.5%(50) of 4-5 year. Important complications observed, abdominal distension 44.5 %(178) loss of neck holding 33.75 %(135), Inability to walk 22.50%, paralytic ileus 19.25% , generalized weakness 14%. Severity of symptoms more in Group I (75)18.75% more number of patients with symptoms in Group II (102)26.75%, Group III (90)22.50%. Common ECG changes flattening of T-wave 51% (204) and ST segment depression 38.5% (154).

Conclusion: In acute diarrhea hypokalemia is common complication in children ranges from mild to severe symptoms like abdominal distension, paralytic ileus, loss of neck holding, and paraplegia and in more severe cases cardiac arrhythmias.

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KNOWLEDGE AND ATTITUDES TOWARDS HUMAN PAPILLOMAVIRUS (HPV). AGREEMENT BETWEEN SPANISH MOTHERS AND THEIRS ADOLESCENT DAUGHTERS

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Background and aims: HPV vaccine coverage is far from ideal in Valencia, Spain. Mothers and adolescent knowledge about HPV and risk perception might influence their decision to vaccinate. In order to design better vaccination campaigns We examined the agreement between mothers and daughters knowledges and perceptions.

Methods: 15 year old female students and their mothers participated. HPV Vaccine was indicated. A questionnaire was filled in by both. Sample selection was performed by a proportional stratified random sampling by clusters by geographic criteria as population of the province of Valencia.

Results: 834 “mother-daughter” couples agreed to participate. 91% of the couples were in favour towards vaccination, in case of disagreement, girls were more supportive of vaccination (OR= 4.25, 95%CI: 1.93-10.62). Regarding risk situations (traffic accidents, cancer, insecurity, new epidemics, AIDS, other Sexually Transmitted Diseases), when disagreement, girls were more concerned than mothers only in the last item (OR: 1.42 CI 95%: 1.11-1.82). 85.7% of couples had heard of HPV. Girls were better informed (OR= 0.51, 95%CI: 0.33-0.78) in case of disagreement. The average HPV knowledge score of mothers was 5.91 (SD: 1.38) and 4.48 (SD: 1.92) in girls. 96% of couples had heard about HPV vaccine. 39.75% of couples agreed that clinicians advised them to get the vaccine. Adverse events was the main reason for not vaccination (20.85% of couples).

Conclusions: There is a general agreement in favor of vaccination, in girls more than mothers. Mothers are more concerned over the vaccine risk. Generally the knowledge of infection is low.

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HIV DIAGNOSIS IN CHILDREN: TWO DIFFERENT POPULATIONS

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Background and aims: Despite worldwide measures to screen and prevent mother-to-child transmission, some children continue to be diagnosed in a later stage. We aim to compare the ones who undergo newborn screening (NBS) to those diagnosed later.

Methods: HIV-infected children diagnosed in our HIV Paediatric Centre over the past 6 years(y) were sorted into Group1 (NBS) and Group2 (non-NBS). Charts were reviewed concerning clinical evolution, laboratorial findings and treatment response.

Results:

Group1 (n=8; 7 HIV1; 1 HIV2): All children were born in Portugal. Seven received prophylactic antiretroviral therapy (ART) and none was breastfed. At presentation, mean CD4+ percentage was 41% (standard-deviation 10,5); none presented immunosuppression. Triple ART was started on six HIV1-infected children, all reaching HIV viral load (VL) < 40 copies/mL after an average of 11,1 months(m). One was diagnosed at age 15m after 3 negative PCR-DNA assays. None presented serious disease.

Group2 (n=15; 14 HIV1; 1 HIV2): 12 children were born in Africa. Median age at diagnosis was 6,8y (1m-15,3y), with 14 of them presenting immunosuppression; 14 were symptomatic. Mean CD4+ percentage was 21% (standard-deviation 16,8). Twelve HIV1-infected children started triple ART; 8 reached undetectable VL at 12m treatment; one after 12m. Treatment failure in 3 children was due to low adherence to ART. None presented disease progression.

Conclusion: Children diagnosed through NBS had neither immunosuppression nor disease and presented better virological outcome on treatment. Clinical suspicion of HIV infection remains crucial, since those evading screening programs will later present with disease, requiring prompt diagnosis and ART.

1154

EFFECTIVENESS OF ORAL RIBAVIRIN AND EXTRACORPOREAL MEMBRANE OXYGENATION IN A 1 YEAR OLD GIRL AFFECTED BY PARAINFLUENZA VIRUS TYPE-3 PNEUMONIA

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Human Parainfluenza viruses (HPIVs) are common respiratory viruses of the Paramyxoviridae family. HPIVs infection can lead to a wide variety of clinical syndromes and Parainfluenza Virus Type 3 (PIV3) is largely known to cause bronchiolitis and pneumonia in the first year of life.

We report the case of a 1-year-old girl who presented acute respiratory distress syndrome, in association with a transitory hypogammaglobulinemia.

Despite supportive care and treatment with endovenous wide-spectrum antimicrobial and steroids therapy, a progressive respiratory failure ensued and Venovenous Extracorporeal Membrane Oxygenation was suddenly started.

Chest radiograph and Computerized-Tomography-Scan showed diffuse bilateral alveolar-interstitial infiltrates, multiple noncavitating nodules with irregular margins, bilateral upper lobes collapse, and pleural effusion.

Screening for Pn.carinii, M.tuberculosis, M.pneumonia, adenovirus, RSV, HHV6, EBV and CMV was negative while PCR examination on nasopharyngeal swab specimens for PIV3 was positive, revealing the diagnosis.

A combination therapy with Ribavirin (120 mg/die for ten days) and intravenous gamma globulin (IVIG)(400mg/Kg/daily for five days) was started with considerable improvement of general conditions. Subsequent blood analysis and more specific immunological assessment resulted normal, thus showing the transient nature of the immune disorder.

This case highlights the importance of a prompt diagnosis and therapy with ribavirin, IVIG and steroids of PIV3 pneumonia in a context of a transitory immune deficiency ECMO can be considered as a successful therapeutic strategy during the early phases of the infection for those cases who rapidly progress to severe respiratory failure.

1155

CONTRIBUTION OF (1-3)-B-D-GLUCAN TO THE DIAGNOSIS OF INVASIVE CANDIDA INFECTION IN NEONATE

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Introduction: Candida species are the third most common cause of late onset sepsis in patients hospitalized in Neonatal Intensive Care Unit. The incidence is 3 % in premature infant < 1500g. The diagnosis of neonatal invasive Candida infections (ICIs) is difficult because the clinical signs are not specific and sensibility of blood cultures is less than 40 %.

Objective: To assess the contribution of serum (1-3)-ß-D-glucan (BDG) levels to the diagnosis of neonatal ICIs.

Methods: This retrospective study was performed at Amiens University Medical Center (Amiens, France) during the period December 2010 - March 2012.

Newborns in whom a BDG assay was performed for a suspected ICI are included in our study. Two groups of patients were constituted: the infected group (n = 18) and the non-infected group (n = 43).

Results: Sixty-one premature infants were included. Patients were (median (25^{th}-75^{th} p)) 28.5 weeks (26.7-30.6) gestational age and 1000 g (910-1440) birth weight.

The BDG level was higher in the infected group (364 pg/ml (131-976) vs. 89 pg/ml (30-127); $p < 0.001$).

The optimal BDG cut-off for distinguishing between non-infected and infected patients was 125 pg/ml (Se = 84%, Sp = 75%).

Conclusion: Our study results suggest that BDG levels were increased in neonatal invasive Candida infections (cut-off for BDG positivity > 125 pg/ml).

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PREVENTION OF THE RECURRENT ACUTE RESPIRATORY VIRAL INFECTIONS IN CHILDREN

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Background: The recurrent episodes of acute respiratory viral infections (r-ARVI) are common for children attending nursery school.

Aim: To evaluate the efficacy of interferon inducer (IFN-i) containing release active antibodies to interferon-γ (anaferon) in prevention of r-ARVI in children.

Methods: The open comparative prospective 2-center clinical trial of efficacy was conducted. The trial was performed in 141 children at the age of 1-5 years. 50 children included in group 1 received IFN-i repeatedly (the previous preventive course was administered 6 months before the trial). 75 children of group 2 took IFN-i for the first time. 16 children of group 3 didn't receive medical prevention of ARVI. For treatment of the ARVI all children received symptomatic medicines, and children of 1&2 groups received IFN-i in the treat regimen. The percent of children becoming ill with ARVI for a first time and recurrent ARVI were evaluated.

Results: For 3 months follow-up period 28% of children suffered from ARVI in group 1, 56% in group 2 and 87,5% in group3. There wasn't registered any case of recurrent ARVI in group 1. Cases of recurrent morbidity were seen in 9,3% of children in group 2 (2 episodes) and in 75% of children in group 3 (44% of children suffered from more than 2 episodes of ARVI).

Conclusions: The repeated preventive administration of IFN-i (anaferon) allows to decrease the morbidity and the frequency of recurrent ARVI episodes in a children attending nursery schools without decreased its efficacy.

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CLINICAL CHARACTERISTICS OF ALVEOLAR AND NON-ALVEOLAR COMMUNITY ACQUIRED PNEUMONIA (CAP): A MULTI-CENTER STUDY

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Background: X-ray defined pneumonia is used for epidemiological studies Alveolar pneumonia (AP) considered as bacterial etiology was use in vaccine evaluating studies. Our aim was to define unique clinical and laboratory characteristics of AP compare with non-AP.

Methods: Prospective multi-center study, children with radiologically confirmed CAP, visiting emergency rooms in 7 different countries of Europe during two seasons: 2010-2011 and 2011-2012 were enrolled. Demographic, clinical and laboratory data were documented. In order to avoid biases, the classification of AP or non-AP was evaluated by one pediatrician.

Results: 949/1339 were AP, 298 were non alveolar and 92 CXR were not available.

Children with alveolar pneumonia were older (32 vs 24 months of age), lived with more children, either at home or at framework ($p< 0.001$) had received more antibiotics in the previous month ($p< 0,01$), had less pneumonias since birth ($p< 0.001$) and less asthma attacks ($p< 0.001$).

Clinically alveolar pneumonia had slightly higher temperature (38.9 vs 38.7; $p< 0.001$) and more rhinorrhea, cough, stomachache and vomits ($p< 0.05$).

Children with alveolar pneumonia had the same O2 saturation and higher respiratory rate related to age ($p=0,02$), white blood cell count (17.5 vs $14.1/10^9$L; $p=0.01$), neutrophil count (11.6 vs $8.2/10^9$L; $p=0.01$) and CRP (75.6 vs 26.1; $p< 0.001$). There was no difference in the ESR and Procalcitonin when available.

Conclusions: Radiologic defined alveolar pneumonia is a unique entity, clinically indistinguishable from non alveolar, and characterized by high WBC, ANC and PCR in previously healthy children.

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BACTERIAL MENINGITIS IN MOROCCO A RETROSPECTIVE STUDY ABOUT 720 CASES

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Bacterial meningitis (BM) is a common disease worldwide;.it was a major public health problem in Morocco with significant morbidity and mortality before integration of vaccines against Haemophilus influenza type b (HIb) and streptococcus pneumonia. The aim of this work is to analyze the evolutionary and epidemiological profile of purulent meningitis at the University Hospital of Casablanca.

Patients and methods: A retrospective review of BM cases reported between January 2001 and December 2012 was conducted. Collected Data included demographic features, causative microbiologic agents and their sensitivity, annual incidence rates, mortality and morbidity.

Results: Our series focuses on 720 cases of BM in children aged 1 month to 14 years. 71% of patients had less than 5 years. The causative agent was identified in 60, 4%. The Neisseria meningitidis (MNO) prevailed with 41% of identified germs, followed by Streptococcus pneumoniae (PNO) and Hib with respectively 32% and 23%. MNO is stable over the past 12 years with a mean of 15 cases a year dominated by serotype B. Mortality is about 4%, complications are at 25% and mortality is around 10%.

Discussion: This study covers two epidemiological periods: pre-meningitis vaccination era and vaccinal eras, the one first began on 2007 with Hib vaccine, the second began on 2010 with pneumococcal conjugate vaccine (PCV). we emphasize a drastic reduction of Hib meningitis which is now occupying the 3rd place after the MNO and PNO. The impact of pneumococcal vaccination is not yet obvious. MNO is currently the main germ of BM.

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POSITIVE PREDICTIVE VALUE OF THE ROTAVIRUS ICD-9 DISCHARGE CODE IN SPAIN

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Aims: To determine the positive predictive value (PPV) of the ICD-9-CM code for rotavirus disease in the Spanish hospital discharge database (CMBD) in order to estimate vaccine effectiveness.

Methods: Retrospective study conducted in Valencia, Spain. Children under 3 yoa born during 2007-12, admitted to public hospitals during January 2008-June 2012, with a discharge code of intestinal infection (001-009). We analysed the PPV of: rotavirus code (008.61) as first discharge diagnosis (A), as first/second diagnosis (B), as any diagnosis (C), or codes 001-009 (excluding 008.61) in first position with 008.61 as second (D).

PPVs using data from the regional laboratory database (RedMIVA) as gold standard were calculated using two definitions:

1) rotavirus test positive vs. negative; or

2) rotavirus test positive vs negative or untested.

Results: There were 4,295 hospitalized cases of intestinal infections, 1,877 (43.7%) were coded as rotavirus. Of all admissions, 3,046 (70.9%) were tested for rotavirus. Of the rotavirus gastroenteritis coded, 1,411 (75.2%) had a positive test result, and 59 (4.2%) had a negative result.

PPVs ranged between 95.9% and 46.5% (Table).

	1	2
A	95.9% (95%CI: 94.5-97.0)%	73.3% (95%CI: 70.8-75.6)%
B	95.9% (95%CI: 94.6-96.8)%	73.8% (95%CI: 71.6-75.9)%
C	96.0% (95%CI: 94.9-96.9)%	75.2% (95%CI: 73.2-77.1)%
D	95.2% (95%CI: 77.3-99.2)%	46.5% (95%CI: 32.5-61.1)%

[PPV]

Conclusion: The moderate-high positive predictive value of the rotavirus discharge code grants the use of CMBD database for analysis of rotavirus vaccine effectiveness and impact.

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UNDER-DIAGNOSIS OF HEPATITIS C IN CHILDREN IN SCOTLAND: DO WE NEED TARGETED ANTENATAL SCREENING?

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Background and aims: Hepatitis C virus (HCV) is a major public health problem in Scotland. Under-diagnosis in adults is well established, with 51% of HCV-infected persons unaware of their status. The epidemiology of HCV in children in Scotland is not well studied and the extent to which under-diagnosis affects this population unknown. This study aimed to describe the epidemiology of HCV, and compare estimated prevalence of vertically-transmitted HCV to reported cases, in children born in Scotland, January 1991-December 2008.

Methods: Prevalence of vertically-transmitted HCV was estimated using national birth statistics, published maternal seroprevalence data and a 5% vertical transmission rate. The Health Protection Scotland (HPS) Hepatitis C Diagnosis database was used to identify reported cases in children under 16 years (January 1991-December 2010). Epidemiological data, including risk factors for HCV, were obtained from medical records.

Results: The predicted prevalence rate of vertically transmitted HCV in Scotland was 1.4/10000 (1.1-1.8/10000) live births. The observed prevalence rate was 0.5/10000 live births. There was a 63% (53-70%) deficit between predicted and diagnosed cases. Maternal intravenous drug use was identified in 77% of paediatric cases where an HCV risk factor was known.

Conclusions: There is a significant deficit between predicted and diagnosed cases of HCV in children in Scotland. This suggests under-diagnosis. The most common risk factor was maternal intravenous drug use. Targeted antenatal screening of women who inject drugs could identify undiagnosed women and infants at risk of HCV. Large population-based paediatric seroprevalence studies are required to establish the true prevalence of HCV.

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DECLINE OF HERPES ZOSTER CASES < 10 YEARS OF AGE AFTER INTRODUCTION OF ROUTINE VARICELLA VACCINATION IN BAVARIA, 2006-2011

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Background: Germany introduced varicella vaccination for all children 11-14 months of age in 2004. We investigated the impact on the epidemiology of herpes zoster (HZ) in paediatric practices.

Methods: HZ cases < 17 years of age were documented monthly from 88 practices in Munich (Bavaria) from October 2006 to September 2011.

Results: The practices reported 274 HZ cases (mean 0.8/0.7/0.7/0.4/0.7 per season and practice). Median age was 9.3 years (IQR 5.5-12.1), previous varicella had occurred at 3.1 years (IQR 1.4-4.3). Children with varicella < 1 year of age (n=32; 12%) developed HZ after a shorter interval than children with later varicella disease (median 3.9 vs. 6.6 years; p=0.03). HZ < 10 years of age declined by 36%, from 3.8 (95%CI 2.7-5.0) cases per 100 practice months in Season 1 to 2.5 (95%CI 1.5-3.4) in Season 3; HZ 10-16 years of age increased by 36%, from 2.2 (95%CI 1.2-3.1) to 3.0 (95%CI 1.8-4.1). For Season 1 to 3, HZ < 10 years of age declined from 39 to 25 cases, HZ 10-16 years of age increased from 22 to 30 cases (Mantel-Haenszel, p< 0.05). However, neither of these trends continued in Season 4/5.

Conclusions: The initial decline of HZ < 10 years of age corresponded to the increase in varicella vaccination coverage in the area (reaching 67% in 2010/11) and may partly be due to herd protection. The increase in children >10 years of age remains unexplained. Similar changes in age groups had been reported by Civen (2009) and Siedler (2011).

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PROSPECTIVE MONITORING OF EPISODES OF FEBRILE NEUTROPENIA IN PEDIATRIC ONCOLOGY PATIENTS

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Background and aims: Febrile neutropenia is an important clinical problem in children with malignant disease. We monitored episodes of febrile neutropenia, complications and available biomarkers.

Methods: Prospective study of episodes of febrile neutropenia (absolute neutrophil count < 1000 cells per mm^3) in children hospitalized in an 18-bed pediatric oncology department over one year period. Documentation of bacterial, viral or fungal infection and estimation of mortality were the endpoints of this study. C-reactive protein (CRP) and procalcitonin were evaluated as predicting biomarkers.

Results: There were 498 admissions and 3490 bed-days during the study period. A total of 85 episodes of febrile neutropenia (91% during induction chemotherapy) were identified in 43 children (median age 7.1 years) with malignant disease (34 hematological malignancies, 9 solid tumors). Documented bacterial infections were found in 27/85 episodes (23 bloodstream infections, 1 urinary tract infection and 3 other infections). Blood cultures revealed that coagulase negative staphylococci were the most frequent pathogens (48%) followed by Escherichia coli (17%), Klebsiella spp (9%) and Pseudomonas aeruginosa (9%). There was 1 documented CMV infection and 1 hepatosplenic candidiasis. There were 3 deaths, one associated to the infection. The median of CRP in children with documented bacterial infection was 70.4, while in children without documented bacterial/viral or fungal infection was 28.6 respectively (p=0.021). Positive procalcitonin (>0.5mcg/l) was associated to documented bacterial infections (p=0.04).

Conclusions: Bloodstream infection was the most frequent complication in episodes of febrile neutropenia. CRP and procalcitonin may provide assistance for guiding prompt treatment of these episodes.

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ETIOLOGICAL DIAGNOSIS OF ACUTE ENCEPHALITIS IN CHILDREN: ARE WE ANY CLOSER?

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Background: Acute encephalitis is a neurological syndrome caused by different agents. Although new laboratory methods have improved the diagnosis, in a great proportion of cases the etiology remains unknown.

Methods: Medical charts from previously healthy children < 16 years old hospitalized with encephalitis were reviewed and demographic, clinical and laboratory parameters analyzed.

Results: From January 2001 to December 2012, 35 children with encephalitis were admitted (60% males; 3.68 [0.95-7.4] years). History of recent infection was found in 43% (15/35) of patients and 71% (25/35) had fever. Cerebrospinal fluid (CSF) was normal in 32% of the 31 children who underwent a lumbar puncture. Children with abnormal CSF had more headaches (p=0.03) and more abnormal electroencephalograms (p=0.05) compared to those with normal CSF. A CT-scan was performed in 26/35 (71%) children while 31/35(88%) had a brain MRI. Almost half of patients had neurological sequelae: neurocognitive deficit (28%), seizures (26%), motor impairment (14%) and others (17%). Etiology was found in 66% (23/35) of the children, 43% of them (10/23) by PCR. The most frequent pathogens isolated were VVZ (21%), HSV I (17%) and Mycoplasma (17%). Compared to the 2001-2007 period we observed an increase in molecular diagnostic tests performance in the 2008-2012 period, especially in blood PCR tests (12.5% vs 47%,p=0.03).

Conclusion: Encephalitis is still associated with an elevated morbimortality in children. An etiological microorganism was identified in two thirds of the patients but diagnosis remains challenging. Further studies as well as unified clinical guidelines are needed to improve management of this disease.

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INTESTINAL PARASITIC INFECTION AMONG PRE-SCHOOL CHILDREN

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Background: Intestinal parasites are common in children. The aim of the study was to determine the prevalence of intestinal parasites in pre-school children, brought to Pediatric Clinic in Prishtina with complaints of gastrointestinal symptoms.

Methods: Fecal samples were taken from 350 children and brought to National Institute of Public Health laboratory. Lugol solution was used during microscopic examination. Statistical significance was analyzed by using Chi-Square test.

Results: Intestinal parasitic infections were identified in 40 children (11.5%). In the total sample, the most frequent parasites found was Giardia lamblia 24 (60%). The second frequency was for Ascaris lumbricoides 15 (37.5%), and the third one for Enterobius vermicularis 1 (2.5%). There is no stastistical difference related to sex.

Conclusions: There is e low prevalence of intestinal parasitosis among pre-school children even though this study emphasizes the need for improved environmental hygiene and health education of the population.

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DERIVATION OF A DECISION ALGORITHM TO PREDICT ACUTE PYELONEPHRITIS IN FEBRILE CHILDREN WITHOUT SOURCE

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Background: The identification of acute pyelonephritis (APN) in children with fever without source (FWS) would be of interest as APN represent half of bacterial infection among those children. Procalcitonin was demonstrated to be significantly associated to APN, and urinary dipstick, a specific screening test for urinary tract infection, could be helpful. We aimed to derive a decision algorithm to predict APN among febrile children without source using simple examinations immediately available (procalcitonin and urine dipstick) at the Emergency Department.

Methods: Data from bi-centre cohort studies of children with FWS were analysed using multilevel regression modelling.

Results: 582 children (15% APN) were included. Procalcitonin, leucocytes and nitrites on dipstick urine were associated with APN in univariate and multivariate analysis. A model was derived based on the logistic regression equation, and yielded an AUC ROC of 0.94 [0.91-0.97] significantly higher than procalcitonin and CRP alone ($p < 0.0001$). According to a decision curve analysis, the model also offered a better strategy than those based on biomarkers considered alone. Dichotomizing the model on an interesting threshold, the model achieved 97% [93-99] sensitivity, 54% [49-59] specificity, 40% [35-45] positive predictive value, and 98% [96-100] negative predictive value.

Conclusion: The derived decision algorithm predicted APN with high sensitivity and negative predictive value, meaning that very few patients were misdiagnosed. Specificity reflected the number of more invasive diagnostic procedures, such as reference techniques for urine collection or early DMSA scan, avoided. These results need further abroad validation.

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MOTHER TO CHILD TRANSMISSION OF HIV ACCORDING TO TIME OF MATERNAL DIAGNOSIS. RESULTS FROM THE GREEK HIV PERINATAL STUDY, 2008-2012

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Background and aims: To evaluate outcomes in infants born to HIV (+) mothers according to time of maternal HIV diagnosis and implemented interventions.

Methods: Retrospective analysis of data, derived from the national HIV perinatal study and followed up in the Pediatric Infectious Disease Unit of Agia Sophia Hospital between 2008 -2012.

Results: From 1990 -2012, 231 infants born to HIV positive women were evaluated in the Unit, 69 of them between 2008-2012. In total 8 infants became infected.

28/69 (40,6%) infants were born to mothers known to be HIV+ before current pregnancy. 17/69 (24,6%)infants were born to mothers diagnosed during antenatal screening. No infants became infected. In all cases a comprehensive approach to reduce mother to child transmission of HIV, according to national guidelines was implemented.

In 12/69 (17,4%) maternal infection was diagnosed during labour. 3 infants became infected despite the prompt initiation of neonatal prophylaxis. The increase in the number of women diagnosed antepartum in 2011 -2012 is related with the recent HIV outbreak among IDUs.

In 6/69 (8,7%) cases the maternal diagnosis followed the diagnosis of the infection in the child. In a twin pregnancy only one child became infected.

In the remaining 6/69 cases the time of maternal diagnosis was unknown but all children were negative.

Conclusions: The availability of effective interventions to prevent mother-to-child HIV transmission has led to a limited number of HIV-infected infants in Greece. Strong coordination of efforts is necessary in order to manage cases presenting late in pregnancy.

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LONG-TERM EXPERIENCE AND METABOLIC EFFECTS WITH ATRIPLA® IN HIV-ADOLESCENTS

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Background: High levels of adherence to HAART in HIV patients are required to achieve viral and immunological control. Atripla is a once-a-day coformulated tablet of efavirenz, emtricitabine and tenofovir, which is a good option in combination antiretroviral therapy (CART). However there is scarce experience with Atripla in patients< 18 years.

Methods: Prospective study of patients with Atripla in an Infectious Disease Unit since January 2009.

Results: A total of 8 patients (6 male) started Atripla when they were less than 18 years old. Currently median age is 15.1 years (10-21). A follow-up period of at least 12 months has been realised in all cases. Median of accumulated time of treatment was 29.6 months (12-46 mo). Median of CD4 before and after the beginning of Atripla was 1181 cells/µL (357-2117) and 865 cells/ µL (592-1135), respectively. Median of HIV viral load before and after of Atripla was 6751.5 copies/ml (37-23.600) and 64.3 copies/ml (37-255.6), respectively. All patients present very good lipid profile after the beginning of treatment, except case 1 and case 4 who have a diet rich in saturated fats. Most of them (7 cases) present an adherence >95%. Case 7 has showed low levels of adherence currently because of rebelliousness of knowledge infection. Main results are exposed in table 1.

	Gender	Age (years)	Viral load before/after Atripla®(copies/ml)	CD4 before/after Atripla® (cells/µL(%))	Total cholesterol before/after Atripla® (mg/dl)	Triglycerides before/after Atripla® (mg/ml)	Adherence before/after Atripla® (%)	Previous treatment to Atripla®
1	F	21	<37/<37	1537(36%)/ 717 (37 %)	151/125	89/150	85-95/>95	FTC+DDI+ EFV
2	M	19	<37/<37	2117(33%)/ 870 (35,7%)	146/131	123/40	>95/>95	DDI/FTC/Fosam+rtv
3	M	14	23600/<37	357(15%)/ 806(24%)	117/122	69/50	- />95	Interrupted for 5 years
4	M	10	<37/<37	1691(51%)/ 1135(46%)	165/246	70/62	>95/>95	ABC/FTC/Lop+rtv
5	M	17	16390/<37	675 (23%)/ 1141 (32%)	110/133	61/113	-/>95	Interrupted for 2 years and 9 months
6	M	11	<37/<37	965 (22%) /1063 (35%)	162/142	45/35	>95/>95	DDI/ABC/EFV
7	M	14	<37/<37	761(33%)/ 599(35%)	211/127	116/97	80-85/80-85	ABC/TDF/FTC
8	F	15	13800/255,6	1346 (28%)/ 592 (37,5%)	140/145	56/41	-/>95	Interrupted for 3 years and 6 months

[Table 1]

Conclusion: In general, Atripla is been well tolerated. The use of this pill is able to achieve viral control and improvement in adherence and quality of life of patients and their families.

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PROPORTION OF HOSPITALISATIONS AND COMPLICATIONS IN INFANCY DURING 14 YEARS OF SURVEILLANCE AND THE INCIDENCE OF PERTUSSIS

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Background and aim: Owing to vaccination coverage for pertussis of 98-99% since 1996 and narrow time interval for each vaccine dose at 3, 5 and 12 months of age there have been a significant decrease of pertussis in childhood in Sweden. Last 4 years only around 40 pertussis cases per year have been reported in infancy. All children with reported pertussis have been followed up in the pertussis surveillance study with structured questions of hospitalisations, complications, vaccinations, antibiotic treatment, etc. But, could the reporting of pertussis differ through the years?

Method: The proportions of complications and hospitalisations of the pertussis cases have been analysed in infants. If these proportions of the severity of pertussis do not change during the years, the assessed incidence of pertussis could be an assumption for the changes in incidence.

Results: During the years 1997-2011 the proportion of infants with complications or hospitalisations due to pertussis were relatively constant. The reported cases were however decreasing. This indicates a real decrease of pertussis among infants, even in the youngest infants not yet immunised. In 2012 there was a preliminary increase of 35% of reported pertussis in infants. Whether this is a real increase or not will be evaluated.

Conclusion: Changes in the incidence of pertussis disease could be evaluated more properly if the proportion of complications and hospitalisation of the disease is analysed. Thus, the changes in incidence would then unlikely be influenced by diagnostic shifts or different awareness of pertussis.

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HAART AND CARDIAC ALTERATIONS IN HIV-INFECTED CHILDREN: A SINGLE CENTER EXPERIENCE

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The introduction of highly active antiretroviral therapy (HAART), had leaded to the transition of HIV disease from an almost uniformly fatal illness to a chronic disease in developed nations. HAART is also associated with clinical cardiovascular concerns. Few is known about cardiovascular risk in children with HIV. Children, living longer with HIV, undergo more intensive and potentially cardiotoxic therapies, with cardiac morbidity and mortality becoming an increasing problem. In this retrospective study, our goal was to assess the cardiac events in a 15 years follow-up in HIV-infected children in treatment in the Infectious Diseases Unit of our Department of Pediatrics.

Methods: We retrospectively studied 23 children treated a combination of drugs since the beginning. In all patients EKG and echocardiography were performed every 6 months, blood sample for lipids profile was also obtain.

Results: Among the 23 patients abnormal ventricular repolarization, left ventricle enlargement and left ventricle dysfunction were present in 5 (21%) children, all of which had zidovudine in their combination therapy. 2 patients died, because of the evolution of HIV disease. Cardiac alterations in the remaining three cases improved with the modification of the treatment regimen.

Conclusions: Our results confirm the data in literature about the cardiotoxic effects of anti retroviral therapy. Additional potentially damaging cardiovascular effects of HAART are present. In HIV-infected individuals, HAART may cause adverse lipid profiles and increased risk for cardiovascular events. Continuing cardiovascular risk evaluations, screening and follow-up of treated patients is necessary.

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MOLECULAR EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL DISEASE IN THE CZECH REPUBLIC FROM THE PERSPECTIVE OF VACCINATION

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Background and aims: The aim of this study was detailed characterization of isolates from invasive meningococcal disease (IMD) in relation to the perspective of vaccination with a new meningococcal vaccines developed by reverse vaccinology.

Methods: Neisseria meningitidis (N. m.) isolates from IMD (n=217) referred to the National Reference Laboratory for Meningococcal Infections in 2007-2012 were characterised by MLST, porA, fetA, and GNA (Genome-derived Neisserial Antigens) sequencing: FHbp (factor H binding protein), NadA (GNA1994), NHBA (GNA2132), OMP (PorA 7-2,4). In total, 168 N. m. B isolates and 49 N. m. non-B isolates were studied.

Results: The following clonal complexes were most frequently found: cc41/44, cc18, cc32, cc269, cc11 and cc23. The FHbp antigen common to new meningococcal vaccines developed by reverse vaccinology was found in all N. m. B and N. m. non-B isolates. FHbp antigenic subfamily B was harboured by 65.4 % of N. m. B and N. m. non-B isolates screened, while FHbp subfamily A was detected in 34.6 %. The NadA antigen was found in 32.6 % of N. m. B and N. m. non-B isolates. The OMP (PorA 7-2,4) was found in one isolate only.

Conclusions: Molecular epidemiology of invasive meningococcal disease is essential to update the vaccination strategy.

Acknowledgement: This work was supported by research grant NT11424-4 of the Internal Grant Agency of the Ministry of Health of the Czech Republic and made use of the Multi Locus Sequence Typing website (http://pubmlst.org/neisseria/) sited at the University of Oxford.

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RECORDING OF CASES OF ERYTHEMA INFECTIOSUM IN VENIZELION GENERAL HOSPITAL OF HERAKLION, GREECE BETWEEN APRIL - AUGUST 2012.

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Background and aims: Parvovirus infection in immunocompetent individuals has usually a mild clinical picture but during pregnancy it can cause serious complications in the fetus. The most common manifestation of infection with parvovirus B19 is erythema infectiosum. Laboratory confirmation is needed to differentiate it from other exanthemas. The aim of our study is to record laboratory confirmed cases of infection with parvovirus , symptoms of the disease in children examined in Pediatric Emergency Department (ED) of our hospital between April and August 2012 and any possible correlation with an epidemic.

Methods: Symptoms of the disease were recorded and laboratory confirmation of the cases was done by detection of IgM and / or IgG against parvovirus in children examined in the Pediatric ED from April to August 2012 with rash compatible with erythema infectiosum .Detection of antibodies was performed using Enzyme-Linked Immunosorbent Assay (ELISA).

Results: A total of 16 children were recorded with confirmed infection with parvovirus B19, 7 boys and 9 girls, aged 22 months - 12 years with a mean age of 6.7 years. 13/16 children had only rash without fever. The duration of rash was from 3 to 15 days (average 8.5 days). No child presented with arthralgias. During the same period in 2011 only 2 children were recorded with confirmed infection.

Conclusion: Between April and August 2012 there was an increased incidence of confirmed Parvovirus infections in Pediatric Emergency Department compared with the same period in 2011. The majority of the cases presented only with rash.

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ABDOMINAL TUBERCULOSIS

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Abdominal tuberculosis is a rare pathology in developed countries. However, due to migratory fluxes from endemic geographical areas, it is becoming more frequent. It shows unspecific symptoms and, in vast majority of cases, thus revealing to be a challenging diagnosis.

11 years-old child, transferred from Guiné-Bissau, by matter of enterocutaneous fistula in the inferior right quadrant of the abdomen, with continuous evolution. During patient admission, it was observed severe pancytopenia and nutritional marasmus which resulted in respiratory failure after 3 days. Immediately started wide spectrum antibiotic therapy, which was stopped after consecutive negative microbiological tests. It was assumed the hypothesis of an abdominal/peritoneal tuberculosis and initiated the respective treatment. The treatment was maintained, even after testing for Mycobacterium Tuberculosis through PCR proved to be negative, due to the healthy clinical response, the location of the lesion and the epidemiological context. After recovering, it repeated the tests of Mantoux® and Quantiferon®, which now scored positive. By persistence of the fistulous trajectory with an high debit, following 2 months of anti-tuberculosis therapy, it was subjected to surgery, with ileocolectomy, to close the fistula. Histological test showed severe granulomatous transmural inflamation and some epithelioid granulomas associated with some areas of necrosis. Abdominal tuberculosis is a strong differential diagnosis in several scenarios. Facing an adequate epidemiological context and existing a strong suspicio, it is legitimate to start anti-tuberculosis treatment immediately. The discovery of alcohol-acid-resistant bacili occurs in a small percentage of cases and their absence should not limit the therapy's suspension, if appropriate.

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ACUTE SUPPURATIVE PAROTITIS: UNCOMMON PRESENTATION

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Introduction: Acute suppurative parotitis is a very rare infection in the neonatal period, lying in the literature only about 100 cases reported.

Case study: Newborn male fruit at term. Maternal serology and viral markers: negative. Screening of group B Streptococcus negative. Eutocic hospital delivery without complications. Anthropometry appropriate for gestational age. Under exclusive breastfeeding. On the eighth day of life, brought to the emergency department for not presenting stools for approximately 48 hours. Objectively had left hemifacial asymmetry, with edema and erythema in the pre-auricular region. Analytically: leukocyte 17.13 * 109 / L (39.8% neutrophils and% lymphocytes, 36.3); amylase < 10 U / L; ionogram serum unchanged PCR and 4.11 mg / L (N: < 3 mg / L). Cervical sonography: findings consistent with acute suppurative parotitis. Collected blood culture and swab exudate channel Stenon. Empirical intravenous antibiotic therapy initiated with vancomycin, ceftazidime and amikacin with progressive clinical improvement and remission of inflammatory signs. The culture of exudate channel Stenon was positive for Staph. aureus. The imunological study was normal. Ultrasound control, showed asymmetry of the glandular volume, by relative increase left without collections. Performed in outpatient MRI that showed no changes in the ducts of the parotid glands.

Comments: Although rare, acute suppurative parotitis should always be part of the differential diagnosis of preauricular erythematous masses, even in the absence of apparent risk factors. The timely institution of appropriate antibiotic treatment is essential to prevent the onset of severe complications, sometimes requiring surgical intervention and consequent increased morbidity.

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KNOWLEDGE, ATTITUDES AND BELIEFS OF MEDICAL STUDENTS REGARDING INFLUENZA VACCINATION

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Background and aims: Influenza vaccine is the most effective mean of preventing influenza infection and its severe complications. Save and effective vaccines are available and are mused more than 60 years. The aim of this cross-sectional study was to analyze knowledge, attitudes and beliefs regarding influenza vaccination among medical students.

Methods: 413 sudents of forth year at the Faculty of medicine in Belgrade were identified an received a self-administered questionnaire.

Results: Influenza vaccination coverage was low at a rate 14,04%. The most common reason for being vaccinated were: self-protection from diseaase, reccomendation from doctors, protection of other people, and the most common reason for not being vaccinated were: lack of time, forgotness, belief that vaccine is not effective and lack of perception of own risk. Vaccinated students think that vaccine is the best preventive measure for influenza infection in comparison to unvaccinated students (p=0,001), that is effective in disease prevention (p=0,031), that they are in risk to spread infection to other people (p=0,005), that vaccine is useful in comparison to adverse effects (p=0,027), that they will vaccinate in the future (p=0,001), and that all medical students should be vaccinated (p=0,001). Vaccinated students are aware od risk among pregnant women.

Conclusion: Vaccinated students are more aware of efficacy and necessarity of influenza vacccine.

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VIRAL SURVEILLANCE IN HOSPITALIZED CHILDREN WITH FEVER AND/OR RESPIRATORY TRACT SYMPTOMS IN AMMAN, JORDAN

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Background: Respiratory illnesses are the leading cause of death and hospitalization in children < 5 years of age.

Objective: To determine the viral burden of hospitalized children admitted with acute respiratory infections in Amman, Jordan.

Methods: We conducted a prospective year-round viral surveillance study in children < 2 years of age admitted with respiratory symptoms and/or fever at the government-run hospital, Al-Basheer. Surveillance was conducted Sunday-Thursday from 3/16/10-4/8/12. Clinical and demographic data including antibiotic use were collected. Nasal/throat swabs were collected, placed into lysis buffer, aliquoted, and frozen at -80°C. Specimen aliquots were shipped to Vanderbilt and tested by real-time RT-PCR for respiratory syncytial virus (RSV), metapneumovirus (HMPV), rhinovirus (HRV), influenza A and B, and parainfluenza viruses 1, 2, and 3 (PIV1-3).

Results: A total of 2024 subjects were enrolled. 60% were male, median age 3.6 months, and 91% with no prior medical history. The most common virus was RSV, detected in 886 cases of RSV. Other viruses detected included: rhinovirus(697); hMPV(217); Influenza A(44); Influenza B(11); parainfluenza viruses 1, 2, and 3 (31, 9, and 61). The most common diagnoses were: bronchopneumonia(680-33.6%), rule out sepsis(528-26%), bronchiolitis(386-19%), and pneumonia(215-10.6%). 820/2022(40.6%) were given an antibiotic prior to hospitalization and 1,802/1996(90.3%) given an antibiotic during their stay. 616/1984(31%) required oxygen. 162/1984(8.7%) admitted to the ICU. 110/1984(5.5%) required mechanical ventilation. 16/1981(0.8%) died.

Conclusion: This study indicates that viruses play a major role in respiratory illness in children hospitalized with lower respiratory tract infection in Jordan which is similar to findings in developed countries.

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VIROLOGICAL SCREENING IN CHILDREN TREATED FOR ACUTE MYELOIC LEUKAEMIA

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Background - aims: Children treated for acute myeloicleukaemia (AML) are at increased risk for infections including virus reactivations. Therefore, virological screening is performed in our institution. We evaluated frequency of selected virus infections and/or reactivations during AML therapy.

Methods: In a retrospective monocentric analysis of 22 consecutive patients treated for AML (age at diagnosis: 0.5-17 years, median 12 years) from the years 2001 to 2011 we evaluated results of virological screening for 6 selected viruses (Adenovirus, Cytomegalovirus, Epstein-Barr Virus, Human-Herpes Virus 6, Parvo-B19 Virus, Varicella-Zoster Virus) by polymerase chain reaction (PCR) which initially was performed intermittently and in recent years weekly during treatment and at follow-up examinations thereafter.

Pre-treatment serological examinations were evaluated to differentiate primary infection from reactivation.

Results: In total 42 reactivations/primary infections were found in 19 (86.4 %) of 22 patients. 10 (91.0 %) out of 11 patients who underwent stem cell transplantations (SCT, allogeneic, n=10, autologous, n=1) showed reactivations and/or primary infections after SCT. Further details for all analysed viruses are provided in table 1.

Conclusions: Virus reactivations and primary infections are very common in patients under AML treatment with EBV and HHV-6 in 50%, PVB19 in one third and ADV and CMV in >20% of patients, respectively. Routine virological screening may help in early detection and decision on pre-emptive therapy of viral reactivations/infections in these high risk patients.

		ADV	CMV	EBV	HHV6	PVB19	VZV
pre-treatment serology	pts pos/pts tested	6/7 (85.7%)	5/13 (38.5 %)	11/13 (84.6 %)	7/12 (58.3 %)	11/14 (78.6 %)	8/9 (88.9 %)
	not available	15	9	9	10	8	13
PCR screening	specimens pos./ specimens tested	22/1218 (1.8%)	57/1135 (5.0 %)	60/839 (7.2 %)	79/775 (10.2 %)	30/753 (4.0%)	1/316 (0.32 %)
	pts pos/pts tested	6/22 (27.3%)	5/22 (22.7 %)	11/22 (50.0 %)	11/22 (50.0 %)	8/22 (36.4 %)	1 /17 (5.9 %)
interpretation	pts tested	22 (100%)	22 (100%)	22 (100%)	22 (100%)	22 (100%)	17 (100%)
	reactivation	3 (13.6 %)	4 (18.2 %)	4 (18.2 %)	3 (13.6 %)	5 (22.7 %)	1 (5.9 %)
	primary infection	0 (0.00 %)	0 (0.00 %)	1 (4.5 %)	2 (9.1 %)	0 (0.00 %)	0 (0.00 %)
	pos screening, no serology available	3 (13.6 %)	1 (4.5 %)	6 (27.3 %)	6 (27.3 %)	3 (13.6 %)	0 (0.00 %)

Table 1. Details on pre-treatment serology, virological PCR screening and interpretation of results (primary infection vs. reactivation) for the analysed viruses (ADV - Adenovirus, CMV - Cytomegalovirus, EBV - Epstein-Barr Virus, HHV6 - Human-Herpes Virus 6, PVB19 - Parvo-B19 Virus, VZV - Varicella-Zoster Virus) in absolute counts (%).

[Table 1]

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PRIVATE INITIATIVE FOR CONTROL OF THE TRANSMISSION OF PERTUSSIS IN A BRASILIAN MATERNITY FACILITY

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Pertussis (whooping cough) targets vulnerability of newborns and it often results in complications and deaths. The principal source of transmission are parents/caregivers and though immunity decreases with time (by vaccine and by natural resistance), adults may transmit the disease. Recommendation of the vaccination of adults requires consideration to reduce morbi-mortality due to the resurgence of pertussis.

Objective: Objective of this report is to recommend vaccinating maternity hospital employees against pertussis.

Methods: Curitiba, capital of Paraná State, Brasil (population 1.8 million), has provided the whole cell pertussis vaccine for children (sponsored by the Brazilian Program of Immunizations) since the1970's.

1994 - 2010, Curitiba's vaccination program resulted in a maximum of 10 documented cases of pertussis per year; however, in last quarter of 2011 - first quarter 2012, there was an increase, totaling 92 confirmed cases.

As a result of this spike, the hospital initiated the following: staff was vaccinated, disseminated alerts in meetings, distributed written notifications and made recommendations for visitors and patients.

Prophylactic measures:

· Employee vaccinations

· Visitor reduction

Guidance measures:

· Meetings

· Written alerts for symptoms

· Dissuasion of infant contact if coughing or been near a sick person

· Direction to vaccinate persons in contact with newborns and their mothers

Conclusions: Protecting a newborn from petrussis requires separate tactics. These tactics comprise a strategy "cocoon" and the plan must include vaccination of parents and other familial caregivers. These actions can reduce and prevent cases of pertussis (whooping cough) among infants.

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MOLECULAR DETECTION OF ENTEROAGGREGATIVE ESCHERICHIA COLI IN FAECAL SAMPLES FROM TUNISIAN CHILDREN

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Background and aims: Enteroaggregative Escherichia coli (EAEC) is an emerging enteric pathogen that causes acute and chronic diarrhea among children. The aim of this study was to assess the usefulness of a multiplex PCR assay for the detection of EAEC. The isolates harbouring selected genes were tested for biofilm formation and adherence profil on HEp-2 cells.

Methods: A 178 stool samples were collected from 124 patients and 54 controls children. After standard identification of isolated bacteria (bacterial culture and biochemical identification), we have exanimate the presence of aggR, CVD432 and aspU genes by multiplex PCR after DNA extraction. The isolates harbouring these genes were also tested for biofilm formation and adherence profil on HEp-2 cells using the HEp-2 cell-adhesion assay.

Results: aggR, aspU or CVD432 was found in E. coli faecal isolates from 29 (23.4%) of 124 diarrheal patients and from 8 (14.8%) of 54 healthy children. Twenty five of the 29 strains (86.2%) isolated from patients and 6 of the 8 strains (75%) isolated from healthy children adhered to the HEp-2 cells in a stacked-brick formation. Six EAEC strains that harboured the aggR gene (n=4) and the aggR and the aspU genes (n=2) were HEp-2 cell test negative.

All EAEC strains isolated from patient and healthy children present a biofilm formation but a wide range of the amount of biofilm formation was scored.

Conclusions: The multiplex PCR assay detects a variety of strains exhibiting characteristics of the EAEC group, making it a useful tool for identifying EAEC strains.

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A VIRAL MENINGITIS OUTBREAK ASSOCIATED WITH ECHOVIRUS 18 IN SÃO PAULO STATE, BRAZIL

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Background and aims: Human enteroviruses (HEVs) are responsible for a wide spectrum of clinical disease. They are the most common cause of viral meningitis and represent a serious public-health problem, especially during outbreaks. The aim of this study was to describe the HEVs serotype responsible for an outbreak of 11 suspected cases of aseptic meningitis among children from two schools in the City of Bauru, São Paulo State, Brazil, between October and November of 2012.

Methods: Cerebrospinal fluid (CSF) samples from 05 children were sent at the Adolfo Lutz Institute for research of HEVs. Cell culture, RNA extraction and Real Time Polymerase Chain Reaction (PCR) were performed on each sample to determine the presence of HEVs. Samples which were positive for enterovirus in cell culture were subject to reverse transcription - PCR (RT-PCR) and VP1 partial sequencing to identify the etiological agent of the outbreak. The serotype of each isolate was determined by BLAST search of the VP1 amplicon sequence available in GenBank.

Results: All CSF specimens were diagnosed as enterovirus-positive by real time-PCR. Phylogenetic analysis of two successfully sequenced samples revealed echovirus 18 (E-18) as the etiological agent.

Conclusions: E-18 was reported as cause of an outbreak of aseptic meningitis in schoolchildren from City of Bauru, São Paulo State, Brazil. Rapid detection and identification of HEV serotypes in clinical specimens are important in appropriate patient management and epidemiological investigation. Additionally, we illustrate the utility of molecular methods for the detection and typing of enteroviral infections.

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IRF8: MOLECULAR CHARACTERIZATION OF THE DENDRITIC CELL IMMUNODEFICIENCY ASSOCIATED MUTATION IRF8^{K108E}

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Disseminated mycobacterial infection following perinatal vaccination with Bacillus Calmette-Guérin (BCG) is an early manifestation of primary immunodeficiencies. We have previously shown that homozygosity for a loss of function allele in the IRF8 gene (IRF8^{K108E}) causes a severe myeloid immunodeficiency associated with a complete absence of circulating monocytes and dendritic cells, absence of production of IL12, and presence of multiple severe infections in this infant. Biochemical characterization of the IRF8^{K108E} variant has been carried out in primary cells and by comparative analysis following transfection of wild type and mutant variants in myeloid (RAW264.7) or epithelial cells (HEK293). In contrast to wild type IRF8, the pathological IRF8^{K108E} variant is retained in the cytoplasm and does not accumulate in the nucleus following stimulation with IFNg, and cannot transcriptionally activate (IL12p40) or repress (ISG15). Introduction of additional variants at position 108 indicates the positive charge at that position is essential for DNA binding and transactivation and is lost when this charge is abolished. Studies in cells treated with cycloheximide show that in comparison to the WT protein, the IRF8^{K108E} variant has a shorter half-life, is highly unstable, and undergoes rapid proteosomal degradation. We are currently testing whether or not the K108E mutation alters other post-translational modifications of IRF8, including ubiquitination and SUMOylation. Finally, we have conducted RNA-sequencing on primary cells from normal and from the IRF8^{K108E} variant to identify myeloid specific IRF8 targets.

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CORRELATION BETWEEN IMMUNOGENICITY AND EFFICACY FROM CLINICAL TRIALS OF THE PENTAVALENT ROTAVIRUS VACCINE

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Background: Since approval in the US in 2006, the pentavalent rotavirus vaccine, RotaTeq™, has been licensed in over 105 countries. Although efficacy against rotavirus gastroenteritis (RVGE) has been demonstrated in clinical settings, a clear correlate of protection or a measure of immune response that could predict efficacy has yet to be identified. This is the first time that data from several clinical efficacy trials with immune responses were pooled and being presented to provide a unique context for evaluating the correlation between immunogenicity and efficacy.

Methods: Data from four Phase II and III clinical trials of RotaTeq™ were pooled for assessing the correlation between immunogenicity and efficacy. Logistic regression models were used to evaluate the correlation between immunogenicity and efficacy based on data from individual subjects, as well as from aggregated data at the population level.

Results: Analyses of individual subject data and aggregated immunogenicity and efficacy data from Phase II and III studies showed that 1) Individual level postdose-3 (PD-3) G1 serum neutralization antibody (SNA) titers are correlated with efficacy, higher PD-3 G1 SNA titers are associated with lower odds of contracting RVGE; 2) Across studies, at an aggregate level, higher PD-3 G1 SNA geometric mean titers (GMTs) are associated with higher efficacy. Efficacy plateaus when the G1 SNA GMTs are within the range observed in the developed world studies.

Conclusions: Both analyses support that PD-3 GI SNA titers can serve as a relative correlate of efficacy against RVGE in children vaccinated with RotaTeq™.

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ACCELERATED NEUTRALIZING ANTIBODY RESPONSE TO RABIES VACCINATION SIX MONTHS AFTER A SINGLE INTRAMUSCULAR PREEXPOSURE DOSE

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Background and aims: Rabies is still a serious public health problem especially in Asia. Management of severe exposures includes using of immunoglobulin which is expensive and scarce. Pre-exposure vaccination of subjects at risk eliminates need for immunoglobulin. Pre-exposure vaccination schedules require 3 injections of tissue culture vaccine. It would be desirable to learn if a single dose might be able to induce an adequate immune response**.**

Methods: Forty healthy volunteers were randomized into 2 groups. Study group (A) received one intramuscular dose of purified vero-cell rabies vaccine. Comparative group (B) received one subcutaneous dose of measles-mumps-rubella vaccine. After 180 days, both groups received 5 doses of simulated intramuscular postexposure rabies prophylaxis (PEP) on days 0,3,7,14 and 28. The geometric mean titers (GMTs) of neutralizing antibody (Nab) titers were determined by Rapid Fluorescent Focus Inhibition Test (RFFIT) on days 0,3,5,7,14,28 and 42.

Results: All group A subjects had detectable neutralizing antibodies six months later and developed an accelerated immune response when given a simulated PEP. On day 7, seroconversions were detected in all group A subjects comparing 16.7% of group B. Nab titers above the WHO recommended level of 0.5 IU/mL were found in 92.3 % of group A subjects comparing 0 % of group B on day 5. Adverse reactions were minor and transient in both groups.

Conclusion: Our study demonstrates that one intramuscular injection of purified vero cell rabies vaccine provides immune memory for at least 6 month. It results in an earlier immune response followed by PEP.

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THE BURDEN OF ROTAVIRUS GASTROENTERITIS IN THE CZECH REPUBLIC, DATA ABOUT THE COVERAGE OF VACCINATION

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Background and aims: Rotaviruses are the most frequent aetiological agent among patients with diarrhoeal disease worldwide. Epidemiological data could be the basis for the recommendation of vaccination.

Methods: The importance of rotaviruses was analysed retrospectively from official reports, and from laboratory data of Czech laboratories in years 2003-2012. Data about the vaccination against rotavirus infections was collected from pediatricians and producers of vaccines.

Results: There were reported 40,991 cases of rotavirus gastroenteritis. Among them 49.6% were children under 3 years, and 64.9% under 5 years. The most common among all aetiological agents of gastrointestinal disease were Campylobacters, the third frequent rotaviruses in the year 2012. The highest incidence rate was between February and April in the analysed period. On the basis of laboratory data and the use of Soriano-Gabarroś method, it is estimated, that 3,596 children under 5 years are hospitalised and another 28,768 are out-patients with more benign rotavirus gastroenteritis annually. There were reported 16 deaths on rotavirus gastroenteritis (among them 3 children under 3 years). On the basis more frequent laboratory confirmation of diarrhoeal disease in last years and better reports rotavirus infections are increasing. Contrary, numbers of vaccinated children are very low. The vaccination started in the year 2007, the coverage of vaccinated children in the first year of life was 16,6% in the end of 2012. Among all pediatricians only 82,9% started with the vaccination against rotavirus infections.

Conclusion: The results indicate the need of universal vaccination against rotavirus infections in the Czech Republic, too.

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EYE PAIN AND EDEMA…AND ZOSTER APPEARED LATER

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Background: Herpes-Zoster Ophthalmicus (HZO) can result from reactivation of endogenous latent Varicella-zoster virus (VZV) in the sensory ganglia towards the ophthalmic division of the trigeminal cranial nerve. At first, eye pain can be the only symptom. Although rarely reported in childhood, this condition might be sight-threatening.

Aim: The main purpose of our report is to emphasize the possibility of atypical presentation in the reactivation of VZV in the ophthalmic division of the trigeminal nerve, and the importance of early diagnosis to avoid ophthalmic complications.

Case report: Five-year-old girl, previously healthy, with severe right eye pain and headache for five days, and on physical examination eyelid edema. Was admitted with diagnostic suspicion of post-septal cellulitis versus orbital pseudo-tumor. A high-resolution computer tomography revealed myositis of inferior and medial rectus muscles. The onset of unilateral vesicular eruption along the three dermatomes of the trigeminal nerve occurred only four days later. Ophtalmologic evaluation documented right eye keratitis. History of previous full-blown varicella in the first year of life was found and a positive VZV viraemia was discovered. Treatment with acyclovir resulted on clinical improvement. A complete resolution of the HZO was achieved without sequelae.

Conclusions: Whenever there are vesicular lesions on the nose (Hutchinson´s sign), the risk of HZO is higher, as it indicates the involvement of nasociliary branch of the trigeminal nerve, which also innervates the globe. Although rare in pediatric patients, early diagnosis in these cases is critical to prevent progressive corneal involvement and potential loss of vision.

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TIMING OF ADOLESCENT BOOSTER AFTER SINGLE PRIMARY MENCC IMMUNIZATION AT YOUNG AGE: THE TIM-STUDY, AN INTERVENTION STUDY AMONG DUTCH TEENAGERS

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Background: Meningococcal serogroup C polysaccharide (MenC-PS) specific antibody levels decline rapidly after single primary MenC conjugate (MenCC) vaccination in young children. A second MenCC vaccination during or prior to adolescence might be needed to attain longer lasting protection and maintain herd immunity.

Aim: To establish an appropriate age for an adolescent MenCC booster vaccination.

Methods: Three age-groups were recruited with healthy 10 year olds (n=91), 12 year olds (n=91) and 15 year olds (n=86). All participants were primed with the MenC-PS tetanus toxoid conjugated vaccine (NeisVac C^{TM}) 9 years earlier, and received the same MenCC vaccination at the beginning of the study. Blood samples were collected prior to (T0) and 1 month (T1) and 1 year (T2) after vaccination. MenC-PS specific IgG levels were measured using a fluorescent-bead-based multiplex immunoassay (MIA). Functional antibody levels were measured using the serum bactericidal antibody assay (SBA).

Results: 268 participants were enrolled, 259 (96.6%) completed all study visits. Table 1 shows the MenC-PS specific IgG levels and SBA titers.

	10 year olds			**12 year olds**			**15 year olds**		
	GMC MenC-PS specific IgG; µg/mL (95%CI)	**GMT SBA (95%CI)**	**SBA ≥8, n (%)**	**GMC MenC-PS specific IgG; µg/mL (95%CI)**	**GMT SBA (95%CI)**	**SBA ≥8, n (%)**	**GMC MenC-PS specific IgG; µg/mL (95%CI)**	**GMT SBA (95%CI)**	**SBA ≥8, n (%)**
T0	0.26 (0.22-0.31)	4.0 (2.9-5.4)	17 (19)	0.32 (0.26-0.39)	8.2 (5.3-12.6)	31 (34)	0.40 (0.31-0.51)	13.1 (8.1-21.0)	39 (45)
T1	134 (117.0-153.4)	31,564 (26,899-37,038)	88 (100)	193.6 (168.2-222.3)	45,175 (38,608-52,859)	89 (100)	174.3 (147.5-206.0)	47,289 (40,422-55.322)	85 (100)
T2	12.2 (10.2-14.4)	1,987 (1,602-2,247)	85 (100)	23.3 (19.3-28.0)	4.165 (3,444-5,038)	89 (100)	33.7 (28.4-39.9)	6,292 (5,272-7,509)	83 (100)

[MenC-PS specific IgG levels and SBA titers]

Conclusion: 9 years after primary vaccination, antibody levels increased spectacularly 1 month after a second MenCC vaccination. One year post-vaccination antibody levels remained high, but decreased faster in the younger age groups.

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CONSIDERATIONS IN THE MANAGEMENT OF HCV-RELATED THROMBOCYTOPENIA WITH ELTROMBOPAG

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Eltrombopag is a 2nd generation thrombopoietin-receptor agonist. It binds with the thrombopoietin-receptors found on the surfaces of the megakaryocytes & increases platelet production. Many recent studies have suggested a potential role for this novel agent in the treatment of thrombocytopenia associated with hepatitis-C infection. Studies have shown that adjunct treatment with Eltrombopag can help avoid dose reductions/ withdrawals of pegylated interferon secondary to thrombocytopenia. It may also have a role in priming up platelet levels to help initiate antiviral therapy. Similarly, chronic liver disease patients with thrombocytopenia who need to undergo an invasive procedure may be potential candidates for short 2-week courses of eltrombopag in the periprocedural period to help reduce the risk of bleeding. Besides the price (deemed very expensive & probably not cost-effective), there are some legitimate concerns about the safety profile of this novel agent (most importantly, portal vein thrombosis, bone marrow fibrosis & hepatotoxicity). In this article, the potential role of eltrombopag in the context of hepatitis C virus (HCV)-related thrombocytopenia is reviewed. To write this article, a MEDLINE search was conducted (1990 to November 2012) using the search terms “eltrombopag,” “HCV,” and “thrombocytopenia.”

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FEATURES OF THE IMMUNE STATUS OF FREQUENTLY ILL CHILDREN

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Recurrent respiratory disease of viral and bacterial etiology can lead to immune dysfunction, so relevant is the study of the immune status in patients with frequent episodes to develop adequate treatment.

Mission: To study the parameters of systemic immunity in the long and often ill children.

Methods: Examined 45 children 3-7 years with recurrent respiratory infections to 8-10 times a year. Age of infectious-inflammatory syndrome ranged from birth to 3.5 years. Allergic reactions in anamnesis occurred in 29% of children. At laboratory examination determines the index of T-cell, humoral immunity, phagocytosis, cytokines.

Results: The absence of marked disorders of CD3 +, CD4 +, CD8 +, CD19 + and CD16 + CD56 + peripheral blood lymphocytes. In 67% of children indices CD16 + CD56 + NK cells were recorded at the lower limit of normal. The level of immunoglobulins A, M, G match age norm in 66% of children. Isolated transient decrease IgG was detected in 6.6% of the children, reduced IgA - at 11,1%, IgM - in 7%, IgG and IgA - a 2.5% decrease in IgG, M, A registered at 2.45 % of children. In 82% of patients surveyed values of IFN-γ and IFN-α did not have a standard deviation of age. Increasing the concentration of IFN-γ and phagocytic activity of neutrophils were detected in 18% of children.

Conclusions: The most frequently ill children haven´t persistent disorders of immunity, which necessitates their comprehensive survey to identify the reasons extraimmune increased infectious disease followed by the appointment of personalized immunotherapy.

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SOME ASPECTS IN DIAGNOSTICS AND TREATMENTS AND ANTIMICROBIAL RESISTANCE OF SEPSIS NEWBORNS

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Background and aims: Sepsis is a great problem in neonatology.Knoledge of antimicrobial resistance and some diagnostic markers of sepsis is an important component of management strategies of diagnostic and treatment of neonatal sepsis.

Methods: There was open prospective research by randomized method. There were studied 96 full-term newborns whis gram-negative bacterial sepsis (Newborns was placed in the NICU-neonatal intensive care unit,whith symptoms of sepsis,age of 0-3days). The diagnosis of sepsis was confirmed with clinical-laboratory stadies. There was stadied bacterial culture of blood by routine culture method. For estimating existence and heaviness of infection was defined by procalcitonini(PC)-by immunoluminometric method and C-reactive protein(CRP) by Latex-agglutination method.Started antibiotics,recommended from WHO was Ampicillini-Gentamitini. Efficiency of antibiotiktreatment was estimate by CRP,PC and by clinical signs. Research was statistically reliable and agreedical bioethical board.

Results: During sepsis, Blood culture was positive in 41% cases-late than 48-72 hours,from this E.Coli was ampicillin and gentamicin resistant- 5%, Ps.Auriginozain was ampicillin and gentamicin resistant-17%, Klebsiella Pneumoniae was ampicillin and gentamicin resistant-11%, Level of CRP was increased: sensitivity was 79%,specificity 84%. Level of PC also was increased, sensitivity was 98%,specificity 97%, until started treatment.In this cases wnan in 72hour CRP and PC was increased was changed antibiotics, until blood culture resalts.

Conclusions:

1. CRP and PC are reliable diagnostic markers of neonatal sepsis, but PC was more informative,quick,than CRP.

2. By CRP and PC we can estimated Efficiency of antibiotiktreatment during sepsis.

3. During gram-negative sepsis in33% was antimicrobial resistance against ampicillini-gentamicini.

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SENSITIVITY OF STREPTOCOCCUS ON ANTIBIOTICS IN NEONATES ON FIVE YEAR'S MATERIALS

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Background and aims: Streptococcus is type of bacteria that is the most common cause of morbidity in newborn babies, due to the fact that 5% to 40% of pregnant women will show positivity on these bacteria.

Presentation of the sensitivity of analysed streptococcus for antibiotics used in the neonatal period.

Methods: Performed analysis over the antibiogram with positive microbiological results with isolated streptococcus, taken in the first 48 hours in neonates after the birth.

Results: During the last five years, 1,751 peripheral swabs were taken. Out of those, 356 (20.33%) were positive, from which 75 (21.06%) were streptococcus. Enterococcus was isolated in 30 (40%) swabs and its sensitivity to antibiotics was as follows: 96.66% to vankomicin, 86.66% to ampicillin, 83.30% to ceftriakson, 76.66% to cefuroksim, 46.60% to amikacin, and 30.00% to cefixime.

Streptococcus agalactiae GRB isolated in 27 (36%) smear showed sensitivity as follows: ampicillin with 92.59%, sensitivity of ceftriakson, cefuroksim and cefixime was 85.18%, vankomicin with 81.48%.

Streptococcus pyogenes isolated in 9 (12%) copies were with sensitivity as follows: ampicillin, ceftriaxone, cefuroxime, vancomycin, cefixime with 88.88% and amikacin with 44.44% sensitivity.

Streptococcus pneumoniae represented by 6 (8%) isolates for which ceftriakson, cefixime, cefuroksim, amikacin and vankomicin with 100% sensitivity and ampicillin with 88.88%. In only 3 (4%) cases, Streptococcus species were with sensitivity of 100% and 50%, retrospective, to ampicillin, ceftriakson, vankomicin cefuroksim; and amikacin and cefixime.

Conclusion: Due to the toxicity of antibiotics and the resistant strains, in the initial therapy, give preference to ampicillin.

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SOME ASPECTS OF DIAGNOSTICS OF NEONATAL SEPSIS

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Background and aim: Neonatal sepsis is a great problem with high mortality (13-25%) in paediatrics. Aim of the work is to study some endocrine functions while sepsis and shock and development of diagnostic-differentiating criteria and correcting therapy.

Methods: There was conducted the prospec studies.There ware studied 108 newborns, placed in NICU whith symptoms of sepsis,age of 0-5 days. The diagnosis of sepsis was confirmed whith clinical-laboratory studies, in 41% cases, we obtained the blood culture. We divided two groups: In the 1st group-there were 108 patients whith the diagnosis of sepsis and in the 2nd group-27patients with sepsis shock. We've studied c reaqtive protein (CRP) in the blood serum,by meansof latex-agglutination techniques, Procalcitonon(PC), by -immune-luminometric method.Thiroxin(T4), three-iodine-thyronin(T3). thiro-stimulating hormone(TSH) radio-immunology methods. Research was statistically reliable.(P< 0,001). Studies were agreed with the department of bioethics of the hospital.

Results: In case of sepsis and sepsis shock the level of CRP was increased,sensitivity was 79%,specificity 84%.level of PC increased even more: sensitivity 98%, specificity 97%. Levels of T4 and T3 decreased, sensitivity 60%, specificity 65%. In case of sepsis the quantity of TSH was increased, sensitivity 68%, specificity 40%.

Conclusions:

1. CRP and PC provide the markers for prompt, fine and reliable diagnostics at the early stage of neonayal sepsis, in addition, PC is more informative, than CRP.

2. While sepsis, there revealed hypo-function of the thyroid gland.

3. Hypo-function of the thyroid gland may aggravate immune defict during sepsis.

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A COHORT STUDY OF OFF-LABEL ANTIRETROVIRAL USE IN PAEDIATRIC HIV INFECTED PATIENTS

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Background and aims: Licensing data for paediatric dosing is often sparse and subsequent studies may result in changes to recommended doses. We measured the extent and consequences of off-label antiretroviral use in HIV-infected children.

Methods: Multicentre cohort study involving 331 HIV-infected children from the Madrid Cohort. The patient clinical notes date from the first recorded off- label prescription in March 1988 to December 2011.

Results: Overall 540 (23%) of 2353 antiretrovirals (ARV) were prescribed off label in 221 (67%) children according to EMA licensing at the moment of prescription. The main reason for starting an off label drug was treatment failure. Adverse events occurred in 34% of children but only 8% discontinued treatment. Problems taking the drug led to withdrawal in 3%, more likely when formulation was not suitable for age ($p< 0.05$). Up to 10% were overdosed and 10% underdosed (25% above or below the current recommended dose respectively). The underdosed patients had treatment failure in 50% vs 26% in non-underdosed ($p< 0.05$). Adverse events in the overdosed group were not more frequent. If the drug also wasn´t approved by the FDA at the time of prescription, it was more likely to be underdosed and less likely to be overdosed ($p < 0.05$).

Conclusions: Off-label use or ARV is common. Adverse events were common but rarely led to withdrawal. Suitable formulation is important in younger children. Pharmacokinetic studies are needed as frequent misdosing may occur when prescribing off label, most importantly, underdosing may lead to treatment failure.

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NEONATAL SEPSIS IN DEVELOPING COUNTRIES - WE ARE ON CLOUDNINE

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Background: Over gowning is one of the meausure of infection control in NICU though the benefits and risks of gowning remain unclear.

Objectives:

(1) To study the sepsis rate by blood culture positivity in a tertiary level NICU.

(2) To compare the sepsis rate and the neonatal mortality rate in our NICU with other available data from rest of the developing world.

Data collection and analysis: Prospective observational study from Cloudnine Hospital, Bangalore, India over a period of 6 years June 2006 to May 2012. Sepsis rate & mortality rate of other developing countries was searched on Pubmed, Ovid Medline, Embase, and Popline.This data was then campared with our study.

Results: During the study period, 6524 babies were born in the hospital out of which 1206 required NICU admission. 763 babies met inclusion criteria out of which blood culture was positive among 34 The incidence of culture positive neonatal infection was 5.2 per thousand live births & 4.4% of all neonatal admissions. We found statistically significant low incidence of neonatal infection, over all death rate & death rate due to sepsis. Non-gowning is not associated with increased systemic nosocomial infection.

Conclusion: Gowning is not required to decrease systemic nosocomial infection, death rate due to sepsis & nosocomial colonisation. The costs associated with gowning are considerable - especially in developing countries. There is an urgent need for studies looking at simple and sustainable interventions to reduce the burden of neonatal infection. Our unit may serve as a role model for developig countries.

1193

DIFFERENCES IN IMMUNISATION SITE PAIN FOLLOWING PNEUMOCOCCAL CONJUGATE VACCINATION

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Background: UK children receive the 13-valent pneumococcal conjugate vaccine (PCV-13) at 2, 4 and 12 months of age. As a secondary objective in a randomised controlled trial, we studied immunisation site pain following booster immunisation of PCV-13 and the 10-valent pneumococcal conjugate vaccine (PCV-10).

Methods: 178 children who had previously been vaccinated with PCV-13 at 2 and 4 months were randomised 1:1 to receive a booster dose of either PCV-13 or PCV-10 at 12 months of age. Immunisation site pain following vaccine injection was determined with the tools as suggested by the Brighton Collaboration. An independent assessor who was blinded to the vaccine the children were given scored pain using the Modified Behavioural Pain Scale (MBPS) and the crying time. Parents were asked to provide a pain score using the Numerical Rating Scale (NRS).

Results: Data were available for 77 (PCV-10) and 80 (PCV-13) participants. MBPS pain scores were significantly higher in the PCV-13 group compared to the PCV-10 group (mean 7.7 vs. 7.2, p=0.039) with non-significant trends towards more pain in the PCV-13 group when measured by NRS and crying time.

Conclusions: We found significant differences in the immunisation site pain between the two currently most used pneumococcal conjugate vaccines with PCV-13 being more painful than PCV-10. Injection pain is a source of distress for both children and parents and a less painful vaccine may therefore increase acceptance of immunisation and reduce future fear of needles.

1194

CLINICAL FEATURE OF HOSPITALIZED CHILDREN WITH INFLUENZA INFECTION FOR SEVEN YEARS

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The relation between influenza subtype and age, clinical symptoms, diagnosis, and clinical course was reviewed in hospitalized children in winter season annually since 2006 to 2013 retrospectively. The diagnosis of influenza was made by rapid diagnostic test kit or PCR test. The clinical features in each type of influenza were evaluated according to respiratory (R: pneumonia), neurological (N; seizure, abnormal behavior), encephalopathy (E), and other symptoms (O; persistent fever, dehydration, gastroenteritis and others).

Results: 245 (147 boys, and 98 girls) cases were admitted due to influenza antigen positive disease in this study period. Seasonal type A was 100 (R; 33, N36, E;2, O;29), H1N1pdm09 was 95 (R:55, N;23, E;3,O;14), and type B was 50 (R;18, N;16, E;1, O;15) cases. H1N1pdm09 virus was detected only in 2009-10 and 2010-11 seasons. The age distribution (0y/1-5y/6-10y/11y-) of these children was 19/47/28/9 in seasonal A, 10/24/40/21 in H1N1pdm09, and 1/24/22/3 in type B. All children recovered and discharged without major complication. In respiratory disorder, percutaneous Oxygen saturation at admission was lower in H1N1pdm09 (median 88%) than seasonal A (96) or B (98), but total admission period was not longer.

Conclusion: Rapid diagnostic kit is useful to know the origin of fever when patient should be admitted. The results support to understand the clinical picture of age related symptoms. Encephalopathy was observed in these types of infection.

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PHILADELPHIA CHROMOSOME POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTED WITH BLOODY DIARRHEA: IS THE REASON DASATINIB THERAPY OR CYTOMEGOLAVIRUS COLITIS?

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A 18-years old girl with Philadelphia (Ph) chromosome positive acute lymphoblastic leukemia (ALL) suffered from bloody diarhhea during the dasatinib therapy. Primarily we think the diarrhea was the side effect of dasatinib and therapy was cancelled. Diarrhea was abate during the time without treatment but patient was not fully recovered so we investigated other reasons which can cause bloody diarrhea including inflamatory bowel disease and infectious microorganisms. We performed computed tomography (CT) and ultrasonogram and marked thickening of the colonic mucosa from ilocecal to sigmoidal area was shown. Cytomegalovirus (CMV) antigenemia was found positive (1,435E+03 IU/ml CMV). Colonoscopy revealed solitary rectal ulcer and colitis. A colonic biopsy specimen showed typical CMV nuclear inclusions. Immunohistological study of the specimen was positive for CMV antigen. Immunological screening revealed hypogammaglobulinemia. Administration of ganciclovir 10 mg/kg/day for 14 days improved the diarrhea and other symptoms. Hemorrhagic colitis can be an adverse effect of dasatinib therapy but other causative agents have to be searched if the bloody diarrhea proceed despite the dasatinib therapy discontinuation.

1196

IMPLEMENTATION OF PERTUSSIS IMMUNIZATION (DTAP) FOR HEALTH-CARE WORKERS IN A UNIVERSITY CHILDREN'S HOSPITAL IN SWITZERLAND

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Background and aim: Infection with B. pertussis is most serious in young infants who frequently acquire it from adults. Pertussis immunization in adults 25-29 years of age and all adults in close contact with infants < 6 months was added to the Swiss national immunization schedule in 2012. We implemented this new recommendation for all health care workers (HCW) in our institution, beginning in April 2012. Here we report our results after 1 year.

Methods: Between April 2012 and March 2013, information about the campaign was advertised to our staff through several channels and appointments for counselling and immunization were offered. After checking indications and contraindications, informed consent for tetanus-diphtheria-pertussis (dTpa) immunization was obtained. Specific adverse events (AE) were assessed by HCW in standardized questionnaires for 7 days.

Results: Of 620 HCW, 422 (68%) had appointments: 62 (10%) had already received dTpa < 10 years ago, 348 (56%) received dTpa now and 12 (2%) declined, resulting in 66% coverage so far. Of 235 returned questionnaires, >1 local AE (swelling or redness >2 cm Ø) was reported in 46 (20%) HCW and fever in 5 (2%); no serious AE occurred. Analysis of reactogenicity in relation to the interval of last dT immunization is currently in progress.

Conclusions: Comprehensive efforts were needed to achieve a pertussis immunization coverage of currently 66% among HCW in our institution. Good tolerability of the vaccine and continous and individual information to our HCW about the rationale and benefits of pertussis immunization contributed to this success.

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EPIDEMIOLOGICAL ASPECTS OF CHRONIC VIRAL HEPATITIS C INFECTION IN CHILDREN FROM SOUTH-EASTERN ROMANIA

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Background and aims: Hepatitis C virus (HCV) infection is affecting more than 180 millions worldwide and has a high propensity for chronicity, especially in childhood. The aim of the study was to evaluate the epidemiological characteristics of children with HCV infection.

Methods: HCV infection was diagnosed, through anti-HCV antibodies detection, in 53 children admitted between January 1991 and December 2012. We reviewed the medical records and analyzed: age, sex, risk factors, viral serologies and comorbidities.

Results: The patients were divided in three groups: 6 patients with negative viral load, 16 that did not undergo HCV-RNA testing and 31 with positive HCV-RNA (chronic hepatitis C). Out of the latter, 80.6% received treatment. The sex ratio was male/female:27/26. The age at diagnosis ranged from 1 to 17 years (mean 7.9). The largest number of patients were diagnosed in 2002, 2009, 2010 and 2011 with 6, 8, 6 and 6 cases respectively. In 30.1% of cases the mother was HCV infected. Risk factors identified in the patients' history were: blood transfusions in 9, chronic use of intravenous drugs in 4 and surgery in 2 cases. Three patients had VHB coinfection. Five patients had underlying comorbidities: von Willebrand disease, celiac disease, cystic pulmonary fibrosis, spherocytosis and thalasemia majora.

Conclusions: Hepatitis C is a public health issue. Nevertheless, it is still a neglected disease in many developing countries. Materno-fetal transmission remains, together with blood transfusion, the main ways Romanian children acquire HCV infection. Controlling HCV infection remains a challenge until an effective vaccine is developed.

1198

SAFETY REPORT IN A COHORT OF HIV-INFECTED CHILDREN AND YOUNG ADULTS IMMUNIZED AGAINST SEASONAL INFLUENZA

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Background and aims: Influenza infections in immunocompromised patients are associated with severe complications and the risk is highest among children. Thus vaccination against flu is recommended annually for this patient population including HIV infected children. The aim of this study is to assess the safety and immunogenicity of inactivated seasonal influenza vaccine in HIV-infected children and young adults and to identify biological markers of immune response using the model of influenza vaccination. Herein we report safety data.

Methods: We performed inactivated influenza vaccine trivalent types A and B, split virion (VAXIGRIP®) in 74 HIV-infected children and young adults and in 28 age- and gender-matched healthy controls. All participants receive one vaccine dose.

Results: The investigational vaccine was well tolerated. No deaths occurred throughout the study. One serious adverse events (SAEs) occurred in control group consisting in a hospitalization for seizures 7 days after vaccine administration in a child with previous CNS infection. All solicited reactions were mild to moderate in severity and resolved within three days of onset. Local and systemic reactions were reported by 24% of subjects in the HIV group and by 12% of subjects in the control group. The most commonly reported solicited reactions were fever, headache and local pain in both groups. No study participants experienced altered HIV load or CD4 + T cell counts during the study.

Conclusions: Administration of inactivated trivalent influenza vaccine resulted safe among HIV-infected children and young adults. The only one serious adverse event reported was judged unrelated to vaccination.

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CONNATAL INFECTION AND APLASIO CUTIS CONGENITA

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The aim of our paper is to inform about the three cases of Aplasia cutis congenita in our

hospital which are the first three after 25 years in more than 75 000 deliveries. All the three were with positive blood culture with the group B Streptococcus.

Perinatal and connatal infection are continue to cause mortality rate and morbidity rate to newborns. Group B Streptococcus is the commonest searious baterial pathogen affecting neonates in the different forms like early on set infection. Early onset neonatal infection is caused by organisms that colonized mothers genitourinary system.

Aplasia cutis congenita is a rare condition. The lesions of the skin apparent at birth,sometimes similar with the wound of some trauma. In the literature, we find that 60% occur on the scalp, but sometimes it may occur as multiple lesions. They occur as well demarcated, and they range in size from 0.5-10 cm. It may be circular, oval, linear, or stellate in configuration.

The depth may involve only the epidermis and the upper dermis, resulting in minimal alopecic scarring, or the defect may extend to the deep dermis, the subcutaneous tissue, or rarely the periosteum, the skull, and the dura.

Our cases were a full term newborns delivered per vias naturalis .....

Without family history. Without super infection and without other anomalies, and all the three were discharge home as well as other well born children, after well implemented antibacterial therapy.

1200

MUMPS OUTBREAK AMONG HIGHLY VACCINATED TEENAGERS AND CHILDREN IN CENTRAL REGION OF PORTUGAL: OCTOBER 2012 -MARCH 2013

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Background and aims: Mumps vaccine was introduced in Portugal in 1987, rapidly reaching >95% 2 dose coverage. The annual incidence rapidly fell to low levels. 16 sporadic cases were notified in the central region of Portugal in 2010 and 13 in 2011. We report an outbreak in this region during 2012-2013.

Methods: Cases of salivary-gland swelling and other symptoms compatible with mumps were investigated. Demographic, clinical, laboratory and vaccination data were analysed.

Results: Between October 2012 and March 2013, 145 outbreak-related cases of mumps were reported. 87.6% (127/145) of cases occurred in 3/13 counties and 73% (106/145) had a known contact. Median age was 16 years (2-62) and 71% were 11-20 years. 61.3% were male. The disease was generally mild. 80% had fever and in 57.2% there was unilateral involvement of the parotid gland. 7.9% (7/89) had orchitis (≥12 years of age) and there was one case of oophoritis. There was only one hospital admission. School transmission predominated but class attack rates were < 10%. 93% of cases were vaccinated of whom 97% had received two doses. 14.5% had received one dose of vaccine containing the Rubini strain. Among cases from whom specimens were available, 50% were laboratory-confirmed by PCR.

Conclusions: This is a report of a mumps outbreak in a consistently highly immunised population in Portugal. School contact appears to have facilitated transmission, overcoming vaccine-induced protection. High rates of two-dose coverage may have reduced the severity and transmission of the infection and, limited the size of the outbreak.

1201

STABLE BONE MINERAL DENSITY IN A COHORT OF VERTICALLY HIV INFECTED ADOLESCENTS TREATED WITH HAART

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Introduction: Many studies in HIV infected-children and adults have described low bone mineral density (BMD) and calcium metabolism abnormalities. These have been attributed to the ARV treatment and to the viral-associated inflammation. There are not many longitudinal studies of BMD in HIV-infected children and adolescents, and especially of a long duration.

Objectives: To analyze the evolution of BMD in a cohort of HIV-infected by vertical transmission children and adolescents treated with HAART.

Methods: Retrospective study describing BMD at two different periods of life (P1 and P2) in a cohort of HIV infected children by vertical transmission in Madrid (Spain). BMD, anthropometry and laboratory data (CD4 and viral load) were collected. We adjusted by height and race for Z score BMD (BMD-a).

Results: Fourty-two HIV infected children were studied. Baseline data included median age 9,6 years (IQR 7-11.5), 66% female, 90% Caucasians, Tanner 1: 66%, clinical CDC C: 27%, immunological CDC 3: 40% and viral load < 50cop/ml: 42%. Median between both periods were 6,3 years (IQR 5,4-7,8). Tanner stage 5 was completed at 58% at P2. BMD Z score < -2 (P1:11%;P2:8,9%) and BMD-a (P1:6,7%;P2:6,3%).

There were no statistical differences between both periods at BMD-a Z score. Only weight and BMI was associated with low BMD at 2P.

Conclusions: In our cohort of children, low BMD (Z score< -2) was not common, after adjusting for height and race. In our population of children treated with HAART for a prolonged period there was no decrease of BMD-a in over time.

1202

SO FAR SO GOOD - HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS AFTER EPSTEIN BARR (EBV) INFECTION

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Introduction: Hemophatocytic lymphohistiocytosis (HLH) is a syndromic acute agressive hyperinflammatory disease, primary/hereditary or secondary (infections, malignancy or rheumatologic disorders are known triggers), and a major diagnostic and therapeutic challenge.

Case report: A fourteen year-old, previously healthy girl, was admitted after 15 days of fever, fatigue and hepatosplenomegaly, and rapid clinical deterioration in the last 36h with irritability, confusion, jaundice and anasarca. EBV-DNA viral load on blood was 28097 copies/mL. Abdominal-US showed alithiasic cholecystitis, Brain MRI was normal. Laboratory data: moderate bicytopenia, non-measurable fibrinogen levels, hyperferritinemia (9036 mcg/mL), hypertriglyceridemia (570mg/dL) and normal ESR. Hemofagocythosis in bone-marrow smear confirmed the diagnosis of HLH. Treatment was started following HLH-2004 protocol with gamaglobulin, etoposide (weekly) and dexametasone daily. She presented good clinical and analytic evolution. EBV viral load was indetectable since day 27. Etoposide was stopped after the third dose, and dexametasone discontinuation was made following the protocol. Genetic studies were conducted in Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet (Stockholm, Sweden)- negative for known mutations. Follow-up has not documented recurrence so far.

Conclusion: The authors present a case of EBV infection complicated with hepatitis/alithiasic cholecystitis and HLH. This is a rare but potentially fatal complication of EBV infection. Prompt diagnosis improves response to treatment and prognosis.

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PERITONITIS IN CHILDHOOD NEPHROTIC SYNDROME

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Background: Patients with nephrotic syndrome (NS) are at increased risk for infection, including peritonitis.

Goals: Identify risk factors for the development of spontaneous bacterial peritonitis in children with NS.

Material and methods: We conducted an analysis of infections in 81 children (64 boys, 17 girls) with NS.

Results: Infectious complications were observed in 38 of the 81 children (47%), and peritonitis in 12%. The frequency of peritonitis was higher in children with frequent relapses, steroid dependent and secondary non-responders (71%). Primary peritonitis was identified In 9 patients (12% rate). Peritonitis was characterized by abdominal pain (98%), fever (95%), abdominal tenderness (85%), and nausea and vomiting (71%). Those patients with a serum albumin level less than or equal to 1.5 g/dl at initial presentation were estimated to have a 7 fold (P=0.06) increase in developing peritonitis than those with an initial albumin greater than 1.5 g/dl. A platelet count greater than 500 cells/mm^3 tended toward a reduced risk (P=0.10) for peritonitis when compared with patients with a platelet count less than 500 cells/mm^3. Hypertension, hematuria, or normal C3, C4 at the time of initial diagnosis were not associated with an increased risk of subsequent peritonitis. Low serum albumin (≤ 1.5 g/dl) at presentation was associated with an increased risk of peritonitis among children with NS at our institution.

Conclusion: Based on our data, it seems reasonable to take into account risk factors and initiate antimicrobial therapy in nephrotic children with suspected peritonitis using a combination of antibiotic therapy.