

MENCC VACCINATION IN CHILDREN; THE DUTCH EXPERIENCE

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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.

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. The level of protective antibodies generated shortly after MenC vaccination in children and adolescents appeared to be age-dependant and decrease in immunity against MenC seems to be inversely correlated with the age at primary vaccination.

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. As teenagers aged between 12-18 years are also at risk, 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.

Several countries have implemented the MenC vaccination into their national immunization program, but age at primary and booster vaccination differs per country. In an attempt to determine the optimal vaccination schedule for MenC, age at MenC vaccination and results from different countries that have introduced the MenC vaccination are compared. In addition, a study currently running in the Netherlands to determine the appropriate age for a booster MenC vaccination will be discussed.

IMMUNOGENICITY OF CONJUGATE MENINGOCOCCUS C VACCINE IN PEDIATRIC SOLID ORGAN RECIPIENTS

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For efficacy reasons, conjugate vaccines are suggested for immunocompromised patients, although clinical trials targeting this issue are rare.

In a prospective study, the immunogenicity of a single dose of conjugate *Meningococcus*C (Men C) vaccine was assessed by analyzing the serum-bactericidal-antibody (SBA) titers in 10 pediatric solid organ transplant (SOT) patients (8 kidney; 1 liver; 1 liver and kidney).

All patients demonstrated an increase of SBA titers after vaccination. Only four patients showed a delayed immune response one month after vaccination. All patients maintained protective SBA titers ($\geq 1:8$) over an observation period of at least 16 months to a maximum of 28 months despite rapidly waning titers starting at 6 months post vaccination. Vaccination was also successful in a case of a 10-year old kidney-transplanted boy with atypical hemolytic uremic syndrome (aHUS) and heterozygous factor H mutation receiving the terminal complement inhibitor eculizumab to avoid recurrence of aHUS in the renal graft.

Despite rapidly waning SBA titers within 6 months after vaccination, protective SBA titers ($\geq 1:8$) were maintained after kidney transplantation under immunosuppressive therapy with mycophenolate-mofetil, tacrolimus, steroids and eculizumab over a 27 months observational period. Despite high immunogenicity of the conjugate MenC vaccine in SOT patients, it remains unclear whether serologically-defined protective SBA titers mediate true protection from invasive meningococcal disease in immunocompromised patients, particularly, under treatment with a complement inhibitor. For immunocompromised patients with significantly decreasing titers, a booster dose may be discussed with close monitoring of SBA titers over time.

LONG-TERM CONTROL OF MENINGOCOCCAL CAPSULAR GROUP C (MENC) DISEASE IN THE UNITED KINGDOM

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The UK was the first country to introduce the meningococcal capsular group C (MenC) conjugate vaccine into the national immunisation programme in 1999. The vaccine was administered in stages over 12 months to all children aged < 18 years and resulted in a 99% reduction in invasive MenC disease across all age groups through a combination of direct and indirect protection.

Data from the enhanced national surveillance of invasive meningococcal disease conducted by the Health Protection Agency in England and Wales along with recent clinical trials and seroprevalence studies were analysed

MenC disease incidence remains low following the introduction of routine MenC immunisation in England and Wales. Although a 12-month booster was added to the national immunisation programme in September 2006, recent clinical trials and serosurveys have shown poor antibody persistence even among those receiving the current schedule. In contrast, higher antibody levels were achieved with school-age and adolescent vaccination, peaking in those vaccinated at 14 years. A recent randomised controlled trial showed infants receiving a single dose of MenC conjugate vaccine in infancy were adequately boosted at 12 months.

Given that MenC disease is rare in infants and toddlers, it has been proposed that the UK MenC immunisation programme should be reduced to a 1+1 schedule and an extra dose of MenC conjugate vaccine offered to adolescents. Although a recent increase capsular group Y (MenY) disease has been observed, the relatively small number of cases is unlikely to support adolescent boosting with a quadrivalent conjugate vaccine.

EVALUATION OF MENINGOCOCCAL C CONJUGATE VACCINE SCHEDULES IN CANADIAN CHILDREN: A GUIDE TO PROGRAM STRATEGY

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The diversity of universal infant meningococcal C conjugate (MenC) immunization schedules in Canada provides an opportunity to evaluate optimal program design. Alberta (AB) offers a 3-dose program (2, 4 and 12 months); British Columbia (BC) provides 2 doses (2 and 12 months) and Nova Scotia (NS) offers 1 dose at 12 months. This interim analysis of a 5-year cohort study presents data to assess differences in protection in provinces providing early priming doses in infancy.

In this prospective comparative cohort study, three similar cohorts of healthy children from BC, AB and NS were enrolled prior to the 12 month MenC dose and immunized with MenC-Tetanus Toxoid conjugate. All sera were assayed for serogroup C bactericidal activity using standardized procedures with rabbit as the exogenous complement source. SBA was measured at baseline (12 months of age) and 1 month after the 12 month MenC dose (13 months of age). Titers < 1:8 were considered non- protective.

Subjects were significantly different in their baseline protective titers according to the number of priming doses received: in AB (2 priming doses) 100% (95% CI 98% - 100%) were protected; in BC (1 priming dose) 84% (75% - 90%) were protected; and in NS (no priming) 27% (21% - 35%) were protected. All subjects were protected after the 12 month MenC dose.

Two priming doses given in infancy afford optimal protection; however substantial protection was seen after one priming dose. Evaluating existing programs is essential for planning immunization strategies to control MenC disease.

ROTAVIRUS VACCINATION: IMPLEMENTATION AND IMPACT**J. Gray***University of East Anglia, Norwich, UK*

Rotavirus causes substantial worldwide morbidity and mortality and is a leading cause of severe dehydrating diarrhoea in children aged < 5 years. Rotavirus is responsible for approximately 5% of all deaths in this age group. In Europe, rotavirus causes up to 56% of hospitalisations due to community-acquired acute gastroenteritis in children aged < 5 years. To reduce the burden of rotavirus disease, an oral live-attenuated human rotavirus vaccine (HRV) was developed to elicit protection against severe illness through mimicking the immunity from natural infection.

Following the introduction of HRV into national immunisation programmes in 2005, studies have been conducted to assess vaccine effectiveness in 'real-world' settings. Data from Europe and Latin America demonstrate the impact vaccination has on rotavirus disease burden. One key Belgian study (213 confirmed cases; 276 matched controls) estimated 90% effectiveness for two doses of the human HRV against rotavirus gastroenteritis hospitalisation among young children.

Studies examining the impact of HRV on childhood gastroenteritis-related mortality have shown substantial reductions in the number of diarrhoea-related deaths. In Mexico, yearly all-cause diarrhoea-related mortality among children aged < 5 years decreased by 46% from an average of 18 deaths per 100,000 in 2003-2006 to 9 deaths per 100,000 in 2008-2010. Similarly, in Panama, 2 years after vaccine introduction, gastroenteritis-related mortality declined by 50% in children aged < 5 years.

Real-world effectiveness data are consistent with efficacy data obtained from clinical trials and demonstrate the potential of HRV to substantially reduce childhood mortality and hospitalisation. Post-licensure effectiveness studies are vital to assure that the expected benefits of HRV programmes are attained.

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IMPROVING VACCINATION STRATEGIES TO HELP PROTECT AGAINST PERTUSSIS THROUGHOUT LIFE**J. Roord***VU University Medical Center, Amsterdam, The Netherlands*

Decades after the introduction of pertussis vaccination, the disease continues to be an important cause of morbidity and infant mortality, and poses a considerable worldwide threat. Despite high vaccination coverage, however, there has been a global resurgence of the disease and outbreaks have been seen in many countries, particularly in infants, adolescents and adults. Pertussis has consequently become the most prevalent vaccine-preventable disease in developed countries.

Infants younger than 3 months, who are too young to be vaccinated, are at the greatest risk of contracting severe pertussis, which can lead to hospitalisations or complications, and have the highest mortality rate due to pertussis. Adults and adolescents with undiagnosed or asymptomatic pertussis infection play an important role in transmitting the disease to young unimmunised infants.

The increasing incidence of pertussis in adolescents and adults may be due to waning of vaccine-induced immunity over a period of 4 to 12 years after vaccination. Pertussis infection in these groups suggest that the protection offered by childhood vaccination is not sufficient and that booster vaccination of adolescents and adults may aid in decreasing the overall disease burden, in addition to decreasing the reservoir for infant infection.

Strategies that could be explored include the development of new vaccines with higher efficacy rates and longer duration of protection, and improvements in vaccination schedules. Appropriate vaccination of healthcare professionals, childcare providers, pregnant women, household contacts of infants and family members of newborns might help protect the most vulnerable infants. Effective booster programmes may be required for preschool children, adolescents and adults to help protect against pertussis throughout life.

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CHALLENGES AND VALUE OF VARICELLA VACCINATION

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Varicella is a highly contagious disease caused by primary infection with the varicella zoster virus (VZV). Over 90% of European children will become infected with VZV in the first 10-12 years of life. Varicella is often considered a benign disease, however, some cases can cause serious complications such as neurological disorders, pneumonia, secondary bacterial infections or even death. Serious complications from varicella can lead to hospitalisation, with European rates ranging from 1.3 to 4.5 per 100,000 population/year. The vast majority of these occur in healthy immunocompetent individuals. In many European countries, a lack of awareness of the true clinical impact of varicella means the burden of the disease is underestimated.

Routine childhood varicella vaccination in Europe has had a positive effect on disease prevention and control. A two-dose varicella vaccination schedule has been shown to further reduce the incidence of varicella and its complications compared with a one-dose schedule, and to reduce the risk of breakthrough varicella cases.

In approximately 10-20% of cases, VZV can reactivate later in life as herpes zoster (HZ). Re-exposure to VZV through contact with an infected person is believed to protect latently infected individuals against HZ. A concern with childhood varicella vaccination is the potential increase in HZ incidence due to the decrease in the spread of VZV. However, a rise in HZ incidence has been observed in countries in the absence of a varicella vaccination programme (Canada and the UK), while in the USA, the age-specific HZ incidence did not differ between states with high and low varicella coverage. It is necessary to characterise baseline trends of HZ in order to monitor the impact of the HZV programme as well as to understand changes in the epidemiology of HZ due to varicella. Continued careful monitoring is required.

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BACTERIAL CONJUGATE VACCINES FOR THE PREVENTION OF MENINGITIS AND INVASIVE DISEASE**D. Goldblatt**

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Bacterial conjugate vaccines were developed to control the severe burden of disease caused by encapsulated bacteria. For the first conjugate vaccine to be licensed in humans (1989), *Haemophilus influenzae* type b (Hib) polysaccharide was conjugated to a carrier protein and found to be immunogenic and protective when used in young children. All forms of invasive Hib disease including meningitis were prevented by use of the vaccine in infancy. In 1999, *Neisseria meningitidis* group C (Men C) conjugate vaccines were next to be licensed and had a notable effect on meningococcal C meningitis when introduced into routine infant immunisation programmes. Pneumococcal conjugate vaccines followed in 2000 with similar success, preventing meningitis caused by serotypes covered in the vaccine. However, the exact mechanism by which the vaccines protect remains unknown. All three vaccines have profound effects on nasopharyngeal acquisition which might be a major mechanism by which meningitis is prevented. Challenges that remain for preventing meningitis include:

i. Maintaining long-term protection through to adolescence when immunising in infancy only. This is important in the context of the possible waning of vaccine-induced immunity combined with the absence of natural boosting due to low circulation of the pathogen

ii. Replacement meningitis by strains of the bacteria not contained in the vaccine. This has not been observed for Hib or Men C but is more of a problem with pneumococcus

Novel strategies, such as non-capsule based vaccines, may be required in the future to augment the conjugated capsular polysaccharide approach.

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IMPACT OF SYNFLORIX™ (PHiD-CV) AGAINST PNEUMOCOCCAL MENINGITIS IN BRAZIL**M. Safadi***Santa Casa de Sao Paulo, Sao Paulo, Brazil*

Between 2007 and 2009 an average of 1,150 cases of pneumococcal meningitis (PM) were reported annually in Brazil, with the highest age-specific incidence occurring in children < 2 years of age and with consistently high overall case-fatality rates, approximately 35%.

In mid-2010 the 10-valent pneumococcal conjugate vaccine (PHiD-CV) was introduced into the Brazilian Immunization Programme in a 3 + 1 schedule for infants, with a one-dose catch-up for children 1-2 years of age.

Data from the National Surveillance System of Notifiable Diseases indicate a 43% reduction in the number of PM cases in children aged < 2 years, the age group targeted for vaccination, by June 2011, compared with the average number of cases in the same period in previous years (2007-2009).

In the most populated State, Sao Paulo, 1 year after the introduction of PHiD-CV, the rates of PM in children aged < 2 years declined from an average of 9.2/100,000 persons in the pre- vaccination baseline period (2007-2009) to 5.1/100,000 in 2011. This represents a 44% reduction in the incidence rate after the introduction of the vaccine. The proportion of PM cases in children aged < 2 years declined by 57%, from 27.6% to 11.8%, after the introduction of the vaccine.

PHiD-CV has been introduced in universal mass vaccination programmes in > 30 countries. The encouraging results experienced in Brazil are promising, showing reductions in invasive disease, including meningitis, in the vaccine eligible age group, and anticipate the potential impact on disease that could follow after implementation of universal vaccination programmes.

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PROTEOMICS AND GENOMICS - CAN THEY HELP US UNDERSTAND THE PATHOGENESIS OF INFECTIOUS DISEASES?

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Unravelling of the human genome and the development of methodology for genome wide transcriptome analysis has revealed a previously unimagined complexity in the host response to infectious diseases. The new technologies of RNA expression profiling by microarray and proteomic analysis of body fluids by mass spectroscopy provide powerful new tools for understanding the pathogenesis and diagnosis of paediatric infectious diseases. This lecture will describe insights into major childhood infectious diseases gained through application through transcriptomic approaches to childhood infection including TB and fulminant bacterial and viral infections.

STRENGTHENING EUROPE'S DEFENCES AGAINST INFECTIOUS DISEASES OF THE YOUNG**J. Giesecke***European Centre for Disease Prevention and Control, Stockholm, Sweden*

The European Centre for Disease Prevention and Control opened in Stockholm in 2005. It is an Agency of the European Union with a remit to give scientific advice and produce risk assessments, to perform European-level surveillance and epidemic intelligence, to provide training and capacity-building, and to generally strengthen European preparedness against infectious disease.

It is important to observe that ECDC only performs risk assessments and gives scientific advice. The actual implementation of measures is up to the Commission and to the Member States.

The work of the Centre is divided into seven Disease Programmes, of which the ones on tuberculosis, vaccine-preventable diseases and influenza are the three most involved specifically with paediatric disease.

The tuberculosis programme has as one of its main activities to follow paediatric TB and to give advice on diagnosis and public health measures.

In the programme for vaccine-preventable diseases, there is now a big thrust to help improve vaccination coverage against measles and rubella in the EU. A report on cases and outbreaks is published monthly, there is an action plan to identify barriers to vaccination and to advice countries how to address these, and there are several activities directed at vulnerable populations. - Other activities are aimed at invasive pneumococcal infection, HPV, pertussis, etc.

For influenza ECDC has supported two big EU-wide projects on vaccines: one to measure vaccine effectiveness and one to assess adverse events.

The remit of ECDC is to assist countries in the prevention and control of infectious diseases for all ages, but it is clear that for many of the diseases prevention in children will be one of the most important factors in decreasing overall incidence. Working with EU-wide Learned Societies, such as ESPID, we will continue this endeavour.

IS TREATMENT REQUIRED FOR ACUTE OTITIS MEDIA?**O. Ruuskanen***Pediatrics, Turku University Hospital, Turku, Finland*

Acute otitis media (AOM) is the most common bacterial infection in young children. Three quarters of children will have one or more episodes of AOM by the age of three years. When considering the treatment of AOM the most important thing is the reliable diagnosis i.e. analysis of the pneumatic otoscopic examination.

Most countries have their guidelines for treatment of AOM and they vary. The treatment of AOM consists of several options: 1. Systemic analgesics 2. Topical analgesics 3. Antibiotics 4. Myringotomy 5. Watchful- waiting. Analgesics are considered beneficial and myringotomy ineffective or harmful. Antibiotic treatment vs watchful- waiting has a continuous subject of debate. In spite of that AOM has been the most common indication of antibiotic treatment in young children in all countries. Since 1968 12 randomized, double-blind and placebo-controlled trials on the efficacy of antimicrobial treatment have been carried out. The main conclusion is that antimicrobial treatment is effective. Two recent high-quality studies, in Turku and in Pittsburgh, show a significant benefit among children who received the drug with respect to the duration of acute signs of illness. On the other hand, in the other study two thirds of the children in the placebo group did not need rescue antibiotic treatment. Amoxicillin or amoxicillin-clavulanate are the most commonly used drugs, with high doses in countries with high prevalence of penicillin resistance. The duration of treatment can be as short as five days.

In conclusion, analgesic and antibiotic treatment is required for most young children with AOM.

WHAT'S NEW TO PREVENT AND TREAT CENTRAL VENOUS CATHETER-ASSOCIATED BLOODSTREAM INFECTIONS

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Central venous catheter-associated bloodstream infections (CVC-BSI) are among the most common pediatric healthcare-associated infection. Many institutions have achieved marked reductions in pediatric CVC-BSI by the consistent application of evidence-based preventive bundles. However, few institutions have been able to completely eliminate CVC-BSI using the common bundles related to catheter insertion and maintenance.

Although data are inconclusive, emerging evidence suggests there *may* be additional interventions that could further decrease CVC-BSI. Factors such as prolonged hub scrubs, use of novel antiseptic or disinfectant products (e.g. baths, caps, and dressing), and antiseptic catheter locks may help to prevent some CVC-BSI in children.

In this session, we will discuss the available data on these new interventions and products. Additionally, we will consider the potential risks and benefits of adoption of any of these new practices.

PREVENTION AND TREATMENT OF CATHETER-ASSOCIATED INFECTIONS

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Catheter-related bloodstream infections (CR-BSIs) are a major problem with intravascular catheters. The morbidity and cost of CR-BSIs is considerable. The use of aseptic techniques during insertion and dressing changes continue to be the most essential actions for prevention. The importance of maximal barrier precautions during insertion of central venous catheters (CVCs) cannot be overemphasized. Other preventive measures include using the appropriate type of catheter for the underlying indication, choosing suitable sites for catheter insertion, changing administration sets at proper intervals, and removing the catheters as soon as possible. Using a >0.5% chlorhexidine skin preparation with alcohol for antisepsis, and selectively using antiseptic/antibiotic impregnated CVCs, if the rate of CR-BSIs is not decreasing despite implementation of maximal sterile barrier precautions are additional preventative measures. Regarding diagnosis of CR-BSIs, it requires that two paired blood samples from the catheter hub and a peripheral vein meet CR-BSIs criteria for quantitative blood cultures or differential time to positivity. Vancomycin is recommended for empirical therapy in settings with an elevated prevalence of MRSA infections. Empirical therapy for gram-negative bacilli should be based on local antimicrobial susceptibility data and disease severity, with particular care for *P. aeruginosa* coverage in neutropenic and septic patients or those known to be colonized with this organism. Antibiotic lock therapy should be used for catheter salvage. Long-term catheters should be removed when CR-BSIs are associated with severe sepsis, positive blood cultures despite appropriate therapy for >72 hours, suppurative thrombophlebitis, endocarditis or infections due to *S. aureus*, *P. aeruginosa*, fungi, or mycobacteria.

CONGENITAL CMV**S. Boppana**¹, V. Papaevangelou²

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Congenital cytomegalovirus (cCMV) infection is an important cause of congenital infection (0.2-2.5% of live births) and a leading cause of non-genetic sensorineural hearing loss (SNHL). Children with symptomatic infection are at risk of developing sequelae such as mental retardation, seizures and SNHL. However, most newborns with cCMV infection are asymptomatic (90%). They are also at risk of developing SNHL (10-15%). Hearing loss may be bilateral, is often progressive or with delayed onset. Only 50% of cases of SNHL caused by CMV are detected by neonatal hearing screening programs. Recently there have been significant advances in the diagnosis and treatment of congenital CMV. Universal newborn screening for cCMV, in dried blood spots (DBS) and saliva, as a tool of early identification of infants at-risk is being discussed. Early diagnosis would enable development of guidelines for evaluation of newborns with cCMV (viral load, head ultrasound or brain MRI), prospective monitoring of hearing and intervention during critical stages of speech and language development. Although, blood viral load at birth has been suggested as a prognostic indicator of SNHL, conflicting results have been reported. Current guidelines for antiviral treatment include newborns with either symptomatic disease or those in which postnatal evaluation has revealed evidence of CNS or severe focal organ disease (hepatitis, thrombocytopenia, etc). Finally, the recent availability of oral formulation of valgancyclovir allows outpatient management of newborns in which antiviral therapy is indicated.

During this session recent developments on cCMV infection will be presented. Management will be discussed using real cases as examples.

GROUP A STREPTOCOCCAL INFECTIONS: MEET THE EXPERT SESSION**A. Efstratiou**

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GAS infections cause significant morbidity and mortality globally, largely attributable to invasive disease and rheumatic heart disease and mainly amongst the young and elderly populations. GAS cause considerable long term morbidity, supporting its global importance, hence the considerable efforts in recent years to produce an effective vaccine. Recent European population-based studies have described the epidemiology and clinical features of GAS diseases ranging from classic sore throat to severe life threatening infections, such as septicaemia, streptococcal toxic shock syndrome (STSS) and necrotising fasciitis. Timely monitoring of incidence, mortality and microbiological characteristics is essential to identify changes in disease patterns and emergence of hypervirulent strains, providing opportunities for alerts to be cascaded to frontline medical staff to facilitate early diagnosis, prompt initiation of life-saving therapy and inform the development of guidelines for control and management. The organism possesses numerous cell surface proteins that play a key role in host-bacteria relationships such as virulence and or adherence and form the basis of the GAS typing scheme. These proteins also represent choice candidates for vaccine developments. M-protein is a surface protein encoded by the emm gene which acts as a major virulence factor. Emm-typing is the molecular gold standard and there are currently more than 180 emm types described worldwide. GAS epidemiology varies with time and is dependent upon geographic location and socio-economic conditions. Monitoring type distributions is essential to identify changes in disease patterns, emergence of hypervirulent strains and essential to epidemiological surveillance studies. All these aspects will be discussed in the session.

THE GROUP A STREPTOCOCCAL CLINICAL ENIGMA: TO RECOGNIZE, TO UNDERSTAND AND TO MANAGE APPROPRIATELY. MUCH EASIER SAID THAN DONE!**E.L. Kaplan***Department of Pediatrics, University of Minnesota Medical School, Minneapolis, MN, USA*

Group A streptococcal (GAS) infections and their sequelae remain among the most frequently encountered infectious diseases in children; they continue to perplex clinicians, public health authorities and basic scientists.

The clinical diagnosis is not always easy. The presentation may vary considerably; specific signs and symptoms are often not obvious in the wide pediatric age spectrum. Clinical algorithms can be misleading. Because of these difficulties, the clinical microbiology laboratory remains important. While rapid antigen detection tests are commonly used, their often reduced sensitivity results in the throat culture remaining the "gold standard." Streptococcal antibody tests (e.g., ASO and anti-DNase B) have essentially no role in the management of acute pharyngitis.

The very difficult-to-understand streptococcal upper respiratory tract "*carrier state*" adds further confusion to the clinical and laboratory diagnosis of GAS upper respiratory tract infections.

The goal of therapy is eradication of the organism from the throat. There has **never** been a GAS clinical isolate resistant to penicillin. Thus, while there are many antibiotics that can be used to treat these infections, many believe that the penicillins - and perhaps the cephalosporins - remain first choice antibiotics. Many believe that short course antibiotic therapy (< 10 days orally) is not optimal.

Group A streptococci and their suppurative and non-suppurative sequelae remain important clinical and public health issues. It is hoped that the future development of a *cost-effective* group A streptococcal vaccine will address this issue. But realistically, since that likely will not be possible for some years, appropriate clinical management remains crucial.

ATYPICAL MYCOBACTERIAL INFECTIONS

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Although *M. tuberculosis* remains one of the most important infective pathogens throughout most of the developing world, infections caused by atypical or opportunistic non-tuberculous mycobacteria (NTM) represent an increasing problem in industrialised countries. Transmission of NTM usually occurs from environmental sources including soil, water, dust, aerosols and animal sources. Nosocomial outbreaks, usually by rapid-growers, have been reported following surgical procedures, including CVL insertions and respiratory manipulations. It may be difficult to distinguish disease from colonisation, as isolating NTM from a clinical specimen does not necessarily indicate it is causing disease. Studies in the USA have estimated prevalence at around 20% of that for Tuberculosis (1-2 /100,000

population), *M. avium*, *M. kansasii* and *M. fortuitum* being the most common. The most frequent sites of infection are lymph nodes, skin, lungs, catheter-related and disseminated disease. In immunocompetent children, lymph node infection of the neck is the most clinically significant, with the majority of cases occurring in children under 5 years of age. The main differential diagnosis is TB lymphadenitis. In industrialised countries, lymph node disease due to NTM is much more common than that due to *M. tuberculosis*. Surgical excision of the involved nodes is the treatment of choice. In immunocompromised children and those with pulmonary disease, extensive cutaneous disease or disseminated disease, treatment with several anti-mycobacterial agents may be required for periods of 9-24 months.

SCREENING FOR NOSOCOMIAL VIRAL INFECTIONS IN A NEONATAL INTENSIVE CARE UNIT

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Background: Nosocomial infections account for a large part of hospital-associated morbidity and mortality in neonates. In many cases they are caused by bacteria. However, little is known about nosocomial infections of viral origin. The aim of this prospective pilot trial was to evaluate the occurrence of viral infections in neonates treated for suspected nosocomial sepsis in a tertiary care neonatal intensive care unit (NICU).

Methods: All neonates in whom antibiotic treatment was initiated due to suspected nosocomial sepsis were enrolled consecutively. Airway secretions were analysed using a multiplex reverse transcriptase PCR technique. This method allows screening for adenovirus, respiratory syncytial virus, influenza virus A and B, H1N1 virus, parainfluenza virus 1 - 4, metapneumovirus, coronavirus and picornavirus in one specimen. Stools were examined for adenovirus and rotavirus using antigen testing and confirmatory PCR.

Results: During a 14-month period 51 cases of suspected sepsis were observed in 361 patients. Blood culture proven bacterial sepsis was verified in two cases. In the remaining cases, respiratory syncytial virus was detected once and picornavirus two times in the upper airways. Hence, in the cases with suspected but non-proven bacterial sepsis the incidence of viral pathogens was 6.1 %.

Conclusions: This prospective study substantiates the occurrence of viral agents as relevant nosocomial pathogens in the NICU. The frequency observed is in line with previous retrospective findings. Underreporting due to variation of viral load and inconsistent swabs must be considered. For further evaluation a subsequent study involving a larger cohort of patients is warranted.

LONG-TERM OUTCOMES OF CONGENITAL CYTOMEGALOVIRUS (CMV) INFECTION IN SWEDEN AND THE UNITED KINGDOM

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Background and aims: Congenital CMV is an important cause of deafness and neurological problems, but its natural history is poorly understood. We report updated findings on children followed to age 5+ years in two large prospective studies.

Methods: Pregnant women in Malmö, Sweden, and London, UK (1977-1986) were enrolled, and newborns screened for CMV in urine or saliva. Cases and matched controls were examined regularly and followed up for 5+ years.

Results: 176 congenitally infected infants were identified among >50,000 screened (Sweden: 76 infants, 4.6/1000 births; UK: 100, 3.2/1000 births); 214 controls were selected. 5% (9/176) of neonates with congenital CMV were classified as symptomatic (e.g. hepatomegaly/splenomegaly, tachypnoea, hypertonia/microcephaly). Transient petechiae alone was not classified as a symptom. Of 86% of children followed up to age 5, 83% (126/151) had no developmental problems; 7% had mild, 3% moderate and 6% severe impairment (no differences by study, $p=0.36$). Among children symptomatic neonatally, 56% (5/9) had some impairment, versus 14% (20/142) of those who were asymptomatic ($p=0.007$). Of note, mothers of 8/14 children with moderate/severe outcomes had probable or confirmed non-primary infection. Three of 10 children with petechiae neonatally had sequelae. All serious outcomes were identified by age 2; only three children had mild developmental impairment first identified after that age. Four controls had sequelae (Sweden: 1/50; UK: 3/111).

Conclusions: Moderate or severe outcomes were reported in 9% of children with congenital CMV. Although 14% of those asymptomatic at birth developed sequelae, there was little evidence of progression of disease after age 2.

GBS AND THE NEONATE: PREVENTION STRATEGIES**P. Melin**^{1,2}

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Streptococcus agalactiae, or group B streptococcus (GBS), remains the leading cause of neonatal sepsis and meningitis, early onset and late onset diseases (EOD, LOD).

Where consensus guidelines to detect and treat intrapartum women with GBS colonization have been widely adopted, incidence of neonatal EOD has dramatically declined. In response to both successful impacts on the incidence of GBS-EOD and analyses of missed opportunities, the first American guidelines for prevention issued in the 90s have since been adapted in several stages to improve their efficacy. In some countries in Europe, nationwide guidelines, whether screening-based or risk-based, for the prevention of neonatal GBS diseases have also been issued and adopted, with the expected impact on incidence of GBS-EOD. In spite of universal screening, in spite of the great progress that has been made, GBS-EOD continues to occur and the GBS burden remains a significant public health issue. Continuous efforts to improve screening for GBS status continue to be important and may be able to take advantage of new rapid diagnostic technologies. The current screening-based strategy for prevention is highly effective but imperfect. Given the challenges, limitations and potential complications of maternal intrapartum prophylaxis, a new approach is still needed.

Maternal immunization against GBS is an attractive alternative for the prevention of not only neonatal diseases but also stillbirths and maternal diseases. Vaccines against GBS may likely become the most effective and sustainable long-term preventive strategy.

MICROBIOLOGY OF CYSTIC FIBROSIS

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The established microbial pathogens in cystic fibrosis (CF) include 1) Respiratory viruses, 2) Bacteria from the normal flora of the upper respiratory tract or the skin e.g. *S. aureus*, *H. influenzae*, *S. pneumonia*, 3) Bacteria and fungi from the environment e.g. *P. aeruginosa*, the *B. cepacia* complex, *A. xylooxidans*, *S. maltophilia*, nontuberculous mycobacteria, *Nocardia*, *Moraxella*, *Enterobacteriaceae*, the anaerobe *Prevotella intermedia*, and *Aspergillus*. The most important is chronic *P. aeruginosa* lung infection caused by biofilm growing mucoid strains. Diagnosis of the various bacterial pathogens in CF is done by microscopy and conventional cultivation-dependent methods whereas PCR is mainly used for research. Sputum, deep throat culture and BAL is contaminated by the oral flora, and the mere detection of bacteria (by cultivation or PCR) which are not recognized CF pathogens gives rise to much confusion. Some criteria used for identifying emerging pathogens in CF are given in the table:

Species identification:	Notably of persistent colonization, be aware of misidentification.
Infection = inflammation:	The role of concomitant other pathogens should be defined.
Decrease of pulmonary function:	Eventually leading to lung transplantation or death, but the role of concomitant other pathogens should be defined.
Chronic infection:	Diagnostic role of antibody response.
Epidemiology:	Spread to other CF patients, genotyping necessary.
Detection of virulence factors:	Neutralising antibodies may occur during chronic infection.
Immune response:	Development of antibodies, specific, or cross-reactive induced by other pathogens?
Pathogenesis:	Immune-complex-mediated infection

[Criteria for identifying emerging pathogens in CF]

(Høiby & Pressler: Emerging Pathogens in Cystic Fibrosis. Eur. Respir. Mon. 35:66-78; 2006. Høiby, N., Ciofu, O., Bjarnsholt, T. *Pseudomonas aeruginosa* biofilms in cystic fibrosis. Future Microbiology 5:1663-1674 ;2010)

FUNGAL PULMONARY SYNDROMES IN CYSTIC FIBROSIS**C. De Boeck***Pediatric Pulmonology, University Hospital Gasthuisberg, Leuven, Belgium*

In patients with cystic fibrosis (CF), lung infection with bacterial pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* is the predominant problem. However fungal infections and complications involving fungal antigens are increasingly recognized. The best known fungal complication, occurring in 5 to 10 % of patients, is 'allergic bronchopulmonary aspergillosis' (ABPA). Patients present with a variety of signs and symptoms: increased cough and wheeze, new chest infiltrate, serum IgE > 500 IU/ml, and specific IgE and IgG antibodies against *Aspergillus fumigatus*. Diagnostic criteria are not clear-cut. Some patients definitely have the full blown picture and in others it is dubious whether they do have ABPA, a type of 'Aspergillus asthma' or mere *Aspergillus* colonization. The treatment of ABPA is controversial, with oral corticosteroids and itraconazole as main stay therapy. Because of incomplete control and relapse, alternative therapies such as omalizumab, nebulized amphotericin B, pulse steroids and newer triazole agents are used. Worse evolution of lung function has been found in patients with persistent isolation of *Aspergillus* from sputum in the absence of ABPA. Whether antifungal treatment improves this course is unclear. Mainly in sicker and older patients, fungal pathogens such as *Scedosporium*, *Exophiala* and others are isolated. The treatment schedules for these are poorly researched. In CF patients, use of voriconazole is complicated by cost, complex drug-drug interactions and side effects. Posaconazole has greater activity against *Aspergillus* and causes fewer drug interactions. Experience in CF is however limited.

INHALED VERSUS INTRAVENOUS ANTIBIOTICS: PHARMACOKINETICS/PHARMACODYNAMICS ISSUES**R. Brüggemann^{1,2}**

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The route of administration is defined as the path by which a drug enters the body. As a consequence of this choice, the pharmacokinetic properties of a drug (absorption, distribution, metabolism, and excretion) are critically influenced by the route of administration. Many different pharmaceutical formulations with as many distinct routes of administration have been registered for therapeutic use at the EMA or FDA. The use of “non-conventional” routes of drug administration (ie other than oral or intravenous) has improved the ability of physicians to succeed in treating specific complications. For instance, the administration of antibiotics by the inhaled route is a widely recognized treatment of pulmonary infections in patients with cystic fibrosis (CF). An antibiotic delivered directly to the site of infection should be most effective.

Dosimetry, safety and the efficacy of drugs in the lungs are critical features in the development of inhaled medicines. The evidence describing the relationships between pharmacokinetic (PK) and pharmacodynamic (PD) measurements after inhalation of drugs is limited. A better understanding of pulmonary PK and PK/PD relationships would help lessen the risk of not encountering full therapeutic success as well as identifying the potential for drug accumulation in the lung or excessive systemic exposure. Underlying concepts and indications for inhalation versus intravenous therapy as a component of anti-infective therapy will be discussed. Drugs such as tobramycin, colistin, zanamivir and amphotericin B are commonly used in CF patients and will be used to illustrate specific challenges.

FATAL HUMAN METAPNEUMOVIRUS PNEUMONITIS POST HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Objectives: Human Metapneumovirus (HMPV) is a common cause of respiratory viral infections in the community. Little is known about its relevance in immunocompromised children.

Methods: Case report of a fatal HMPV infection in a patient with Graft-versus-Host-Disease (GVHD) following hematopoietic stem cell transplantation (HSCT).

Results: The patient was a 10-year-old girl with secondary CML and HSCT from a matched sibling donor after conditioning with busulfan, cyclophosphamide and melphalan. Recurrent CML post transplant was controlled by nilotinib plus donor lymphocytes, resulting in molecular remission but also, in chronic GVHD. Eight months after transplantation, while on 0.2mg/kg/day of prednisone, the patient presented with dry cough and progressive respiratory distress. Laboratory investigations revealed a normal CBC and a CRP of 2.2 mg/dL. Total and CD4+-lymphocyte counts were 1920 and 328/uL, respectively. X-ray and CT imaging revealed bilateral patchy lung infiltrates and ground glass opacification. Bronchoscopy with BAL and thoracoscopic lung biopsy demonstrated interstitial and intraalveolar pneumonitis with signs of alveolar damage, no evidence of bronchiolitis obliterans, CMV, PCP and fungi, but HMPV type-B by PCR. Despite a 14-days course of intravenous ribavirin plus IVIG, steroid boluses, empiric antibacterial/antifungal treatment and maximum respiratory support, the patient did not recover and died three weeks later from irreversible lung failure without clearance of HMPV from respiratory secretions.

Conclusion: Although it is unclear whether HMPV was the sole or a contributing cause of fatal lower respiratory tract disease, the case demonstrates that HMPV needs to be considered a potentially serious respiratory viral pathogen in immunocompromised children.

MENINGOCOCCAL DISEASE AND AGE-RELATED MACULAR DEGENERATION SHARE GENETIC SUSCEPTIBILITY LOCI

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Background and aims: Host genetic variation in complement factor H(CFH) show very strong evidence of association with individual susceptibility to meningococcal disease(MD).

Methods: We performed a meta-analysis of two GWAS in Spain (ESIGEM-network) and the UK, totaling 894 MD cases and 5,645 controls,with replication in a further 565 MD cases and 2,600 controls of West European descent.The MD cases were genotyped using the Illumina Human-610K Quad Bead Chips for UK and the Illumina Human-660W Quad Bead Chips for Spain. Replication genotyping was done using the Sequenom-MassArray platform.

Results: We note strong evidence of association at the previously reported *CFH* locus on Chromosome 1(rs1065489, $P = 1.18 \times 10^{-8}$ and rs11582939, $P = 1.95 \times 10^{-8}$).The second most significant SNP was observed within *ABCA4*(rs544830, $P = 2.93 \times 10^{-6}$, per-allele OR = 1.30).Strong statistical association of this locus with MD was corroborated by two other neighboring SNPs(rs550060, $P = 4.48 \times 10^{-6}$, per-allele OR = 1.29 and rs497511, $P = 4.55 \times 10^{-6}$, per-allele OR = 1.29). These findings within *ABCA4* were further replicated in the Western European collection($P = 8.72 \times 10^{-5}$, $P = 1.81 \times 10^{-4}$, and $P = 6.59 \times 10^{-5}$ respectively), leading to genome-wide significant findings for all three *ABCA4* SNPs($P = 8.46 \times 10^{-10}$, $P = 5.28 \times 10^{-9}$, and $P = 2.36 \times 10^{-9}$, respectively) when data from all MD sample collections were jointly analyzed.

Conclusion: As mutations in both *CFH* and *ABCA4* also confer susceptibility to macular degeneration, our observation points to shared mechanisms of pathogenesis between macular degeneration and MD.

POST-TRANSPLANT INFECTIONS IN CHILDHOOD LIVER DONOR RECIPIENTS

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Background and aims: Retrospective assessment of post-transplant infections in childhood liver donor recipients at one center in a developing world country.

Methods: Between 1998 and 2011 there were 73 patients who received a liver transplant. The transplantations were conducted in hepato-pancreato-biliary surgery unit, and patients were followed by pediatric gastro-entero-hepatology and pediatric infectious disease division of Istanbul University Medical Faculty. During post-transplant follow-up period patients were divided into 3 groups (1st post transplant month, 2-6th post transplant months, after 6th post transplant month). Infection rates during these periods were statistically evaluated.

Results: 73 patients (46 female / 27 male) who received 76 liver donor transplantation were enrolled in the study. Children aged 4.3-212 months were followed up during 1-267 days post transplantation. Most frequent reasons of transplantation were metabolic diseases. Post-transplant overall mortality was 8.2%. In the 1st month gram-positive bacteria were the most encountered, gradually replaced by gram-negatives. The most frequently isolated species of gram negative bacteria was *Acinetobacter spp.* and gram positive bacteria was *MRCNS*. The frequency rate of bacterial infection reduced statistically significantly after the first month of liver transplantation. CMV was the most frequent serologically proved viral infection. *Candida albicans* was the unique isolated pathogen in fungal infections.

Conclusions: Our post-transplant infection rate was in accordance with previous published data. To know the frequency and the type of isolated microorganism in liver donor recipients is important for infection prevention and also for increase in survival rate at centers performing liver transplantation.

MANNOSE-BINDING LECTIN DEFICIENCY IN PAEDIATRIC STEM CELL TRANSPLANTATION**A. Heitger¹, S. Heitzeneder¹, M. Seidel², S. Matthes²***¹Transplantation Immunology, Children's Cancer Research Institute, ²Stem Cell Transplantation Unit, St. Anna Children's Hospital, Vienna, Austria*

Stem cell transplantation (SCT) is associated with severe immunosuppression in the immediate post-SCT period. During this period, the susceptibility to severe infections, including opportunistic infections, is significantly increased. Mannose-binding lectin (MBL), part of the complement system, has a significant role in the host defence. Due to genetic polymorphisms, MBL deficiency in the normal population is present up to 30%, but its clinical impact in otherwise healthy individuals is an ongoing matter of debate. Here, we investigated whether MBL deficiency constitutes a risk factor for severe infections after allogeneic SCT. Up to December 2011, 94 allogeneic SCT recipients were enrolled in the study and monitored during the time of neutrophil recovery. By ELISA technique, 14 % of patients had low MBL serum levels (50 - 500 ng/ml), and further 5% patients had extremely low levels (< 50 ng/ml). As assessed by high resolution melting analysis (HRMA), MBL genetic testing including exon 1 variants and promoter polymorphisms were discovered in ~ 30% of the patients, indicating that MBL polymorphisms are not stringently associated with low MBL serum levels. While final results are pending, preliminary analyses suggest that neither MBL serum levels nor MBL genetic variants were significantly associated with an increased rate of severe infections arguing against perceiving low MBL levels a significant risk factor in paediatric allogeneic SCT recipients. If confirmed, these findings do not support prophylactic MBL substitution as an effective means to ameliorate susceptibility to infections in allogeneic paediatric SCT.

RISK FACTORS FOR SEVERE INFECTION IN A COHORT OF CHILDREN WITH CANCER AND FEVER ADMITTED TO THE HOSPITAL

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Background: Cancer is an important risk factor for severe infection. We present a cohort of children prospectively enrolled with cancer and fever to evaluate risk factors for a severe infection.

Methods: All children with cancer and fever admitted to the hospital were prospectively enrolled in this study. We performed physical examination (PE) and a minimum of laboratory tests including procalcitonin (PCT) on admission, initiated a standardized treatment and evaluated their outcome. We analyzed the data dividing the cohort in two groups: group 1, children with the final diagnosis of severe infection; group 2 children with the final diagnosis of fever without source.

Results: Forty six children were enrolled in the study with 8 children (17.4%) diagnosed with severe infection (group 1). Median age was 141 months (30 for group 1 vs 148 months for group 2; $p=0.013$), with no differences in sex distribution. More children in group 1 had leukemia (75 vs 29%; $p=0.038$). There were no differences in PE or laboratory parameters except in PCT levels (0.9 vs 0.1, respectively; $p=0.005$). PCT at 48 hours (1.5 vs 0.1; $p=0.021$) and days with fever (4 vs 2; $p=0.022$) but not CRP at 48 hours were also higher in group 1. Group 1 also had a trend towards more days with severe neutropenia (5.5 vs 3; $p=0.07$).

Conclusions: In our cohort younger age, prolonged fever and PCT on admission and at 48 hours were the parameters that better predicted severe infection in children with cancer and fever.

WEST NILE VIRUS IN GREECE AND OTHER EMERGING VIRUSES IN EUROPE**A. Papa***Aristoteles University of Thessaloniki, Thessaloniki, Greece*

Global warming contributes to the spread of arboviruses, especially those transmitted by mosquitoes. Recently, in summer 2010, a large West Nile virus (WNV) outbreak occurred in Greece, resulting in thousands of human infections. Apart the asymptomatic and the mild febrile cases, 197 neuroinvasive cases were observed. Most of them (88%) were encephalitis cases, and 33 (17%) had a fatal outcome. The patients with neuroinvasive disease were elderly persons with an underlying disease. The incidence of the neurological disease was 15 per 100,000 population. Molecular testing of mosquitoes collected at the sites where the cases were observed showed that the strain belonged to WNV lineage 2, genetically closest to a WNV strain detected in 2004 in birds in Hungary, carrying the mutation H249P in NS3 gene, which has been previously associated with increased pathogenicity in WNV lineage 1 strains. Identical sequences were recovered from blood donors, as well as in additional mosquito pools, in wild birds and, later, in spring 2011, in sentinel chickens. WNV outbreak occurred in Greece also in 2011. Apart the mild cases, 76 neuroinvasive cases have been reported, 8 of them fatal. In 2011 the incidence was lower (0.68/100,000) than in 2010, the cases were more dispersed (North and Central Greece), and the fatality rate was lower (10.5%). During 2010-2011, WNV outbreaks occurred also in Romania, Russia, Israel, while less cases were detected in other European countries.

A large outbreak of Chikungunya virus (CHIKV) infections took place in 2007 in Italy, while autochthonous, 2 each, dengue virus (DENV) and CHIKV infections occurred in France in 2010. The same year, a cluster of dengue fever cases was observed in Croatia, in regions where *Aedes albopictus* mosquitoes predominated. The recent emergence and establishment of many "tropical" viruses in Europe, constitutes a warning signal for public health authorities to enhance surveillance and design prevention and control measures.

SEVERE PERTUSSIS AMONG INFANTS < 90 DAYS OF AGE ADMITTED TO PEDIATRIC INTENSIVE CARE UNITS. SOUTHERN CALIFORNIA, SEPTEMBER 2009-JUNE 2011

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Background: Pertussis can cause severe illness and death among infants. Ten infants died during the 2010 pertussis epidemic in California. Data on the most effective management of critically ill infants is needed.

Methods: We collected information on infants ≤ 90 days of age admitted to five pediatric intensive care units (PICU) with pertussis from September 1, 2009-June 30, 2011. Infants who were diagnosed with pulmonary hypertension or died were considered to have more severe infections. We compared more severe with less severe infections.

Results: There were 31 infants (55% female, 94% Hispanic); 8 had more severe infections, of whom 7 had pulmonary hypertension and 4 died. Infants with more and less severe infections were demographically similar, and no significant differences in time from illness onset to initial medical care were identified. Infants with more severe infections had higher peak white blood cell counts (WBC), 74,200 vs. 26,900 ($p < 0.01$) and their WBC exceeded 30,000 more rapidly after illness onset, 5.1 vs. 14.6 days ($p < 0.01$). Infants with more severe infections were more likely to have a 50% increase in WBC in ≤ 24 hours, (50% vs. 0%, $p = 0.01$).

Conclusions: Infants with more severe pertussis were more likely to have higher WBC and more rapid increases in WBC than infants with less severe infections. Identifying these infants early during the course of illness through early WBC measurement might allow for more rapid implementation of interventions like exchange transfusion that could potentially reduce the severity of disease and prevent death.

SHIFT OF MEASLES EPIDEMIC FROM CHILDREN TO ADULTS: THE EXPERIENCE OF THE REGIONAL UNIVERSITY HOSPITAL OF CLERMONT-FERRAND, AUVERGNE, FRANCE 2008-2011

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Background and aims: A measles outbreak developed in France from 2008 to 2011. Its incidence was high in Auvergne. We describe its evolution towards involvement of adults, its clinical consequences and their explanations.

Methods: Measles cases were defined as a rash associated with IgM positive serology and/or salivary test. We recalled all the cases registered through mandatory notification and patients referred to the university hospital.

Results: From 2008 to 2010 the epidemic affected mainly children and adolescents in gipsy groups with few secondary cases. Since mid-2010 and mostly in 2011 the outbreak developed largely in the community. 376 cases were notified in the district: 160 children (42,6%) ; 216 adults (57.4%). Among the adults, 113 (52%) were referred to the university hospital (median age 26.7 y). 71 (63%) were hospitalised: pneumonia was confirmed in 31, diarrhea occurred in 29, biological hepatitis in 47, thrombopenia in 39. An encephalitis case needed intensive care. No death. Previous exposition was identified in 30 (27%) and secondary cases occurred in 18 (16%). 19 patients were healthcare workers, 5 infections were hospital-acquired. 92/110 were unvaccinated, 18/110 (16%) had received one dose of measles vaccine. Unvaccinated patients were more likely to be hospitalised ($p=0.005$) and suffer from complications.

Conclusion: Despite a vaccine coverage of children $\geq 85\%$ (with 1 dose) in Auvergne, measles epidemic expanded from children in restricted groups to the community; it peaked when it affected insufficiently immunised adults. These observations highlight the need for improving the vaccine coverage especially in young adults.

Q-FEVER IN THE NETHERLANDS

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Q fever is an ubiquitous zoonosis that is caused by *Coxiella burnetii*. In the last four years there was a large outbreak of Q fever in The Netherlands with almost 4000 confirmed cases. Infection occurs through inhalation of infected aerosols. The reservoir mainly consists of dairy cattle. Clinical symptoms of acute Q fever are non-specific and resemble a mild flu-like illness. Reports on Q fever in children are scarce, although, based on seroepidemiological data, they often seem to be exposed to *C. burnetii*. Children usually present with gastrointestinal symptoms and rash. Rarely, chronic infection develops. This is usually manifested by endocarditis, vascular infection and, in children, osteomyelitis. Diagnosis is based on serology and nucleic acid amplification. Doxycycline is the treatment of choice for acute infection. An alternative for young children and pregnant women is cotrimoxazole. Chronic infection requires long term treatment of doxycycline combined with hydroxychloroquine.

Although a better understanding of the disease has been gained, many questions including those about optimal treatment still remain. An overview of the epidemiological and clinical aspects of Q fever is presented, with emphasis on pediatric cases.

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF PEDIATRIC PATIENTS WITH DENGUE HOSPITALIZED AT COSTA RICA'S (CR) NATIONAL CHILDREN'S HOSPITAL: 2005-2010

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Background and aims: Dengue is the most frequent and rapidly spreading arboviral disease in the world. In CR, dengue has become a public health problem since 1993, with 203,313 cases being diagnosed since then (2003-2010). Its incidence has increased 30 times especially in both coasts, and then spread to inlands. Our main objective was to describe the epidemiology of dengue in hospitalized children at the only pediatric tertiary referral hospital of CR.

Methods: Retrospective chart review of children < 13 years of age who were hospitalized and had confirmed dengue by ELISA IgM or PCR. Study period was January/1/2005-December/31/2010.

Results: 31 patients were included, 45% were male; 59% of patients were 6-11 years of age. Half of hospitalizations occurred during 2010. The most common presenting symptoms and signs were: fever, 97%; rash, 74%; vomiting, 39%; and abdominal pain, 32%. Hypotension occurred in 35% of patients but only 10% had tachycardia. Pleural effusion was documented in 6.4% patients. Hemorrhagic dengue occurred in 19% of patients. Thrombocytopenia at admission was documented in 25 (80.7%) patients, median 84,000 (range 30,000-154,000) platelets/mm³. Admission to the PICU was required in 2 patients, 1 of whom died due to dengue shock.

Conclusions: Dengue has spread to CR cities over 1000 meters above sea level, therefore it has to be considered in the differential diagnosis of fever and rash, and children with fever, hypotension, and bradycardia. In this study, there was very low incidence of complications probably due to early medical suspicion at the primary care level.

EHEC OUTBREAK IN GERMANY

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Enterohemorrhagic *Escherichia coli* (EHEC) belongs to a highly diverse group of Shiga toxin (Stx)-producing *E. coli* (STEC). They can cause bloody diarrhea and cause in up to 30% of the cases of infection a severe disease called Hemolytic Uremic Syndrome (HUS). These bacteria showed their epidemic potential during their recent outbreak in May 2011 in Germany. More than 3300 patients suffered from bloody diarrhea, more than 800 developed an HUS and 52 patients died. This was the largest described outbreak in Europe known so far. The question remains, how we can prevent such dramatic events. As there is still no specific therapy or vaccine available for EHEC infections and antibiotic therapy in the initial phase of the diarrhea is considered to increase the chance of inducing a HUS, preventive strategies lie in the focus of controlling EHEC-associated infections. Therefore, an early and specific detection of the EHEC is necessary. Conventional and molecular methods used in today's microbiological laboratories are not sufficient to distinguish an STEC from an EHEC infection. Furthermore, there is a lack of knowledge about possible co-infections with other microorganisms (e.g. viruses) or the isolated presence of stx-converting bacteriophages in patients with diarrhea. Identification of the role of co-infections and Stx-lacking EHEC, would allow a correct assessment of clinical importance of STEC. It has been described before that several stx-subtypes are associated with the severity of STEC-disease. Therefore, early stx-subtyping and molecular characterization could possibly allow a risk assessment useful for the clinical management of the patient. An early monitoring of the patient could lead to secondary prevention of severe EHEC-disease.

Therefore, new and innovative techniques need to be developed in order to improve the diagnostic and the management of the patient. A molecular risk assessment is necessary to advise the public health service and to take appropriate measures in order to prevent in future such large outbreaks with highly virulent EHEC.

OF MAN AND MICRO: THE CHILD AS THE FATHER OF THE MAN**A.J. Cant**

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Microbes are constantly evolving to better exploit the wonderful niche that man offers. Man's immune system is evolving attempting to prevent microbes succeeding. Some mutations in immune response genes enhance immunity; most lead to greater susceptibility to infection. Children are in the forefront of this struggle being both naïve to infectious agents and most likely to show the consequences of immune defects. As paediatric infectious diseases physicians we share a unique opportunity to recognise and delineate these ever changing scenarios, from influenza pandemics to drug resistant TB, FARS and many others, and develop new ways to meet microbes new challenges by therapeutics, vaccination and immune modulation as well as better treatment for children who suffer the consequences of experiments of nature that failed. If we don't who will?

ANTIBACTERIAL AGENTS FOR RESISTANT GRAM NEGATIVE INFECTIONS (COLISTIN, TIGECYCLINE, FOSFOMYCIN)**C. Antachopoulos**

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The emergence of infections caused by multi-resistant Gram-negative bacteria over the last years has been associated with increased morbidity and mortality both in adult and pediatric patients. As these infections are often resistant to many classes of conventional antimicrobial agents (including the carbapenems and aminoglycosides) the remaining therapeutic options likely to be effective are limited. A number of antimicrobial compounds active against these bacteria have been lately introduced, such as tigecycline, whereas others, already known for decades, have been "re-discovered", such as colistin and fosfomycin. Unfortunately the pharmacokinetics, safety and efficacy of these three agents in pediatric patients have not been systematically studied across all range of ages (from infancy to adolescence). In some cases (colistin), dosing recommendations for children are based on data from previous decades, generated using microbiological methods for determination of drug concentrations whose validity is currently questioned. The present lecture will summarize available data on pharmacokinetics, safety and efficacy of colistin, tigecycline and fosfomycin in infants and children and will highlight gaps in our knowledge as well as areas where current practise or recommendations are likely to change in the near future. Questions to be answered and future areas for research regarding the pediatric use of these antimicrobials will also be discussed.

NEW ANTIFUNGAL IN PEDIATRICS

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Substantial achievements have been made in the development of new antifungal agents over the last decade. Unfortunately, clinical trials involving pediatric patients, or focussed neonatal or pediatric clinical trials are lacking. The recognized necessity to establish appropriate neonatal and pediatric dosages has led to an increase in pharmacokinetic/pharmacodynamics studies and experimental models. The results of these studies show us indeed what we did not know about the old and new antifungal agents with respect to their use in paediatrics.

The two most recent developed antifungals, posaconazole and anidulafungin, are not yet approved for use in paediatrics. Two case series of paediatric patients show a favourable safety and tolerance profile and efficacy as salvage therapy. A twice daily dosing algorithm for posaconazole prophylaxis in children with chronic granulomatous disease was developed and led to an adequate exposure. Anidulafungin, probably distinctive to the other echinocandins due to its unique pharmacokinetics, should be avoided in children until more pharmacokinetic and clinical data become available.

For the two other echinocandins, caspofungin and micafungin, having an approval for use in children and neonates for specific indications, robust data sets and models are available to distillate appropriate dosages. An optimal dosage for voriconazole in children > 2 years of age (has been approved for this age category) is still not established. Results of recent pharmacokinetic data of fluconazole and echinocandins dosing in neonates warns us that for effective treatment of neonatal candidiasis, much higher dosages might be needed.

HIGH PREVALENCE OF X4-TROPIC VARIANTS IN CHILDREN AND ADOLESCENTS INFECTED WITH HIV-1 BY VERTICAL TRANSMISSION

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Background and aims: We aimed to characterize co-receptor use in antiretroviral-experienced pediatric patients infected with HIV-1 by vertical transmission in order to predict the proportion of HIV-infected children and adolescents who could maximally benefit from treatment with CCR5 antagonists.

Methods: 118 multidrug-resistant pediatric patients (36 children and 82 adolescents) were enrolled in a cross-sectional study from September 1st, 2009 - October 30th, 2010. Viral tropism was assessed using the new phenotypic HIV-1 tropism assay (TROCAI) and Trofile (ES).

Results: The 57.0% (n=49) DM and 23.3% (n=20) X4. Only 19.7% (n=17) showed R5 variants. HIV-1 co-receptor usage was not reportable in 39/118 (33%) patients. When analyzed independently children adolescents who obtained reportable TROCAI (n=24 and n=62, respectively), 70.8% (n=17/24) children and 82.2% (n=51/62) adolescents showed viruses with DM or X4 variants. Independently, Trofile (ES) was performed in 42/118 patients who had HIV-1 RNA >1000 copies/mL. No patient showed X4-tropic variants and DM viruses were observed in 28.6% (n=12/42) of patients. In 14.3% (6/42) of patients HIV tropism could not be reported.

Conclusions: X4 variants are present in more than 80% of the antiretroviral experienced older children and adolescents infected with HIV by vertical transmission enrolled in our cohort that may limit the use of CCR5 antagonists' family.

CD4-ASSOCIATED IMMUNOSENESCENCE PATTERNS IN VERTICALLY HIV-INFECTED SUBJECTS

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Background: Vertical HIV-transmission represents an important world-wide health problem although the incidence in developed countries has been drastically reduced by the extensive use of HAART. Vertically HIV-infected subjects have been exposed to the virus during their immune system's maturation and have suffered a persistent chronic activation throughout their full lifetime; consequences of such situation in their immune system are not fully understood. The objective of this study was to analyze immunosenescence-related parameters in different CD4 T-cell subsets.

Methods: Fifty seven vertically HIV-infected subjects and 32 age-matched healthy subjects were studied. Activation (HLA-DR+), senescence (CD28-CD57+) and proliferation (Ki67+) were analyzed on different CD4 T-cell subsets; such are naïve (CD45RA+CD27+), memory (CD45RO+CD27+), effector memory (CD45RO+ CD27-) and TemRA (CD45RA+CD27-).

Results: Compared to healthy individuals, vertically HIV-infected subjects showed increased naïve and memory CD4 T-cell frequencies ($p= 0.035$ and $p= 0.010$, respectively) but similar frequencies of both effector subsets. Whereas naïve CD4 T-cells were not further altered, memory CD4 T-cells presented increased levels of senescence and proliferation markers ($p< 0.001$), effector memory CD4 T-cells presented increased levels of activation, senescence and proliferation markers ($p< 0.001$) and TemRA CD4 T-cells presented increased levels of activation and senescence ($p< 0.001$) than those of healthy subjects.

Conclusions: Despite long-periods of infection, vertically HIV-infected subjects show specific patterns of immunosenescence, revealing a preserved CD4 T-cell homeostasis mainly regarding subset differentiation and distribution. Nevertheless, excepting the naïve subpopulation, all subsets experienced immunosenescence features, pointing to uncertain consequences of the future aging process in these subjects.

PERINATAL HIV INFECTIONS IN THE UK, 2001-2010

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Background and aims: Despite high uptake of antenatal screening, mother-to-child HIV transmission (MTCT) still occurs. MTCT rates from diagnosed women are now < 1%, with fewer than 10 transmissions annually. However, perinatally-infected children are also reported whose mothers were undiagnosed at delivery. Perinatal infections are described in relation to timing of maternal and child diagnosis.

Methods: Surveillance data on pregnancies in diagnosed women, and HIV-infected children, is collected through the UK and Ireland's National Study of HIV in Pregnancy and Childhood. Only UK data are reported here.

Results: 10,209 infants born to diagnosed women 2001-2010 were reported by end 2011, rising from 480 in 2001 to 1288 in 2007; numbers have now stabilised. Infection status was reported for 8895 (87%) children and 82 (0.9%) were infected; among 1314 children with unconfirmed status, fewer than 15 are expected to be infected. 90% of infected children born to diagnosed mothers are diagnosed by 12 months.

Another 189 (69.7%) perinatally-infected children were reported whose mothers were undiagnosed at delivery. About half were diagnosed under age one, but 29 were 3 years or older at diagnosis, and the oldest so far was aged 8. Some children born since 2001 are likely to still be undiagnosed; the overall proportion diagnosed at older ages will increase.

Conclusion: Although some undiagnosed women probably had long-standing infection, others may have seroconverted in pregnancy or after delivery while still breastfeeding. Audit of perinatally-acquired infections and expert review of cases to identify remaining barriers to prevention of MTCT is underway.

ATAZANAVIR (ATV) USE AND DOSING IN HIV-1-INFECTED CHILDREN IN THE UK AND IRELAND

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Background and aims: In the EU the protease inhibitor (PI) atazanavir (ATV) is indicated for treatment of HIV-1-infected children ≥ 6 years of age in combination with other antiretrovirals. However data outside of clinical trial settings are limited in paediatrics. Our aim was to describe demographics, clinical characteristics, antiretroviral therapy (ART) use and dosing in children receiving ATV in the Collaborative HIV Paediatric Study (CHIPS), a cohort study of all HIV-diagnosed children living in the UK/Ireland.

Methods: Descriptive analysis of data reported to CHIPS to 30/09/11.

Results: 1,405(82%) of 1,704 HIV-infected children ever reported to CHIPS received ART, of which 152(11%) had ever taken ATV. Characteristics for the 113(8%) receiving ATV at last follow-up were as follows: 68 (60%) female; median age 15 years (IQR 14-17); 35(31%) ever CDC C; 24(21%) previous mono/dual therapy. For the remaining 39 not on ATV at last follow-up, 11(28%) were on a treatment interruption, 23(59%) continued on another PI-based regimen and the rest an NNRTI-based regimen. In 35 children reasons for stopping ATV were available: 18(51%) poor adherence; 1(3%) severe adverse event; 3(9%) potential toxicity; 13 (37%) other. Only 11(6%) of 196 recorded doses of ATV were below the adult 300mg once daily dose.

Conclusion: ATV is prescribed to older children who are given adult doses. Most children stopping ATV but continuing ART remain on PIs. The relatively high proportion of children off ART at last follow-up is likely to be related to poor adherence in adolescence.

UPDATE IN PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV**C. Thorne***University College London, London, UK*

More than 1000 infants are infected with HIV worldwide daily and there is a global commitment to reduce mother-to-child transmission (MTCT) to < 5% by 2015. However, in high income settings in Europe and elsewhere, “virtual elimination” of MTCT of HIV has been achieved, with transmission rates of < 1-2% reported. An overview of the epidemiology of HIV in antenatal populations across Europe and of fertility trends in women living with HIV will be given. A brief history of approaches to prevention of MTCT (PMTCT) in Europe will be provided, contrasting the situation in Western versus Eastern Europe, followed by an overview of current policies and practices. Use of antiretroviral drugs in pregnancy and within neonatal prophylaxis forms the cornerstone of preventive strategies. In Western Europe today, the vast majority of HIV-positive pregnant women receive combination antiretroviral therapy (cART) for their own health and/or for PMTCT. Practices in Eastern Europe are more varied, but several countries have transitioned from use of abbreviated antiretroviral regimens to cART for PMTCT (WHO Option B). HIV and antenatal ART have both been associated with adverse pregnancy outcomes, including preterm delivery, and recent data will be reviewed. Trends in the use of other PMTCT interventions will be discussed, including mode of delivery and neonatal prophylaxis. Challenges with respect to PMTCT in Europe will be described, including the needs of specific groups such as women who inject drugs, those with co-infections and those with presenting with advanced HIV disease for the first time in pregnancy.

EPIDEMIOLOGY AND MANAGEMENT OF MULTIDRUG-RESISTANT AND EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS IN CHILDREN

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The World Health Organization estimated that 440 000 incident cases of multidrug-resistant tuberculosis (MDR-TB) occurred during 2008. Of all TB cases world-wide, 10-15% occur in children. As the incidence of MDR-TB in children closely follows that of adults, it could be expected that ~50 000 childhood MDR-TB cases occur annually. However, as a definite diagnosis of MDR-TB requires microbiological confirmation of *Mycobacterium tuberculosis* plus drug susceptibility testing (DST), only few cases are reported. Childhood TB cases who are in contact with adult MDR- or extensively drug-resistant (XDR)-TB cases should be suspected of having the same resistant TB. DST in adult and child TB cases should become more feasible with new rapid diagnostic tests.

Treatment of MDR/XDR-TB requires the same second-line anti-TB drug regimens as in adults. Treatment duration depends on the extent of disease, with advanced disease requiring treatment for 18 months after first negative culture. Drug adverse effects are more difficult to assess in children than in adults. Special attention should be given to hearing impairment (second-line injectable drugs) and hypothyroidism (thionamides and para-aminosalicylic acid). Outcome in children has generally been good (cure/treatment completion in >80% of cases), even in XDR-TB cases. Outcome is improved by early diagnosis and aggressive treatment with most appropriate anti-TB drug regimens. Newer drugs, such as the fluoroquinolones and linezolid, have been used with success and with minimal adverse effects in children.

Young or HIV-infected child contacts of MDR/XDR-TB cases should be screened for disease. Once TB disease is excluded, clinical follow-up is most important. Evidence is increasing that chemoprophylaxis of these high-risk MDR-TB contacts could effectively prevent disease.

PROSPECTS FOR NOVEL TUBERCULOSIS VACCINES: WHERE DO WE STAND?**S. Hoff***Department of Infectious Diseases Immunology, Statens Serum Institut, Copenhagen, Denmark*

Tuberculosis (TB) continues to be a major cause of morbidity and mortality throughout the World, with approximately 8.8 million new cases and an estimated 1.1 million deaths in 2010 (WHO report 2011). Infants and younger children (below 5 years) are at risk of rapid, disseminated disease, which can cause high mortality unless aggressively treated. There is also a growing threat from multidrug resistant TB (MDR-TB). To control the TB epidemic there is a great need for an effective TB vaccine and improved TB diagnostics. The existing vaccine against TB, the bacille Calmette-Guérin (BCG) vaccine provides partial protection especially against disseminated TB disease in infants and younger children, but although globally very widely used, varying vaccine efficacy estimations have made BCG vaccination policies vary across countries. Currently much effort is ongoing in the search for a new vaccine against TB to either boost or replace the existing BCG vaccine. A number of TB vaccine candidates are undergoing clinical trials and include both live mycobacterial vaccines, viral vectored vaccines and adjuvated protein based vaccines. These novel TB vaccine candidates explore various vaccine strategies including prophylactic vaccination, post-exposure vaccination and therapeutic vaccination. In parallel immune based TB diagnostics have evolved from the Tuberculin PPD skin test to interferon gamma release assays and a second generation skin test, which detects *M. tuberculosis* infections with high specificity.

CURRENT MANAGEMENT ALGORITHMS OF URINARY TRACT INFECTIONS IN INFANTS

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During the last decade there has been a major change in both the treatment and investigations of infants who have experienced a UTI. Previously all these infants were hospitalised for iv antibiotic treatment and they were all investigated with a combination of ultrasound, DMSA scintigraphy (sometimes both on the acute phase and after 6 month) and a MCUG.

Recent guidelines suggest a more individualised approach. Infants who are not septic appearing and who can take medicines by mouth are already from onset treated with oral antibiotics. Imaging is decided according to clinical criteria to meet the need of each particular child.

The background to these major changes and the details of this modern approach will be presented.

PROBLEMS IN PREVENTION AND TREATMENT OF INFLUENZA**S. Esposito, N. Principi**

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Antiviral medications with activity against influenza viruses are an important adjunct to influenza vaccine in the control of influenza. Influenza antiviral prescription drugs can be used to treat influenza or to prevent influenza. Two influenza antiviral medications are recommended for use in Europe as well as in the United States during the 2011-2012 influenza season: oseltamivir (Tamiflu®) and zanamivir (Relenza®). Oseltamivir and zanamivir are chemically related antiviral medications known as neuraminidase inhibitors that have activity against both influenza A and B viruses. Antiviral resistance to oseltamivir and zanamivir among circulating influenza viruses is currently low, but this might change. Also, antiviral resistance can emerge during or after treatment in certain patients (e.g., immunosuppressed). Clinical and observational data show that early antiviral treatment can shorten the duration of fever and illness symptoms, and reduce the risk of complications from influenza (e.g., otitis media in young children, pneumonia, respiratory failure, and death). Antiviral treatment is recommended as early as possible for any patient with confirmed or suspected influenza who is hospitalized or has severe, complicated, or progressive illness or is at higher risk for influenza complications. In addition, antiviral medications are 70% to 90% effective in preventing influenza and are useful adjuncts to vaccination. Worldwide, health authorities do not recommend widespread or routine use of antiviral medications for chemoprophylaxis so as to limit the possibilities that antiviral resistant viruses could emerge. An emphasis on early treatment and monitoring is an alternative to chemoprophylaxis after a suspected exposure for some persons.

TOXOPLASMOSIS: TREATING IN PREGNANCY AND INFANCY**P. Ambroise-Thomas***National French Academy of Medicine, Paris, France*

Toxoplasmosis is one of the most frequent congenital infections. As soon as maternal infection (generally asymptomatic) is serologically suspected, preventive treatment must be prescribed to avoid the mother to child transmission or, if this transmission has already occurred, to avoid or limit its consequences. Spiramycin is first line prenatal treatment. It does not cross the placenta to the fetus, but is present in high concentrations in the placenta, and thus it has been reported to decrease the frequency of vertical transmission. This treatment with spiramycin is changed to a combination of pyrimethamine-sulfonamide and folinic acid if fetal infection is proved (serology, PCR, mouse inoculation of amniotic fluid). As soon as *Toxoplasma* infection is confirmed, infected children are treated with the pyrimethamine-sulfonamide and leucovorin combination for at least several months (consensus does not exist about the duration of this post natal treatment: 3 months in Denmark, 12 months in France). The efficacy of this treatment is discussed and according to recent multicenter studies, it could be active against serious neurological sequelae disorders (SNSD, risk reduced by three-quarters) but it does not prevent ocular lesions. Finally, these results relate to the relatively benign type II strain of *T. gondii*, which predominates in Europe and North America. Trials are urgently needed to determine the most effective timing and type of prenatal treatment for the more virulent parasite strains that predominate in other continents and particularly in South America.

PREVENTION OF SEXUALLY TRANSMITTED INFECTIONS IN ADOLESCENCE; A FOCUS ON HIV**C. Foster**

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Vaccine preventable sexually transmitted infections (STIs) include Hepatitis B and Human Papilloma virus, however most agree an effective vaccine against HIV is unlikely for many years. Globally, ~50% of new HIV infections reported in 2009 occurred in 15-24 year olds. Whilst behaviour change messages are central to most sub-Saharan national AIDS programs, the impact of individual behavioural interventions on HIV incidence remains disappointing. In the same setting male circumcision in heterosexuals reduces HIV incidence by up to 60% with wide scale roll out of safe circumcision services recommended by the WHO.

The use of antiretroviral therapy (ART) in HIV prevention, established in mother-to-child transmission, practised as post exposure prophylaxis (PEP) where available, continues to be explored as topical and oral pre-exposure prophylaxis (PrEP). Tenofovir (TDF) vaginal gel reduced HIV incidence by a third, oral TDF and Emtricitabine PrEP, had protective efficacy in MSM and heterosexual populations and may have a role in select groups. ART has been shown to massively reduce onward transmission to sexual partners by 96%. Universal testing and treatment has been proposed, however the acceptability/feasibility are unproven and complex.

Increasing numbers of perinatally infected adolescents, sexually active at an age comparable to their uninfected peers, join a global cohort of behaviourally infected adolescents. Evidence suggests that unprotected sex is associated with poorer ART adherence, increasing risk of transmission to partners and offspring. Within the paediatric setting, sex/relationship education in late childhood/adolescence, retention in care, effective ART, engaging uninfected partners in testing and education, judicious use of PEP/PrEP provides a framework for robust combination HIV prevention, an area where, as yet, no single intervention has proved to be effective.

PREVENTION OF HORIZONTAL TRANSMISSION OF MICROBES: INFECTION CONTROL ISSUES IN THE HOSPITAL**D. Pittet***Infection Control Programme and WHO Collaborating Centre on Patient Safety, University of Geneva Hospitals, Geneva, Switzerland*

The impact of healthcare-associated infection is important due to its high incidence associated with significant mortality and substantial extra-costs. It occurs in every healthcare facility in every country and affects hundreds of millions of patients annually worldwide. Infection rates differ dramatically between countries with the greatest burden in developing nations. Although some differences can be explained by patient mix diversity, others suggest a wide variability of policies and practices in healthcare-associated infection prevention, such as differences in adoption and application of guidelines and protocols, beliefs and attitudes among healthcare workers, staffing patterns, available resources, or barriers to implementing best practices. The World Health Organization (WHO) launched the First Global Patient Safety Challenge "Clean Care is Safer Care" in 2005 to tackle the problem of healthcare-associated infection worldwide with hand hygiene recognised as the single, most important preventive measure. To date, 126 countries have pledged their support at governmental level to implement actions to reduce healthcare-associated infection, corresponding to 90% coverage of the world population, and approximately 43 countries have reported the existence of formal hand hygiene campaigns. The major challenge for the next decade will be to demonstrate sustainability and continue to show a significant impact on infection prevention across the world. To truly protect our patients, it will take leadership, commitment, a range of actions, and time. The efforts of WHO, together with countries and hospital facilities, should help bring true ownership to healthcare workers in relation to microorganism transmission and its prevention and, subsequently, long-term patient safety improvement.

MANAGEMENT OF INFECTIONS CAUSED BY RESISTANT (RB) AND PAN-RESISTANT BACTERIA (PRB) IN CHILDREN**R. Cohen^{1,2}**¹CLIN, CHI Créteil, Créteil, ²ACTIV, Saint Maur des Fossés, France

Infections caused by Gram-negative bacilli (GNB) are become the main concern: *P. aeruginosa*, *Acinetobacter* sp, *B. cepacia*, *S. maltophilia*, *K. pneumoniae* and other enterobacteria, including *E. coli*...If some compound developed specifically for GNB are in the pipeline, no new options will be available in the next 5 years. These last ten years several change have been occurred for RB and PRB infections:

- the main mechanism of resistance is the production of extended spectrum β -lactamases (ESBL) and carbapenemases,
- many resistant strains harbor several mechanisms of resistance,
- these infections are not limited to hospitalized patients but are also community acquired, sometimes for patients without underlying diseases and who have never received antibiotics.

Even for experienced PIDs, the management of these infections is complex, and no longer "ready to wear" but "tailor-made". It must be based on:

- enhanced cooperation with microbiology laboratories (for detailing the resistance mechanisms, MICs and the role of associations,
- thorough knowledge of PK/PD.

For treatment of infections due to ESBL, penems are the reference. However, their overuse inevitably leads to the emergence of penem-resistant strains. For these reasons we must choose whenever possible alternatives, according to the strain susceptibility: aminoglycosides, or unconventional treatment, ceftazidime + /- inhibitor, temocillin, tigecycline, fosfomycin.

For strains resistant to carbapenems, colimycin is the corner stone of treatment. However, high doses and association with another antibiotic are required. Most often the cooperation with microbiologist is necessary for the choice of the second antibiotic: penems, rifampin, tigecycline, sulbactam, fosfomycin...

IMPROVING THE EVIDENCE BASE FOR ANTIBIOTIC USE IN EUROPE - WHAT DO WE DO AND WHY DO WE DO IT**N. Spyridis***Paediatric Infectious Diseases, University of Athens, Athens, Greece*

The increasing prevalence of antimicrobial resistance remains an issue of concern to patients as well as health care professionals. There is overwhelming evidence that antibiotic misuse is a key factor driving this process. Highly resistant pathogens may not be treatable with available antimicrobials and at the same time there are very few new antibiotics in the production pipeline. Resistant pathogens can be food-borne, community-acquired or hospital-acquired. In the community, antibiotic prescribing for children increased in late 1990s in Europe and the US showing some signs of improvement in the early 2000. Alarmingly, the rates of antimicrobial resistance rose as well. Most of those prescriptions given for common uncomplicated infections of the upper respiratory tract, namely: otitis media, sinusitis, cough/bronchitis, pharyngitis and nonspecific upper respiratory tract infection (the common cold).

Currently there is very limited information on antimicrobial consumption and antibiotic resistance for children in Europe. Existing European surveillance schemes such as ESAC (European Surveillance of Antimicrobial Consumption), and EARSS (European Antimicrobial Resistance Surveillance System) have limited age-specific data. There is also a wide variation or absence of antibiotic prescribing guidelines in many countries in Europe. Some countries have robust evidence-based guidance, which aim to reduce the use of antibiotics for minor viral upper respiratory tract infection. In the other countries there are either no guidelines in place, or guidelines advocate the use of very broad spectrum antibiotics. There is also only limited data on the impact of immunisation campaigns on EU wide antibiotic prescribing for specific clinical indications and rates of antimicrobial resistance.

FALSE-POSITIVE RESULTS OF RAPID ANTIGEN DETECTION TESTS (RADT) FOR GROUP A STREPTOCOCCUS (GAS) PHARYNGITIS: A CASE-CONTROL STUDY

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Background: Rapid antigen detection tests (RADT) false-positives (FP) are positive RADT with negative throat culture for group A streptococcus (GAS). Several mechanisms have been proposed to explain these FP: GAS nutritional variants, non-viable GAS (related to prolonged office-to-laboratory delay or bacterial interference with *Staphylococcus aureus*), or cross-reaction with *Streptococcus milleri*.

Methods: This prospective study, performed between 2009 and 2011, assessed the performances of a RADT in 1482 children with pharyngitis. Consecutive samples of FP cases, true-negative (TN) and true-positive (TP) controls were analyzed with tryptone-glucose-yeast (TGY) broth enrichment, GAS-specific polymerase chain reaction assay (GAS-PCR), mannitol salt agar culture, and biochemical identification in case of α -hemolytic colonies.

Results: 51 FP cases, 58 TN and 117 TP controls were analyzed. No GAS nutritional variant was isolated after TGY broth enrichment in FP cases or controls. The rate of positive GAS-PCR was significantly higher in FP cases than in TN controls (74% vs 2%, $p < 0.001$). There was no difference in the mean office-to-laboratory delay between FP cases and TP controls (2.5 vs 2.6 days, $p=0.53$). The rate of *S aureus* was higher in FP cases than in TP controls (74% vs 14%, $p < 0.001$), and 65% of FP cases were GAS-PCR positive and *S aureus* positive. No *S milleri* was found in FP cases or controls.

Conclusions: Most RADT FP results are due to non-viable GAS (mainly explained by the inhibitory presence of *S aureus*). Therefore, RADT specificity can be considered close to 100% in clinical practice.

ROLE OF PROCALCITONIN IN THE DIAGNOSIS OF SEVERE INFECTION IN PEDIATRIC PATIENTS WITH FEBRILE NEUTROPENIA-A SYSTEMIC REVIEW AND META-ANALYSIS

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Objective: To determine the accuracy of the procalcitonin (PCT) test for diagnosis of bacterial sepsis in pediatric cancer patients with febrile neutropenia (FN).

Methods: MEDLINE, EMBASE and the Cochrane Library were searched for studies that evaluated PCT alone or compared with other laboratory markers such as CRP to identify bacterial sepsis in children with FN. Bivariate model was used to derive summary sensitivity and specificity of the diagnostic tests.

Results: A total of 9 studies looking into PCT tests and 8 studies looking into CRP tests were included in the final analysis. The prevalence of bacterial sepsis was 172/482 (35.7%) in PCT studies and 741/1316 (56.3%) in CRP studies. In terms of area under the ROC curve (AUC), PCT has a better discrimination than CRP (AUC: 0.81 vs. 0.74). However, PCT is not as sensitive as the CRP test. The pooled sensitivity of PCT was 0.63 (95% CI: 0.41-0.80) as compared to 0.77 (95% CI: 0.61-0.88) for CRP. PCT is more specific than sensitive while CRP is more sensitive than specific in this population. The pooled specificity was 0.80 (95% CI: 0.71-0.87) for PCT and 0.62 (95% CI: 0.49-0.73) for CRP. PCT has the best likelihood ratio positive (LR+: 3.17, 95% CI: 2.37-4.24), making it the best rule-in test.

Conclusions: Of three markers potentially useful for diagnosing bacterial sepsis in children with FN, PCT has better overall diagnostic accuracy than CRP. The results of this meta-analysis may have important clinical implications for the management of children with FN.

DETECTION OF EIGHT RESPIRATORY VIRUSES WITH A NOVEL POINT-OF-CARE MULTIANALYTE ANTIGEN DETECTION TEST IN CHILDREN WITH ACUTE RESPIRATORY TRACT INFECTION

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Background: Rapid etiological diagnosis of a respiratory virus infection has potentially impact on patient cohorting, antiviral and antibiotic therapy, and prediction of the clinical course. Most point-of-care tests for detection of respiratory viruses have limitations in diagnostic performance and clinical usability.

Methods: We evaluated a novel, automated multianalyte point-of-care antigen detection test system (MariPOC, ArcDia, Finland) in comparison with multiplex reverse transcription polymerase chain reaction (RT-PCR) in a pediatric emergency department setting. The MariPOC test system detects eight respiratory viruses (respiratory syncytial virus (RSV), influenza A and B viruses, adenovirus, parainfluenza type 1, 2, and 3 viruses, and human metapneumovirus) from a single nasopharyngeal swab specimen by a fully automated random-access immunoassay method. Samples were taken from 158 children 0-17 years of age (mean, 1.8 years) with respiratory symptoms and/or fever and analysed both by MariPOC and by RT-PCR.

Results: The sensitivities and specificities of the MariPOC test were 83% and 99% for RSV (n=36), 85% and 96% for influenza B (n=20), 50% and 99% for influenza A (n=6), 25% and 97% for adenovirus (n=12), and 50% and 100% for metapneumovirus (n=8). Parainfluenzaviruses were detected only in five patients.

Conclusions: This novel point-of-care test system is rapid, practical, and specific method for simultaneous detection of several respiratory viruses. Compared with RT-PCR, the sensitivity is moderate for detection of RSV and influenza viruses, and low for adenovirus.

COMPARATIVE ANALYSIS OF 3,961 NASOPHARYNGEAL SAMPLES FOR PERTUSSIS DIAGNOSIS USING RT-PCR AND CULTURE IN 2010/2011, SÃO PAULO - BRAZIL

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Background and aims: Pertussis occurs worldwide, and despite the introduction of the primary immunization and the good coverage of the programs, *Bordetella pertussis* still continues to circulate. Laboratory diagnosis of Pertussis is based on culture, considered the "gold standard" for detection of *B. pertussis*. Although culture method is highly specific, its sensitivity is variable and more sensitive diagnostic methods are needed. The Instituto Adolfo Lutz, São Paulo, Brazil was introduced Real-time PCR (RT-PCR) as an additional method for laboratory diagnosis. The aim of this study was to evaluate the positivity of RT-PCR and culture for detection of *B. pertussis* in nasopharyngeal swabs from suspected cases of pertussis and their contacts.

Methods: In this study, we analyzed a total of 3,961 nasopharyngeal swabs collected from Jan/2010 until Dec/2011 to test by culture and RT-PCR. The samples were cultured using standard methods. RT-PCR reaction was performed in the thermocycler model LightCycler® 480 Software release 1.5.0 SP3 - Roche®, including specific primers and probes for detection of toxin gene *ptxS1* and the insertion element IS481.

Results: Among 3,961 swabs analyzed, 266 (6.7%) were culture and RT-PCR (*PtxS1/IS481*) positive for *B. pertussis*; 608 (15.3%) swabs were positive only by RT-PCR; 06 (0.1%) were positive only culture and the remaining 3,081 (77.8%) swabs were negative for both techniques.

Conclusions: The introduction of RT-PCR for pertussis diagnosis was an excellent additional method, demonstrating high sensitivity and greater positivity, but should always be performed simultaneously to culture, which is the golden standard for diagnosis.

REFINEMENT OF A RISK SCORE, THE LAB-SCORE, FOR IDENTIFICATION OF SEVERE BACTERIAL INFECTION IN CHILDREN WITH FEVER WITHOUT SOURCE

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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, associated CRP, procalcitonin and urinary dipstick (UD) to predict SBI. However, all biomarkers values were a priori dichotomized, and the fever duration was not included; these points may decrease the algorithm power and transportability. We aimed to refine this algorithm.

Methods: Data from bi-centre cohort studies of children with FWS were analysed using multilevel regression modelling.

Results: 606 children (24% SBI) were included. All following co-factors were associated with SBI in univariate analysis: fever duration, maximum temperature, CRP, procalcitonin, neutrophiles count, and UD results. However, multivariate model only kept CRP, procalcitonin in a categorical form because of model convergence, and UD. The model achieved an AUC ROC of 0.94 [0.92-0.96] significantly higher than all biomarkers alone, as well as significantly higher than the Lab-Score (0.91; 0.89-0.94; p=0.007). According to a decision curve analysis, the model yielded a better strategy than those based on biomarkers considered alone, as well as the extreme strategies (all or none were considered as SBI). A first model threshold the model offered 98% [94-100] sensitivity) with 53% [48-57] specificity. Another cut-off led to 90% [83-94] sensitivity and 82% [79-85] specificity, which is significantly higher than the lab-score on this sample (90% sensitivity, 87% specificity).

Conclusion: The modified Lab-score demonstrated higher prediction ability for SBI than the original Lab-Score, with promising wider transportability across settings. These results need further abroad validation.

BRUCELLOSIS AND RICKETTSIOSES IN EUROPE

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Brucellosis and rickettsioses are the two main anthrozooses classically present in Europe, especially in southern countries.

Human rickettsial diseases are a variety of clinical entities caused by α -proteobacteria of the order *Rickettsiales* belonging to genera *Rickettsia*, *Orientia*, *Ehrlichia* and *Anaplasma*. Until recently, it was thought that Mediterranean spotted fever due to *Rickettsia conorii* was the only tick-borne rickettsiosis in Europe. However, in recent years, many more species or subspecies within the spotted fever group of the genus *Rickettsia* have been described as emerging pathogens in this continent. Furthermore, cases of infection due to flea-borne rickettsioses (*R. typhi*, *R. felis*) have been described. Finally, the mite-transmitted *Rickettsia akari*, the agent of rickettsialpox, is also known to be prevalent in Europe. Cases of human anaplasmosis have been described in many European countries.

Brucellosis is a global zoonosis. European countries with the higher incidence of human brucellosis are the Former Yugoslav Republic of Macedonia, Albania, Greece, Bosnia and Herzegovina, Spain and Portugal. In Italy, a steady decline in the number of annual cases has been consistently observed over the past 30 years. Brucellosis-free status has been granted by the European Union to Sweden, Denmark, Finland, Germany, the UK (excluding Northern Ireland), Austria, Netherlands, Belgium, and Luxembourg. Norway and Switzerland are also considered brucellosis-free countries. Brucellosis is not endemic in eastern Europe. Brucellosis in Russia nowadays is mainly a disease of the Caucasian districts.

The principal aspects of these diseases will be considered with particular attention to the paediatric population.

MALARIA IS STILL HERE**J. Okebe***Medical Research Council Unit, Banjul, The Gambia*

The past decade has witnessed an unprecedented decrease in the malaria burden in several endemic countries, some of them considering the prospect of elimination. Key to this process has been the widespread use of effective drugs and interventions targeting the parasite and vector backed by a strong global financial commitment. The global estimates of reduction in disease burden and the prospects of meeting the millennium development goals however do not appear as optimistic.

In several countries, though diagnosis has improved through the implementation of rapid tests, the true malaria burden may still be underestimated as access to centres where these services are available may be difficult, quality control mechanisms unavailable and the reporting system weak.

The decreasing endemicity has been marked by heterogeneity in transmission. The persistence of pockets of transmission in some locations partly explains the less than optimal results observed despite the interventions implemented. There are also indications of a shift of the risk of infection and disease towards older populations, possibly due to a delay in the acquisition of immunity due to the declining transmission.

As the march towards elimination gains momentum, control efforts must come to terms with the new challenges from an old adversary. Understanding these changes is essential to our ability to frame control strategies towards the global elimination of the disease.

VISCERAL LEISHMANIASIS AND HEMOPHAGOCYtic LYMPHOHISTIOCYTOSIS (HLH)

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Background and aims: Hemophagocytic lymphohistiocytosis (HLH) is a primary or secondary entity characterized by an uncontrolled activation of T-lymphocytes and natural killer cells. The prevalence of HLH among visceral leishmaniasis (VL) has not been well established.

Methods: A multicentric retrospective study was conducted among all public hospitals in Madrid between January 2010 and December 2011. Patients younger than 18 years diagnosed of VL in whom *Leishmania spp.* was isolated by conventional culture, PCR and/or direct visualization in blood, bone marrow or spleen were included in the study.

Results: Among 28 children with clinical suspicion of VL, 24 fulfilled inclusion criteria. Mean age at diagnosis was 2.8 years (SD=2.74 years). Bone marrow biopsy was performed in 21, and findings of hemophagocytosis were present in seven of them (33.3%). Ten patients (41%) met the HLH criteria proposed by the HLH Study Group

	Neutrophils (μ L)	Platelets (μ L)	Hemoglobin (gr/dl)	Ferritin (μ g/L)	Triglycerides (mg/dl)	Fibrinogen (gr/L)	Soluble CD25 (U/ml)	Duration of fever before treatment (days)	Duration of fever from 1st day of treatment (days)
All children Mean (SD)	839.6 (370.9)	98238 (45268)	7.8 (1.38)	3527.9 (65956)	323.57 (164.91)	2.94 (1.36)	1778.62 (636.4)	12.9 (5.78)	2.48 (2.76)
Children with HLH criteria Mean (SD)	794.38 (414.9)	95222.2 (64669.9)	6.97 (1.04)	7149.3 (8864)	440.8 (182.5)	2.25 (1.19)	1822.16 (726.5)	13.8 (5.2)	2.30 (2.31)
Children without HLH criteria Mean (SD)	867.54 (355.8)	100500 (40659)	8.42 (1.3)	742.3 (1224.8)	233.38 (67.8)	3.56 (1.24)	1648 (387.5)	12.09 (6.4)	2.64 (3.23)
p value	0.672	0.81	0.015	0.049	0.006	0.032	0.76	0.51	0.78

[table1]

All children were treated with liposomal amphotericin B. One child had a relapse of VL 6 months after the first episode and there were no deaths. Three patients received specific treatment for HLH.

Conclusions: Up to 41% of children with visceral leishmaniasis met the criteria for HLH. In Spain, we recommend to rule out visceral leishmaniasis in children with HLH criteria.

MORBIDITY AMONG CHILDREN TRAVELERS WITH SICKLE-CELL DISEASE VISITING TROPICAL AND SUB-TROPICAL AREAS; A RETROSPECTIVE STUDY

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Background: Increasing numbers of children with sickle-cell disease are travelling to tropical areas.

Objective: To examine the morbidity among children with sickle-cell disease during and after a travel to a tropical area.

Methods: Children (< 18 y) with a sickle-cell disease managed at a french pediatric sickle cell disease national referent center, who traveled to a tropical area between June and December 2009 were included in a retrospective study.

Results: Thirty-nine children were included. Their median age was 7.8 years [4.3-11.7]. Ten children were treated with hydroxyurea, three were in transfusion exchange programs, and six received a "preventive" transfusion before travelling. All the children and their parents attended a pre-travel visit focusing on prevention of travel-related diseases. Three children (7,7%) were hospitalized and 12 children (30%) consulted a physician during the stay. No child was transfused. Within 3 months after returning, 15 children (38.5%) visited the emergency room and 12 (30.7%) were hospitalized. The most frequent diagnosis in the three months following the return were the vaso-occlusive crisis (n = 8) and pneumonia (n = 5). Two children had minor salmonella bacteremia complicated for a child with a severe multifocal osteomyelitis. The number of hospitalizations was higher in the months after the trip from the month before the trip (respectively, n=1 and n=9).

Conclusion: Travels to tropical areas in children with sickle-cell disease are associated with a high morbidity. Salmonella infection is a particularly important threat, and empirical antibiotic therapy should be used routinely for traveler's diarrhea in this population.

PETS, KIDS, AND PAEDIATRIC INFECTIOUS DISEASES**E. Galanakis**

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Humans have lived for millennia with domestic animals, companion animals, service animals, and pets, which are often considered to be family members. Pets are not a major source of human infection but they do transmit bacterial, viral, fungal, and parasitic diseases ranging from self-limited colonization to life-threatening conditions.

Transmission, depending on the pet and the pathogen, usually requires close contact and is facilitated by bites and scratches, or through cutaneous, mucous, digestive and respiratory routes, or via fleas and ticks. Non-traditional pets in particular may facilitate transmission of emerging and re-emerging zoonoses. Children are at higher risk for pet-related infections.

Pet-related infections can be prevented by keeping pets healthy, avoiding contact with sick animals, and hand washing. Prevention measures include advice on hygiene, vaccines for pets and humans, veterinary care, appropriate pet foods, selection of the appropriate pet for the individual child, and communication between child physicians and veterinarians.

History and recent research have shown that pet companion provides health and emotional benefits for children. Risk of transmission of infectious diseases can be minimized with appropriate prevention and kids should be supported to enjoy the pet companion.

ADDRESSING CONCERNS ABOUT VACCINES**G. Marshall***Department of Pediatrics, University of Louisville, Louisville, KY, USA*

Despite unprecedented successes in the elimination and control of infectious diseases through vaccination, providers now find themselves challenged to justify universal vaccine programs to parents. As diseases have disappeared from the public's eye, adverse events related to vaccines have taken on more importance. Many parents, fearing that vaccines are dangerous or unnecessary, are refusing to have their children vaccinated, or are demanding tailor-made schedules; many adults are also opting out. This program explores some of the myths and truths surrounding vaccines and provides the audience with a framework with which to understand the current dilemma and address public concerns. The lecture is centered on 10 truths about vaccination, among them the facts that fear of vaccines can lead to public harm, that vaccines are not 100% safe, and that ultimately parents want what's best for their children. Providers should learn to identify heuristic thinking about vaccines and move parents and patients from belief to a scientific basis for action.

INFANT IMMUNIZATION: STARTING FROM PREGNANCY**E.C. Dinleyici***Department of Pediatrics, Eskisehir Osmangazi University, Faculty of Medicine, Eskisehir, Turkey*

Infections during early life cause significant morbidity and mortality and are incompletely protected by existing vaccine strategies due to current schedules are initiated too late or no licensed vaccines. Several immunization strategies currently exist to prevent infections early in life, including maternal immunization, neonatal immunization, maximize herd immunity and use existing vaccines more effectively. Maternal immunization not only protects the mother but also allows protective antibodies to be passively transmitted to the fetus, which protect the newborn until active immunization. Elimination of neonatal tetanus through the use of maternal vaccination is an important example of this success of these methods. Recent epidemics of pertussis and pandemic influenza make clear that pregnant women and their infants are at risk for infections that can be prevented safely and effectively. The tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine has been shown to be safe and immunogenic during pregnancy. Furthermore following vaccination the umbilical cord titers for pertussis antibodies are higher than the maternal titers and Tdap immunization is now recommended during pregnancy as the preferred method for preventing neonatal pertussis. The maternal influenza vaccination has also been associated with the reduction of laboratory-confirmed influenza infections and hospitalizations prior to six months of age. In contrary, maternal derived antibodies may modulate neonatal immune function and interfere with the infant's response to vaccines. Preventing infection with maternal antibodies could become shorter for rubella, varicella and measles, which necessitate the development of new and earlier immunization policies.

To date, studies have been conducted on neonatal immunization at birth, including hepatitis B, BCG, oral polio, acellular pertussis and pneumococcal vaccines. Current knowledge suggests that the neonatal immune system is not immature but that it is appropriate for early postnatal life and develops over time. Further information about the principles of adaptive immune responses, the neonatal innate and mucosal immune system can be used to guide the rationale design of vaccination strategies to protect young infants against early life infections. In addition, new vaccine technologies (e.g. new adjuvant/vector, antigen delivery systems, mucosal vaccination) have opened new immunization possibilities against respiratory syncytial virus, Group B streptococcus and cytomegalovirus infections as well as existing vaccine-preventable diseases.

HOW PAEDIATRIC INFECTIOUS DISEASE SPECIALISTS MAY ASSIST INTERNISTS TO DEVELOP A LIFETIME VACCINATION SCHEDULE

U. Heininger

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Most primary immunizations are recommended in early childhood, several of which are then followed by one or more regular booster doses in later childhood, adolescence, or adulthood.

Unfortunately, many adolescents - which are in a phase of transition from primary care provided by paediatricians to general practitioners - do have immunization gaps for various reasons. Frequently, immunizations are not actively declined by adolescents but lack of knowledge about recommended immunizations prevails. In such and other situations, the paediatric infectious disease specialist is predestined to make a difference and assist the internist by 1) identifying immunization gaps in individual patients, 2) counselling the adolescent and provide a perspective on future needs of immunization including those needed for family planning (e.g. immunizations against varicella, rubella, pertussis) and 3) at any age of the paediatric patient, exploring the immunization status of other family members (parents, grandparents) with the goal of recommendation of immunizations which need updating or catch-up. Given the expertise in immunization issues, the PID specialist can have an instrumental role in assisting internists (and other medical specialties) to develop a lifetime vaccination schedule.

PARALLEL SESSION 7: ANTIBIOTIC PK/PD FOR THE PEDIATRICIAN**J. Standing**

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Understanding pharmacokinetics (PK) allows estimation of the time course of circulating antimicrobial concentration following a dose. Concentrations of antimicrobial can easily be inferred for highly perfused tissues, and estimated using physiological concepts for poorly perfused areas. Understanding pharmacodynamics (PD) allows for predictions of how antimicrobial concentrations will affect pathogen proliferation. Mathematical models quantify dose-concentration-effect relationships, and as our experimental units (patients) differ from each other, statistical methods known as nonlinear mixed effects are useful to quantify and separate between subject and residual variability.

This session will review basic principles of antimicrobial PKPD. An introduction to nonlinear mixed effect modelling will provide useful guidance for how to read papers using 'population' approaches, and how to plan and undertake PKPD studies. Finally, scaling of PK between adults and children of different ages will be discussed, so by the end of the session participants will no longer wonder why some drugs are dosed by age, some by weight, and others by body surface area.

EFFECTIVENESS OF BENZNIDAZOLE IN PEDIATRIC CHAGAS DISEASE INSPITE OF LOWER PLASMA CONCENTRATIONS THAN ADULTS. A POPULATION PHARMACOKINETICS STUDY

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Introduction: Chagas disease, caused by *Trypanosoma cruzi* infection, can lead to severe long term complications. Treatment with benznidazole is effective, in children, despite lack of information on its pharmacokinetics.

Patients and methods: Children with Chagas disease, aged 2-12 years were enrolled in a population pharmacokinetics study (clinicaltrials.gov #NCT00699387) and treated with oral benznidazole 5-8 mg/kg/day BID for 60 days. Blood samples for benznidazole measurement were obtained after the first dose, at steady state or after the last dose. Benznidazole was measured by HPLC method developed by our group.

Results and discussion: 38 children were enrolled. Mean age was 7.3 years (SD: 3.6, range 2.1-12). Mean benznidazole dose was 6.4 mg/kg/day (SD:1; range 5 - 8.7). Median benznidazole highest observed concentration (C_{max}) was 4.3 mg/L (range 1 - 12.2). Estimated pediatric clearance (corrected for weight) was significantly higher than that reported for adults. All children treated had a positive response, with negativization of PCR for *T. cruzi* DNA, and marked decrease in anti *T. cruzi* antibody titers.

We observed benznidazole concentrations in children were lower than those reported in adults treated with comparable mg/kg doses. However, treatment was effective and well tolerated, with few adverse drug reactions (ADRs), unlike adults. If confirmed, our results would suggest that dosing modifications in adults may be beneficial, as it is possible that the lower blood concentrations, while still providing therapeutic effect, may be responsible for lower incidence of ADRs.

AN ACUTE OTITIS MEDIA MIDDLE EAR MICRODIALYSIS MODEL IN THE CHINCHILLA WITH IMPLANTED TYMPANOSTOMY TUBES

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Background and aims: This study was conducted to develop a model to assess the distribution of ciprofloxacin into middle ear fluid (MEF) following administration of an otic suspension formulation (Ciprodex®) in uninfected and infected chinchillas whose tympanic membranes had been fitted with tympanostomy tubes.

Methods: Uninfected and infected chinchillas were studied. Infected ears were inoculated (100 CFU) with *S. pneumoniae* (A66.1 serotype 3). After surgical insertion of tympanostomy tubes, 0.15ml Ciprodex® (450µg of ciprofloxacin) was introduced into the external ear. The ear flap was gently manipulated, allowing the dose to enter the middle ear through the tympanostomy tube. Unbound ciprofloxacin concentrations in MEF were continuously monitored (every 16min) by HPLC for up to 48hr, using on-line microdialysis, with retrodialysis to determine ciprofloxacin recovery. Animals were freely moving, with access to food and water.

Results: Unbound MEF ciprofloxacin concentrations were determined in uninfected (N=6) and infected (N=7) ears. Mean maximum MEF ciprofloxacin concentrations (C_{max}) were 986 and 349µg/ml, respectively. Ciprofloxacin exposure, assessed in both groups by the mean area under the curve (AUC), was 334,000 and 121,000µg-hr/ml, respectively. MEF concentrations remained above 10µg/ml for 15 to 48hr. C_{max} and AUC were more variable in the infected ears.

Conclusion: External ear dosing of Ciprodex® in chinchilla ears with implanted tympanostomy tubes produced unbound concentrations of ciprofloxacin in middle MEF well above the minimum inhibitory concentrations identified for bacteria found in middle ear fluid in children with acute otitis media.

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COULD WE HAVE A UNIFIED EUROPEAN VACCINATION SCHEDULE?**P.L. Lopalco**^{1,2}

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Childhood vaccination programmes in the European Union (EU) member states are all effective and sustainable. Those programmes led either to the elimination or to a good control of dangerous infectious diseases. The current vaccination schedules vary a lot across Europe: the same vaccine product is used according to different schemes and the vaccination offer is very diverse. Vaccination programmes are exclusive competence of the member states and no European harmonisation can be achieved by law. Large consensus towards a common vaccination schedule might improve the efficiency of the vaccination programmes, i.e. achieving the same results by reducing the number of vaccine administrations, and would certainly promote equity throughout the EU. Moreover, increasing harmonisation would benefit those families that move across the EU with small children.

DECREASED SENSITIVITY OF CANDIDA SPECIES TO ANTIBIOTICS IS COMPENSATED BY MULTISYNERGISTIC ANTI-CANDIDA ACTION OF PROBIOTIC LECTINS AS NEW ANTIMICROBIALS

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Background: Probiotic lectins are perspective regulators of metabolism [1]. The aim was to compare anti-*Candida* action of probiotic bacterial lectins (PBL) and antibiotics.

Methods: Standard conditions of growth of freshly isolated clinical strains of *C.albicans*, *C.glabrata*, *C.krusei* or *C.tropicalis* on *Sabouraud* agar in the presence of standardized preparations of disc-applied L of lactobacilli (acidic and cationic LL: aLL, cLL) - Acilact ingredients, and L of bifidobacteria (aLB, cLB) - Bifidin and other cellular probiotic ingredients. Standard disc-antibiotics included: amphotericin-B (A), fluconazol (F), itraconazol (I), ketoconazol (K), clotrimazol (C), and Nystatin (N).

Results: *Candida* growth inhibition depended on type of PBL or antibiotic, and biotope nature of clinical strain. As a rule, antifungal effectiveness of PBL was observed as aPBL > cPBL, aLB > aLL, cLL > cLB. The orders of antibiotic sensitivity of *C.albicans* ([K>F] > C > I > A > N), *C.krusei* (C > I > [K>F] > A > N) and *C.tropicalis* (C > [K>F] > I > A,N) were differed in [K>F] position correlating to the expected level of *Candida* species hydrolase metabolism. PBL reveal both antibiotic-like (symmetrical) and distant assymetrical anti-*Candida* activities. aLB preferentially interacted to *C.albicans* or *C.tropicalis*, and aLL preferentially interacted to *C.krusei*. PBL in combinations with antibiotics revealed anti-*Candida* multisynergistic action. PBL were able to inhibit antibiotic-resistant strains. Compared to PBL, grass lectins revealed less anti-*Candida* selectivity.

Conclusion: Results indicate prospects of PBL in combinations with azoles.

Reference: [1] M. Lakhtin, V. Lakhtin, V. Alyoshkin, S. Afanasyev. *Benef. Microbes* (2011) 2: 155-165.

BACTERIAL PATHOGENS AND RESISTANCE PATTERNS IN CHILDREN WITH COMMUNITY-ACQUIRED URINARY TRACT INFECTION: A CROSS SECTIONAL STUDY**S. Afsharpaiman***Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran*

Background: Recent studies on antimicrobial susceptibility of bacterial pathogens causing urinary tract infection (UTI) in children showed high levels of resistance to antibiotics in clinical settings. We tried to determine the common types of bacterial pathogens causing UTI in children and their antimicrobial resistance patterns at a sample of Iranian children.

Methods: The study subjects consisted of 114 children (58.8% were female) categorized in the three age groups of neonate (< 28 days, n=45), breastfeeds (28 days to 2 years, n=41), and infants (>2 years, n=28) who had culture-proven UTI. Sensitivity testing was performed by the disc diffusion technique.

Results: The most frequently cultured pathogens included *Escherichia coli* (71.7%) and *Enterobacter* (28.9%). UTI caused by *Enterobacter* was commonly detected in neonates (60.6%) in comparison with infants (21.2%) and children (18.2%). Imipenem was the most active agent (97.3% susceptible) followed by ciprofloxacin (90.4%) and amikacin (82.9%) against *Escherichia coli* isolates. Bactrim, cefalotine and cephalixin were the least active agents with 76.3%, 75.0% and 73.7% of *Escherichia coli* isolates exhibiting resistance respectively. Also, imipenem and ceftizoxim were the most efficient antimicrobials against *Enterobacter* with the sensitivity rate 85.2% and 71.4%, respectively. However, nitrofurantoin, ceftazidime and cefalotine were the least active agents against *Enterobacter* with the resistance rate 92.3%, 66.7% and 62.5% respectively.

Conclusion: Low susceptibility of cephalosporines to common UTI pathogens can be due to high administration of these drugs against children UTI in our population. Change of empiric therapy especially in neonate group should be considered.

ANTIBIOTIC RESISTANCE IS ASSOCIATED WITH LONGER BACTEREMIC EPISODES AND WORSE OUTCOME IN FEBRILE NEUTROPENIC CHILDREN WITH CANCER

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Purpose: With the increasing emergence of multiresistant pathogens, better understanding of these infections is necessary. The aim of the present study was to evaluate the risk factors associated with isolating a multiresistant organism (MRO) from a positive blood culture in pediatric cancer patients with febrile neutropenia (F&N), and to study its impact on clinical course and outcome of febrile episodes.

Patients and methods: The association between MRO with underlying malignancy, age, disease status, hospitalization during episode, absolute neutrophil count, absolute monocyte count, clinical foci of infection, and pathogens isolated was assessed in bacteremic pediatric cancer patients. The MRO phenotype was defined as diminished susceptibility to more than 3 of the broad spectrum antibiotic classes.

Results: Among 239 episodes of blood stream infections (BSI), Gram-positive, and Gram-negative organisms were detected in 180 (75%), and 59 (25%) episodes, respectively; with 38% of isolates showing multiresistance (n = 92). Significant risk factors (P < 0.05) for MRO were hospitalization, Gram-negative organisms, presence of clinical focus of infection, reduced ANC, prolonged duration of neutropenia, and previous intake of antibiotics. Of the episodes with prolonged duration of fever extending for more than 7 days 62% (64/93) were associated with a multiresistant phenotype, while it accompanied 72% (18/25) of the cases with an unfavorable outcome; P-value < 0.001.

Conclusion: Isolation of MRO is more likely to be associated with a prolonged course and an unfavorable outcome. Continuous multidisciplinary surveillance of BSI is warranted to develop strategies for antimicrobial resistance control.

FREQUENCY OF BACTERIA ISOLATED FROM CHILDREN'S BLOOD CULTURE IN A UNIVERSITY HOSPITAL IN IRAN AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERN

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Introduction: Bacteremia is associated with significant mortality in children worldwide. Study of frequency of bacteria isolated from children's blood culture and their antibiotic susceptibility patterns can be help in selection of empirical therapy. In this study, the frequency of bacteria isolated from blood culture of children suspected to bacteremia admitted to a university hospital in Tehran, Iran, during a 1 year period were determined and their antibiotic susceptibility pattern were studied.

Method: Culture of blood and determination of antibiotic susceptibility was done by standard methods. The result of kind of isolated bacteria, antibiotic susceptibility and age and sex were analyzed by SPSS software.

Results: During study period, blood culture was done for 5116 children and bacteria were isolated in 912 cases (17.8%). Three most frequently groups of bacteria in blood cultures of patients were non-fermentative gram negative bacteria (*Pseudomonas* and *Acintobacter* spp), coliforms (*Escherichia coli*, enterobacter and klebsiella spp.) and coagulase negative staphylococci, respectively, which were isolated in 63.4%, 17% and 12.8% of patients, and constituted 93.2% of positive blood cultures. The susceptibility of different isolated bacteria was variable but highest susceptibility in most isolated bacteria was shown to ciprofloxacin.

Conclusion: This study was shown that gram-negative bacteria were prevalent in bacteremia of children in Iran and many of isolated bacteria were multidrug resistant.

NASAL CARRIAGE OF METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* ISOLATES FROM JORDANIAN CHILDREN AND YOUNG ADULTS AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERNS

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Background and aims: Nasal *Staphylococcus aureus* is a major source of community and hospital associated staphylococcal infections. In Jordan, MRSA rate was reported as high as a 60% in some medical centers making this a particularly serious problem. This study determined the prevalence of nasal *S. aureus* isolates and MRSA community acquired isolates and investigated their antimicrobial resistance profile in Jordanian children.

Methods: Nasal specimens of the children and young adult individuals in Alkarak province were cultured and screened for *S. aureus* and MRSA using standard microbiological protocols and their antibiotic profile susceptibility was investigated using disc diffusion techniques. *MecA* gene and other antibiotic resistance genes (*MupA* and *Ant-2*) were determined by the polymerase chain reaction.

Results: A total of 10 (5.6%) *S. aureus* isolates were obtained from 180 nares specimens screened. Two (1.1%) of the isolates were MRSA. The isolates showed an overall 65% resistance to ampicillin, 42.5% to doxycycline, 37.5% to chloramphenicol, 25% to erythromycin, 12.5% to cotrimoxazole, 5% to gentamicin and clindamycin; with 20% methicillin resistant. No isolate was resistant to mupirocin, vancomycin, linezolid and fusidic acid. Four of all the isolates were multi-drug resistant.

Conclusions: We conclude that the rate of colonization by *S. aureus* is low in healthy children and colonization with MRSA is not common in our area. Clindamycin, gentamicin or trimethoprim-sulfamethoxazol could be used in mild to moderately severe diseases caused by CA-MRSA.

CHARACTERIZATION OF NASOPHARYNGEAL ISOLATES OF TYPE B HAEMOPHILUS INFLUENZAE AND IDENTIFICATION OF PLANTS SHOWING ANTIBACTERIAL ACTIVITY

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Background and aims: Increasing incidence of antibiotic resistance has made treatment and management of *Haemophilus influenzae* infection more difficult. Nasopharyngeal *H. influenzae* isolates are excellent surrogate for determination of antibiotic resistance prevalent among invasive *H. influenzae* isolates. We characterized nasopharyngeal *H. influenzae* isolates obtained from healthy school going children in Delhi and evaluated antibacterial activity of medicinal plant extracts from North East India.

Methods: Nasopharyngeal *H. influenzae* isolates were collected from healthy school going children and subjected to serotyping, fimbrial typing and antibiogram profiling. ESBL production was recorded using phenotypic as well as molecular methods. Multi Locus Sequence Typing (MLST) of 13 representative nasopharyngeal *H. influenzae* isolates was performed. Antibacterial activity of medicinal plant extracts collected from North-East India was evaluated through disk diffusion method.

Results: 32.5% of isolates were identified as serotype b. Fimbrial gene was detected in 28.75% of the isolates. Antibiotic resistance was observed to be high. ESBL production was observed in 6.25% of isolates. MLST identified several novel alleles and sequence types. Some plant extracts showed considerable antibacterial activity against multi drug resistant isolates.

Interpretation and conclusions: We report here the prevalence of high resistance against common antibiotics and detection of ESBL in *Haemophilus influenzae*. Detection of *H. influenzae* type b capsular gene and the presence of fimbrial gene (*hif A*) suggest virulence potential of these strains. Discovery of novel alleles and presence of new sequence types suggests wider genetic diversity. Validation of potent plants used in traditional knowledge will help identify the future drug candidates.

GENOTYPIC AND PHENOTYPIC CHARACTERIZATION OF AMPICILLIN-RESISTANT *HAEMOPHILUS INFLUENZAE* STRAINS ISOLATED FROM CHILDREN IN BULGARIA

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Background and aims: To investigate the mechanisms of ampicillin resistance of clinical strains *H. influenzae* from children with meningitis, acute otitis media and respiratory tract infections.

Methods: A total of 186 *H. influenzae* clinical strains were collected from children, aged 0 to 14 years: 53 cerebrospinal fluid (CSF), 5 blood, 24 sputum, 36 middle ear fluid and 68 upper respiratory tract samples. Serotyping was done by a coagglutination test and by PCR capsular genotyping. Beta-lactamase production was determined by the chromogenic cephalosporin test with nitrocephin. The antimicrobial susceptibility was done by microbroth dilution method. According to the ampicillin minimal inhibitory concentrations (MIC), all ampicillin non-susceptible strains were investigated for point mutations in their *ftsI* gene, indicating amino acid substitutions in PBP3.

Results: Overall, 58 strains *H. influenzae* belonged to serotype b (31.2%), 1 strain was type e, and 127 isolates (68.3%) were non-typeable. The total ampicillin non-susceptibility rate by MIC was 22.6%. Of all the 186 isolates, beta-lactamase positive ampicillin-resistant (BLPAR) strains were 14.3%, 5.6% were beta-lactamase negative ampicillin-resistant isolates (BLNAR). Another 2.7% were beta-lactamase positive amoxicillin/clavulanate-resistant (BLPACR) strains, implying the presence of both enzymatic and non-enzymatic mechanisms. The most frequent (80%) amino acid substitution was Asn-526 -> Lys which places the isolates in group II and the rest in group I due to Arg-517 -> His substitution.

Conclusions: The only mechanism of ampicillin resistance within the meningitis isolates was due to beta-lactamase production. BLNAR strains were found only among *H. influenzae* from respiratory tract infections and acute otitis media.

WHAT A PETTY! ANTIBIOTIC RESISTANCE OF HEALTHCARE ASSOCIATED INFECTIONS AMONG HEMATOLOGY ONCOLOGY PATIENTS

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Background: Antimicrobials are probably one of the most successful forms of chemotherapy that saved a lot of lives and contributed to the control of infectious diseases that were the leading causes of human morbidity and mortality. Unfortunately antibiotic resistance is increasing and brings with it the possibility of untreatable infections and a return to the antibiotic era.

Aim: To determine the antibiotic resistance profile of pathogens associated with health care associated infections (HAI) among adult hematology-oncology patients.

Methods: 66 hematology-oncology male patients clinically suffering from signs and symptoms of HAI were enrolled in the study. According to the site of infection blood, urine, sputum, throat swab and skin swab samples were obtained and properly cultured for isolation of the causative pathogen. All isolated bacteria were identified then subjected to antibiotic susceptibility testing using single disc diffusion method following CLSI guidelines.

Results: The 66 patients involved in this study suffered 50 laboratory confirmed health care associated infections. Gram positive cocci represented 52% of isolates while Gram negative bacilli represented 44% of isolates. Staphylococcus aureus showed high percentage of resistance to antibiotics where > 90 were Methicillin resistant with an alarming resistance to Vancomycin (9%). Imepinem resistance was noticed in 14.3%, 33.3% and 50% of P. aeruginosa, Citrobacter spp. and Acinetobacter baumannii respectively. Also 40% of isolated Enterobacteriaceae were extended spectrum beta lactamase (ESBLs) producers.

Conclusions: Emergence of multi-drug and pan-drug resistant Gram positive and Gram negative bacteria in HAIs.

KLEBSIELLA PNEUMONIAE CARBAPENEMASE PRODUCER ORGANISMS IN THE CHILDREN IN BURN UNIT: FIRST REPORT FROM IRAN

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Background and aims: Pseudomonas, Acinetobacter and Klebsilla are the most important cause of infection in burned patients. Carbapenem resistant isolates make some complications in treatment of infections related to these organisms in burned patients especially in children.

The objective of this study was to determine the phenotypic detection of *Klebsilla Pneumonia* Carbapenemase (KPC).

Method: From March to September 2011, Twenty-one Children hospitalized one week at least in Motahary burn hospital in Tehran that have more than 20% Total Burn Surface Area (TBSA) accepted in this study. Identification of isolates were confirmed and antibiotic susceptibility testing and then KPC determined by Modified Hodge Test according to CLSI guideline.

Results: Thirteen KPC- producing strains were isolated from nine out of 21 patients (*P. aeruginosa*. *A. baumannii*, *K. pneumonia*. 6, 4 and 3 respectively). One patient colonized by 3, tow patients colonized by 2 producer-KPC organisms and six patients infected by one KPC-producing organism. All of these isolates were Multi drug Resistant (MDR) that 8 out of 13 were susceptible to Colistin alone. One patient expired.

Conclusions: High percentage of MDR strains in our hospital with positive KPC and high recurrent risk can cause increase in morbidity and mortality among hospitalized burn children. Findings of this study also highlight the importance of implementation of an effective infection control strategy to prevent and decrease the prevalence of KPC-producing organisms.

SENSITIVITY AND RESISTANCE PATTERNS OF PSEUDOMONAS AERUGINOSA IN CLINICAL SAMPLES OF IRANIAN EDUCATIONAL HOSPITALS

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Introduction: *Pseudomonas aeruginosa* is a gram-negative, aerobic, rod shaped bacterium with unipolar motility. The symptoms of such infections are generalized inflammation and sepsis. It is recognized as a serious opportunistic pathogen that causes infections in hospitalized patient. We aimed to determine sensitivity and resistance patterns of *Pseudomonas aeruginosa* against various antibiotics among clinical samples of educational Hospitals of Iran, Urmia university of medical science.

Material and methods: This prospective study was carried out in Iran, Urmia University of Science between 2009 and 2011. Strains of *Pseudomonas* were isolated from different samples, after being microbiologically tested in clinical laboratory. We applied standard Kirby-Baur disk diffusion method to isolated samples according to the anti-biogram of Muller-Hinton environment. All collected data were analyzed using SPSS(ver.18) software.

Results: Totally 233 of *Pseudomonas* strains were isolated from different clinical samples. Sixty patients(25.75%) were resistant to all antibiotics, Where the majority of them found in transplantation and burns ward. The maximum antibiotic resistance 99.5% was observed against Trimtoprine Solfametoxole. The most effective antibiotics for *Pseudomonas aeruginosa* were ciprofloxacin (55.33%), Amikacin (61%) and Imipenem (33%).

Conclusion: Statistics showed that this bacterium has developed its resistance pattern against Amikacin and Ciprofloxacin in comparison to previous years. So the use of effective infection control practices can go along way to limiting the development and spread of antimicrobial resistance ensuring that these agents continue to find a place in treatment of *Pseudomonas aeruginosa* infections.

MULTIPLE ANTIMICROBIAL RESISTANCE IN ESCHERICHIA COLI URINARY TRACT INFECTION IN HOSPITALIZED CHILDREN IN HONG KONG: 2006 TO 2011

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Background: Antibiotic resistance has become an increasingly pressing threat to public health worldwide. Being the most common pathogen for urinary tract infection (UTI) in children, *Escherichia coli* (*E. coli*) is also the most common antibiotic-resistant bacterial urinary pathogen. Furthermore, *E.coli* has been observed to develop resistance to multiple groups of antibiotics and therefore be highly challenging to clinicians when managing children with UTI. We aimed to describe the evolving trend of multiple antimicrobial resistance in urinary *E.coli* in hospitalized children in Hong Kong.

Methods: Hospital microbiology laboratory database of Prince of Wales Hospital, a University hospital in Hong Kong, from 1 January 2006 through 31 December 2011 were queried for culture-confirmed *E.coli* urinary tract infection in paediatric patients hospitalized during the 6-year study period. The patients from one month of age to less than 18th birthday were included in the analysis.

Results: There were 568 cases of *E.coli* urinary tract infection included in the analysis. A high prevalence of resistance for *E.coli* was observed against ampicillin and 1st generation cephalosporin (71% and 49% respectively). Other antibiotic resistance rates were: cotrimoxazole (46%), gentamicin (32%), ciprofloxacin (23%), amoxicillin/clavulanate (22%), 3rd generation cephalosporins (23%) and nitrofurantoin (19%). Extended-spectrum beta-lactamase (ESBL) producing *E.coli* was found in 24% of cases. Furthermore, we detected that 48% of *E.coli* cases were resistant to 3 or more groups of antibiotics.

Conclusions: Our results documented the emergence of multiple antimicrobial resistance among urinary *E. coli* in children and highlighted the need to explore strategies for their containment.

REVIEW OF INCIDENCE AND ANTIBIOTIC SUSCEPTIBILITY PATTERN OF *KLEBSIELLA PNEUMONIAE* NEONATAL SEPSIS IN A NEONATAL ICU OF KARACHI, PAKISTAN

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Klebsiella pneumoniae (Kp) is an important nosocomial pathogen with increasing drug resistance associated with high morbidity and mortality in neonatal intensive care setting. We report the incidence and antibiotic susceptibility pattern of Kp in our NICU over the last five years (2006-2010).

Methods: Medical records of all neonates with discharge diagnosis of sepsis due to Kp from Jan 2006 till - Dec 2010 were retrieved and reviewed by using HIMS. Demographic features, gestational age, date and year of admission and antibiotic susceptibility of isolates were recorded. Kp incidence per 1000 NICU admissions and incidence of early or late onset Kp sepsis were calculated.

Results: 99/2355 neonates developed Kp sepsis during the five year period. The overall incidence of Kp sepsis was 4.2% (42/1000 NICU admissions); highest was 63/1000 in the year 2010. Majority were males (64%) and premature neonates (61%). Twenty-one developed early onset neonatal Kp sepsis. High level of antimicrobial resistance for ampicillin, gentamicin, aztreonam and cephalosporins were noticed. Almost all isolates were extended spectrum beta lactamases (ESBL) producing. Increasing trend of resistance was seen for amikacin, fluoroquinolones, piperacillin / tazobactam and carbapenem. In 2010, 31% of the isolates were carbapenem resistant. No significant difference in antibiotic susceptibility was observed for early vs. late onset neonatal Kp sepsis.

Conclusion: This study documents the rise in Kp incidence and carbapenemase resistant Kp at our NICU in the last five years. There is a need for continuous surveillance to have timely information on the antibiotic susceptibility of these organisms.

METHICILLIN-RESISTANT AND METHICILLIN-SUSCEPTIBLE COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS INFECTION: AN ELEVEN-YEAR STUDY

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Background and aims: Over the past few decades, infection due to community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has been reported worldwide. We aimed to report the spectrum of CA-MRSA infections and to compare the patients infected with methicillin-susceptible or methicillin-resistant strains.

Methods: This retrospective cohort study on patients aged < 20 years included 90 cases of community-acquired *S. aureus* infections in an 11-year period. Clinical and microbiological data were registered.

Results: Fifty-nine (66%) were males and the median age was 2 years. The majority (87%) of the patients was hospitalized and chronic underlying illnesses were detected in 27 (30%) cases. Overall, 34 (37.8%) patients had skin and soft tissue infections and 56 (62.2%) patients had deep infection. Four (5.1%) patients were transferred to the intensive care unit and two (2.6%) died. Complications were detected in 17 (18.9%) cases, such as pleural effusion (41.2%), osteomyelitis (23.5%) and sepsis (17.6%). Six (6.7%) methicillin-resistant strains were detected. There were no significant differences on the baseline characteristics or on the outcome of patients infected with methicillin-susceptible or methicillin-resistant strains. Approximately 93% of the cases received systemic antibiotics, out of which 59 (65.5%) used oxacillin or cephalothin. Four bacteraemic patients infected with methicillin-resistant strains improved without receiving vancomycin.

Conclusions: Both methicillin-susceptible and methicillin-resistant *S. aureus* strains resulted in morbidity and death among children in this setting.

ANTIBIOTICS RESISTANCE PATTERNS OF ISOLATES IN CHILDREN WITH GASTROENTROITIS IN HAMADAN, WEST OF IRAN

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Background and aim: Gastroentrotitis is very common in particular in devoloping countries and is still one of the most causes of mortalities in children. The aim of present study was to identify the most common of bacterial agents causing gastroentrotitis in children and detection of their resistance to antibiotics in patients who referred to university hospitals of Hamadan, west of Iran.

Methods: During two years, 610 samples obtained from children under 14 years old with gastroentrotitis were investigated for bacterial cultures, frequency of age, and antibiogram patterns. Antibiogram tests were also performed by gel-diffusion method of Kirby-Bauer. The data were gathered through a questionnaire and analysed using spss software.

Results: Out of 610 tested samples, 155 cases (25.4%) had positive culture for intestinal pathogenic bacilli. The most common isolate was; *Escherichia coli* (EPEC) with 105 cases (67.8%) and the lowest isolate was Shigella with 18 cases (11.6%). The most common serogroups of Salmonella were *S. typhi* (34.4%) and *S. typhimurium*. The most common serogroup of Shigella was *S. sonnei* (55.6%). The most effective antibiotics against bacteria were ceftriaoxone, cefoxime, nitrofurantoin, imipenem, amikacin and gentamycin.

Conclusion: The present study showed that *Escherichia coli* (EPEC) and *Salmonella species* are predominant causes of gastroentrotitis in children in this region. In many other countries, the most common serogroups of *E. coli* are O157 and O55, but in our study the serogroup of O128 was common. Most species showed high resistance to routine antibiotics such as ampicillin, amoxicillin, trimethoprim and chloramphenicol.

MICROBIOLOGICAL MONITORING IN PEDIATRIC POPULATION. SOFIA, BULGARIA**N.S. Hadjieva**¹, M. Christova², M.M. Petrov³, E. Christova⁴

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The aim of the study is an analysis to be made with respect to the microbiological surveillance in the paediatric clinics of the University Paediatric Hospital (UPH), and the control respectively, over the collection and testing of the samples. CLSI, ECDC and EUCAST standard procedures are used for the strains identification and antibiotic susceptibility testing. The microbiological monitoring in UPH has been performed for the period 2010-2012. The significant amount of information of the separate clinics has been interpreted in view of the strains circulation according to the type of samples tested and isolates antibiotic resistance. The Gram positive microorganisms account for 58.1 %, and the Gram negative for 41.9 % of all the bacterial isolates. The most common multiresistant strains as percentage of the total number have been as follows: *S. aureus* - MRSA = 49 %; *S. epidermidis* Oxa R - MRSE = 80 %; *S. pneumoniae* Pen R (PRP) = 38 %; *E. coli* CAZ-R = 22 %; *Klebsiella pneumoniae* CAZ- R = 65 %; *Acinetobacter* MEM- R = 40 %. One of the main conclusions refers to the highly reduced number of the microbiologically tested patients, thereby reflecting both over their inexact antibiotic therapy, and the elevated resistance patterns percentages in the hospital. The estimates of the work accomplished and the data about high resistance of some of the isolates for the current period emphasize the necessity of increasing the number of microbiological testing, the constant and systemic monitoring, and the continuing training of staff.

DETECTION OF ESBL TYPES BLA-CTXM, BLA-SHV, BLA-TEM AMONG CLINICAL ISOLATES OF ACINETOBACTER BAUMANNII IN PATIENTS FROM TABRIZ, IRAN

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Acinetobacter spp. has been recognized over the last two decades as important opportunistic pathogens. Extensive use of antimicrobial chemotherapy in clinical environments has contributed to the emergence and dissemination of multidrug resistant nosocomial *Acinetobacter (A.) baumannii* infections. These bacteria are resistant to all known antibiotics. The most common mechanism of- β lactam resistance is enzymatic degradation by β -lactamase enzymes. The aim of this study was to determined the genotype of ESBL (TEM, CTX-M, SHV) produced by *A. baumannii* clinical isolates in patients from Tabriz north-west of Iran.

A total of 100 *A. baumannii* strains isolated from different clinical specimens were identified by standard microbiological methods. Production of ESBL was determined by testing resistance of the isolates against ceftazidime, cefotaxime, ceftriaxone and verified by Double Disk Synergy Test. Prevalence of *bla*TEM, *bla*SHV and *bla*CTX-M was determined among ESBL positive isolates by PCR technique.

Antimicrobial susceptibility testing showed that the lowest resistance rate was against polymixin B (16%) and colistin (19%) whereas the highest resistance rate was observed against Ticarcillin (100%), Cefixim (100%) and Ceftizoxim (100%). PCR results showed that among 60 ESBL positive *A. baumannii*, 31.6% of isolates were positive for *bla*SHV, followed by *bla*CTX-M (13.3%) and *bla*TEM (12%).

A high frequency of ESBL production was observed among studied *A. baumannii* isolates. The prevalence of SHV gene in this isolates was more than TEM and CTX-M genes.

VARIATION IN ANTIBIOTIC SENSITIVITY TESTING: POTENTIAL RELEVANCE FOR THE INTERPRETATION OF CHILDHOOD BACTERAEMIA RESISTANCE PATTERNS FROM ROUTINE CLINICAL DATA

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Background and aims: Laboratory methods can introduce bias in surveillance of antimicrobial resistance based on routine data. We aimed to establish the degree of variation in antibiotic sensitivity testing (AST) in a sample of European children's hospitals processing neonatal and paediatric blood cultures.

Methods: Thirteen partner laboratories in a large European project were asked to indicate their AST practices for six key EARS-Net pathogens (*S.aureus*, *S.pneumoniae*, *E.faecalis/faecium*, *E.coli*, *K.pneumoniae* and *P.aeruginosa*). A survey was conducted to establish whether a total of 68 pre-defined bug/drug combinations formed part of local routine AST.

Results: Individual laboratories indicated that 29.6-81.8% of the 68 possible bug/drug combinations across all 6 pathogens formed part of their routine first line panels. Up to 49.1% of bug/drug combinations were never used in AST by specific laboratories.

Second line AST was specifically assessed and pre-defined based on resistance detected towards any of the antibiotics tested in the first line panel. Three centres used less than 40% of the specified bug/drug combinations in first line AST, but additionally reported including up to 28.3% of the bug/drug combinations in second line panels. Conversely, 3/4 centres testing more than 60% of bug/drug combinations as first line did not use any further combinations in second line AST.

Conclusions: Variation exists in testing panels for neonatal and paediatric bacteraemia, with laboratories significantly differing in the breadth of routine AST and use of second line AST. When not formally considered, this could potentially bias observed antimicrobial resistance patterns based on surveillance using routine laboratory data.

HOW DOES ROUTINE FIRST LINE ANTIBIOTIC SENSITIVITY TESTING FOR CHILDHOOD BACTERAEMIAS IN EUROPEAN LABORATORIES CORRESPOND TO EARS-NET SURVEILLANCE PROTOCOLS?

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Background and aims: The European Antimicrobial Resistance Surveillance Network (EARS-Net) aims to measure comparable and valid antimicrobial resistance bacteraemia data in Europe. We aimed to establish whether routine data from laboratories processing neonatal and paediatric blood cultures were likely to cover the bug/antibiotic-group combinations requested by EARS-Net.

Methods: Thirteen laboratories mostly from large children's hospitals were surveyed on their antimicrobial sensitivity testing (AST) practices for *E.coli* and *S.pneumoniae*, amongst other pathogens. We reviewed whether the standard EARS-Net bug/antibiotic-group combinations were covered by first line AST panels for these pathogens.

Results: For *E.coli* 6/13 laboratories used at least one antibiotic from each of the 5 specified bug/antibiotic-group combinations (aminopenicillins, third generation cephalosporins, aminoglycosides, fluoroquinolones, carbapenems) in first line AST. Another 6/13 covered all groups except carbapenems, and 1/13 indicated only testing antibiotics out of 2 groups as first line. All laboratories included aminopenicillins in first line AST.

For *S.pneumoniae* only 2/13 laboratories indicated testing antibiotics from all 5 bug/antibiotic-group combinations (penicillins, macrolides, third generation cephalosporins, fluoroquinolones, moxifloxacin) as first line. Another 4/13 used antibiotics from 4 groups, but not moxifloxacin in first line AST. The remaining 7/13 covered 3 or fewer bug/antibiotic-group combinations in first line panels. All laboratories included penicillins and macrolides in first line AST.

Conclusions: European laboratories processing neonatal and paediatric blood cultures do not consistently generate comprehensive data relevant to EARS-Net reporting. Therefore any paediatric AMR data based on EARS-Net reporting may not be fully representative of current AMR rates in European children's hospitals.

THE PREVALENCE OF ENTEROBACTERIACEAE ESBL PRODUCING ISOLATED FROM URINARY TRACT INFECTION IN CHILDREN IN NORTHERN LEBANON

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Background: The aim of this study is to determine the prevalence of ESBL producer Enterobacteriaceae implicated in urinary tract infection (UTI) in children in northern Lebanon.

Methods: The study took place between 1-1-2008 and 23-12-2011 in the microbiology Laboratory of Nini Hospital Northern Lebanon.

Culture is considered positive if the following tests are positive: Leucocytes esterase, nitrites, protein and the presence of microscopic leukocytes (> 10 cells / microscopic field (40 ×)) with culture growth ≥ 10⁵ CFU / ml. the Susceptibility was determined by disk diffusion method.

Results: In total we studied 457 strains isolated from children aged < 15 years (174 from hospitalized children and 283 children from outpatient children).

Escherichia coli (*E. coli*) was the major species (85%), followed by *Klebsiella* spp. (7%) and *Proteus* spp. (5%).

Of the 457 isolates there were 81 isolates were ESBL producers (17.7%) (table 1). The prevalence of ESBL strains was 23.5% in hospitalized children and 14.1% for out-patient children. *E.coli* was the dominant species in both categories (97.5% in outpatients' children and 90.2% among hospitalized children). Conclusion The study shows the high prevalence of ESBL in UTI in children. The presence of high level of resistance to cotrimoxazol, amoxiclave and quinolones. There was a good susceptibility with imipenem, cefoxitin, fosfomycin, nitrofurantoin and tigecyclin.

External patient	ATB	AMP	AMC	TIC	TCC	PIP	TZP	IMP	ATM	CXM	FOX	CTX
	TOTAL= 283	27.9	72.1	33.9	72.8	33.9	92.9	99.3	81.3	78.8	92.6	81.3
	ESBL n= 40 (14.1%)	0	35	0	27.5	0	82.1	100	0	0	97.5	0
		CAZ	FEP	LEX	CFM	GEN	NET	TOB	AMK	COL	SXT	PPA
	TOTAL= 283	81.3	82.9	69.3	81.3	83	90.1	81.6	98.2	89	50.5	66.8
	ESBL n= 40	0	0	0	0	50	75	50	92.5	100	20	42.5
	CIP	OFX	FOS	NIT	TGC							
TOTAL= 283	85.9	81.3	95.3	87.6	93.5							
ESBL n= 40	65	62.5	97.5	95	97.5							
Internal Patient	ATB	AMP	AMC	TIC	TCC	PIP	TZP	IMP	ATM	CXM	FOX	CTX
	TOTAL= 174	21.8	60.9	24.1	61.5	24.1	89.6	99.4	69.5	69	93.1	69.5
	ESBL n= 41 (23.5%)	0	19.5	0	22	0	87.5	100	0	0	97.6	0
		CAZ	FEP	LEX	CFM	GEN	NET	TOB	AMK	COL	SXT	PPA
	TOTAL= 283	69.5	70.7	59.2	69.5	80.5	88.4	75.9	99.4	97.7	42.5	57.5
	ESBL n= 41 (23.5%)	0	0	0	0	56.1	78	46.3	100	100	19.5	36.6
	CIP	OFX	FOS	NIT	TGC							
TOTAL= 283	80.9	77.6	96.5	92	96							
ESBL n= 41 (23.5%)	65.9	63.4	97.5	100	100							
Total	ATB	AMP	AMC	TIC	TCC	PIP	TZP	IMP	ATM	CXM	FOX	CTX
	Total = 457	25.6	67.8	30.2	68.5	29	91.6	99.3	76.8	75.2	92.8	76.8
	ESBL n= 81 (17.7%)	0	27.2	0	24.7	0	84.8	100	0	0	97.5	0
		CAZ	FEP	LEX	CFM	GEN	NET	TOB	AMK	COL	SXT	PPA
	Total = 457	76.8	78.2	65.4	75.4	82.1	89.5	79.4	98.7	92.3	47.5	63.2
	ESBL n= 81 (17.7%)	0	0	0	0	53.1	76.5	48.1	96.3	100	19.8	39.5
	CIP	OFX	FOS	NIT	TGC							
Total = 457	84	79.9	95.8	89.3	94.5							
ESBL n= 81 (17.7%)	65.4	63	97.5	97.5	98.8							

ATB= Antibiotic; AMP= Ampicillin; AMC= Amoxicillin-clavulanic acid; TIC= Ticarcillin; TCC= Ticarcillin-clavulanic acid; PIP= piperacillin; TZP=piperacillin-tazobactam
 IMP= imipenem; ATM= Aztreonam; CXM= ceftiozime; FOX= cefotaxim; CTX= cefotaxime; CAZ= ceftazidime; FEP= cefepime; LEX= cefalexin; CFP= cefixime;
 GEN= gentamicin; NET= netilmicin; TOB= tobramycin; AMK= amikacin; COL= colistin; SXT=Trimethoprim-Sulfamethoxazole; PPA=piperimidic acid ;CIP= ciprofloxacin
 OFX= ofloxacin; FOS= fosfomycin; NIT= netilmicin; TGC= Tigecycline. ESBL= Extended-spectrum beta-lactamase; n = total ESBL strains.

[table 1]

PHENOTYPIC AND MOLECULAR CHARACTERIZATION OF B-LACTAMS RESISTANCE, BIO- CAPSULAR TYPING OF NASOPHARYNGEAL COLONIZING *HAEMOPHILUS INFLUENZAE* FROM PRESCHOOL CHILDREN IN NORTH-LEBANON

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Background: The aim of this study is to determine the prevalence, the percentage of biotype, capsular typing, comparing the classical method of identification versus the molecular one of nasopharyngeal colonizing *Haemophilus influenzae* (*H.influenzae*) and determine the overall percentage of susceptibility to β -lactams, detection of β -lactamase production, resistance by modification of penicillin binding protein (PBP) - β -lactamases Negative Ampicillin Resistant (BLNAR) and level of macrolide resistance.

Material and methods: 21 isolates of clinical *H. influenzae*, were isolated from 87 nasopharyngeal specimens. The phenotypic identification method was compared versus the molecular one by PCR of all isolates, the presence of ornithin decarboxylase, urease and tryptophanase was differentiate the strain biotype, and capsular types were determined by standard slide agglutination serotyping (SAST). The prevalence of β -lactams resistance and β -lactamase production as well as their level of macrolide resistance was recorded for each strain using disc diffusion and E-test strip methods; then a chromogenic cephalosporin test (cefinase) was done, after which their β -lactams resistance genes (*bla_{TEM}* and *bla_{ROB}*) were determined by PCR.

Results and conclusion: Slide agglutination serotyping showed that 42.8 % of the strains were type b, Biotypes I, II and III were the prevalent biotypes whereas biotypes IV, VI and VIII was not found. The majority of capsule type b belonged to biotype II.19.0 % of the 21 strains were resistant to ampicillin; all of them produced type TEM-1 β -lactamase. All these isolates had an intermediate susceptibility to erythromycin.

INFECTIONS DUE TO CARBAPENEM-RESISTANT GRAM-NEGATIVE PATHOGENS (CRPs) IN CHILDREN: PRELIMINARY RESULTS FROM THE NATIONAL SURVEILLANCE SYSTEM IN HOSPITALS IN GREECE

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Aim: CRPs are emerging as a major cause of nosocomial infections with an increased impact on morbidity, mortality, and health-care costs. Our knowledge about infections due to CRPs in children is very limited. We present the characteristics and outcome of children with infections due to CRPs notified through the National Surveillance System in Greece.

Methods: Data were collected prospectively from Greek hospitals.

Results: During January-October 2011, 47 children (19 boys; 40.4%) with a median age of 2 years (1 month-14 years) were notified. Underlying conditions existed in 72% of patients. Infections were: pneumonia (16 cases; 34%, including 13 (81.3%) ventilator-associated), bacteremia (13; 27.7%), urinary tract infection (12; 25.5%), and surgical site infection (6; 12.8%). Isolates were: *Acinetobacter baumannii* (20; 40.8%), *Pseudomonas aeruginosa* (19; 38.8%), and *Klebsiella pneumoniae* (10; 20.4%). 66.7% of *Klebsiella* isolates were KPC-producing; the remaining were VIM. The first positive culture occurred a median of 22 days (0-256) after admission. At the onset of infection, 31 (65.9%) were hospitalized in an Intensive Care Unit. Regarding risk factors for colonization, 15 (31.9%) had a history of hospitalization in the previous 6 months; 30 (63.8%) and 25 (53.2%) had received broad-spectrum antibiotics or carbapenems in the previous 6 months, respectively; 34 (72.3%) were on mechanical ventilation; 29 (61.7%) had a central vascular catheter and 26 (55.3%) a urine catheter. Eleven (23.4%) children died a median of 7 days (0-47) after the first positive culture.

Conclusions: Infections due to CRPs are associated with an increased morbidity and mortality among hospitalized children.

CARBAPENEM RESISTANCE IN ACINETOBACTER BAUMANNII ISOLATES CAUSING INFECTIONS IN CHILDREN AT UNIVERSITY HOSPITAL CENTER ZAGREB

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Carbapenems have potent activity against Acinetobacters and are often used as last resort for the treatment of infections due to multiresistant *Acinetobacter baumannii*. However, Acinetobacters may develop resistance to carbapenems through various combined mechanisms including decreased permeability and overexpression of efflux pumps.

Nine *Acinetobacter baumannii* strains were isolated from children's specimens at intensive care units during last three months of 2009 at Clinical Hospital Center Zagreb. The aim of the study was to characterize carbapenem-resistance mechanisms in these isolates. The antimicrobial susceptibility to a wide range of antibiotics was determined by broth microdilution method. Modified Hodge Test was used to screen for production of carbapenemases. E-test was used to screen for production of metallo- β -lactamases. Genes encoding oxacillinases and metallo-beta-lactamases were detected by multiplex PCR. Genotyping of the strains was performed by pulsed-field gel electrophoresis (PFGE) and determination of sequence groups by multiplex PCR.

Three of nine strains were resistant to imipenem and meropenem. They were found to produce OXA-24 β -lactamase, belonged to sequence group 1 (EU clone II) and were clonally related by PFGE. Other six strains were susceptible or intermediate susceptible to carbapenems but showed resistance to gentamicin, expanded-spectrum cephalosporins, piperacillin/tazobactam and ciprofloxacin. Multiplex PCR revealed only the intrinsic, naturally occurring OXA-51 β -lactamase of species *A. baumannii*. These strains showed distinct PFGE profiles and were not clonally related.

The study demonstrated occurrence of carbapenem resistant OXA-24 producing *A. baumannii* at paediatric units of University hospital center Zagreb. Infections with such multiresistant isolates are associated with increased mortality and morbidity.

DETERMINATION OF EXTENDED-SPECTRUM B-LACTAMASES (ESBLs) IN ENTEROPATHOGENIC ESCHERICHIA COLI (EPEC) STRAINS ISOLATED FROM CHILDREN WITH DIARRHEA

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Background and aims: Enteropathogenic Escherichia Coli is a major cause of diarrhea in children in developing countries. The aim of this study is to determine the antibiotic resistance pattern and considering the prevalence of ESBLs coding genes including TEM, SHV, CTX-M and OXA gene and insertion sequence of ISE-CP1 in EPEC strains isolated from children with diarrhea.

Methods: Totally, 192 strains of EPEC isolated from children with diarrhea were included. The susceptibility of isolates to 14 antimicrobial agents was determined by the disc diffusion method and interpreted according to the CLSI recommendations. Production of ESBL in the isolates was determined by combined disk test and the presence of CTX-M, SHV, TEM, OXA and ISE-CP1 genes was detected by PCR.

Results: The results showed that these strains had the most resistance to cefpodoxime (97%), trimethoprom (60.7%), tetracycline (58.4%) and ampicillin (45.8%). Multidrug resistance was 68.7 percent. These strains showed the most sensitivity to imipenem, ceftriaxone, and ciprofloxacin antibiotics. The percentage of ESBLs prevalence in EPEC strains was estimated 79.7 %. PCR approach showed that different ESBL gene prevalence, including, TEM, SHV, CTX-M, OXA and ISE-CP1, respectively are 13.5, 11.9, 10.9, 7.3, and 61.7 percent.

Conclusion: This study highlighted the needs to establish antimicrobial resistance surveillance networks for *EPEC strains* to determine the appropriate empirical treatment regimens. The high prevalence of multidrug resistance and production of ESBLs in *EPEC* isolates confirms the necessity of protocols considering these issues and the exact application of antibiogram test before antibiotic prescription for complete treatment.

COLONIZATION OF NEONATES WITH CARBAPENEMASE-PRODUCING ENTEROBACTERIACEAE (CPE)

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Background: Carbapenemase-producing Enterobacteriaceae (CPE) have emerged as a major public health threat worldwide with particularly high rates in adult ICUs in Greece. There is a lack of data about the epidemiology of CPE in children. We aimed to determine the prevalence of CPE in neonatal intensive care units (NICU).

Method: A point prevalence study was conducted between November, 2011 and January, 2012 in 8 NICUs in 5 public hospitals in Athens, including the 2 largest children's hospitals. We collected rectal and umbilical swabs from infants in 8 NICUs. All the specimens were inoculated on McConkey agar plates containing meropenem and incubated for 48 hours. Enterobacteriaceae were identified to the species level by the API 20E method. All isolates were examined for production of carbapenemases by combined disk synergy test utilizing disks containing meropenem, EDTA and boronic acid. The bla_{VIM} and bla_{KPC} genes were detected by PCR using specific primers. Demographic and clinical data were extracted from the patients' medical records.

Results: 157 neonates were included in our study, 79 were males (50%). The mean age was 40 days and 67% were born prematurely. Out of 314 samples, only one CPE strain (VIM) was isolated in both rectal and umbilical cultures from the same neonate.

Conclusions: *We found a low prevalence of colonization with CPE in NICU patients. Our finding contrasts significantly with colonization rates in adults. Factors associated with this phenomenon need to be further determined in order to design interventions to prevent the emergence of CPE in children.*

PREVALENCE AND RESISTANCE PHENOTYPES OF THE PHARYNGEAL STREPTOCOCCUS PYOGENIS IN PEDIATRIC POPULATION

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Background: Streptococcus pyogenis (GAS) induced pharyngotonsillitis is one of the most frequent diseases and frequent causes for antibiotic intake among pediatric patients.

Aim: Prevalence of GAS induced pharyngotonsillitis in pediatric population and determination of the phenotypes of resistance to antibiotics.

Methods: During the period 2009-2010, 4384 children were examined at the pediatric office with symptoms of pharyngotonsillitis. Cultures of throat smear were performed and for preliminary biochemical identification a 0.04U disc was used. The results were confirmed with specific Lancefield antiserum. The resistance phenotypes (MLSB) to macrolides and lincosamides were investigated using double ERY and clindamycin (CL) in 12 mm distance.

Results: 1312 (29.9%) clinical strains of GAS were isolated (2009: 2084/661, 31.7% and 2010: 2300/651, 28.3%). During the study, 2 cases of septicemia were recorded. The resistance rate of GAS to macrolides was 15% in 2009 and 11% in 2010. The intermediate sensitivity rates were 3% in 2009 and 3.5% in 2010. The resistance rates for clindamycin were the same with those for macrolides and strains with intermediate sensitivity were not recorded. The inducible resistance phenotype was detected more frequently over those of phenotype M (mefA) and of constitutive resistance (CR-MLSB-ermB). All of the GAS strains were sensitive to penicillin, ofloxacin, glycopeptides and b and c generation cephalosporins.

Conclusions: Penicillin remains the treatment of choice and alternatively cephalosporins may be used. The resistance to macrolides may be correlated with their overuse.

ANTIMICROBIAL EXPOSURE AS A RISK FACTOR FOR RESISTANCE TO FIRST LINE ANTIBIOTICS IN URINARY TRACT ISOLATES IN CHILDREN

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Background: Resistant organisms have emerged worldwide due to several factors. Among them, the selective antimicrobial pressure seems to be a major risk factor. We aimed to explore the relationship between prior antibiotic exposure and the risk of antibiotic-resistant pathogens in Urinary Tract Infection (UTI) in children.

Methods: We enrolled all patients with a clinically suspected UTI in the emergency department of a tertiary care Hospital. Clinical and microbiological data were recorded, including previous history of antibiotic exposure. Among those with positive cultures, patients whose urine isolates were susceptible to the antibiotics tested were considered controls, and those with pathogens resistant to “first-line” antibiotics were cases.

Results: 155 episodes corresponding to 128 patients between 1 month and 15 years of age were included. 65% were female. Etiologic isolated agents were *E. coli* (80,3%), *Proteus* spp. (11.6%), *Enterococcus* spp. (4,2%), *Enterobacter* spp. (2,%) y *Klebsiella* spp. (1,4%). 73,6% of the isolates were resistant to amoxicillin, 36% to Sulfamethoxazole/Trimethoprim, 23% to amoxicillin-clavulanate, 8,3% to second generation cephalosporin and 6% to phosphomycin. 43% of children had been exposed to antibiotics in the previous three months, 52% considering the previous six months. There was a statistically significant association between exposure to amoxicillin (OR 2.5, $P < 0.05$) and amoxicillin-clavulanate (OR 4.2, $P < 0.001$) and the isolation of an amoxicillin-clavulanate resistant pathogens.

Conclusions: Previous exposure to antibiotics should be taken into account when prescribing antibiotics for UTI in children. The reduction of antibiotic pressure is a clinical priority for paediatricians to decrease antibiotic resistances.

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* PEDIATRIC ISOLATES WITH COMMUNITY-ASSOCIATED PHENOTYPE IN SÃO PAULO, BRAZIL

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Background and aims: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the community have increased worldwide in the past decade. Community-associated MRSA isolates (CA-MRSA) have specific characteristics of virulence and resistance. Usually the CA-MRSA strains are susceptible to clindamycin, cloramphenicol and TMP-SMZ and resistant to erythromycin. The objective of this study was to observe the clinical features and the antimicrobial resistance profile of *Staphylococcus aureus* isolates in children.

Methods: We analyzed the medical records of children with *Staphylococcus aureus* isolated from blood culture or pleural fluid or secretion of abscess from July 2009 to December 2011, at Santa Casa São Paulo Hospital, a general tertiary school hospital. *Staphylococcus aureus* were identified previously by Gram stain and production of catalase, and coagulase test. Antimicrobial susceptibilities were determined by disk diffusion tests in accordance with guidelines issued by the Clinical and Laboratory Standards Institute (CLSI) 2011.

Results: A total of 61 *Staphylococcus aureus* strains were isolate in children in of the study period. The median of age was 4,375 year. Fifty six strains were isolated from blood culture, one strain was isolated from pleural fluid and four strains from secretion of abscess. Twenty three strains were MRSA. Of these strains, four had a phenotype of CA-MRSA (methicillin and erythromycin resistance; clindamycin, cloramphenicol and TMP-SMZ susceptibility), five were methicillin resistant only, two strains were multi-resistant. All MRSA strains were susceptible to TMP-SMZ.

Conclusions: Of 61 *Staphylococcus aureus* isolates in children during a 30 month-period, 23 were MRSA and 4 had a phenotype of CA-MRSA.

PREVALENCE OF ANTIBIOTIC RESISTANT *ENTEROCOCCUS SPP* IN FRESH VEGETABLE SALAD IN THE CITY OF BOGOTÁ

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Nowadays, the antibiotic resistance of microorganisms has become a worldwide health problem. *Enterococcus spp* are ubiquitous and opportunistic pathogens resistant to several antibiotics. In Colombia, research on resistant *Enterococcus spp* has been focused on the clinical area, so there are no reports on the prevalence and the role that may be playing in food as a way of dispersion of resistant bacteria. The aim of this study was to characterize the antibiotic resistance of *Enterococcus spp* strains isolated from fresh vegetable salads in different establishments in Bogotá. 30 samples of vegetable salads were collected and 31 strains were isolated and identified by 16S rRNA gene sequencing and classical microbiology. Evaluation of antibiotic resistance was performed by susceptibility testing. Antibiotic resistance of 31 *Enterococcus spp* isolates to 13 antibiotics (amikacin, ampicillin, ciprofloxacin, gentamicin, nitrofurantoin, imipenem, meropenem, kanamycin, penicillin, rifampin, tetracycline, vancomycin and cotrimoxazole) was tested. It was found that 12.90% was susceptible to all antibiotics, 38.71% was resistant to three antibiotics, 9.68% to four antibiotics, 9.68% to 5 antibiotics and 6.45% to 6 antibiotics. All antibiotics tested presented at least one strain with resistance. The highest percentage was co-trimoxazole (54.84%), nitrofurantoin (41.94%) and rifampicin (38.71%). It is necessary to clarify the role that food can play as a route of transmission of antibiotic resistant bacteria and how they can be involved in the increase of infections in hospitals and in the community.

THE STUDY OF ANTIMICROBIAL RESISTANCE AMONG SHIGELLA FLEXNERI STRAINS ISOLATED IN TEHRAN, IRAN

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Investigate antimicrobial resistance of and acute diarrhea in Tehran, Iran.

Major hospitals in Tehran.

Resistance testing was performed according to the standard guidelines of the Clinical and Laboratory Standards Institute. All strains were resistant to streptomycin. More than 96.4% of the strains were resistant to tetracycline and amoxicillin, 89% to co-trimoxazole, 72.6% to ampicillin, 33.3% to chloramphenicol, 9.5% to kanamycin, 1.2% to ce None of the tested isolates were resistant to ceftriaxone, ceftizoxime, ceftazidime, gentamicin, ciprocefotaxime, cephalaxine, nalidixic acid and nitrofurantoin. More than 96% of the strains showed multi-drug resistance phenotype.

Seventeen resistance patterns were identified R6 streptomycin/amoxicillin/tetracycline/co-trimoxazole/ampicillin). This study indicates an increase in incidence of multiple drug resistance among the strains of *Shigella flexneri*. Shigellosis is one of the major causes of morbidity in children with diarrhea in Iran. The aim of this study was to identify *Shigella flexneri* (S. *flexneri*) strains isolated from clinically diagnosed cases of gastroenteritis. *Shigella* strains were isolated from stool samples of patients who visited the several S. *flexneri* was preliminarily identified by biochemical tests as well as by API20E. Antimicrobial rifampin, amikacin and furazolidone, floxacin, cephalothin, identified among the strains, however the most prevalent phenotype (36.9%) was S. *flexneri* isolated in Tehran, Iran.

THE PREVALENCE AND SUSCEPTIBILITY OF BACTERIAL UROPATHOGENES OF PEDIATRIC POPULATION

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Aim: To study the results of urocultures of pediatric patients, admitted in hospital and the prevalence and susceptibility of isolated bacteria to antibiotics.

Material: A total of 334 urine specimens were collected from pediatric patients with median age 3,4±2 . During the period 2008 -2011 were performed 334 urine cultures of 163 (47.1%) females and 171 (52.9%) males. Only 46 of the 334 (13,7%) patients with positive uroculture had leukocytosis. Fever as a clinical symptom was found in 37 of the 334 cases (11,0%).

Method: Urine specimens were cultured in McConkey-Blood Agar and cultivated at 37 °C. The identification and control of sensitivity were performed by Vitek 2 test (BIOMERIEUX), and diffusion disk test by Kirby-Bauer method.

Results: In total 58,8% of the strains belonged to *E.coli* and was followed by *Proteus mirabilis* (20,6%), *Pseudomonas aeruginosa* (8,8%), *Klebsiella spp.* (4.9%), *Staphylococcus spp.*(3.9%), *Enterobacter cloacae* (1.5%), *Citrobacter freundii* (1%), *Burkholderia cepacia* (0,5%), *E.coli* was isolated in 35% of males and in 65% of females. The susceptibility to antibiotics, is presented:

SENSITIVITY		Ampicillin	Amoxicillin-Clav.acid	Cefaclor	Cefuroxime Axetil	Amikacin
	<i>E.coli</i>	61.1%	83.3%	77.8%	88,9%	99%
	<i>Proteus mirabilis</i>	71,4%	85%	73%	85,7%	95%
	<i>Pseudomonas aeruginosa</i>	-	-	-	-	88%
	<i>Klebsiella spp.</i>	71,4%	27%	25%	37%	91%

[Table 1]

Conclusions: *E.coli* was isolated from the highest number of cases followed by *Proteus mirabilis* and *Pseudomonas aeruginosa* .Amikacin has good activity against gram negativebacteria. Strainsof *Klebsiella* show increased resistance to Cefalosporins of second generation.

STREPTOCOCCUS PNEUMONIAE ANTIBIORESISTANCE IN CHILDREN WITH ACUTE UPPER RESPIRATORY CONFIRMED INFECTION

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Background: Acute respiratory infections caused by *Streptococcus pneumoniae* (SP) bacteria are common in children in collectivities. In Romania pneumococcal vaccination is not included in the national immunization program. The first intention antibiotics used for treating confirmed SP infection in symptomatic patients are in macrolides/ betalactamine classes.

Objectives: Assessment of SP antibioresistance, from nasopharyngeal/ ear secretions in symptomatic, outpatient children, in Dr V Babes Diagnosis and Treatment Center Bucharest.

Methodes: We considered 68 children aged between 8 months and 16 years, with confirmed SP infection. None of the patients were immunized against SP. All patients were symptomatic for acute upper respiratory infection (51% rhinoadenoiditis, 37% acute middle otitis, 12% sinusitis). In this patients were also performed blood counts, blood inflammatory markers evaluation. Antibioresistance assessment for SP isolated from samples was done using both Kirby Bauer test procedure and E test, for macrolides and betalactam antibiotics.

Results: In 25 cases SP was isolated from ear sample and in 60 cases from nasopharyngeal secretion. The most affected age group was 0- 5 years (70%). Antibioresistance to macrolides appeared in 42% cases of isolated SP strains and towards betalactamines appeared in 38% cases. Both betalactamines and macrolides antibioresistance was higher in the acute middle otitis group (45% and 44%).

Conclusions:

1. Recently excess use of macrolides in SP infections, due to their facile administration, can lead to alarming increase of resistance, compared to previous years.
2. Vaccination may be an alternative to reducing the number of macrolides resistant *Streptococcus pneumoniae* infections.

THE PREVALENCE OF ANTIBIOTIC RESISTANCE AMONG *ESCHERICHIA COLI* ISOLATED FROM COMMUNITY-ACQUIRED URINARY TRACT INFECTIONS

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Aim: To determine the resistance to antibiotics in *Escherichia coli* strains from community urinary tract infection in children (< 16 years of age) and adults and molecular characterisation of a selected group of extended spectrum beta-lactamases producers (ESBL).

Methods: Susceptibility to antibiotics was tested by the participating laboratories (n=43) by the disk diffusion method in isolates causing community-acquired urinary tract infection in April 2011. The isolates producing ESBL were typed by pulse-field gel electrophoresis (PFGE), multilocus sequence typing (MLST) and PCR determination of phylogenetic group. Plasmids were analyzed by PCR-based replicon typing with sequencing of the amplicons.

Results: The resistance rates to ampicilin and co-trimoxazole were rather high (48.1%, respective 24.1%). The resistance to norfloxacin was different in children and adults, 2.7% in children versus 13.4%. Five ESBL isolates were recovered from children and thirty three from adult patients. All of the isolates isolated from children belonged to the pathogenic B2 phylogenetic group and were clustered into 5 different PFGE patterns. MLST results demonstrate the presence of ST131 clone. Among pediatric isolates, three expressed CTX-M-15 and two the CTX-M-9. The plasmids possessed FII (type 1 and 2), FIA (type 1 and 5) and I1 replicons. Similar data were obtained also from adult population.

Conclusions: The presence of ESBL producing strains causing community-acquired infection was found in children and adults. The molecular typing shown the homogeneity of the ESBL strains.

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ANTIMICROBIAL SUSCEPTIBILITY OF ENTEROBACTERIACEAE CLINICAL ISOLATES PRODUCING EXTENDED-SPECTRUM BETA- LACTAMASE (ESBLs) IN A PEDIATRIC HOSPITAL IN ROMANIA**G. Baciu**^{1,2}, G. Gurau^{3,4}, C. Florea^{3,5}, M. Zisu⁶

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Background and aims: The antibiotic resistance mediated by extended spectrum beta lactamases (ESBLs) is a phenomenon that creates serious therapeutic problems around the world. The aim of this study was to detect the prevalence of ESBLs enzymes in Enterobacteriaceae isolated during 2011-2012, and evaluation of susceptibility of the strains to selected antibiotics.

Methods: 30 isolates of *Escherichia coli*, 43 *Klebsiella pneumoniae*, 6 *Enterobacter spp.*, 1 *Citrobacter spp.* and 4 *Klebsiella oxytoca*, 2 *Salmonella group*, 1 *Shigella group* were tested for production of ESBLs and antibiotics susceptibility with Vitek 2 Compact System. The MICs of selected antibiotics were determined according to EUCAST recommendations. In our region, the presence of ESBLs among enterobacteria is high and there are indications of their spread among species other than *Escherichia coli* and *Klebsiella pneumoniae*.

Results: A total of 2 strains were positive with *Escherichia coli* (6,6 %) and 18 strains with *Klebsiella pneumoniae* (41,86%) were producing ESBLs. Most of the ESBL-producing strains were also resistant to aminoglycoside antibiotics and to tetracycline. High sensitivity of ESBL-producing *Escherichia coli* strains (100%) and *Klebsiella pneumoniae* strains (over 90%) to fluoroquinolones was demonstrated.

Conclusion: The obtained results confirm the necessity of continuous and reliable monitoring of ESBL-producing strains among enterobacteria isolated from clinical isolates. Increasing prevalence of this infection is a multifactorial problem with great significance for public health, requiring a complex analysis and implementation of specific measures to different levels

COMMON BLOOD ISOLATES AND SUSCEPTIBILITIES OF NEONATAL SEPSIS CASES ADMITTED IN PEDIATRIC TERTIARY HOSPITAL IN QUEZON CITY, 1996- 2010

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Background and objective: Establishing epidemiological and statistical information regarding neonatal sepsis is needed for establishing a sound program for early detection of infection/outbreak. This study is done to determine the most common blood culture isolate and susceptibilities among neonatal sepsis admitted in a pediatric tertiary hospital in Quezon City, 1996 - 2010.

Methods: Charts of neonates admitted at a pediatric tertiary hospital in Quezon City from January 1996 - December 2010 with final diagnosis of Neonatal sepsis and with at least 1 positive blood culture were collated. Blood culture and sensitivity results were reviewed. Other data included gender, birthweight, gestational age, mode of delivery and maternal history. Data were analyzed using frequency and percentage.

Results: 25% of 263 neonates were diagnosed with neonatal sepsis and had at least one blood culture. Coagulase negative staphylococcus (52%) was the most common bacteria isolated followed by *Enterobacter aeruginosa* (10%) and *Klebsiella pneumoniae* (8%). Gentamycin, Vancomycin and Chloramphenicol were the 3 most common susceptible drugs for Coagulase negative Staphylococcus. Male neonates (58%), term (66%), weight > 2.5 kg (81%), delivered by normal spontaneous delivery (69%), and mothers with history of infection (69%) were frequently noted to have neonatal sepsis.

Conclusion: Coagulase Negative Staphylococcus is the most common pathogen seen in this study. This organism is susceptible to Gentamycin, Vancomycin and Chloramphenicol. Male term neonates with birth weight of more than 2.5 kg delivered by normal spontaneous delivery and mothers with history of infection prior to delivery were commonly noted to have neonatal sepsis.

FACTORS ASSOCIATED WITH REDUCE COMPLIANCE WITH TREATMENT GUIDELINES FOR PEDIATRIC ACUTE OTITIS MEDIA (PAOM)

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Background: Publication in Israel of guidelines recommending delayed antibiotic therapy for PAOM has been associated with reduced antibiotic use. We examined the effects of physician and visit characteristics on PAOM treatment.

Methods: Physician visit data from 2002-2009 of large Health Medical Organization in Israel were used to identify children aged 0.5 to 15 years with PAOM. Antibiotic treatment was defined as purchase of an antibiotic prescribed by the diagnosing physician within 3 days of the visit. We considered the following covariates: physician specialty (pediatrician, otolaryngologist, family physician), day of the week, setting (urgent care/clinic), and clinic location (peripheral/central).

Results: Antibiotic purchasing dropped from 2002 to 2009 respectively in cases treated by otolaryngologists (47% to 36%, $p < 0.001$), and pediatricians (46% to 42%, $p < 0.001$), and increased in cases treated by family physicians (43% to 50%, $p < 0.001$). Purchasing was higher on weekends (Friday and Saturday), as compared to weekdays (Sunday through Thursday) (48%, and 44% respectively $p < 0.001$), in children treated in urgent care as compared to physician offices (51%, and 44% respectively $p < 0.001$), and in children leaving in the most peripheral as compared to central areas (52%, and 38% respectively, $p < 0.001$). Multivariate modeling demonstrated that independent factors associated with increased treatment rates were: being a family physician, and day of the week.

Conclusions: Successful implementation of delayed treatment of PAOM requires addressing factors associated with increased prescribing such as: physician specialty, geographic location, setting and week day of the visit.

HOW SHOULD ADHERENCE TO PAEDIATRIC PERIOPERATIVE ANTIBIOTIC PROPHYLAXIS GUIDELINES BE ASSESSED?

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Background and aims: Perioperative antibiotic prophylaxis (POAP) has been shown to be effective in preventing postoperative infections. The aim of the study was to assess the impact of using different adherence criteria in evaluating POAP at a tertiary paediatric surgical centre.

Methods: POAP administered to consecutive children undergoing surgical interventions under anaesthesia was reviewed prospectively. Information was collected on indication, antimicrobial agent, administered dose and duration of POAP. The proportion of interventions with POAP adherent to institutional guidance adapted from national recommendations was assessed.

Results: 218 POAP prescriptions for 620 children and 710 procedures were analysed. Median age of included patients was 6 years (range 0.01-23.2). Overall POAP was administered for 30.7% (218/710) of procedures. POAP was administered for 68% of procedures in cardiothoracic surgery with more than 50% of procedures carried out with POAP in craniofacial/neurosurgery (57%) and orthopaedic/trauma surgery (52%) and the lowest proportion in ENT surgery (4.3%). The need for POAP was correctly identified in 95% (208/218) of procedures where POAP was administered. However, applying additional criteria for correct antimicrobial choice, correct dosage and correct duration of POAP only 41% (89/218) of POAP administration was adherent to local guidelines. Incorrect antimicrobial choice and duration were the largest sources of error in our cohort.

Conclusions: Although the need for POAP was correctly identified in 95% of cases, with the application of further criteria only 41% of prescriptions were appropriate. The choice and successive application of criteria in assessing POAP is of key importance.

IMPACT OF A RAPID ANTIGEN DETECTION TEST FOR STREPTOCOCCAL PHARYNGITIS ON ANTIBIOTIC PRESCRIBING PRACTICES

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Background and aims: Current management of acute pharyngitis in Ireland is inconsistent. Although Group A Streptococcus (GAS) accounts for only 15-30% of cases, it's difficult to clinically differentiate viral from bacterial causes. Antibiotics are frequently prescribed inappropriately, contributing to the burden of antimicrobial resistance. Use of Rapid Antigen Detection Tests (RADTs) for GAS in the US appears to reduce empirical prescribing, but questions remain regarding the test's sensitivity. Our aim was to evaluate the impact of a RADT-based management protocol on antibiotic prescribing in a small private hospital.

Methods: The RADT was implemented for a six-month period from March-August 2010. Antibiotic use in children (N=27) with clinically-suspected pharyngitis was audited and compared via chart review to that of a retrospective control group (N=48) who presented during March-August 2009.

Results: There was no significant difference in antibiotic prescribing rate between test and control periods (55.6% vs 60.4%; P=0.868). RADT sensitivity and specificity were 50% and 100%, respectively. 'Red ears' and 'sore throat' were the strongest clinical predictors of antibiotic treatment with odds ratios of 8.1 and 4.7, respectively. Individual physician prescribing pattern also significantly influenced likelihood of treatment, for both periods combined (P=0.002) and the test period alone (P=0.008).

Conclusions: Use of the RADT did not alter antibiotic prescribing practices. This may be attributable to its variable performance leading to lack of local acceptance with superseding 'clinical judgement'. Considering its high specificity, it may still have a role as a supportive tool in a diagnostic algorithm, facilitating prompt treatment where needed.

A STUDY OF GENTAMICIN DOSAGE AND LEVELS IN BABIES ADMITTED TO SPECIAL CARE BABY UNIT

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Background and aims: Gentamicin is one of the most commonly used antibiotics in newborns. As Gentamicin has a narrow therapeutic index, therefore trough and peak levels are measured to indicate of toxicity and treatment adequacy. We performed this study to review the Gentamicin dose of 4mg/kg once daily by analysing drug levels and the incidence of drug errors. We also analysed whether there are any benefits of measuring peak levels.

Methods: Gentamicin levels performed on babies more than 33 weeks gestation in the last 4.5 years were analysed. We selected the babies with high peak and/or trough levels to obtain specific information about the Gentamicin dose and action taken. We also assessed whether there was any additional benefit of performing peak levels.

Results: The study revealed that 120 Newborns underwent Gentamicin levels. In total 36 (30%) babies had either high trough or peak level out of which 8 (7%) newborns were found to have high trough only. Our study found that presence of a high peak level did not alter management (i.e. subsequent dose). Gentamicin dosage was prescribed and administered incorrectly for 11% and 3% babies respectively.

Conclusions: We conclude that our current dose of 4 mg/kg/day once a day is extremely safe. When compared with the studies using 5mg/kg, we recommend the use of 4 mg/kg as the standard dose rather than the current recommendation of 5 mg/kg. We also noticed that there is little information gained by measuring peak levels in addition to trough levels.

PAEDIATRIC ANTIBIOTIC PRESCRIPTIONS IN THREE EUROPEAN COUNTRIES BETWEEN 1995 AND 2010: AN ARPEC STUDY

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Background and aims: As part of the ARPEC project (Antibiotic Resistance and Prescribing in European Children), we studied characteristics of paediatric antibiotic prescribing in primary care in the Netherlands (NL) (1996-2010), United Kingdom (UK) (1995-2010) and Italy (IT) (2001-2010).

Methods: We conducted a retrospective cohort-study using data from three electronic medical records databases; Integrated Primary Care Information (IPCI) (NL), The Health Improvement Network (THIN) (UK) and Pedianet (IT).

We included 2,196,163 children (0-18 years) with a total of 12,101,125 person-years (PY) of follow-up.

Yearly prevalence of antibiotic prescriptions, defined as the number of children with at least one antibiotic prescription per year, was calculated. Type and proportion of most prescribed antibiotics were measured using the DU90%-methodology.

Results: The yearly prevalence of antibiotic prescriptions was 17 users/100PY in NL, 30 users/100PY in UK and 42 users/100PY in IT and remained stable over time. Prevalence was highest for the youngest children (0-2 years); 32/100PY (NL), 48/100PY (UK), 53/100PY (It).

Based on the DU90%, we found that almost half of all prescriptions were for amoxicillin+/-clavulanic acid in all countries. Cephalosporins were frequently prescribed in Italy but rarely in the other countries.

Netherlands	United Kingdom	Italy
Amoxicillin (45%)	Amoxicillin (44%)	Amoxicillin (25%)
Amoxicillin / clavulanic acid (13%)	Phenoxymethylpenicillin (13%)	Amoxicillin / clavulanic acid (23%)
Azithromycin (8%)	Erythromycin (10%)	Azithromycin (10%)
Clarithromycin (7%)	Flucloxacillin (9%)	Cefaclor (9%)
Pheneticillin (6%)	Trimethoprim (5%)	Cefixime (7%)
Nitrofurantoin (4%)	Amoxicillin / clavulanic acid (4%)	Ceftibuten (3%)
Flucloxacillin (3%)	Cefalexin(3%)	Cefpodoxim (2%)

[DU90% (0-18 years)]

Conclusions: The prevalence of antibiotic prescribing was high and varied with age - in the youngest age category a third to a half of all children were prescribed an antibiotic during one year of follow-up. Amoxicillin+/-clavulanic acid is the most frequently prescribed antibiotic used overall. In view of this large variation, more consistency in prescribing antibiotics to children seems justified.

ANTIMICROBIAL STEWARDSHIP IN NEONATAL INTENSIVE CARE: MORE THAN JUST GUIDELINES AND PROTOCOLS

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Background and aims: Antimicrobial stewardship is the optimisation of antibiotic prescribing. Effective antimicrobial stewardship consists of selecting an appropriate empirical product, prompt de-escalation based on laboratory data and a daily review of prescriptions. We evaluate the antibiotic prescribing practice in a level 3 UK neonatal intensive care unit.

Methods: Neonatal clinical and laboratory data was prospectively collected over 4 months. Antimicrobial agent, duration and indication were collected.

Results: 189 suspected septic episodes were recorded from 151 neonates, whose mean gestational age was 35 weeks plus 5 days. Ninety percent of the blood cultures were negative and 63% of all prescriptions were discontinued after 72 hours. 16% of neonates underwent more than 1 antibiotic prescription during their inpatient stay.

No of antibiotic Prescriptions	% of Numbers of patients (n=151)
1	84.1
2	10.6
3	2.6
4	1.3
5	0.6
6	0.6

[Antibiotic Prescriptions per patient]

In those babies treated for more than 120 hours, 79% had a negative blood culture. Reasons for continuation of antibiotics included prenatal risk factors, laboratory markers and clinical correlates of sepsis.

Conclusions: There are currently no consistent scoring tools for neonatal sepsis, due to variability in clinical presentation. Even with robust protocols and guidelines, the antibiotic treatment of suspected sepsis in neonates should be individualised and reviewed on a daily basis. Laboratory diagnostic tools, such as blood cultures should not be regarded as a gold standard, and thus should not be solely relied upon for cessation of antibiotics.

THE NEONATAL AND PAEDIATRIC ANTIMICROBIAL WEB-BASED POINT PREVALENCE SURVEY (PPS): BROAD-SPECTRUM ANTIBIOTIC USE FOR COMMUNITY-ACQUIRED PNEUMONIA IN EUROPE IN 2011

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Background and aims: The Point Prevalence Survey (PPS) is part of the Antibiotic Resistance and Prescribing in European Children (ARPEC) Project (<http://www.arpecproject.eu/>). We report the variation in use of antibiotics prescribed for children admitted with community-acquired pneumonia (CAP).

Methods: A one-day PPS of antibiotic use in hospitalised children was conducted in September 2011 in 37 hospitals of 14 European countries. Paediatric European antibiotic use for CAP was analysed by age (4 months - 5 years compared with 6-18 years) and underlying disease.

Results: Overall, 2294 antibiotics were used in 872 children. 171 (7%) antibiotics were prescribed for LRTI of which 135 (79%) were for CAP. Around half of the antibiotics were used in children under 5 years of age (56%). For those aged under 5, 49 % had no underlying disease, while for those aged over 5, 63% had an underlying disease (24% with a chronic lung disease).

The main antibiotics prescribed for CAP to children aged under and over 5 years of age were third-generation cephalosporins (25% versus 22%), macrolides (20% - of which 80% was clarithromycin - versus 31%), aminopenicillins (17% versus 11%) and co-amoxiclav (12% versus 11%). The great majority of these antibiotics were prescribed empirically. Penicillin G was not prescribed for CAP in this survey.

Conclusion: The predominant antibiotics empirically prescribed for children hospitalised with CAP in this survey were cephalosporins and macrolides, which may reflect the high rates of underlying disease. Further prospective cohort studies are required to determine the appropriateness of such broad-spectrum prescribing.

USE OF AN ANTIBIOTIC MANAGEMENT SCORE IN PEDIATRIC PATIENTS WITH BACTEREMIA

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Background: Studies on antimicrobial stewardship interventions show much variability in the outcome variables used. It is unknown which variables are most relevant for patient outcome in pediatric populations and should be used for assessment of antimicrobial stewardship programs (ASPs).

Objective: To define outcome variables relevant for patient outcome and for identifying areas of non-optimal antibiotic use at the Children's Hospital at Downstate in Brooklyn, NY, USA.

Methods: A retrospective chart review identified episodes of bacteremia in pediatric inpatients. 7 antibiotic management variables (e.g. dose, choice of drug(s)) were evaluated for each episode and appropriate management determined. A score of 0 was considered optimal management. For each inappropriate management variable 1 point was added to the antibiotic management score (AMS), up to a maximum of 6 (7 if drug levels were relevant) per episode. Nonparametric statistics were used.

Results: 53 children (aged 0-20y) with bacteremia in a 1y period were identified. 51.8% received non-optimal antibiotic therapy (AMS>0) with a mean AMS of 1.25 per episode. The most common inappropriate variables were duration and deescalation. The AMS was significantly increased in pediatric compared to neonatal units and patients with poor outcome (death/microbiological failure) had significantly higher AMS (median AMS=4) than those with good clinical outcomes (median AMS=0) ($p < 0.05$).

Conclusions: A composite score of major antibiotic prescribing variables such as the AMS may reflect the quality of antibiotic management and its effect on patient outcome accurately and deserves further study. It remains critical to establish relevant universal benchmarks for ASPs.

THE COMPARABILITY OF DIFFERENT STUDY METHODOLOGIES FOR EVALUATING ANTIBIOTIC CONSUMPTION IN NEONATAL INTENSIVE CARE UNITS (NICU)

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Background and aims: Various methods like long term prospective cohort studies (PrCS), point prevalence studies (PPS) and short-term service evaluation surveys (SES) are used to evaluate consumption of anti-infectives (AI). We aimed to assess the comparability of PrCS, PPS and SES results in characterising systemic AI use in neonates in both Estonian third level paediatric hospitals.

Methods: AI use was recorded from patient's charts. In PrCS and PPS individual data plus number of admissions were registered over 6 months in 2007/2008 and one day in fall 2011, respectively. In SES all AIs were registered over 3 days in summer 2011. AI consumption in PPS was expressed as number of treatment days (TD) per 100 hospital days (HD).

Results: In PrCS 64% of admitted neonates (210/490) received a total of 552 prescriptions for 19 AIs resulting in 73TD/100HD. In PPS 8 agents were given to 13% (7/53) patients and in SES 5 agents were registered. In PrCS gentamicin (37%; 23/100) and ampicillin (24%; 13/100) accounted for 61% of prescriptions. Same agents were also most commonly used according to PPS (3 and 2 prescriptions, respectively) and were registered in SES. Other AIs recorded in all 3 studies were meropenem and fluconazole (4/100 in PrCS both), but third commonly used AI in PrCS, penicillin G (6.3/100) was not recorded in PPS.

Conclusion: On a single (small) country level short-term surveys likely underestimate the extent and variety of AI use. Which method to prefer depends on the problem addressed and the cohort studied.

LINEZOLID TREATMENT OF NOSOCOMIAL RESISTANT GRAM-POSITIVE BACTERIA IN NEONATES

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Background and aims: Linezolid is used for the treatment of infections caused from resistant Gram-positive bacteria. Linezolid use in children has already been approved in USA, but not yet in Europe and limited data exists regarding use in neonates.

Methods: We retrospectively analyzed the medical records of neonates who received linezolid from 1/2009-12/2011 in neonatal units.

Results: During the study period, linezolid was used in 37 neonates (23 females, 14 males), 25 of them were (67.6%) preterm. The median age on admission was 4 ± 3.03 (median \pm SE) days (IQR:1-23) and the median age at linezolid administration was 49 ± 11.19 days (IQR:23-156.50). The duration of therapy ranged from 2 to 25 days. Reasons for linezolid administration were Vancomycin Resistant Enterococcus (VRE) bacteremia (35.1%, 13 cases), VR S.aureus bacteremia (10.8%, 4 cases), gram-positive bacteremia that did not respond to vancomycin or teicoplanin (40.5%, 15 cases) and VRE colonization in neonates with fever (8.1%, 3 cases). The administration of linezolid was not clearly justified in 2 cases (5.4%). Linezolid was used as second line therapy and co-administered with other antibacterial or antifungal agents depending on patients' situation. Complications including thrombocytopenia, elevation of bilirubin concentration, anemia, leucopenia and neutropenia occurred in 7 neonates (18.9%). Administration was stopped in 1 neonate due to severe thrombocytopenia. Linezolid administration led to clinical improvement in 30 neonates (81.1%) while 7 (18.9%) died.

Conclusions: In the neonates studied, linezolid was generally effective, well tolerated and can be proved valuable for the treatment of resistant bacteria in this age group.

SAFETY, TOLERANCE AND OUTCOME OF TREATMENT WITH VORICONAZOLE IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS

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Background: Whereas voriconazole (VRC) is an approved option for management of invasive fungal infections (IFI), little is known about its use in pediatric patients. We conducted a retrospective, single-center study of safety, tolerance and antifungal efficacy of VRC in immunocompromised children and adolescents requiring VRC therapy.

Methods: The cohort included 107 patients (0.2-18y; mean:10.1y; 62 males) with hematological disorders (85; 42 post allo-HSCT), immunodeficiencies (9), AIDS (4), metabolic diseases (5) and solid tumor (4) who received 252 courses of VRC for possible (12) and probable/proven (25) IFI, as primary (127) or secondary (79) prophylaxis or as empiric therapy (9). VRC was given IV (10) and (37)/or (205) PO at recommended dosages until intolerance or maximum efficacy.

Results: VRC was administered at a median maintenance dosage of 5.9 mg/kg BID (r, 2.2-22.0) for a median of 65 days (r, 1-1002). Increases in hepatic transaminases (53.5%), bilirubin (23.6%) and alk. phosphatase (10.9%), skin eruptions (5.6%) and neurological adverse events (AEs) (4.8%) were mostly mild to moderate; AEs necessitating discontinuation of VRC occurred in 18 courses (7.1%). While mean alk. phosphatase, AST and bilirubin values were slightly elevated at end of treatment (EOT) ($p < 0.01$), mean ALT and serum creatinine values were not different from baseline. Treatment success was observed in 16/37 pts with proven/probable/possible infections, and in 203/215 courses of empiric therapy/prophylaxis. Overall survival was 97.6% at EOT and 92.1% at 3 month post EOT, respectively..

Conclusions: VRC displayed acceptable safety and tolerance and was effective in the management of pediatric IFIs.

IMPACT OF A TARGETED EDUCATIONAL TRAINING PROGRAMME ON REDUCING INAPPROPRIATE ANTIBIOTIC PRESCRIBING FOR CHILDREN IN A&E

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Background and aims: Increasingly, children in the UK are attending Accident & Emergency (A&E) with common infections, but there are limited data on antibiotic prescribing in this setting. We therefore developed an education programme on optimal antibiotic prescribing for otitis media and tonsillitis via tutorials, online interactive cases and posters and conducted a before and after audit to monitor its impact.

Methods: The post education audit of antibiotic use in children aged less than 16 years attending A&E ran from 14th and 26th of November 2011. Data collected through a standardised questionnaire included patient demographics, diagnosis, doctor's training-grade, and antibiotic therapy.

Results: Of 1127 children with a median age of 3 years, (IQR1.1,8.4) attending A&E over a 14day period, 130(11.5%) received antibiotics. The commonest antibiotics prescribed were amoxicillin 42(30%), co-amoxiclav 31(24%), and phenoxymethylpenicillin 16(13%). 13(5.6%) of 231 children with surgical and 114(13%) of 854 medical diagnoses received antibiotics.

The six main medical diagnoses were upper respiratory tract infection 157(18.4%), gastroenteritis 66(7.7 %), bronchiolitis 44(5%), lower respiratory tract infection 35(4%), tonsillitis 30(4%) and 18(2%) otitis media, with 9%, 0%, 0%, 77%, 50% and 56% receiving antibiotics, respectively. After the educational intervention a reduction of antibiotic prescribing was observed by 25% and 32% for tonsillitis and otitis media, respectively.

Conclusions: An overall reduction of antibiotic prescribing was observed following the educational initiative, particularly for the focused intervention on otitis media and tonsillitis. However there is a need to determine the optimal methodology to maintain these outcomes within an antibiotic stewardship program.

PAEDIATRIC ANTIMICROBIAL STEWARDSHIP PROGRAMME IMPLEMENTATION STUDY**S. Vaughan**¹, K. Doerholt², A. Brett², M. Sharland²¹*Paediatric Medicine*, ²*Paediatric Infectious Diseases, St Georges Healthcare NHS Trust, London, UK*

Background and aims: Antimicrobial stewardship aims to reduce inappropriate prescribing and optimise antimicrobial use to improve outcomes, minimise adverse effects and limit resistance. There is however little published data on its successful implementation in the European Paediatric population.

In 2011 the UK government published Antimicrobial Stewardship guidance 'Start smart - then focus' which outlined best practice for UK hospitals. It described the Antimicrobial Prescribing Decision - a clinical review with 5 prescribing options: **Stop**, **Switch** IV to oral, **Change**, **Continue** and **OPAT** (outpatient antibiotics).

We performed a study to evaluate the implementation of this guidance for UK Paediatric patients.

Methods: Patient episodes involving IV antimicrobials were prospectively assessed from October to December 2011 for Paediatric Medical, Oncology and Surgical patients.

Clinical information, investigations and microbial results were reviewed and the recommended Antimicrobial Prescribing Decision determined and fed back to clinical teams as appropriate.

Outcome data was reviewed to determine any readmission or microbiological relapse after decision implementation.

Results: 81 patient episodes were assessed with an average of 9 patients receiving IV antimicrobials per review day. There was a total recommended intervention rate of 45%.

There were no microbiological relapses and 3 readmissions, unrelated to the prescribing decision made.

The process was calculated to have taken 30 minutes to perform per patient episode.

Conclusions: Implementation resulted in a 45% recommended intervention rate.

The process was however time consuming, in part due to the current lack of electronic data capture.

Clearer outcome and process measures are required to further measure impact.

USE OF COLISTIN IN PEDIATRIC PATIENTS AT A PEDIATRIC INTENSIVE CARE UNIT IN TURKEY

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Background and aims: The aim of this study is to document the clinical characteristics and outcomes of use of colistin in pediatric patients at a pediatric intensive care unit (PICU) in Turkey.

Methods: We reviewed the medical and laboratory records of 29 critically ill children who were treated with colistin for 38 courses between January 2011 and December 2011 at the Department of PICU in Ankara University Medical School, Turkey.

Results: The age ranged from 3 to 217 months with a mean age of 51,2 months and male-to-female ratio was 1:1.37. Chronic neurological or neuromuscular disease (34,2%), primary immun deficeiciency (18,4%), congenital heart disease (18,4%), and malignant (15,7%) were the most common underlying diseases. There were frequently mechanical ventilation, central venous catheter, urinary catheter, ventriculoperitoneal shunt, tracheostomy cannula, chest tube, peritoneal dialysis catheter, and broad spectrum antibiotic usage as the risk factors. Ventilator-associated pneumonia (24 patients) was the leading diagnosis followed by, catheter related blood stream infection (7 patients), bacteremia (3 patients), CNS shunt infection, peritonitis and pneumonia (1 patient). The most commonly isolated microorganisms were *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Serratia marcescens*, *Stenotrophomonas maltophilia*, and *Enterobacter cloacae*. Twenty-eight of 38 courses had a favorable outcome and six of the ten deaths were infections-related. We did not determine nephrotoxicity and neurotoxicity associated with use of colistin.

Conclusions: Use of colistin in severe nosocomial infections caused by multidrug resistance gram negative bacteria appears to be well tolerated and efficacious in most of the cases in PICU.

ANTIBIOTIC PRESCRIBING IN EUROPEAN NEONATAL INTENSIVE CARE UNITS: SERVICE EVALUATION STUDY OF THE EUROPEAN STUDY OF NEONATAL EXPOSURE TO EXCIPIENTS

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Background: Little is reported about variations in antibiotic (AB) prescribing practice between different neonatal units (NICU) in Europe.

Aims: To describe the variability and extent of off-label AB use in NICUs across Europe.

Methods: Subanalysis of data from a Europe-wide service evaluation questionnaire of the ESNEE project recording all medicines prescribed to neonates within a 3-day period. AB were classified as frequent - used in >50% of units where AB was prescribed; moderate - in 25-50% and rare - in < 25% of units. AB were analysed with regard to their labelling status according to UK electronic Medicines Compendium (UKeMC) and the Thomson Micromedex database (TMd).

Results: Of 31 invited European countries, 22 with 126 NICUs (60% 3rd and 30% 2nd level) joined the study (response rate 71%) with overall coverage of 758,333 births. AB were prescribed in 112 (88.9%) units with 65 different active ingredients involved. The number of different AB per unit varied from 1 to 17 (median 5), the most common being gentamicin used in 83 (74%) and ampicillin in 58 (52%) units. Moderately used AB included vancomycin (48%), benzylpenicillin (33%), cefotaxime (32%), fluconazole (29%), metronidazole (29%) and meropenem (28%). Of eight commonly used AB only meropenem is off-label for term neonates, but 7 and 3 agents are off-label for preterm neonates according to the UKeMC and TMd, respectively.

Conclusions: Despite variable labelling status a wide list of AB are prescribed to neonates. More research focusing on the most frequently used AB in preterm neonates is needed.

THE NEONATAL AND PAEDIATRIC ANTIMICROBIAL WEB-BASED POINT PREVALENCE SURVEY (PPS): VARIATION IN ANTIBIOTIC TREATMENT IN 57 HOSPITALS WORLDWIDE IN 2011

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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 (<http://www.arpecproject.eu/>). The study aimed at analyzing paediatric and neonatal antimicrobial prescribing patterns in hospitals within Europe and globally, to identify targets for quality improvement.

Methods: A one-day PPS on antibiotic use in hospitalised children was conducted in September 2011 in 36 hospitals of 14 European countries and 21 hospitals of 8 countries worldwide (Australia, Gambia, Georgia, Ghana, Iran, Malawi, Saudi Arabia, USA), 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 3801 paediatric and 1363 neonatal inpatients reported. Overall, 1517 (40%) paediatric patients and 399 (29%) neonates received at least one antibiotic.

Overall, 16 antibiotics accounted for 75% of total paediatric use (DU75%). These included 6 oral administered antibiotics which accounted for 16% of use. Paediatric top four 'therapeutic' antibiotic classes were third-generation cephalosporins (22%), aminoglycosides (14%), broad-spectrum penicillins (9%) and glycopeptides (7%).

Neonatal DU75% included 9 antibiotics. Neonatal treatment of systemic infections included antibiotic combinations in 64% of neonates. Most frequently prescribed were combinations of aminoglycosides (46%) with ampicillin or amoxicillin (15%), benzylpenicillin (12%) (mainly African countries) or third-generation cephalosporins (9%).

Conclusion: We identified two quality indicators: predominant therapy with third-generation cephalosporins for paediatric patients and prescription of antibiotic combinations with broad-spectrum antibiotics for neonates in Europe and globally, except for Africa.

THE NEONATAL AND PAEDIATRIC ANTIMICROBIAL WEB-BASED POINT PREVALENCE SURVEY (PPS): SURGICAL PROPHYLACTIC ANTIBIOTIC USE IN 57 HOSPITALS WORLDWIDE IN 2011

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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 (<http://www.arpecproject.eu/>). We aimed at analyzing paediatric and neonatal surgical prophylactic antibiotic prescribing patterns, to identify targets for quality improvement.

Methods: A one-day PPS on antibiotic use was completed in September 2011 in 14 European and 8 countries worldwide (Australia, Gambia, Georgia, Ghana, Iran, Malawi, Saudi Arabia, USA), using a validated and standard method.

Results: Out of 2311 and 718 antibiotics prescribed for children (n=1517) and neonates (n=399), 256 (11%, n=209 children) and 48 (7%, n=26 neonates) were prescribed for surgical prophylaxis, respectively.

For paediatric surgical prophylaxis, mainly first-generation (22%), second-generation (18%) and third-generation cephalosporins (16%) followed by a combination of penicillins (11%) were prescribed. 19% of the children received a combination of 2 or 3 antibiotics for surgical prophylactic use.

For neonatal surgical prophylaxis, mainly third-generation cephalosporins (29%) were prescribed, followed by an aminoglycoside (21%) in combination with either a glycopeptide (30%), metronidazole (30%) or a third-generation cephalosporin (30%). Most neonates received a combination of 2 (46%) or 3 (19%) antibiotics for surgical prophylactic use.

The duration of surgical prophylaxis was >1 day in 78% for children and 100% for neonates.

Conclusion: We identified three quality indicators: surgical prophylaxis with cephalosporins, the substantial number of antibiotic combinations used for surgical prophylaxis; and a high proportion of surgical prophylaxis prescribed for more than 1 day.

ANTIBIOTIC SUSCEPTIBILITY OF AEROBE BACTERIA ISOLATED FROM COMMUNITY-ACQUIRED APPENDICITIS IN CHILDREN. HOW MUCH TREATMENT RECOMMENDATIONS FIT IN EVERYDAY PRACTICE?

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Background and aims: Intra-abdominal infection is a common complication of appendicitis. Enterobacteriaceae and anaerobes are the major pathogens involved. The empirical monotherapy with ampicillin-sulbactam or ertapenem is recommended by recent Consensus Conference and Guidelines in pediatric patients. We evaluated the applicability of these two recommendations in children with community-acquired secondary peritonitis treated at our hospital from 2005 to 2011.

Methods: All strains isolated from peritoneal fluid in acute, primary appendicitis were retrieved from the Laboratory of Microbiology database. Identifications of the strains and susceptibility tests were performed by the automated system Phoenix 100 (BD). The Minimal Inhibitory Concentrations (MIC) was interpreted using EUCAST breakpoint.

Results: 114 bacterial strains were isolated: E.coli represented the most frequent pathogen (73%), followed by P.aeruginosa (13%) and enterococci (5%). 30% of E.coli were resistant to ampicillin-sulbactam, but 24 of them were susceptible to gentamycin. All P.aeruginosa resulted susceptible to gentamycin. All enterococci resulted susceptible to ampicillin-sulbactam and gentamycin. All strains tested to ertapenem resulted susceptible.

Conclusion: Antimicrobial therapy plays an integral role in the management of appendicitis with intra-abdominal infections. In our series, monotherapy with ampicillin-sulbactam would have presented an overall failure rate of 36% (41/114). However, the addition of gentamycin to the initial therapy would reduce the failure rate to 0.9%. Meanwhile, all the other bacteria isolated were susceptible to at least one of these. In light of our data we suggest that gentamycin should be added to ampicillin-sulbactam or ertapenem for the initial empirical therapy of aerobes that cause secondary peritonitis in children.

ANTIBIOTIC PRESCRIBING IN CHILDREN FOR COMMUNITY ACQUIRED PNEUMONIA IN ESTONIA; IN A COUNTRY WITH LOW PNEUMOCOCCAL PENICILLIN RESISTANCE

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Background and aims: Penicillin G (100,000 IU/kg/daily) and amoxicillin (40-60 mg/kg/daily) are the first line and clarithromycin the second line treatment for uncomplicated CAP in our hospital. To look into the adherence to the guidelines we conducted a service evaluation survey in Tartu University Children's Hospital.

Methods: We retrospectively reviewed 100 consecutively admitted cases of CAP starting from 01.01.2010. CAP diagnosis was based on typical clinical and radiological findings; all chest X-rays were reviewed by a paediatric radiologist.

Results: The survey included 99 cases admitted over a period of 13 months; the median age was 3.0 years (IQR 1,7; 7.0) and median duration of hospitalization 3 days (IQR 2; 4). Etiology was confirmed in 9 cases. Overall 22% of patients had received antibiotics (AB) prior to hospitalization. The most common AB used in hospital were penicillin G (n = 33; mean dose 122,300 IU/kg/daily) and clarithromycin (n =26; 14.5 mg/kg/daily). Oral amoxicillin (55 mg/kg/daily), cefuroxime (106 mg/kg/daily) and phenoxymethylpenicillin (95,100 IU/kg/daily) were given to 11, 12 and 9 patients, respectively. In half of the patients AB was started intravenously and switched to oral agents on a median of day 3. A total of 8 patients (5 with chronic condition) were admitted to intensive care unit and treatment initiated with 3rd generation cephalosporins. All but 1 patient (who died) recovered completely.

Conclusions: We found a good adherence to local CAP treatment guidelines and suggest that penicillin G and clarithromycin still remain the optimal treatment for mild to moderate CAP.

PATTERNS AND TRENDS OF ANTIMICROBIAL USE IN A PEDIATRIC INTENSIVE CARE UNIT (PICU) USING DAYS OF THERAPY

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Background and aim: Monitoring of antimicrobial use is essential for antimicrobial stewardship programs. We studied pattern and time trends of antimicrobial use in PICU.

Methods: A retrospective analysis of monthly antimicrobial agent use at a patient-level was conducted in an 8-bed polyvalent PICU of a general university hospital from 2009 to 2011. Days of therapy (DOT) of each antimicrobial agent/category divided by 100 bed-days (DOT/100BD) was used.

Results: During study period there were 403 admissions and a median monthly rate (MMR) of 167 bed-days. Aminoglycosides constituted the most common used antimicrobial class (MMR 64 DOT/100BD), but showed a significant decrease during study ($p=0.002$). Cephalosporins were the second most used antimicrobial class (MMR 40 DOT/100BD) with 3rd generation cephalosporins (GC) being the most prevalent (MMR 21 DOT/100BD). Use of 2nd GC was frequent (MMR 8 DOT/100BD), but showed a significant decrease ($p=0.046$); whereas, use of 4th GC was lower (1DOT/100BD) but with increasing rates ($p=0.005$). Utilization of glycopeptides (vancomycin and teicoplanin) had a constant MMR of 32 DOT/100BD. Carbapenems (mainly meropenem), piperacillin/tazobactam (the most used penicillin) and colistin had MMR of 23, 15 and 15 DOT/100BD, respectively. Both metronidazole and clindamycin had a MMR of 12 DOT/100BD with the latter showing a constant decrease ($p=0.014$). Use of other antimicrobials included macrolides, ciprofloxacin and cotrimoxazole with MMR of 6, 5 and 5 DOT/100BD, respectively. Linezolid use was infrequent but with increasing trends ($p=0.002$).

Conclusion: High prevalence of antimicrobial use, especially of aminoglycosides, was found. Constant utilization of colistin is of concern.

ANTIMICROBIAL PRESCRIBING GUIDELINES FOR THE TREATMENT OF RESPIRATORY TRACT INFECTIONS IN EUROPEAN COUNTRIES

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Background and aims: Respiratory tract infections (RTIs) are among the commonest indications for antibiotic use in children. The aim of this study was to explore the existence of antimicrobial prescribing guidelines within different European paediatric hospitals and seek for possible variation in first line drugs, dose calculation and length of treatment.

Methods: In this pilot survey which is part of the ongoing European project "Antibiotic Resistance and Prescribing in European Children" (ARPEC), a web-based preformed questionnaire was used during the last 2 weeks of September 2011 to assess availability of guidelines, and recommended antibiotic treatment of RTIs.

Results: 25 hospitals from 16 countries responded to the guidelines questionnaire. For URTIs an average of 50% reported the existence of guidelines. Almost 85% of hospitals use penicillin and amoxicillin for tonsillitis and 90% use amoxicillin for otitis. Co-amoxiclav was suggested in 50% of respondents for sinusitis. Treatment duration varied between 5-10 days. In terms of LRTIs 80% and 60% of the participants reported no existence of treatment guidelines for bronchitis and pneumonia respectively. Amoxicillin is the sole recommended first line drug for pneumonia in < 5 year old children while in older children a macrolide is recommended by 40% of the participants. The duration of therapy for pneumonia varied between 7-10 days for younger children and 5-10 days for older children.

Conclusions: Guidelines for respiratory infections follow most recommendations from reference sources. However we need to link guidelines to actual antibiotic use and identify factors that may influence guideline implementation.

CASPOFUNGIN EXPERIENCE IN PEDIATRIC PATIENTS

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Caspofungin, the first licensed echinocandin, is a novel class of antifungal and is approved for use in children 3 months of age or older for the treatment of invasive candidiasis, salvage therapy for invasive aspergillosis and as empirical therapy for febrile neutropenia. One hundred and eighteen male, 180 female total 298 children having ages between 1 months-20 years (mean:7,47±5,48) were administered caspofungin using body surface area regimen (first day 70/mg/m² and then 50 mg/kg/m²/day). Of the patients 151 (50,8%) of them had the therapy because of neutropenic fever, 43(14,4%) because of pneumonia, 38 (12,8%) because of sepsis, 36 (12,1%) empirically because of underlying disease, 25 (8,4) because of microorganism obtained from culture and 5 of them because of unresolving fever with unknown etiology. As side effects and adverse reactions 3 patients had rash, 2 had diarrhea and 1 had hypokalemia. This retrospective data shows that caspofungin is generally well tolerated.

ANTIMICROBIAL PRESCRIBING GUIDELINES FOR THE TREATMENT OF NEONATAL SEPSIS IN EUROPEAN COUNTRIES

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Background and aims: Our aim was to explore the existence of treatment guidelines for severe infections such as neonatal sepsis within different European paediatric hospitals, and seek for possible variation in first line drugs.

Methods: In this pilot survey which is part of the ongoing European project "Antibiotic Resistance and Prescribing in European Children" (ARPEC), a web-based preformed questionnaire was used during the last 2 weeks of September 2011. Questions referred to availability of guidelines, source (national or local guidelines) and specific information on the recommended treatment of sepsis in neonates.

Results: 25 hospitals from 16 countries participated in the survey. Nine hospitals responded to neonatal sepsis questionnaire. Lack of guidelines was noted in 60% of the participants. In all reports combined therapy is recommended. Five different combinations are proposed as first line treatment for early onset (EO) sepsis and 9 different schemes for late onset (LO) sepsis. In particular for EO sepsis 7:9 of participants recommend penicillin with aminoglycoside as first line drug, 1:9 ampicillin with 3rd generation cephalosporin and 1:9 ampicillin with 3rd generation cephalosporin plus aminoglycoside. For LO neonatal sepsis 5:9 of hospitals use penicillin with an aminoglycoside, 2:9 antistaphylococcal penicillin with aminoglycoside, 1:9 ampicillin with a 4th generation cephalosporin and 1:9 3rd generation cephalosporin plus aminoglycoside.

Conclusions: There is a significant variation on antibiotic guidelines for the treatment of neonatal sepsis between different European hospitals. It needs to be clarified if local epidemiology and antimicrobial resistance justifies this great variation.

EFFICIENCY OF ORAL ACYCLOVIR TREATMENT OF HERPETIC GINGIVOSTOMATITIS IN PRESCHOOL CHILDREN

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Background and aims: Herpetic gingivostomatitis (HG) has the general course which lasts 10-14 days. Children refuse to eat and drink and require hospitalisation because of dehydration. We investigated the efficiency of oral acyclovir applied 30mg/kg/day for HG in preschool children.

Methods: For retrospective clinical study data was collected between March 1st 2005 and December 31th 2011. 95 immunocompetent children aged 1-7 years with clinical manifestations of HG were divided into three groups. Group one- G1 (33) were given acyclovir 30mg/kg/day in first 72 hours after illness onset. Group two-G2 (30) started with acyclovir therapy after this period, and control group - CG (32) was receiving only antipyretics. We compared duration of fever, oral lesions and eating difficulties between groups.

Results: G1 had oral lesions for a shorter period than G2 and CG (6.15 v. 8.97 and 8.22 days respectively, $p < 0.001$) and shorter duration of fever (4.27 v. 5.83 and 6.28 days respectively, $p < 0.001$); and refusing to eat (4.42 v. 6,27 and 5,88 respectively, $p < 0.001$). There were not significant differences between any outcomes in children in G2 and CG.

Conclusion: Oral acyclovir given 30mg/kg/day for HG, started within the first three days of onset, shortens the duration of all clinical manifestations in affected children. There were no proven benefits if therapy started after this period.

MANAGEMENT OF PARENTS WITH LEFTOVER ANTIBIOTICS, PRESCRIBED TO THEIR CHILDREN**E. Huijssen-Huisman**^{1,2}, G. Van Berlaer¹, L. Faverey¹, Y. Vandenplas¹, F. Brus², M. Ruigen², I. Hubloue¹¹*UZ Brussel - Vrije Universiteit Brussel, Brussels, Belgium*, ²*Juliana Kinderziekenhuis, The Hague, The Netherlands*

Introduction: In Belgium, antibiotics are sold by package, in The Netherlands by dose. We hypothesize that when sold by package, parents risk to have more often antibiotics left. When thrown away, it is burden for the environment or by reusing on own initiative, it adds to the risk of bacterial resistance.

Methods: Survey (hold in Brussels and The Hague)

Results:

Belgium pilot: 60 surveys (25 Dutch, 35 French).

Tablets: almost equally mentioned to been thrown away, stored or returned to the pharmacy, Only 4 times it was reused on own initiative.

Syrups/crèmes: It was often reused or brought back to the pharmacy. Less often thrown in the bin of toilet. 63% of the parents checked the expiry date on a new and 58% on a used product.

Dutch pilot: 47 surveys

Tablets: It was most often returned to the pharmacy, then thrown in a bin, sometimes reused.

Syrups/crèmes: it was most often thrown away or flushed in the toilet, then returned to the pharmacy. It was quite often re-used.

91% of the parents checked the expiry date on a new and 81% on a used product.

Conclusion: In both countries tablets were more often returned to the pharmacy then syrups/crèmes. Both are often thrown away. Self-medication is mentioned by parents. This seems to be more often the case for syrup/crèmes. Dutch people return more often old medication to the pharmacy.

Discussion: Based on this pilot, the survey has been adapted, expecting the results by the end of February.

TEETH AND TONGUE DISCOLORATION AFTER INTRAVENOUS TREATMENT WITH LINEZOLID IN THREE CHILDREN

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Linezolid treatment is administered more often in children because of the increasing frequency of methicillin-resistant *Staphylococcus aureus* in the community. As with any new medication, some rare side effects are reported during post-licensure surveillance.

We describe three children that developed teeth and tongue discoloration while receiving intravenous linezolid for 2-3 weeks. The teeth discoloration was superficial and reversible and the teeth color returned gradually to normal with dental cleaning. The tongue discoloration lasted shorter and returned gradually to normal after linezolid was discontinued. Linezolid was co-administered with piperacillin-tazobactam or meropenem. Tongue discoloration after linezolid administration was initially reported in clinical trials. However, teeth discoloration has been reported in post-licensure use. There are only two separate case reports in the current English literature about tooth discoloration in two children receiving linezolid treatment per os.

We report a rare association of linezolid administration with teeth and tongue discoloration in children, which was reversible with discontinuation of the drug.

MACROPHAGE TARGETED SYSTEM(S) FOR EFFECTIVE MANAGEMENT OF TUBERCULOSIS**D. Dube***Dr. H. S. Gour University, Sagar, India*

In the last two decades, tuberculosis has gone from being a forgotten disease to a modern and recrudescing pathology. Tuberculosis is a curable bacterial infection and most of the negative therapy outcomes are related to extremely low patient compliance, which could be solved by new drug delivery approaches. The purpose of the present study was to develop antitubercular drug loaded surface modified PLGA particles which may significantly enhance the rate and extent of uptake and provide controlled delivery for treatment of tuberculosis. The study further investigates the role of particles as potential stimulators of the macrophage's innate microbicidal responses. Plain and surface modified PLGA particles were prepared and parameters such as particle shape and size, zeta potential, % entrapment efficiency, *in vitro* drug release, *in vitro* cytotoxicity, macrophage uptake, *in vivo* biodistribution and hepatotoxicity were determined. The average particle size of surface modified particles was found to be 489 ± 16.4 nm. The drug entrapment was found to be appreciable. FACS analysis depicted better internalization efficacy of surface modified particles than plain particles. The organ distribution studies demonstrated the superiority of the particulate formulation for preferential accumulation of drug in macrophage rich organs. Thus the results confirm that the developed delivery systems possessed an enhanced antitubercular activity in mice and are capable of reducing hepatic toxicity induced by antitubercular drug.

CAGA+ HELICOBACTER PYLORI IN DENTAL PLAQUE AND GASTRIC BIOPSY OF IRANIAN CHILDREN IS RELATED TO SEVER GASTRIC DISEASE

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Background and aims: To establish whether presence of *cagA+* *Helicobacter pylori* in both dental plaque and gastric biopsy of children is related to sever clinical manifestations.

Methods: One hundred dyspeptic children referred for upper gastrointestinal endoscopy participated in this study. After precise clinical examination, Cumulative dental plaque specimens and gastric biopsies were submitted to histological examination, rapid urease test and polymerase chain reaction (PCR) assays with two sets of primers for *ureC* and *cagA*, to detect the presence of *cagA*.

Results: All children attending this study were under 10 years old and had gastric complications. We looked for a relationship between presence of *cagA* + *Helicobacter pylori* in dental plaque and gastric biopsy with severity of clinical findings assesses via histological examination. Our results show that 85 cases(85%) had h. pylori in their stomach, due to results of PCR with ureC. 69 (59%) had helicobacter pylori in their dental plaque and gastric biopsy. 29 cases(39 %)of these patients had *cagA+* *Helicobacter pylori* in their dental plaque and gastric biopsy and based on histological examinations, 21 (73%) had active gastritis, 7(25 %)had peptic and duodenal ulcers and 1 of them(2%)had premalignant lesions, such as gastric atrophy.

Conclusions: Our results revealed that *cagA* is a virulence factor which results in sever clinical gastric disease in many cases .Also It is confirmed that the rate of infection in childhood is very high, so it may be helpful to carry out the screening test in children.

NEISSERIA MENINGITIDIS W135 INVASIVE INFECTIONS IN CHILDREN: EPIDEMIOLOGICAL, CLINICAL AND GENOTYPIC FEATURES IN A FRENCH NATIONAL SURVEY

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Background and aims: Invasive Meningococcal Disease (IMD) due to W135 serogroup has been described since 40 years, but few data are available, especially for children. The epidemiological, clinical and microbiological features of W135 IMD collected from 2001 to 2008 in two French national surveys are presented here.

Methods: The French National Reference Center for meningococci and the GPIP/ACTIV network of 252 pediatric wards prospectively collected the cases of IMD: W135 IMD was defined by a positive culture or PCR in a normally sterile site. Genotyping was performed to classify positive cultures according to clonal complex.

Results: A total of 119 cases of W135 IMD (4% of IMD) were reported in children, among which 54% were infants (peak incidence between 6 and 9 months). The M/F sex ratio was 1.2. The number of cases decreased from 24 in 2002 to 9 in 2008. The initial clinical status was meningitis (66%), arthritis (8%), purpura fulminans (5%) or meningococemia (21%). Among the 99 genotyped isolates, 53 were ST-22, 42, ST-11, 3, ST-174 and 1, ST-23. Clonal complex ST-11 prevailed in greater Paris, Reunion island and Mayotte, and ST-22 in the rest of France. Meningitis was more frequent for ST-11 (83% vs. 57% for ST-22, $p = 0.007$). Mortality was 6% (7/119) and did not differ according to clonal complex.

Conclusions: Isolates of the clonal complex ST-22 were the most prevalent in W135 IMD and were frequently associated with non-meningeal presentation. Further investigations of clinical tropism of W135 isolates are warranted.

CLINICAL PRESENTATIONS, LABORATORY RESULTS OF PATIENTS WITH KIKUCHI'S DISEASE: THE ASSOCIATION BETWEEN MYCOPLASMA, STREPTOCOCCUS INFECTION AND THE PATHOGENY OF KD

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Background: Kikuchi's disease(KD), also known as histiocytic necrotizing lymphadenitis (HNL), is a benign and selflimiting disease. Past studies suggest that viral infection is associated with KD. There is limited data on the association between mycoplasma, streptococcus infection and the pathogeny of KD. **Materials and methods:** Between August 1999 and October 2011, a total of 19 patients who were younger than 18 years underwent cervical lymph node biopsies and received a diagnosis of KD. Clinical features, laboratory values of our pediatric patients, and long-term follow-up results are discussed. The follow-up period averaged 5 years.

Results: There were 5 girls and 14 boys with a mean age of 11.9. Overall, 94.7%(18) of our patients presented with tender lymphadenopathy, 89.5%(17) with fever and 78.9%(15) with tender lymph nodes. The most common laboratory findings were elevated erythrocyte sedimentation rate 94.7%(18), elevated serum lactate dehydrogenase 55.5%(10), elevated C-reactive protein 38.9%(7), lymphocytes 42.1%(8) and leukopenia 42.1%(8). In addition, 2 patients had an elevated Antistreptolysin "O", 2 patient with prodrome of upper respiratory tract infection, had mycoplasma IgM antibody-positive in the serum, 17 patients followed a benign course, with spontaneous resolution of fever and lymphadenopathy. However, 2 patients with follow-up of more than 6 months had clinical recurrence of KD. No patients developed an autoimmune disease.

Conclusion: In addition to virus infection, mycoplasma and streptococcus infection may also be associated with KD. The prognosis for KD patients is generally optimistic; however, a concurrent autoimmune disease or the risk of developing an autoimmune disease requires long-term follow-up.

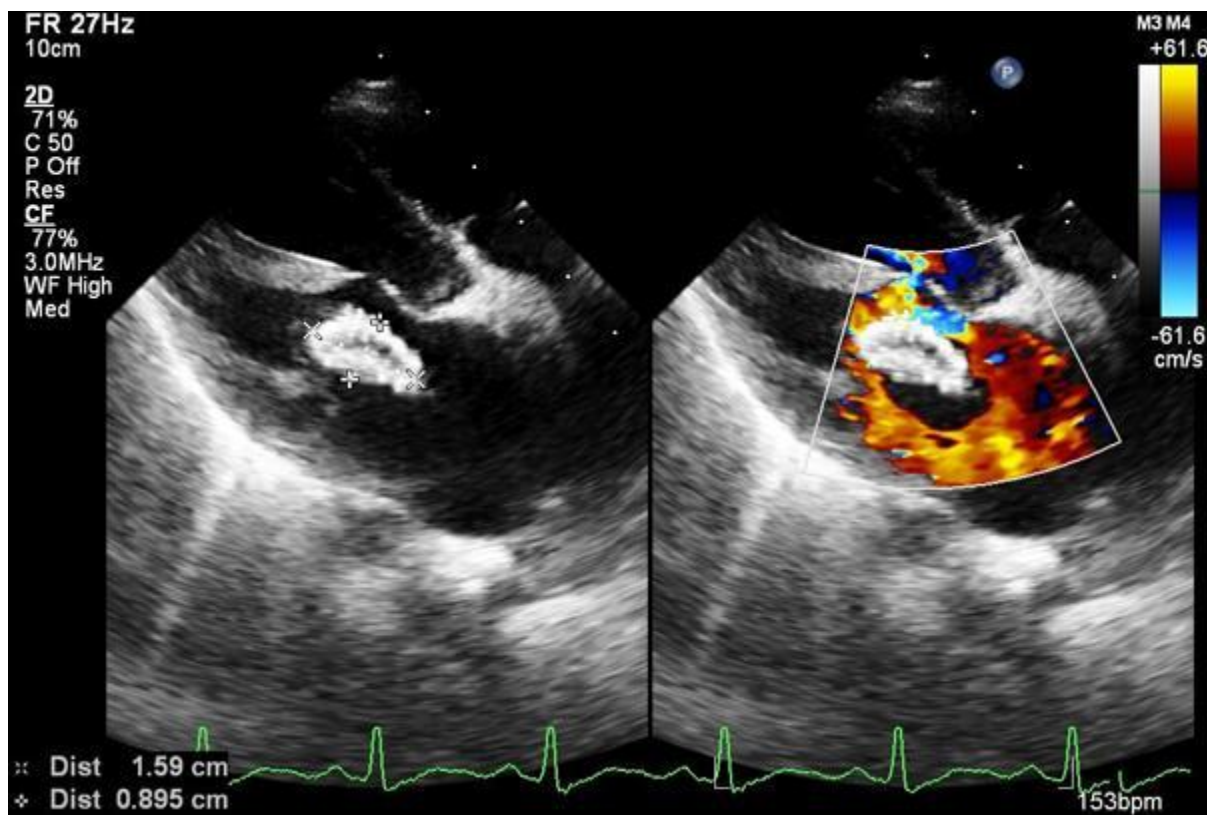
A RARE CASE OF FULMINANT KINGELLA ENDOCARDITIS IN A TODDLER WITH MILD PYREXIA

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Background and aims: We present a year old noted to have mild grade pyrexia for about four weeks and was prescribed oral antibiotics. He continued to be pyrexial and was progressively breathless. He developed a systolic murmur and was referred to paediatric cardiologist.

Methods: On examination he had profound signs of cardiac failure with a loud pan systolic murmur and enlarged Liver. He was ventilated and transferred to a tertiary cardiac unit. His 2D ECHO showed massive vegetation on his posterior mitral valve leaflet measuring about 1.5 * 1.2 cm with torrential mitral valve regurgitation and a large dilated left atrium. His heart was otherwise normal. He was started on broad spectrum antibiotics and Inotropes but continued to deteriorate.



[Mitral valve Endocarditis]

Results: He was taken for mitral valve repair/replacement. Intraoperative findings showed a massive vegetation on the posterior leaflet of mitral valve. The Mitral valve was damaged beyond repair, hence Mitral valve was replaced. The tissue analysis and blood PCR were both positive for kingella, a rare organism of HACEK group. He made a dramatic recovery after surgery and his cardiac function had normalised in few weeks.

Conclusions: Mild grade pyrexia is a very common symptom in children but if persistent can potentially be serious. Infective Endocarditis is rare in a child with a structurally normal heart, but prolonged pyrexia should alert to it and a prompt referral to a cardiologist is crucial in making a diagnosis and prevent a potentially fatal condition.

PECULIARITIES OF SALMONELLA CARRIER STATE AFTER ACUTE GASTROENTERITIS IN CHILDREN**M. Marengolciene**¹, E. Tamuleviciene², G. Leviniene², V. Cirvinskaite²¹*Outpatient Department of Children Infectious Diseases,* ²*Lithuanian University of Health Sciences, Medical Academy, Clinic of Children Diseases, Kaunas, Lithuania***Aim:** To analyse the peculiarities of Salmonella carrier state after acute gastroenteritis in children.**Method:** Data of 29 cases of children (boys - 13, girls -16) acute gastroenteritis, caused by *Salmonella* was analyzed in outpatient department of Kaunas Clinical Hospital in 2011. *Salmonella spp.* was identified microbiologically and the stool culture was repeated after 2 weeks, 1 - 2mo and till clearance in carriers group.**Results:** Gastroenteritis was caused mostly by *S.enteritidis*.20 (69%) carriers were found when the stool culture was repeated after 2 weeks, 59% (17) - after 1mo and 14% (4) carriers after 3mo and longer Patient's age was from 2 mo to 6y old. In carriers group mean age was 35,9 mo, in non carriers - 46,8 mo and the age difference between groups was significant ($p < 0,05$). Though the carrier state had more girls 13 (83,8%), than boys 7 (81%), but the difference was not significant. Antibacterial treatment was given to 17 patients, 12 (70,6%) among them were carriers. Less carriers where in not treated group - 8 (66,7%), but the difference was not significant.**Conclusions:** 69% of children had a carrier status after salmonellosis most often caused by *S.enteritidis*. Children with carrier state were younger than non carriers. The carriers and non carriers groups didn't differ significantly by gender and antibacterial treatment.

THE CLINICAL STUDY ON CD64 EXPRESSION IN INFECTED CHILDREN PRESENTING TO A HOSPITAL INTENSIVE CARE UNIT

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Objective: To evaluate the clinical value of CD64 index in Intensive Care Unit infected patients.

Methods: 60 febrile children presenting to the hospital intensive care unit from 2009.11 to 2010.03 for a retrospective nested case-control study, fever was defined as a body temperature of 38°C or higher, disease group specifically for the bacterial infection or was highly suspected with bacterial infection in 28 cases, 32 in the viral infection group, and exclusion of non-infectious diseases such as juvenile rheumatoid arthritis, Kawasaki Disease; the controls were 50 healthy children of surgical or medical examination. all cases were measured CD64 by flow cytometry, disease group also were detected for blood, ESR, PCT, blood culture and sputum culture simultaneously. all of the statistical analyses were performed using SPSS 16.0, Data are given as means \pm SE, Categorical variables were analyzed using χ^2 test.

Results: 57.1% of the bacterial group and 71.9% of the viral group showed common pneumonia. CD64 index of bacterial infection group, viral infection group and the control group were 12.6 ± 9.7 , 5.4 ± 2.42 and 2.9 ± 0.77 , bacterial and virus group relative to the control group, the CD64 index appeared increased, while the bacterial group significantly higher than the increase of the virus group, the differences between the two groups were significant ($F=11.002$, $P=0.004$).

Conclusion: CD64 index in infected children presenting to a hospital intensive care unit can be clearly distinguished with bacterial infections or viral infections, provided an important basis and a viable strategy for clinical treatment and determine the timing of withdrawal.

RISK FACTORS AND BACTERIOLOGICAL PROFILE OF NEONATAL SEPSIS IN A TEACHING HOSPITAL IN KERMANSHAH, IRAN

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Background and aims: Sepsis is the most common reason of mortality in developing countries. The pattern of bacterial agents of neonatal sepsis changes depend on geographic locations. Maternal, neonatal and environmental risk factors contribute for the development of sepsis in neonates. This study was done to determine the pattern of bacterial agents causing neonatal sepsis. We also attempted to investigate the role of maternal and neonatal risk factors responsible for neonatal sepsis.

Methods: This cross-sectional prospective study was conducted in a teaching hospital in Kermanshah, Iran. During 2006-2010, 639 neonates admitted to the hospital with a clinical diagnosis of neonatal sepsis. Blood cultures were performed from these patients. Bacterial agents identified using standard microbiological and biochemical methods. Data analysis was performed using SPSS software.

Results: Of the 639 neonates, 57.7% were males and 42.3% were females. The mean age of the neonates was 0.88 ± 9.4 days. 41.9% were preterm and 45.2% had low birth weight (< 2500 g). Of the 639 neonates investigated for sepsis, 53 (8.3%) were positive for blood culture. The most common isolated organisms were *Staphylococcus aureus* (28.3%) and *Citrobacter spp.* (21.6%) and Coagulase-negative Staphylococci (17%). Maternal risk factors such as urinary tract infection, hypertension and eclampsia were strongly associated with blood culture proven neonatal sepsis ($p < 0.05$).

Conclusions: *Staphylococcus aureus* and *Citrobacter spp.* were the most common organisms causing neonatal sepsis. We found strongly association between maternal risk factors such as urinary tract infection, hypertension and eclampsia with blood culture proven neonatal sepsis.

MULTI LOCUS SEQUENCE TYPE COMPARISON OF INVASIVE AND COMMENSAL *HAEMOPHILUS INFLUENZAE* ISOLATES FROM DELHI

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Background and aims: The most virulent strain is *H. influenzae* Type b (Hib) responsible for 95% of bloodstream and meningeal Haemophilus infections in children. Hib also constitutes a major portion of nasopharyngeal commensal flora in otherwise healthy individuals. This study was undertaken to analyze if there exist any significant genetic differences between invasive and commensal *H. influenzae* isolates.

Methods: Isolates causing invasive disease were cultured from sterile body fluid. Commensal isolates were obtained from the nasopharynx of healthy schoolgoing children aged 5-14 years. Isolates with type b serotype from both invasive and commensal isolates were detected through capB polymerase chain reaction and slide agglutination serotyping. In total 15 invasive and 13 commensal isolates were characterized through multi locus sequence typing.

Results: Serotyping revealed that all 15 invasive isolates in this study were of Type b. Seven out of 13 commensal isolates were of serotype b and 6/13 were non-Type b. MLST results showed presence of two sequence types (STs) previously described and five new STs among the Indian invasive *H. influenzae* isolates tested.

Amongst the 13 nasopharyngeal isolates tested through MLST, nine distinct STs were discovered each of which were novel.

Interpretation and conclusions: In our study of MLST involving Hib of invasive and commensal origin, it was observed that invasive Hib did not demonstrate much variation in their genome. In contrast, genetic diversity among commensal Hib was much more common implying existence of two distinct evolutionary lineages among invasive and commensal Hib.

THE INCIDENCE OF LOWER RESPIRATORY TRACT INFECTION (LRTI) ON PRESCHOOL CHILDREN

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Goce Delcev, Stip, FYR Macedonia

Introduction: Respiratory illnesses on children are common, serious and important. Chronic respiratory disease is also the second most common reason for hospitalisation.

Aim of the study: To confirm the incidence of LRTI on preschool children because that includes its large burden of disease and the effect of illness on the children.

Material and methods: The diagnosis is consist of further careful observation, auscultation and percussion. A careful routine of observation is essential to identify LRTI early because most often lower respiratory tract infection (LRTI) is accompanied by fever and may be preceded by a typical viral upper respiratory tract infection (URTI).

Results: In January to march (2011) in Clinical hospital in Shtip (R. of Macedonia) were hospitalized 392 preschool children. 79 of them had LRTI and they were hospitalised twice in the year and 3% were hospitalised five times or more. Lower respiratory infections (LRI) include bronchitis, bronchiolitis, pneumonia, empyema, endobronchial infection, suppurative lung disease, lung abscesses, croup and pertussis. Chronic respiratory infection has been demonstrated in 26% of children.

Conclusion: Results suggest that LRTI usually consist in the firs mounts of the year and they rapidly incresed every year. LRTI is an independent risk factor for cardiovascular illness.

INFECTIVE ENDOCARDITIS AT COSTA RICA'S CHILDREN'S HOSPITAL, PERIOD 2008-2011

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Background: Reports about infective endocarditis (IE) in Latin American children are scarce, and no studies from Central America have been published in the English language literature. A previous study of IE at our only pediatric tertiary referral and teaching hospital of Costa Rica (period January 2000-December 2007), documented a 25% rate of MRSA among children with staphylococcal endocarditis. Our objective was to describe and update the epidemiology and microbiology of IE at this center.

Methods: Retrospective chart review of children < 13 years of age with a hospital discharge diagnosis of IE, from January 1st, 2008 to December 31th, 2011.

Results: Twelve patients were discharged with a diagnosis of IE. 7/12 (58.3%) patients were female. Overall, 41.7% were < 5 years of age and 2/12 (16.7%) were newborns. Among risk factors, previous use of central venous catheters was documented in 33.3%, a congenital cardiac defect in 25%, and recent cardiac surgery in 8.3% of patients. Blood cultures were positive in 10 (83.3%) pts. The most common etiologic organisms included: *Staphylococcus aureus* (58.3% pts, of which 71.4% were MRSA), *Staphylococcus epidermidis* (8.3%), *Staphylococcus saprophyticus* (8.3%), and *Enterococcus faecalis* (8.3%). Surgical exploration, including removal of vegetations and valvular repair, was required in 75% of patients. No deaths occurred.

Conclusions: Due to the increasing and high rates of MRSA among children with IE at our center, oxacillin is no longer the first antibiotic choice for children with suspected staphylococcal IE and therefore vancomycin should be the first treatment option.

EVALUATION AND MANAGEMENT OF ORBITAL COMPLICATIONS OF ACUTE SINUSITIS IN PEDIATRICS**P. Izadi¹, M. Yarmohammadi¹, B. Izadi²***¹Shahed University, Tehran, ²Kermanshah University of Medical Sciences, Kermanshah, Iran*

Acute sinusitis is often a mild self-limiting disease but it can easily spread to the orbit due to close anatomic relationship and venous drainage. The most common complication in acute sinusitis is orbital infection and occur more frequently in pediatric population and it is a therapeutic emergency.

Orbital inflammation is classified by Chandlers classification into five stages as: 1) periorbital cellulitis, 2) orbital cellulitis, 3) subperiosteal abscess, 4) orbital abscess and 5) cavernous sinus thrombosis.

Fever, headache and orbital or facial swelling are most common presenting symptoms. Computed Tomography is the basis for early recognition and evaluation and sufficient treatment. Broad spectrum antibiotics and emergency surgical drainage of the affected sinus and the orbital abscess form the mainstay of treatment.

In this study we conducted the results of patients with orbital complication due to acute sinusitis in 5 years period.

Computed Tomography and ophthalmological examination are two important component in the management. Most orbital infections respond to medical treatment, but in abscess formation endoscopic sinus surgery proved to be safe and reliable as the mainstay of treatment.

NEURO PSYCHIATIC DISORDER DUE TO GABHS STREPTOCOCCAL INFECTION IN CHILDREN: A CASE CONTROL STUDY

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Background: Recent evidence suggests that group A β -hemolytic streptococcal infection may increase the risk for PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection). Object of this study was comparison the titer of antibodies against GABHS (ASOT, Anti-DNase B, and Anti streptokinase) between children with PANDS (obsessive-compulsive disorder, and attention deficit hyperactive disorders) and control group.

Methods: A cross sectional/cases control study had done in pediatric psychology clinics in Tehran (Rasoul Hospital) g 2008-2010. We compared serum antibodies against GABHS (streptolysin O, deoxyribonuclease B, and Streptokinase) quantitatively (ABCam-ELISA, USA) between 79 cases with OCD, ADHD and 39 controls (age matched). The antibody titers (IU/ml) in their sera were compared and analyzed statistically. The area under ROC, sensitivity, specificity and positive predictive value of tests calculated.

Results: Most of cases studied in summer (57%) and spring (23%). 3 type of antibodies were higher in cases ($p=0.000$). Antistreptolysin O (cut off level 195) had 90% sensitivity; 82% specificity PPV 92%, AUC: (CI= %95; 0.99-0.91). Anti streptokinase (cut off level 223) had 82% sensitivity; 82% specificity; PPV 95%; AUC: (CI= %95; 0.934-0.735). Anti DNase (cut off level 140) had 82% sensitivity; 82% specificity, PPV 95%; AUC: (CI= %95; 0.99-0.91).

Conclusion: It presents possible role for streptococcal infection in OCD&ADHD disorder. We found a significant higher antibodies against GABHS in OCD&ADHD cases in compare with healthy children. Treatment of streptococcal infection is achievable by using of long acting penicillin in our country. Use of aggressive treatment like plasmapheresis, IVIG needs future RCT studies.

TWO CLOSELY RELATED STRAINS ASSOCIATED WITH PERTUSSIS RESURGENCE IN ISRAEL

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Background: Despite Israel's vaccination rate of 95%, pertussis incidence has peaked at 37/100,000 (2007). Antigenic divergence between clinical isolates and vaccine strains may lead to the circulation of *Bordetella pertussis* (*Bp*) strains that are antigenically distinct from vaccine strains, thereby possibly contributing to the increasing numbers of pertussis cases in western countries. To date, there has been no attempt to identify the strain specific clone(s) of circulating *Bp* in Israel.

Objective: To employ Pulsed-Field Gel Electrophoresis (PFGE) to evaluate the polymorphism of the circulating *Bp* strains in Israel during a period of high disease activity.

Methods: We analyzed 82 isolates of *Bp* collected during high incidence rate years, 2007-2008 using PFGE. The *SpeI* restriction enzyme was utilized.

Results: Four strains of *Bp* were found, named A, B, C and D. Types A and B were the most common, are *closely related* and constitute 95% of the isolates. Notably, Strains A and B are identical to the 2010 European strains referenced at the Pasteur Institute (Paris), FR4803 (PFGE group IV β) and FR4736 (PFGE group IV α), respectively. The most common Israeli strain, A, has the same PFGE cluster of the dominant European BpSR11 strain (PFGE group IV β) identified in the 1999-2004 EUpertstrain II project (Hallander, 2007). Strain clonal expansion may represent an adaptive response to high vaccination coverage.

Conclusion: The dominant European PFGE cluster (PFGE group IV β) was also predominant in Israel, 2007-2008. International pertussis strains monitoring among highly vaccinated population should be pursued to track *Bp* polymorphism.

10-YEAR LENGTH DISSEMINATED ABSCESES DUE TO MYCOPLASMA FAUCIUM IN AGAMMAGLOBULINEMIC PATIENT

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Background and aims: Immunocompromised patients sometimes have unusual infections. New diagnostic tools might make diagnosis easier.

Case report: A 16-year-old girl with 2-year history of recurrent peritoneal collection, which had been treated with multiple drainage



[Abdominal MRI]

Personal history: Agammaglobulinemia on replacement with subcutaneous gammaglobulin, CD4-lymphopenia and 10-year history of multiple suppurative cutaneous abscesses and abscessified lymphadenopathy, receiving several courses of antibiotics (rifampicin, azithromycin and cephalosporins). All cultures had been sterile. On physical examination she was stunted, facial and arm skin abscesses, with right fistulized axillary lymphadenopathies, 5-6cm hepatomegaly and giant splenomegaly.



[Face and neck abscesses]

On her back, there was a 10x15cm, elastic, neither tender nor inflamed mass. Normal CBC except for lymphopenia (470cells/mm³). CT and MR confirmed giant splenomegaly and a left retroperitoneal abscess close to psoas muscle, without affecting it. Chronic granulomatous disease was excluded. Blood culture was negative. Retroperitoneal abscess was drained. Cultures were negative for bacteria, fungi and mycobacteria. Cutaneous biopsy showed deep suppurative folliculitis. No microorganism grew in skin cultures. 16S rDNA PCR and sequencing of drained pus as well as pus of skin abscesses 99% homology with database sequencing for *Mycoplasma faucium*. Polidocanol sclerotherapy of her retroperitoneal abscess was performed. Combination antibiotherapy (doxycyclin and ciprofloxacin) was started. Three days after cutaneous abscesses stopped draining. Two months after all her skin lesions were cured as well as her retroperitoneal abscess.

Discussion and conclusion: Rare species of *Mycoplasma* spp and *Helicobacter/Flexispira* spp has been related to invasive infections and recurrent abscesses in agammaglobulinemic patients. They are difficult to cultivate, so 16S rDNA PCR and sequencing may be a useful tool for diagnosis of chronic or recurrent infections with persistent negative cultures.

PEDIATRIC INVASIVE HAEMOPHILUS INFLUENZAE (HI) INFECTIONS IN ISRAEL IN THE HAEMOPHILUS INFLUENZAE TYPE B VACCINE ERA: A NATIONWIDE PROSPECTIVE STUDY

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Background: Hib vaccination (since 1994) resulted in a marked decrease in Hib morbidity. Presently, pediatric Hi invasive disease (PHiID) is caused primarily by *non-capsulated Haemophilus influenzae (ncHi)*. We studied the epidemiological trends and selected clinical characteristics of PHiID in Israel in the Hib vaccine era.

Methods: This is an ongoing, nationwide, prospective study. Cases with Hi isolated from blood or cerebrospinal fluid were enrolled during 2003-2009.

Results: 278 cases of ncHi (64.5%), Hib (26.5%) and *non-b encapsulated Hi* (9%), were identified. The overall mean incidence (/100,000 children < 16 years \pm SD) was 1.8 ± 0.3 , and was stable for all serotypes. Serotype-specific mean incidence was 1.1 ± 0.2 , 0.5 ± 0.2 and 0.2 ± 0.1 , respectively. The highest incidences ($P < 0.0001$) occurred in children < 1 year: 6.3, 5.3 and 1.4 respectively. PHiID incidence decreased with increasing age, and was rare >4 years. PHiID incidence was higher in non-Jewish vs. Jewish children: 2.3 vs. 1.6, ($P < 0.006$, IRR:1.42; 95% CI:1.11-1.82), respectively. This trend was more accentuated in girls. Bacteremia without focus was the most common manifestation in non-b Hi (60%), whereas meningitis was the most common manifestation in Hib (43%). Case-fatality rate was 5.9%, (75% of deaths from ncHi). 11% of the patients had comorbidity with no differences between serotypes; the mortality among this group was 20%.

Summary: In the Hib vaccine era, PHiID and its associated mortality are primarily attributed to ncHi. The low rate of invasive Hib is sustained. Additional studies to investigate differences in population-specific disease and risk factors associated with invasive disease are warranted.

EARLY-ONSET INFECTIONS CONNECTED WITH *ENTEROBACTERIACEAE* IN POLISH NEONATAL INTENSIVE CARE UNITS*

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Aim: The objective of this study was to investigate the incidence, risk factors and outcomes of Early-Onset Infections (EOIs) connected with *Enterobacteriaceae* in very-low-birth-weight newborns in Polish Neonatal Intensive Care Units (NICU).

Methods: Continuous prospective infection surveillance conducted during 2009 at six Polish NICUs and included 910 newborns whose birth weight was < 1500 grams. Infections were defined according to the Gastmeier's criteria. EOIs were diagnosed < 3 days after delivery.

Results: The incidence of *Enterobacteriaceae* Early-Onset Septicemia was 0.7% and of *Enterobacteriaceae* Early-Onset Pneumonia: 1.3%. EOI connected with *Enterobacteriaceae* accounted for 12.7% of the total of all EOI. The factors significantly increasing the risk of EOI were a low gestational age, small birth weight, a low score in the CRIB and Apgar score as well as maternal chorioamnionitis, additionally: bacterial vaginosis in the child's mother during pregnancy for EO-Pneumonia. The perinatal prophylaxis did not have an influence on the occurrence of EO-S. The most important *Enterobacteriaceae* organisms were: *Escherichia coli* (18,5% of all EOI) and *Enterobacter spp.* (6,2%). Mortality was: 33,3% for *Escherichia coli* and 25% for *Enterobacter spp.*

Conclusions: The observed frequency of EOS did not differ from the one described in the literature, whereas the incidence of EO-Pneumonia was higher. The bacterial etiologies suggest the vertical transmission of the pathogens and a close relationship between the observed EOIs with maternal environment. The applied perinatal antibiotic prophylaxis was ineffective.

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POST- DIPHTHERITIC NEUROPATHY IN CHILDREN IN A TERTIARY CARE HOSPITAL IN NORTH INDIA**S. Kanwal**, D. Yadav, V. Kumar*Pediatrics, Lady Hardinge Medical College and Kalawati Saran Children's Hospital, New Delhi, India***Objective:** To study the clinical profile and outcome of post-diphtheritic neuropathy in children in a tertiary care hospital in North India.**Design:** Descriptive retrospective study.**Setting:** Pediatric ICU of tertiary care hospital at Delhi.**Patients:** 48 consecutive patients with post- diphtheritic neuropathy treated between Jan 08 and Dec 10.**Methods:** The case records of 48 children admitted with post- diphtheritic neuropathy were reviewed and information regarding personal details, clinical features, recovery parameters and outcome was recorded using a predesigned Performa .The data was analyzed using SPSS version 16.**Result:** Median age was 4.25 years. All of cases were either unimmunized or partially immunized. Median latency period was 15 days. 52% children had palatal palsy whereas 48% had limb weakness initially. Median duration of progression of weakness was 5 days. 94% had limb muscle weakness during their clinical course. Respiratory muscles were involved in 85.4% cases and 60.4% required mechanical ventilation. 41.7% children had post diphtheritic myocarditis. While 14.6% had fatal outcome and 10.4% had hypoxic neurological injury.**Conclusion:** Boys were affected more. Children greater than 5 years of age were 40% of total admission. Median duration of latency was shorter, muscle weakness, progression and recovery was faster as compared to observational adult studies. There was no significant difference in the progression of the disease complication rate, recovery in children less than 5 years and greater than 5 years of age.

BACTERIAL PATHOGENES CAUSING SEPTICEMIA IN INFANTS PATIENTS AND ANTIBIOTICS RESISTANCE PATTERN IN HAMEDAN, WEST OF IRAN

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Background and aims: Resistance pattern of different bacteria and pathogen frequency may vary significantly from country to country and also in different hospitals within a country. Thus, regional surveillance programs are essential to guide empirical therapy and infection control measures. The aim of present study was the evaluation of bacterial pathogens that causes septicemia and their antimicrobial sensitivity, at Educational hospitals, Hamedan, Iran.

Methods: This descriptive cross-sectional study comprised 746 blood cultures, which were taken from infant patients in Hamadan hospitals during 2 years. Positive blood cultures, the etiology of septicemia, antimicrobial sensitivity and resistance of strains to antibiotics were entered the questionnaires. Data were statistically analyzed, using SPSS 13.

Results: From 746 blood cultures evaluated, 93 cases (12.5%) were positive and 51.6% of positive blood cultures were due to gram negative bacteria. The most common causes of septicemia included: *Staphylococcus epidermidis* 37.6%, *E.coli* 25.8% and *Staphylococcus aureus* 8.6%, respectively. Gram negative bacteria were resistance to common antibiotics: cloxacillin 100%, tetracycline 84.6%, cephalotin 69%, ampicillin 66.7%, nalidixic acid 62.5%, cephalexin 61.5%, amoxicillin 61.5%, and TMP-sulfamethoxazole 53.1%; while resistance was lower in gram positive organisms: cloxacillin 66.7%, penicillin 75%, nafazoline 75%, amikacin 50%, doxycycline 50%, TMP-sulfamethoxazole 41.7%, and gentamicin 40%.

Conclusion: The present study showed that gram negative organisms, in particular, *E.coli* are the most common causes of sepsis in this region. It also indicated that gram negative strains causing septicemia showed most common resistance to current antibodies, so that more than 50% resistance was observed in most of these organisms.

EMPYEMA THORACIC IN CHILDREN; COMPARISON OF MANAGEMENT OPTIONS. A STUDY FROM KARACHI, PAKISTAN

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Management of pediatric pleural empyema remains controversial; as there is no definite consensus on the superiority of one on another (medical or surgical). We aim to compare surgical and medically managed patients (identify etiology, clinical manifestation, management and complications of children with empyema thoracic) in a tertiary care hospital from Karachi, Pakistan.

Methods: We retrospectively reviewed the medical records of children aged (>1 mo. - 15 years) with discharge diagnosis of parapneumonic effusion, empyema or complicated pneumonia during 1996-2010 period. Cohort was further divided on the basis of managed either only medically and/or surgically.

Results: Among the 112 patients more than half (54%) were 5 year or less in age. Males (74%) were predominant. Most cases were admitted during winter and spring (67%) season. Unvaccinated were (32%) and 27% were severely malnourished. Fever, cough, and dyspnea were the major presenting symptoms. Sixty-six (59%) were on some antibiotics prior to admission. *Staphylococcus aureus* followed by *Streptococcus pneumoniae* were the commonest organism isolated from blood and pleural fluid cultures. Patients were divided into medical (n=26) and surgical (n=86) groups. Surgically managed children were younger ($p=0.01$); less weight ($p=0.05$); had prolonged fever ($p=0.06$); cough ($p=0.09$) and they stay more in hospital ($p=0.003$) as compared to medically managed children. Complications rates were similar in both groups. Three patients died; two in surgical group and one in medical group.

Conclusion: Empyema thoracic in children required early identification along with right antibiotics choice and prompt treatment according to individual basis to prevent complications.

SEVERE INFANTILE *BORDETELLA PERTUSSIS* PNEUMONIA IN MONOZYGOTIC TWINS WITH A CONGENITAL C3 DEFICIENCY

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Bordetella pertussis or whooping cough is a vaccine preventable disease that still remains a serious infection in neonates and young infants. Most deaths occur before receiving the first dose of pertussis vaccine. These deaths might be partially explained by low antibody titers against this pathogen in neonates, due to lower maternal antibodies and less transport of these antibodies across the placenta. We describe 2 young infants, monozygotic twins, with a severe *B. pertussis* pneumonia of whom one eventually was treated with extracorporeal membrane oxygenation (ECMO). Diagnostic work up of unexplained hematuria and proteinuria during the illness revealed low serum C3 levels with normal C4 levels, suggesting alternative complement pathway involvement. Extensive analysis of the persistent low C3 levels demonstrated a unknown heterozygous mutation in the C3 gene in both siblings and their mother. The mutant protein is almost 46% shorter than wild type C3, resulting in the loss of important binding sites for factor B and the loss of the thioester bond important for the function of the protein. In combination with the premature birth of the twins and the specific virulence mechanisms of *B. pertussis* this C3 mutation might have contributed to the severe disease course in this case. This case provides indirect in-vivo evidence for the role of complement inhibition by *B. pertussis* when establishing an infection. When confronted with a severe case of *B. pertussis* infection, genetically caused complement disorders should be ruled out.

VIRULENCE PROPERTIES OF HAEMOPHILUS INFLUENZAE TYPE B, F AND AN UN-ENCAPSULATED STRAIN ISOLATED FROM CHILDREN IN IRAN**N. Mojgani***Biotechnology, Razi Vaccine Research Institute, Karaj, Iran*

Haemophilus influenzae (Hi) is a Gram-negative, exclusively human pathogen responsible for a wide variety of respiratory infections and potentially life threatening invasive diseases such as meningitis. Hi pathogenicity varies depending on the presence or absence of capsule and the specific capsule type. An important goal of this study was to determine the importance of specific capsule type in the pathogenesis of invasive *H influenzae* disease. We compared the virulence of a type b, type f and unencapsulated (NTHi) strains, by determining the ability of the strains to produce bacteremia with subcutaneous and intraperitoneal inoculation in an animal model. The organisms were passed through mice several times to insure their virulence. Subcutaneous inoculation of 10^3 colony-forming units of strains with the type b capsule in mice models, produced bacteremia at a greater frequency than did the strains with the type f capsule. Infection by the intraperitoneal route was followed by progressive peritonitis and bacteremia with subsequent infection of the brain and meninges, and death. Death occurred between twelve and 72 hours after infection with type b strains. No death was seen in mice infected with 10^6 cfu of type f strains, while higher doses of the strain caused only bacteremia in these mice models. Capsule deficient strain was unable to cause bacteremia when inoculated by any route.

ANTI-ADHESIVE EFFECTS OF BIOTECHNOLOGICAL SYNTHESIZED HUMAN MILK OLIGOSACCHARIDES**S. Weichert**¹, S. Jennewein², S. Schmohl¹, H. Schrotten¹, J. Putze¹¹*Pediatric Infectious Diseases, University Children's Hospital, Medical Faculty Mannheim, Heidelberg University, Mannheim*, ²*Jennewein Biotechnology GmbH, Rheinbreitbach, Germany*

Background: Beyond nutritional aspects human milk provides further health benefits by preventing adhesion of pathogens to epithelial surfaces, which is attributed to human milk oligosaccharides (HMOs). In this study, we were for the first time able to use enzymatic engineered HMOs to investigate the antiadhesive effects on pathogen attachment.

Methods: Adherence of *Pseudomonas aeruginosa* strain DSM 1707, enteropathogenic *Escherichia coli* (EPEC) strain O119 and *Salmonella typhis* on two epithelial cell lines (A549, Caco-2) in the presence of lactose, mannose, 2'-fucosylated lactose (2'-FL), 3-fucosylated lactose (3-FL) and human milk was determined by cultural enumeration.

Results: Adherence of *Pseudomonas aeruginosa* on A549 cells was highly significantly inhibited by 2'-FL and 3-FL (25% and 23% inhibition, respectively), whereas no inhibition was observed with lactose. 2'-FL and 3-FL highly significantly inhibited adhesion of *Pseudomonas aeruginosa* to Caco-2 cells by 28% and 39%, respectively, as well as did human breast milk (inhibition of 59%). Adhesion of the enteropathogenic bacteria *Salmonella typhis* and EPEC O119 to Caco-2 cells was significantly inhibited by 2'-FL and 3-FL, as well as by mannose (inhibition of 17%, 16%, 68%, and 18%, 21%, 24%, respectively), whereas with lactose no inhibitory effect was shown. Furthermore, adhesion of EPEC O119 to Caco-2 cells was significantly inhibited by human breast milk (33% inhibition).

Conclusion: We were for the first time able to proof the efficient inhibition of different pathogens by enzymatic engineered HMOs in two human cell culture models. HMOs might play an important role as supplementary infant formula ingredients in near future.

STAPHYLOCOCCUS AUREUS BACTERAEMIA IN CHILDREN - NATIONWIDE STUDY ON INCIDENCE AND MORTALITY

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Background and aims: *Staphylococcus aureus* bacteraemia (SAB) is an important infection in all age groups. Less is known about its epidemiology in children than in adults. The study objective was to describe the incidence and mortality of childhood SAB in Iceland.

Methods: All children (< 18 years) with a positive blood culture for *S. aureus* in 1995-2008 were retrospectively identified by clinical microbiological laboratories performing blood cultures in Iceland. Episodes occurring within 90 days from previous SAB were classified as relapses and not counted as separate infections. Clinical data was collected from medical records. National population statistics and dates of death were retrieved from the National Registry.

Results: In the study period 130 children had 136 distinct episodes of SAB. Additional 14 blood cultures (9.3%) were regarded as contaminations and excluded. Overall annual incidence of SAB was 12.4 per 100,000 children, with no significant temporal changes being observed. Incidence per 100,000 children was 68.3 in the age group < 1 year, 6.3 in 1-5 years, 10.5 in 6-11 years and 10.0 in 12-17 years. Sixty-nine cases (50.7%) were community-acquired, 47 (34.6%) nosocomial and 20 (14.7%) healthcare-associated. All cause 7-day, 30-day and 365-day mortality were 0% (0/136), 1.5% (2/136) and 3.8% (5/133), respectively. Seven cases (5.2%) experienced a relapse of SAB. No episode with methicillin-resistant *S. aureus* (MRSA) was identified.

Conclusions: While incidence of childhood SAB in Iceland is similar to that described in most other populations, the mortality rate is one of the lowest reported. MRSA was not found.

CIRCULATING VEGF RECEPTOR-2 IN CHILDREN WITH MENINGOCOCCAL SEPSIS

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Background: Several studies have shown that circulating soluble VEGF Receptor-1 (sVEGFR-1) is increased in experimental and clinical sepsis and is associated with worse outcome. No data on sVEGFR-2 in clinical sepsis are available. Aim of our study was to determine the serum levels of soluble VEGFR-2 in children with meningococcal sepsis admitted to the intensive care unit.

Methods: 28 children were included who were enrolled in a clinical trial of inactivated protein C concentrate at the Pediatric Intensive Care Unit of the Sophia Children's Hospital, Erasmus Medical Centre (16 boys, 12 girls; age 4.8 years \pm 4.8; PRISM III score 23.6 \pm 9.2; mortality 8/28). The control group consisted of 16 children presenting with fever in the emergency room at the University Medical Center Utrecht, for whom a diagnosis of serious bacterial infection was excluded (12 boys, 4 girls; age 4.5 years \pm 4.3). Ethical approval was obtained. sVEGFR-2 in serum was measured by ELISA (Quantikine R&D Systems).

Results: Serum sVEGFR-2 at the time of PICU admission was significantly decreased in children with meningococcal sepsis compared to controls (6882 pg/mL \pm 2335 vs. 16174 \pm 3540; $P < 0.001$).

Serum sVEGFR-2 levels at the time of PICU admission were more decreased in non-survivors compared to survivors (5640 pg/mL \pm 1940 vs 7378 \pm 2336; $P = 0.037$).

Conclusions: Serum levels of soluble VEGFR-2 (sVEGFR-2) are decreased in children with meningococcal sepsis. Serum sVEGFR-2 levels are decreased greatest in non-survivors.

PARENTAL AWARENESS AND KNOWLEDGE ABOUT INVASIVE MENINGOCOCCAL DISEASE (IMD): RESULTS OF A MULTINATIONAL SURVEY

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Background: Parental knowledge about diseases influences decisions about preventive or therapeutic interventions for their children. Infants commonly receive multiple vaccines against pathogens that cause meningitis and sepsis, which can cause confusion.

Methods: To assess knowledge and opinions among parents of infants and healthcare providers, the New Vaccinations of Infants in Practice Survey was conducted online in Australia, Canada, France, Germany, Spain, Sweden, and UK.

Results: Overall, 2460 parents responded; most understood that invasive meningococcal disease (IMD) may cause death (1355/2460; 55%), progress rapidly (1470/2460; 60%), and cause disability (1538/2460; 63%). Parents in Australia and UK, countries with meningococcal immunization campaigns that included disease education, had the greatest disease awareness. Relatively few German (148/403; 37%) and Swedish (79/203; 39%) parents were aware of IMD lethality. Overall, few parents (390/2460; 16%) knew that 0-12 month-olds are at highest risk of contracting IMD, while approximately one-third (856/2460; 35%) did not. After exposure to disease information, more parents (1672/2460, 68% vs. 1336/2460, 54%) were highly likely to accept vaccination of their infants against meningococcal serogroup B. Further, 37% (900/2460) knew that their child had already received some meningococcal vaccine; yet 61% (1491/2460) were unsure whether it covered all causes of meningitis.

Conclusions: Parents had a moderate degree of knowledge about IMD and were unlikely to report that their infants had received meningococcal vaccination. Education should be recommended to increase parental awareness of the types and causes of meningitis and sepsis and the age groups that are most at risk.

MENINGOCOCCAL MENINGITIS IN CHILDREN: FRENCH SURVEILLANCE NETWORK FROM 2001 TO 2009

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Background: Since 2001, the GPIP/ACTIV set up an active surveillance network to analyze the epidemiological, clinical and biological features of meningococcal meningitis in France.

Methods: From 2001 to 2009, 252 French pediatric wards and 166 microbiology laboratories enrolled all children (0-18 years old) with bacterial meningitis. The inclusion criteria were a clinical meningeal syndrome, cerebrospinal fluid (CSF) pleiocytosis and at least one positive microbiological test (positive culture, PCR, slide agglutination or smear detection in CSF and/or blood culture). Risk factors, signs and symptoms, vaccination status, CSF analysis, treatments and case fatality rate were recorded.

Results: During the period of the study, 1661 meningococcal meningitis were reported among 3769 (44.1%) bacterial meningitis. Serogroup distribution of the isolates was 61.3%, 27.0%, 2.4%, 0.6% and 0.3% for serogroups B, C, W135, Y and A, respectively. Mean age was 4.4-year-old (median 2.5) and 2/3 of cases occurred in children under 5-year-old. Cases peaked in < 1 year, 33.8% for the serogroup B and 23.4% for the serogroup C. 27.5% of children had received an antibiotic treatment up to 24 hours before lumbar puncture. A shock was reported in 31.0% of cases. No vaccine failure was reported with MenC conjugate vaccine. All patients had received beta-lactamin. Global case fatality rate was 6.5% but was higher (9.2%) for serogroup C than for serogroup B (5.9%) (p=0.02).

Conclusion: This is among the largest series of meningococcal meningitis to date. Effective meningococcal serogroup B vaccine and serogroup C vaccination recommendations could control the burden of meningococcal meningitis.

DEEP NECK INFECTIONS IN CHILDREN: EXPERIENCE IN A TERTIARY-CARE CENTER IN TURKEY DURING 2005-2011 PERIOD

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Background and aims: Deep neck infections are rare in children but associated with significant morbidity and mortality. This study reviews our experience in the diagnosis and management of deep neck infections in children.

Methods: Retrospective study of the patients who were diagnosed with deep neck infections from 2005 to 2011 in our tertiary-care center was performed. Medical records of patients were reviewed as clinical, microbiological, therapeutic data.

Results: Over a 5-year period from 2005 to 2011 a total of 25 cases were included in the study. There were four peritonsillar abscess, 11 parapharyngeal abscess, seven retropharyngeal abscess and three prevertebral abscess. Of the patients, six (24%) were female and 19 (76%) were male. The mean age was 47.9 ± 39.0 months (5 months- 12 years). A total of 15 (60%) children had a history of taking oral antibiotics before admission (beta-lactams in 52%). The most frequent symptoms and clinical findings were fever (100%), neck mass (92%), neck stiffness (40%), odynophagia (40%) and difficulty in breathing (24%). Etiological agent was detected in only one patient. The diagnosis was confirmed by computed tomography in 23 patients. Ten (40%) patients treated with surgical intervention and parenteral antibiotic therapy. Fifteen (60%) patients treated with parenteral antibiotics alone. We successfully treated patients by early diagnosis.

Conclusion: Because of potentially fatal complications, deep neck infections should be considered in the differential diagnosis of children who presented with fever and neck mass even though the absence of the more specific findings like odynophagia and respiratory distress.

FATAL LEGIONELLA PNEUMOPHILA SEPSIS IN A 7 MONTHS OLD INFANT**C. Pantazis**¹, S. Ghosh², B. Henrich³, C. MacKenzie³, S. Braunstein⁴, T. Höhn¹

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Legionella is a very rare infectious agent in childhood. Legionella pneumophila is the responsible agent about 90% of cases and causes both, legionnaires' disease and Pontiac fever, the latter a disease without the typical respiratory involvement. We introduce the case of a 7 months-old boy who was hospitalized due to prolonged bronchitis and onset of high fever. We initiated antibiotic therapy with ampicillin and oxacillin, and added gentamicin on the second day. The boy deteriorated and was transferred to our PICU. We changed the regimen to piperacillin-tazobactam and meropenem. In the further clinical course the boy was intubated and required catecholamine support. Few hours later he died in irreversible septic shock.

In serial blood cultures, no responsible agent could be detected. On microscopy of the blood smear plenty of bacteria could be seen, thus we performed further investigations. In the blood culture Legionella pneumophila was verified through PCR post mortem and Legionella pneumophila was cultivated in special culture medium. The parents consented to autopsy, which revealed numerous pyogenic spots in lungs and liver.

Lethal Legionella pneumophila infection are extremely rare in infancy and childhood. At the present state we can neither confirm nor refute any underlying condition putting this particular infant at risk to suffer and die from this bacterial infection.

ACUTE MASTOIDITIS: GOOD OUTCOME WITH LOW RATE OF TEMPORAL BONE CT SCAN AND MASTEIDECTOMIES

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Background and aims: Acute mastoiditis is the most frequent complication of acute otitis media (AOM) and it can lead to severe intracranial complications. We retrospectively analysed all the cases of acute mastoiditis admitted at our institution in the last ten years.

Methods: The medical records of children with acute mastoiditis, managed at the University Hospital of Udine, Italy, between January 2001 and December 2011 were reviewed. Inclusion criteria were post-auricular swelling and erythema with evidence of co-existent or recent AOM at presentation. Criteria for cortical mastoidectomy were intracranial complication or lack of clinical improvements after 24-48 hours of antibiotic intravenous therapy with a third generation cephalosporin at full dosage, without miringotomy.

Results: 45 patients (6 months-10 years of age, sixteen younger than 2 years) fulfilled the entry criteria. Twenty-nine were males (64%), with a rate of 3.4 per 10.000 E.R. admissions. Twenty-four (54%) were already on oral antibiotics for AOM before hospital admission. Post-auricular fluctuation was detected in eight cases (24%). Only two patients underwent a contrast-enhanced CT scan of the temporal bone. Mastoidectomy was carried out in five children (11%), in one case for neurological symptoms at presentation, in the other four for mastoiditis medical therapy failure. All the patients recovered without sequelae.

Conclusion: in our experience a conservative approach for acute uncomplicated mastoiditis, with a low rate of diagnostic CT-scan, was curative in almost 90% of cases even in the majority of patients with post-auricular fluctuation at presentation.

DISABILITY ADJUSTED LIFE YEARS FOR MENINGOCOCCAL DISEASE: INDICATOR FOR PRIORITIZING PREVENTION

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Background: Meningococcal disease(MD) is a major cause of illness worldwide. Vaccination is considered the best strategy for prevention. Disability Adjusted Life Years(DALYs) is a measure that estimates burden of disease and is useful for evaluation of the impact on health policies. We assessed the burden of MD(ICD-10:A39) in Argentina, Chile and Brazil, for 2008, estimating DALYs(years of life lost to premature death-YLL- plus years lived with disability-YLD-).

Methods: We analyzed mortality data from the Bureau of Vital Statistics of the Ministry of Health of the countries. YLL were calculated for each stratum, using the criteria of life expectancy, discount rate of 3% and non-uniform age weights. For YLD, the methodology was based on the reasons YLD/YLL, already known for the Region of the Americas(WHO-2004). Populations were standardized to evaluate the performance of DALYs among different countries of this study(WHO populations for 2000-2025).

Results: For 2008, deaths by MD were 25 in Argentina, 12 in Chile and 428 in Brazil. Argentina had 829 DALYs(YLD/YLL:164/665), Chile 483 DALYs(106/377) and Brazil 16659 DALYs(3233/13426). Ratios YLD/YLL were 0.2-0.3, indicating a higher weight of YLL vs. YLD. The greatest impact of DALYs was in children < 4years (53.8%;49.3%;49.1%,respectively) and followed by the 5-14year old group (19%;43.7%;20.3%,respectively). The country with the highest burden of MD was Brazil(8.8 lost DALYs/100.000 hab.) followed by Chile and Argentina (3.3 and 2.2 respectively).

Conclusion: estimating the burden of MD may help to define priorities in prevention and resource allocation in health policies to incorporate vaccines into National Immunization Programs.

HELICOBACTER PYLORI IN CHILDREN'S GASTRITIS IN A PEDIATRIC CLINICS FROM ROUMANIA**O. Marginean¹**, C. Marginean², M. Marginean²¹*Pediatric Gastroenterology, University of Medicine and Pharmacy, ²Medicine University, Târgu Mures, Romania*

Helicobacter pylori infection is an important cause in child gastritis. Some cases are resistant to therapy although the correct treatment.

The purpose of this study was the analyze of cases of gastritis with Helicobacter pylori in children and their evolution.

Methods: The study was a prospective realised on children admitted between january 2008 and december 2010. We had 218 cases of gastritis with Helicobacter pylori; for these patients it was prescribed treatment according to internationally recommendations accepted today in order to eradicate the infection and to cure gastritis.

Results: The average age of patients in the study group was 13.6 years, with a higher incidence in groups 13 - 18 years (57.33%), female gender (62.38%). From patients diagnosed with gastritis with Helicobacter pylori, 193 cases presented for review; after proper treatment. Clinical-histological changes had disappeared in 165 cases (75,68%) and Helicobacter pylori was negative in 186 (86,11%) cases 1 months later . A number of 22 patients (13,89%) remained positive. We found other favoring factors and infection with Helicobacter pylori to children's parents in 8 cases from the 22 resistant to treatment.

Conclusions: The resistance of Helicobacter pylori infection to therapy is caused by continued action of favoring factors, the existence of the same infection to other members of family, the virulence of microorganisms in association with genetic predisposition present in some individuals. *„This paper is supported by the Sectoral Operational Programme Human Resources Development, financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/89/1.5/S/60782”*

COMPLEMENT FACTOR H-RELATED 5 (CFHR5) PROTEIN LEVELS ASSOCIATED WITH THE CLINICAL SEPSIS PHENOTYPE IN CHILDREN WITH MENINGOCOCCAL DISEASE

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Background and aims: A genome-wide association study^[1] identified complement factor H (CFH) gene family variants in meningococcal disease (MD). The CFH family comprises CFH itself, and five genes that encode structurally similar proteins termed CFH-related proteins. Of the five CFH-related proteins, CFHR5 has been proposed to be important in the regulation of complement within the kidney^[2]. Here, we measured serum CFHR5 protein levels in a healthy paediatric cohort and in children with MD.

Methods: Serum CFHR5 was quantified by ELISA in 57 patients with MD and 40 controls. Serum CFHR5 levels were correlated with MD phenotype.

Results: The mean serum CFHR5 was significantly lower in MD patients during the acute phase (1.219 µg/ml) compared to healthy controls (2.348 µg/ml, $p < 0.0001$). However, there was no significant difference in the mean CFHR5 in convalescent MD samples when compared to controls. Mean serum CFHR5 was higher in convalescent than acute MD samples ($p < 0.0001$). Levels did not differ between males and females.

Acute CFHR5 levels were compared to sepsis severity scores, there was significant positive correlation with: ICU free days ($p=0.042$) and negative correlation with: Rotterdam score ($p=0.055$), GMSPS ($p=0.002$), PRISM ($p=0.033$). Mean acute CFHR5 ($p=0.019$) and C3 ($p=0.012$) levels were lower in the patients requiring renal support (haemodialysis) on PICU.

Conclusions: Serum CFHR5 levels in MD follow those of C3 and CFH, falling acutely and normalising during convalescence. We hypothesise that this represents sequestration of serum CFHR5 by (1) binding to the pathogen directly or (2) binding to tissue C3 during sepsis.

RETROSPECTIVE EVALUATION OF INFECTIONS BY *RICKETTSIA TYPHI* AND *RICKETTSIA CONORII* AMONG CHILDREN IN CENTRAL GREECE

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Background and aims: To present our experience on epidemiology of *Rickettsia typhi* and *Rickettsia conorii* infections in a pediatric population in Greece, during the last 9 years (January 2003-October 2011).

Methods: Serum samples from children hospitalized for prolonged fever were tested for *R. typhi* and *R. conorii* with serological assays in a pediatric hospital in Athens. Serological evaluation was performed with an indirect immunofluorescence assay. The IgM diagnostic titer was set at $\geq 1:64$ and the IgG was set at $\geq 1:128$.

Results: A total of 2720 serum samples were tested. Overall, 26 children (15 male, 11 female, aged 6 months to 15 years old) were screened positive for *R. typhi* or/and for *R. conorii*. Of those, 14 children exhibited positive antibodies only for *R. typhi*, 4 exclusively for *R. conorii*, while 8 children yielded positive results for both species. The serum samples were tested for antibodies against *R. conorii* and/or *R. typhi* 6 to 20 days after the onset of fever. The major clinical manifestations of the infection were, as follows: rash, mainly maculopapular, 47%; splenomegaly, 36%; lymphadenopathy, 29%; hepatomegaly, 21%. The most frequent laboratory finding was increased transaminase activity 56.5% (AST: 21 to 240 U/L and ALT: 11 to 170 U/L). The majority of cases (73%) were identified from June to September. The outcome was favorable for all 26 patients.

Conclusions: Although rickettsiosis is rare in our country, this infection should be considered in every child with prolonged fever, rash and slight or moderate elevations of both transaminase activity.

DETECTION OF H.PYLORI ANTIGEN IN THE STOOL SAMPLES OF CHILDREN IN TEKIRDAĞ, TURKEY

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Introduction: *Helicobacter pylori* infection shows worldwide distribution, predominantly in countries or regions with poor socioeconomic conditions. This study was designed with the aim of investigating the presence of *H. pylori* antigen in the stool specimens of children, in Tekirdağ, Turkey

Material and methods: A total of 1441 children (aged 0 months to 15 years)- with complaints of anemia, gastroenteritis, abdominal pain, nausea and vomiting- were screened for *H.pylori* antigen. The stool specimens were collected within two years (01.01.2010-31.12.2011) and tested with HP Ag (DIA.PRO, Diagnostic Bioprobes, Italy) according to the recommendations of the manufacturer. The subjects were divided into three groups based on their ages: Group A (0 months to 5 years), Group B (6-10 years) and Group C (11-15 years).

Results: The median age of children with *H.pylori* positive samples was 6.6 ± 4.1 , 47.9% girls and 52.1% boys. Overall positivity of *H. pylori* stool antigen was 6.6%, decreasing with age, as 41.7%, 39.6%, 18.8% in groups A, B and C, respectively ($\chi^2=9.3$, $p=0.01$). No difference due to gender was obtained ($\chi^2=0.17$, $p=0.68$).

Conclusion: Some serological studies conducted in Turkish children, showed the overall *H.pylori* seropositivity rates ranging between 30.9% and 78.5, increasing with age. Our results with higher antigen positivity in 0-5 years group, correlates with these results, showing exposure to the agent in the early years of childhood. In conclusion, the importance of preventive measures for the development of *H.pylori* infection in children, especially in developing countries was emphasized.

MENINGOCOCCAL GENOTYPE ST-11 AND CORTICOSTEROIDS THERAPY: WHICH IMPACT ON PEDIATRIC INVASIVE MENINGOCOCCAL INFECTIONS?

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Background: The indication of Corticosteroids (CS) in acute bacterial meningitis (ABM) remains debated, particularly in meningococcal disease. We hypothesized that CS may be beneficial in highly pro-inflammatory genotypes such as ST-11 isolates.

Methods: We performed a retrospective study and matched microbiological data from invasive meningococcal infections (IMI) to clinical data of pediatric cases with ABM and purpura fulminans (0 to 18 years old). We analysed all patients data with CS documented treatment regardless of time of administration. Severe IMI cases were defined as presence of one of the following: shock, coma, purpura fulminans, artificial ventilation or seizures.

Results: From 2001 to 2009, among the 805 patients with IMI, 270 (33.5%) have received CS. The distribution of serogroups, genotypes (available for 410 cases; 51%) and age for IMI cases did not differ between children with and without CS treatment. Mortality was higher for patients who received CS than those without CS (12.7% vs. 4.5%, $p < 0.001$). ST-11 isolates were associated with a higher mortality (OR 2.38, [1.29-4.41], $p=0.004$). In the absence of CS treatment, ST-11 isolates were associated with increased mortality (OR 4.68, [1.91-11.46], $p=0.001$) but this increase was not significant when only severe cases due to ST-11 isolates were analyzed (OR 1.71, [0.95-3.09], $p=0.073$).

Conclusion: In absence of CS treatment for IMI pediatric cases, ST-11 isolates seem to increase the risk of death. CS therapy would have an anti-inflammatory role stopping the noxious effects of these hyper-invasive isolates and helping to improve outcome.

LEMIERRE SYNDROME IN CHILDHOOD: MANAGEMENT OF SEVERE OTOGENIC VARIANT

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Background: Lemierre-syndrome is associated with severe head and neck infections. Anaerobic bacteria are most commonly isolated. Early diagnostic and correct management are important due to its considerable morbidity and mortality. We report the successful management of 2 cases with otogenic variant of Lemierre-syndrome.

Case reports: 2-year old girl, previously healthy presents with acute high fever (39.5°), otalgia and prostration. Blood test results (neutrophils 13.500/mm³ and CRP 340mg/l) were suggestive of invasive bacterial infection. Due to progressive clinical impairment, PICU admission and empiric antibiotic treatment for otogenic/CNS infection with cefotaxime and clindamycin were initiated and myringotomy realized. After isolation of *Fusobacterium nucleatum* in blood culture, treatment was switched to penicillin mono-therapy. Heparin was added after detection of an internal jugular vein thrombosis by CT scan. After 42 days of antibiotic therapy (21 days IV and VO each) complete clinical recovery was achieved.

3-year old previously healthy girl was admitted with a 2-weeks history of fever, otalgia, otorrhea and postauricular fluctuation. CRP (177.9mg/l), neutrophils (11.950/mm³) were elevated. CT of head and neck revealed acute mastoiditis, subperiosteal abscess and thrombophlebitis of the sigmoid sinus and internal jugular vein. She underwent mastoidectomy and abscess drainage being culture positive for *Fusobacterium necrophorum*. Amoxicillin-clavulanic acid was administered for 7 weeks, however osteomyelitis of the temporal bone as well as reoccurrence of raised inflammatory markers delayed clinical recovery and required antibiotic-switch to metronidazole for further 3 month.

Conclusion: Early diagnosis, aggressive and prolonged antibiotic therapy in combination with surgical drainage when indicated result in satisfactory outcomes of Lemierre-syndrome.

MYCOPLASMA PNEUMONIA INFECTION - A SERIES OF A DEPARTMENT OF PEDIATRICS (2005-2010)**B. Maia Vale**¹, M.M. Zarcos²¹Hospital Pediátrico Carmona da Mota, Coimbra, ²Centro Hospitalar Leiria-Pombal, Leiria, Portugal

Background and aims: *Mycoplasma pneumoniae* is one of the most common etiologic agents of community-acquired pneumonia, with higher incidence between ages of 5 and 20 years. Definitive diagnosis requires documented seroconversion with 2 to 4 weeks apart. This study aims to characterize patients observed in a Department of Pediatrics with positive serology for *Mycoplasma pneumoniae*.

Methods: Retrospective descriptive study of children and adolescents admitted to the ward or seen in consultation with positive serology for *Mycoplasma pneumoniae* from January 2005 to August 2010. Serology is positive if IgM by ELISA \geq 1RU/ml. Demographic and clinical variables were analyzed.

Results: We obtained 24 cases of children and adolescents with positive serology for *Mycoplasma pneumoniae*. There was a predominance in female (66%), in the age group 5 to 15 years (66%) and in Winter. Most common symptoms were fever and cough. Complementary tests revealed leukocytosis with neutrophilia in 38% and C-reactive protein increased (32%). The most prevalent pattern on chest radiograph was unilateral interstitial infiltrate (55%) and 35% had pleural effusion. The diagnoses were pneumonia (20 cases) and pleurodynia, arthritis, erythema nodosum and upper respiratory tract infection, 1 case each. Macrolide were prescribed in 54%. All patients had good outcome.

Conclusions: The results obtained are identical to those described in literature. The differences observed are: winter predominance, higher percentage of diagnosis other than pneumonia and unilateral interstitial infiltrate unilateral as the most frequent radiological pattern. We stress the importance of epidemiological documentation of seroconversion in suspected cases of infection by this microorganism.

THE FACTORS AFFECTING CULTURE POSITIVITY IN BRUCELLOSIS

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Background: Brucellosis constitutes a public health problem in Turkey. In endemic *Brucella melitensis* areas such as Turkey, children represent 20-25% of cases.

Patients and methods: This study was designed and conducted as a retrospective study including the patients with the diagnosis of brucellosis during the period of January 2007-January 2012. In this study the demographic and clinical features of the patient with the positive blood cultures or cultures from bone marrow aspirations were compared with the brucellosis patients with negative brucella cultures.

Results: During the period between January 2007 to January 2012 totally 116 patients were treated with the diagnosis of brucellosis. Among the 116 patients, in 40 patients (34,5%) *Brucella* species were isolated. Forty seven (40,5%) patients were female; while sixty-nine patients (59,5%) were male. The mean age of the patients were $9,33 \pm 4,01$ years (minimum 0,2 months to 15 years). The ratio of fever in culture positive patients (82,5%) were found to be significantly higher in culture negative patients (63,2%). However the ratio of previous antimicrobial treatment and constitutional symptoms were found to be indifferent in two groups ($p > 0,05$).

Conclusion: While handling patients with suspected brucellosis; sampling for blood culture has a great importance especially in presence of fever. Additionally in our study previous antimicrobial therapy did not play an important role for culture negativity.

HEMOLYTIC UREMIC SYNDROME CAUSED BY BORDETELLA PERTUSSIS INFECTION

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Background: Hemolytic uremic syndrome (HUS) is a clinical syndrome characterized with hemolytic anemia, thrombocytopenia, and acute renal failure. It has great clinical importance due to its being one of the leading cause of acute renal failure in children. While typical HUS develops due to shiga toxin producing *Escherichia coli* (STEC), several viruses and bacteria were reported to be associated with atypical HUS.

Patient: We report the case of a 5-week-old infant with severe *Bordetella pertussis* infection resulting in hemolytic anemia, thrombocytopenia, and acute renal failure leading to a diagnosis of hemolytic uremic syndrome (HUS) associated with pertussis. She was treated with macrolides in the eraly period and periton dialysis and plasma transfusions were performed later. However; the patient died on the 15 th day of hospitalization. Pertussis diagnosis depended on the clinic and positive PCR results for from the nasofarengeal aspirate samples.

Conclusion: The cases with pertusis had been increasing for the last decade; however HUS due to *Bordetella pertussis* had been rarely reported. As in our case; in infants with pertussis with any problem in the renal functions and associated thrombocytopenia should remind the clinician about the possibility of developing HUS.

PROSPECTIVE OBSERVATIONAL STUDY ON CURRENT PRACTICE IN SUSPECTED SEPTIC CHILDREN ADMITTED TO A PEDIATRIC HOSPITAL

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Background and aims: Sepsis is one of the main cause of morbidity and mortality in pediatric population. An observational study regarding microbiological diagnosis and treatment of sepsis was prospectively conducted with the aim to evaluate current practices in our pediatric hospital. **METHODS** Any immunocompetent child aged 0-12 years admitted to immunological and infectious pediatric wards between July-December 2011 with possible diagnosis of sepsis has been enrolled. At discharge every patient was classified on clinical judgment and microbiological results as having confirmed, probable or no sepsis.

Results: We enrolled 35 patients (31% < 3 month-old), with mean age of 5.2 months. Results about proportion of microbiological diagnosis and type/duration of treatment are shown in the table. Our collected data revealed that 77% of children received double therapy for a mean duration of 14 days (including iv plus oral treatment after discharge). Noteworthy, length of treatment was significantly different between patients with confirmed sepsis and no sepsis (p 0.032) but there was no significant difference in duration of treatment among patients with probable and no sepsis.

Conclusions: Our data revealed that there is a tendency to over length of treatment in all categories. In consideration of these we will implement a stricter policy of antibiotic prescription and keep the observational studies for further six months.

	Confirmed sepsis	Probable sepsis	No sepsis
< 3 months old	4	12	8
Double vs Single therapy (mean days duration)	4 vs 0 (17.5)	10 vs 2 (12.9)	5 vs 3 (11.5)
> 3 months old	2	6	3
Double vs Single therapy (mean days duration)	2 vs 0 (15.5)	4 vs 2 (11.5)	3 vs 0 (13.7)

[Cohort characteristics]

SEPSIS CAUSED BY SERRATIA SPECIES IN PRETERM INFANTS: CLINICAL CHARACTERISTICS AND OUTCOME

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Aim: To determine clinical characteristics and outcome of sepsis caused by Serratia species in preterm infants.

Methods: 87 consecutive preterm infants with the Serratia species sepsis confirmed by positive blood cultures were retrospectively evaluated. Patients were analyzed for maternal, demographic, clinical and therapeutic variables, as well as for the outcome. Cox regression analysis was used to determine predictors of outcome.

Results: Study group consisted of 54 male and 33 female neonates; average birthweight was 1614±586 grams and average gestational age was 31±4 weeks. A total of 13 (14.9%) patients died during initial hospitalization. Mechanical ventilatory support was used in 39 (44.8%) and pneumothorax developed in 5 (5.7%) patients. Cox regression analysis, that included maternal (peridelivery infections, premature rupture of membranes, type of delivery), demographic (sex, birthweight, gestational age), clinical (Apgar score in 1. and 5. minute, insertion and duration of central venous line insertion and intubation) and therapeutic variables (use of surfactant, initial antibiotic regimen consisting of amikacin and ampicillin), identified birthweight (B -0.002, exp B 0.918, p=0.005) and gestational age (B -0.201, exp B 0.815, p=0.002) as predictors of outcome, but only Apgar score in 1. minute (B -0.429, exp B 0.651, p=0.002) was identified as an independent predictor of outcome.

Conclusion: Our data indicate that sepsis caused by Serratia species in preterm infants have poor outcome. Only Apgar score in 1. minute is an independent predictor of outcome.

TWO PEDIATRIC CASES OF GRANULICATELLA ENDOCARDITIS SUCCESSFUL TREATED WITH MEROPENEM

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Background and aims: Granulicatella spp. is a difficult growing bacteria responsible for endocarditis and sepsis which are fatal in about 20% of the cases. Here we report two case of Granulicatella endocarditis in children.

Case reports: The first case concerns a 7-years-old female with Shone syndrome, a history of cardiac surgery, and a subtotal obstruction of conduit. The second one was a 5-year-old male with infundibular pulmonary stenosis and cardiac catheterization 3 weeks before the hospitalization. Both were diagnosed with endocarditis according to modified Duke criteria.

In the two patients blood cultures turned positive for Granulicatella adiacens. Due to the inefficacy of first line treatment (Vancomycin+Gentamycin in the first patient and Cefotaxime+Gentamycin in the second one), the therapy was changed with a double therapy with meropenem. In both patients symptoms improved significantly and after 4 weeks of intravenous therapy they shifted to per os and were discharged in good clinical condition. On follow-up visit, 6 months after discontinuation of therapy, the two patients were doing well with negative blood cultures.

Conclusions: Given the particular antibiotic susceptibility profile of these bacteria, and the inconstant feasibility of AST, we suggest that, in the pediatric population, combined antibiotic regimen including meropenem should be considered as a second line treatment in non-responding patients or even as a first line treatment in high risk patients.

THE CLINICAL FEATURES AND SEQUELAE OF PAEDIATRIC INVASIVE MENINGOCOCCAL DISEASE**C. Stein-Zamir**, H. Shoob, N. Abramson, G. Zentner*Jerusalem District Health Office, Jerusalem, Israel*

Background: *Neisseria meningitidis* is an important cause of childhood meningitis and septicaemia. Invasive meningococcal disease (IMD) is associated with considerable mortality and life-long debilitating sequelae.

Methods: Population-based epidemiologic study of IMD in the Jerusalem district, focusing on children under 15 years, including follow-up interviews.

Results: Between 1999 and 2011, 222 IMD cases occurred in Jerusalem, 189 (85%) of them in children aged 0-14 years. The annual incidence rate was $2 \pm 0.6/100,000$ population peaking among infants under 1 year ($20.9 \pm 9.5/100,000$). Most of the children (83%) were from low socio-economic Arab and Jewish ultra-orthodox communities. The case fatality rate was higher among Arab than among Jewish children (17.1% vs. 7.5%). Most cases (64.5%) were culture-confirmed by positive blood (32.9%) or cerebrospinal fluid (19.4%) culture or both (12.2%). Significantly fewer positive cultures were seen in those treated with antibiotics prior to admission. Serogroup B comprised 77.8% of the bacterial isolates. Pulsed-field gel electrophoresis showed considerable resemblance between the isolates from Arab cases. The most common symptoms were vomiting, headache and photophobia; clinical signs included fever, seizures, petechial rash and meningismus or a bulging fontanelle. Short-term complications were infrequent and included sterile arthritis and prolonged fever. Among survivors of the acute illness, the long term sequelae included hearing loss in 5.4% and neurological impairment in 14%.

Conclusions: IMD causes significant mortality and sequelae in children. *Neisseria meningitidis* group B was found to be the leading pathogen in our population; hence, accelerated development of a specific vaccine against group B disease is crucial.

SUCCESSFUL MEDICAL TREATMENT IN A CHILD WITH *E. COLI* ESBL MENINGITIS, COMMUNICATING HYDROCEPHALUS AND VENTRICULAR EMPYEMA: A CASE REPORT

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Background and aims: ESBL producing organisms are increasingly emerging and implicating an outbreak in both community and hospital settings. We report a successful non-surgical, medical treatment in a child with *E. coli* ESBL meningitis, communicating hydrocephalus and ventricular empyema.

Case report: An eight-month-old boy with multiple anomalies presented with fever and mucous diarrhea. Ceftriaxone was initiated with gradual improvement of diarrhea. On the third day of admission, he developed generalized tonic-clonic seizure. CSF showed WBC of 16,560 (99% PMN), protein of 279 mg/dL, sugar < 2 mg/dL and gram stain demonstrated gram negative bacilli. High dose cefotaxime and phenytoin were given. After three days of treatment, the patient developed recurrent seizures with decremented sensorium. Endotracheal intubation was placed and CT demonstrated marked communicating hydrocephalus with ventricular empyema. CSF culture revealed *E. coli* ESBL, antibiotic was switched to meropenem and neurosurgical consultation was made. The parents did not consent to ventriculostomy with preference to antibiotic treatment with regular lumbar puncture. After treatment installation, gradual improvement was observed and CSF culture was negative for organisms after 14 days of treatment. Meropenem was continued for 42 days. His sensorium and CSF profile returned to normal before stopping the antibiotic. Serial CT brain showed improvement of hydrocephalus. Phenytoin was stopped with no recurrent seizure.

Conclusions: Incidence of infections from ESBL producing organisms are increasingly emerging and causing wide spectrum of illnesses which prompts for both aggressive medical and surgical intervention. Antimicrobial agents must be vigilantly utilized to prevent possible development of new highly-resistant organisms.

AN UNUSUAL ASPECT OF BARTONELLOSIS MIMICKING AN AUTOIMMUNE DISEASE**D. Zarganis**¹, G. Papaioannou², G. Vartzelis¹, D. Maritsi¹¹*General Pediatrics, ²Radiology, Mitera Hospital, Athens, Greece*

Background: Although previously considered a rare cause of pyrexia of unknown origin (PUO), with the aid of new diagnostic tools the clinical spectrum of bartonella henselae infection has expanded.

Methods: We present a case of a seven year old immunocompetent female patient who developed systemic symptoms mimicking an autoimmune rather than an infectious disease.

Results: The patient, offspring of an unrelated Caucasian couple with uneventful past medical history, presented with erythematous papular rash, biquotidian fever, night sweats and arthralgias. There was no antecedent history of cat contact. Investigations showed increased inflammatory markers (ESR, CRP), thrombocytosis, hypercalcemia raised ALP and angiotensin converting enzyme (ACE). Quantiferon test was negative. Abdominal imaging showed multifocal calcified granulomas of the liver and spleen, CXR showed enlarged hilar lymph nodes; ophthalmology review showed low grade panuveitis. Clinical, laboratory and imaging features pointed towards sarcoidosis. Subsequently, raised titers (IgM 1:32, IgG 1:256) against bartonella confirmed the diagnosis of B. henselae infection. She was treated with gentamycin followed by ciprofloxacin; repeat investigations showed complete resolution of findings.

Conclusion: The presence of hepatic and splenic lesions in children with bartonellosis is well documented. Our case however, exhibited certain unusual findings such as the co-existence of ocular and solid organ involvement as well as the presence of calcifications during the acute phase. Serological testing is an inexpensive and effective way to diagnose bartonellosis in immunocompetent patients; we suggest that bartonella serology is included in the baseline tests performed in children with PUO even in the absence of contact with cats.

PRIMARY CARE PHYSICIANS' ASSESSMENT AND MANAGEMENT OF CHILDREN WITH ACUTE PHARYNGITIS IN AUCKLAND, NEW ZEALAND

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Background and aims: In New Zealand acute rheumatic fever (ARF) in children is still a serious and common sequelae of group A Streptococcus (GAS) throat infections. Those most at risk are children aged 5-14 years and Maori/Pacific Island people. Timely diagnosis and accurate management of group A streptococcal pharyngitis is a crucial step in the primary prevention of acute rheumatic fever.

The National Heart Foundation of New Zealand and the Cardiac Society of Australia and New Zealand have published guidelines on ARF, including the assessment and management of acute GAS pharyngitis.

Our aim was to assess how primary care physicians in Auckland manage sore throats in children, including whether they have implemented these guidelines.

Methods: Primary care physicians in Auckland, NZ, were invited to complete an online survey looking at how they managed a child with a sore throat and any factors that may influence their decisions.

Results: There were 48 eligible responses to the survey; 19 (40%) did not follow a guideline or policy regarding sore throat management; 34 (71%) primary care physicians correctly identified a child with likely GAS pharyngitis, however only 12 (24%) followed a management plan in keeping with the ARF guidelines for a child with pharyngitis suggestive of GAS.

Conclusions: Greater clinical awareness of the risk factors for GAS sore throat and the availability of the guidelines through health policy and educational approaches could be suffice to improve the quality of sore throat management by primary care physicians.

COMMUNITY ACQUIRED PSEUDOMONAS SEPSIS PRESENTING WITH ECTHYMA GANGRENOSUM**E. Moraitis**^{1,2}, D. Lianou¹, K. Kotsonis¹, S. Papadaniil¹, K. Kassiou¹¹*1st Dept of Pediatrics, Aghia Sophia Children's Hospital, Athens, Greece,* ²*Rheumatology, Great Ormond Street Hospital for Children, London, UK*

Background: Pseudomonas aeruginosa sepsis is uncommon in children with no underlying immunodeficiency. Ecthyma gangrenosum is a known cutaneous manifestation of Pseudomonas sepsis. It consists in dermal necrosis resulted from vascular thrombosis secondary to bacterial multiplication in the wall of the vessels.

Methods: A previously healthy six-month-old girl presented with a three-day history of high fever, and one-day history of diarrhea and lethargy.

The examination on admission showed a lethargic infant, with a deep and large anal ulcer with a grey- yellowish plateau and surrounding erythema. The investigations of note revealed leukopenia and neutropenia, and significantly raised inflammatory markers. Pseudomonas aeruginosa was isolated from the cutaneous lesion, stool and blood cultures.

The patient received a 15-day course of intravenous ceftazidime and amikacin according to the culture sensitivity.

The clinical picture has improved relatively quickly, with defervescence on day 2 of treatment and subsequent resolution of the necrotic lesion with no need for surgical debridement.

The initial haematological abnormalities have corrected within the first days of treatment and the patient remained normopenic at follow up.

Results: In view of the higher prevalence of Pseudomonas sepsis in immunocompromised children, a work-up for immunodeficiency has been performed. The quantitative immunoglobulins test, neutrophil oxidative burst assay, leucocyte adhesion and lymphocyte subsets were normal.

Conclusion: Ecthyma gangrenosum associated with neutropenia in an unwell child should raise the suspicion of Pseudomonas aeruginosa infection. Subsequent evaluation for immunodeficiency should be performed in these patients. Early recognition of ecthyma gangrenosum will prompt us to start appropriate therapy.

PARAPNEUMONIC EMPYEMA IN CHILDREN IN GERMANY - FIRST RESULTS ON THERAPEUTIC MANAGEMENT FROM A NATIONWIDE SURVEILLANCE STUDY

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Introduction: An increase in the incidence of paediatric parapneumonic empyema (PPE) has been observed in several countries. The superiority of either conservative or operative treatment is discussed controversially.

Methods: Since 10/2010, surveillance has been conducted in all 472 German paediatric departments using the German Surveillance System for Rare Paediatric Diseases (ESPED). Children with pneumonia accompanied by pleural effusion persisting for >7 days or necessitating pleural drainage were included. Clinical, diagnostic and therapeutic details and outcome were analyzed.

First results: Between 10/2010 and 07/2011 155 children with PPE were analysed. Median hospitalisation duration was 15 days (IQR 11,0-21,0). 49% of the children needed intensive care. In 102 cases (66%) pleural space was opened by puncture (65/42%), drainage (85/55%) or surgical intervention (26/17%). 23(15%) children received video assisted thoracic surgery with a median delay of 9 days post hospitalisation, in 13 cases with decortication. Fibrinolysis, pleural lavage or open decortication were performed in 23(15%), 19(12%) and 3(2%) children respectively.

An association with surgical intervention (VATS: n=23; open decortication: n=3) was identified for *S. pneumoniae* ($p < 0,01$) PPE as well as for sonographic stages reflecting organisation of pleural fluid according to the American Thoracic Society ($p < 0,05$). In 34(22%) children persistent sequelae were documented, mostly chronic pleural/pulmonary changes.

Discussion: For almost one third of the children the pleural space was not opened and surgical intervention was necessary only in few children. Further analyses will be necessary to identify diagnostic parameters for which an invasive procedure seems advantageous.

THE THR164ILE POLYMORPHISM OF THE BETA-2 ADRENERGIC RECEPTOR ASSOCIATES WITH SUSCEPTIBILITY AND OUTCOME IN CHILDREN WITH SYSTEMIC MENINGOCOCCAL DISEASE

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Background: Meningococcal disease may present as sepsis, meningitis or a combination of both. The major clinical symptom of septic shock is reduced blood pressure. The adrenergic system acts as major player for short-term blood pressure regulation via controlling vascular tone and cardiac output.

Septic patients show a severe dysregulation of haemodynamics. Peripheral vascular failure, as seen in meningococcal septic shock, may be facilitated by distinct single nucleotide polymorphisms in the adrenergic receptors. A rare polymorphism in the β_2 adrenergic receptor gene (ADRB2 Thr-164 to Ile-164) leads to "loss of function" of the receptor, dramatically reducing receptor densities on vascular smooth muscles. This prospective, multicentre study examined the relationship between meningococcal disease and the ADRB2 Thr164Ile variant.

Methods: 424 previously healthy children with meningococcal infection from 107 paediatric hospitals in Germany, Switzerland, Italy, and Austria were included in this study. Cord blood samples of healthy, unrelated newborns (n = 474) were used as controls. The ADRB2 Thr164Ile polymorphism was analysed in all subjects using a TaqMan assay.

Results: Carriers of the Ile164 variant showed a 3.6 increased OR for fatal outcome (95%CI = 1.0 - 13.8, P = 0.043). In addition, the Ile164 variant conferred a significantly higher risk for meningococcal disease (3.5% in patients vs. 1.1% in healthy controls, OR = 3.4; 95%CI = 1.2 - 9.5, P = 0.011).

Conclusion: In our study we provide first evidence that the rare ADRB2 Thr164Ile polymorphism is not only associated with outcome in meningococcaemia but also the risk for meningococcal disease.

THE GLN27GLU POLYMORPHISM OF THE BETA-2 ADRENERGIC RECEPTOR ASSOCIATES WITH HAEMODYNAMICS AND OUTCOME IN CHILDREN WITH SYSTEMIC MENINGOCOCCAEMIA

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Background: Meningococcal disease (MD) may present as sepsis, meningitis or a combination of both. Peripheral vascular failure, as seen in meningococcal septic shock, may be facilitated by distinct single nucleotide polymorphisms in adrenergic receptor genes. The Gln27Glu polymorphism in the β_2 adrenergic receptor gene (ADRB2) leads to attenuated down-regulation of the receptor, resulting in constant receptor densities on vascular smooth muscles, despite agonist action. This prospective, multicentre study examined the relationship between MD and the ADRB2 Gln27Glu variant.

Methods: 420 previously healthy children with MD from 107 paediatric hospitals in Germany, Switzerland, Italy, and Austria were included in the CEMGS study. Another cohort of 360 confirmed paediatric cases of MD recruited through a national research network (ESIGEM - www.esigem.org) from 41 Spanish hospitals, was used for replication analysis. The Gln27Glu polymorphism was analysed using a MALDI-TOF MS (ESIGEM) and a HRM assay (CEMGS).

Results: Patients homozygous for the Gln27 variant (Gln27Gln) showed significantly higher systolic blood pressure nadirs (83.5 mmHg vs. 75.7 mmHg, P -value = 0.02) and improved outcome (2.9% vs. 9.5% fatality rate, P -value = 0.009, OR = 3.5, 95%CI = 1.2-10.3). Refractory hypotension was rare in this group (7.6% vs. 17.6%, P -value = 0.04, OR = 2.6, 95%CI = 1.1-6.7), and length of vasopressor use (2.2 days vs. 6.7 days, P -value < 0.0001) was markedly shorter than for patients with other genotypes.

Conclusion: In our study we provide first evidence that the ADRB2 Gln27Glu polymorphism directly interferes with sepsis haemodynamics and is associated with outcome in meningococcaemia.

SURVEILLANCE OF HOSPITAL-ASSOCIATED INFECTION IN AN PEDIATRIC INTENSIVE CARE UNIT IN İZMİR, TURKEY

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Background: In this study we aimed to determine the frequency of hospital-acquired infection (HAI), the microorganisms that cause HAI, the antibiotic resistance patterns of these microorganisms and the risk factors for the development of HAI at Pediatric Intensive Care Unit (PICU).

Patients and methods: Between the January 2010-January 2011, a total of 320 children who admitted the PICU were evaluated retrospectively. HAI developed in 61 of 186 patients. Hospital-acquired infection positive and negative patients were compared to each other according to gender, age, total duration of stay in PICU and in hospital, the PRISM and PIM scores, mortality rates, intubation, tracheostomy, central venous catheter, urinary catheter, nasogastric tube, total parenteral nutrition (TPN), antibiotic use and hospital admission story. In statistical analysis, Student-t, Mann-Whitney U, Chi-Square and Logistic Regression tests were used.

Results: The HAI rate was calculated as 33.3%. The most common type of nosocomial infection was bloodstream infection (73.2%), the most common pathogenic group was gram-negative bacteria and the most frequently isolated microorganism was methicillin-resistant coagulase-negative staphylococci (26.7%). In 86% of these microorganisms, multi-drug resistance was determined. Between the HAI (+) and (-) groups, we found a statistically significance by logistic regression analysis in terms of presence of underlying chronic disease, length of stay in hospital, the presence of central venous catheter, the blood product transfusion status, the application of sedation and the total parenteral nutrition support.

USING DATA LINKAGE METHODOLOGY TO DETERMINE RATES OF HOSPITAL-ACQUIRED BLOODSTREAM INFECTIONS IN CHILDREN IN ENGLAND

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Objectives : To determine the epidemiology of hospital-acquired (HA) bloodstream infection (BSI) and antimicrobial resistance (AMR) in children aged 1 month-18 years in England.

Methods : Episodes of BSI and associated AMR data in children voluntarily submitted to the Health Protection Agency's microbiological database between January 1st 2009 and March 31st 2010 were extracted. Microbiological reports were probabilistically linked to England Hospital Episode Statistics (HES) in-patient data to capture admission and discharge dates. Reports of positive blood cultures from children taken ≥ 2 days after admission were defined as hospital-acquired (HA) and were analysed in terms of pathogen and AMR.

Results : A total of 8,718 episodes of paediatric BSI were reported during the study period, of which 82% were linked with HES data. A total of 1,734 (23%) episodes were HA, equating to a rate of 4.89/1,000 admissions lasting ≥ 2 days. Median age at BSI was 1 year, and 54% occurred in males. The most commonly reported organisms were coagulase-negative staphylococci (30%), *Enterococcus* spp. (13%), *Staphylococcus aureus* (11%), *Escherichia coli* (8%) and *Klebsiella* spp. (7%). AMR for Gram-negative organisms was 4% for piperacillin/tazobactam and gentamicin and 5% for meropenem. AMR in Gram-positive organisms was 3% for vancomycin therapy.

Conclusion : This study outlines the first national estimates of HA BSI rates in children in England and characterises the causative organisms. AMR to common antibiotic treatments was low. This study demonstrates the value of data linkage for conducting epidemiological investigation at a national level.

CHARACTERISTICS OF SALMONELLA INFECTIONS IN AN INDUSTRIALISED COUNTRY

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Introduction: Salmonella infections are common in children from developing countries and associated with increasing antibiotic resistance.

Objectives: To evaluate specificities of Salmonella infections in children cared for in a paediatric university hospital in Brussels.

Methods: Cases were identified through laboratory records from January 2005 until December 2011. Charts were retrospectively reviewed for demographical and clinical data. Serotyping and antibiotic susceptibility data were analysed. Incidences were calculated using number of emergency department/primary care visits as denominator.

Results: 239 children had a positive clinical sample. Incidence of Salmonellosis increased steadily from 27/10⁵ in 2005 to 37/10⁵ in 2011. Over the 7 years, there was a marked seasonality with a monthly infection rate peaking in September. 40% of the children had a previous history of travel, mostly in Africa (2/3). The majority of the children had gastroenteritis, 20 (8.5%) had bacteraemia and one had osteomyelitis. 8 children were tested positive in the adoption screening. For 72 (30%) children Salmonella was the source of hospitalization. 53 (22%) children received antibiotic treatment, 28 of which were administered intravenously. The most common Salmonella serogroups were B, D and to a lesser extent C. *S. typhi* was only recovered in 5 imported cases. Only 11% and 10% of the strains were ampicillin and cotrimoxazole non-susceptible respectively. Among blood isolates, all were susceptible to ceftriaxone and one was resistant to quinolones.

Conclusions: Paediatric Salmonella infection is not uncommon in Brussels, often after returning from endemic countries. The incidence has been increasing since 2005. Antibiotic resistance remains low.

LYME DISEASE IN CHILDHOOD: REPORT OF A CASE

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Background and aims: The aim of the current study is to present an unusual case of a pediatric patient suffering from Lyme disease and remind clinicians of the natural course and treatment of this uncommon clinical entity.

Material and methods: A 13 year old, immigrant boy was admitted to our pediatric department because of high fever, up to 40 Celcium degrees, since a 7 day period time, along with dizziness and fatigue. He mentioned persistent muscle pains and arthralgia of pelvic limbs for at least 3 weeks. He could not recall a tick bite. There was not present any erythema migrans. He undertook a thorough clinical, imaging and laboratory examination and evaluation of acute phase reactants as part of the diagnostic procedure that would allow the application of the appropriate treatment therapy and the consequent patients recovery.

Results: Serologic tests for antibody to *Borrelia Burgdorferi* that were positive helped the establishment of diagnosis. Consequently, the patient received the appropriate antibiotic medication.

Conclusion: Even though, the true incidence of Lyme disease in Hellenic child population is not estimated, pediatricians should always be aware of this clinical entity because of its severe neurological and cardiac complications.

GROUP A STREPTOCOCCAL TOXIC SHOCK SYNDROME COMPLICATED WITH PERIPHERAL ISCHEMICAL GANGRENE AND NECROTIC FASCIITIS: A CASE REPORT

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Aim: We report a case of group A streptococcal toxic shock syndrome (STSS) complicated with peripheral ischaemic gangrene and necrotizing fasciitis.

Methods: A previously healthy 11-year-old boy presented with a 2-days history of fever and pain of both ankles and right forearm. Clinical examination revealed a toxic appearance, poor peripheral perfusion, hypotension, tachycardia, fever, swelling and erythematous rash of the right forearm. A magnetic resonance imaging shown fasciitis of the right forearm and surgical debridement with extensive fasciotomy were performed. Rapid pharyngeal test and blood cultures were positive for group A β -haemolytic *Streptococcus*. Consequently multiorgan dysfunction and peripheral symmetrical gangrene of toe fingers and left thumb were established. However, after combined antibiotic treatment, inotropic support, intravenous immunoglobulin (IVIG) administration, mechanical ventilation for 57 days and hospitalisation in PICU for 61 days, his clinical condition improved. Plastic reconstruction of the right forearm was necessary as well as amputation of toe fingers.

Discussion: STSS is a distinct, aggressive entity that most often affects patients with underlying diseases; however, it can also occur in healthy individuals. In rare cases, STSS can be complicated by necrotizing fasciitis. In addition, peripheral symmetrical gangrene constitutes a very rare complication of invasive streptococcal infections due to disseminated intravascular coagulation, which often results to amputations.

Conclusions: This case indicates that despite the exponential nature of the illness and the rapid progression to shock and multiorgan dysfunction, complete recovery can be achieved by maintaining a high index of suspicion, early treatment and aggressive organ support.

PATTERN AND RESISTANCE RATES OF BACTERIA ISOLATED FROM BLOODSTREAM INFECTIONS IN PEDIATRIC INTENSIVE CARE UNIT (PICU)

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Background and aims: BSIs constitute common nosocomial infections in PICU. The aim of this study was to characterize BSI bacterial pathogens and their susceptibility rates in a PICU.

Methods: We conducted a retrospective analysis of BSI isolates in an 8-bed PICU of a tertiary-care level hospital from 2005 to 2011. Bacterial identification and antimicrobial susceptibility were done using Vitek2 automated system. Duplicate and repetitive bacterial isolates were excluded.

Results: Of 154 pathogens, Gram-negative and Gram-positive bacteria were isolated in 41% and 59% of cases, respectively. Among Gram-negatives 34% were *Acinetobacter baumannii*, 34% *Pseudomonas spp* (91% *P. aeruginosa*, 9% *Stenotrophomonas maltophilia*) and 32% Enterobacteriaceae (70% *Klebsiella pneumoniae*, 20% *Serratia marcescens*, 10% *Enterobacter cloacae*). Among Gram-positive bacteria 92% were coagulase negative staphylococci (68% *S. epidermidis*, 14% *S. hominis*, 12% *S. haemolyticus*, 6% *S. warnerii*), 7% *Enterococcus spp* (*E. faecium*, *E. faecalis*) and only 1% *S.aureus*. Increased resistance rates of *A. baumannii*, *P. aeruginosa* and *K. pneumoniae* were found to 3rd generation cephalosporins (100%, 61%, 92%), piperacillin/tazobactam (100%, 15%, 42%), meropenem (64%, 33%, 0%) and ciprofloxacin (100%, 27%, 42%), respectively. Among aminoglycosides amikacin and gentamicin had the best in vitro activity against to *K. pneumoniae* isolates (75%) whereas tobramycin to *P. aeruginosa* (20%). Colistin resistance was found in 7% of *A. baumannii* isolates. All staphylococci and enterococci were susceptible to glycopeptides, linezolid and daptomycin. CoNS were 95% resistant to oxacillin.

Conclusion: Predominance of non-fermenters and high levels of resistance especially to beta-lactams among Gram-negative bacteria isolated from BSI in PICU is of great concern.

NEONATAL CONJUNCTIVITIS: 4 YEARS WITHOUT PROPHYLAXIS

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Background and aims: The need of eye prophylaxis is questioned: oxytetracyclin is effective for *Neisseria gonorrhoeae* but ineffective for *Chlamydia trachomatis*. Due to improvement in pre-natal care, infection with *Neisseria gonorrhoeae* is now seldom encountered.

Our objective was to know the prevalence of neonatal conjunctivitis in the era of non-prophylaxis.

Methods: A retrospective, descriptive study, with consultation of medical records of newborns with ocular exudate culture between January 1st of 2008 to December 31st of 2011.

Results: We included 8972 newborns in the study. About 292 (3,3%) developed conjunctivitis, 55% were from masculine gender with a median of age of 6 days at the time of the beginning of the symptoms. The median cases/year was 73 with a decrease in the incidence over the years (incidence of 4.9 cases per newborn in 2008 vs 2.5 in 2011). About 60% of all conjunctivitis there was a identifiable germ: *S. aureus* (23%), *E. coli* (20%), *C. trachomatis* (6,4%), *S. epidermidis* (3%) other (11%). In any case of conjunctivitis was isolated *Neisseria gonorrhoeae*

The age at onset of *C. trachomatis* (9,9 days) was similar to the age of *S. aureus*, and higher than *E.coli* conjunctivitis (2,6 days), or when no microorganism was isolated (5,3 days).

Conclusions: In the era of non-prophylaxis with oxytetracyclin, we conclude that there is no incidence of neonatal conjunctivitis of *Neisseria gonorrhoeae*. We also conclude that, despite the non-use of prophylaxis, the incidence of neonatal conjunctivitis continues to decline. So, the need of topical oxytetracyclin remains doubtful.

ACUTE MASTOIDITIS IN CHILDREN IN THE ERA OF PNEUMOCOCCAL CONJUGATE VACCINE IN MADRID

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Background: The incidence of mastoiditis has recently increased. This has been related to the emergence of new serotypes or more aggressive drug-resistant strains. Universal program of PCV7 was set up in Madrid in 2008, and modified to PCV13 in June, 2011.

Methods: Retrospective study of all consecutive mastoiditis diagnosed in children below 15 years from October-2006 to December-2011 in Getafe Hospital. Cultures were obtained from tympanocentesis and placement of ear tubes. Antibiotic resistances to *S.pneumoniae* were assessed using EUCAST 2012 criteria. Epidemiological and clinical characteristics were analyzed. Statistical analysis was performed with SPSS 15.0.

Results: 31 children (18 women) were included. Median age at was 2.3 years (2 months, 12 years). The most common clinical presentation was auricle protrusion, retroauricular swelling, otalgia and fever. Median leukocytosis and PCR were 16.686 and 84.3 respectively. *S.pneumoniae* was the most common microorganism isolated in 7 cases (26%). Serotypes were: 19 A (2009), 11A (2010), 10A (2010) and non-typable but non-vaccine related in 2 cases (2009 and 2010). After introduction of PCV7, only non-vaccine related serotypes were isolated. No pneumococcal mastoiditis has been diagnosed after PCV 13 introduction. Two cases (11A and 19A) of penicillin resistance (MIC \geq 2 mg/l), and three cases (11A, 19A and non-typable) cefotaxime intermediate resistance (MIC = 1 mg/l) were observed.

Conclusions: Epidemiological changes in mastoiditis could be related to the introduction of pneumococcal conjugated vaccines. The best empirical treatment needs to be defined, when incidence of pneumococcal mastoiditis remains low but drug-resistant strains are of concern.

EPIDEMIOLOGY OF DEATHS AND HOSPITALIZATION REASONS DUE TO INFECTION FROM RESISTANT-PATHOGENIC MICROBES, IN A GENERAL HOSPITAL IN THESSALY, GREECE

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Introduction-Aim: The first cause of death among severe hospitalized- immunosuppressed patients are hospital-acquired infections by resistant pathogenic strains.

The aim of this study was to map the percentage of deaths by sex and reason, in the different departments of the Hospital, to comment on the results and suggest solutions.

Methods: We studied 1040 microbial cultures performed from samples in the affected systems and tissues of severely affected hospitalized patients, during a 6 month period, to identify pathogens resistant strains such as *Acinetobacter*(A), *Klebsiella*(K), *Pseudomonas aeruginosa*(PA).

Results: Among 184 cultures taken from 143 patients hospitalized, among all departments of the hospital, the following pathogenic resistant strains were isolated (descending order): (A): 83,3%, (K): 11,1% and (Ps): 5,6%. 18 of the patients died (12,6%), (13 males, 5 females), primarily in the ICU (44,4%) (Intensive Care Unit) and secondarily in the pathology clinics (38,85%), mainly due the *Acinetobacter* pathogenic resistant strain (susceptible Colymycin: 88,9% and then to TGC). In a percentage of 11,6% of the cultures, of those who died, 2 or 3 pathogenic resistant strains were isolated (K, or Ps). 50% of the deaths occurred during the summer period peaking in August (33.3%).

Conclusions: The main resistant pathogenic strains accounting for heavy fatal infections were the (A) followed by (K) and (Ps). These regard severely affected patients hospitalized in ICU as well as elderly-immunosuppressed patients of other departments and especially the pathology clinics. Epidemiological surveillance and vigilance of experts on infection is required. Appropriate hygiene, safety and prevention measures should be taken against these resistant pathogens.

BACTERIAL INFECTIOUS DISEASES IN THE NEWBORN INFANTS

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Background and aims: Infections are a frequent and important cause of morbidity and mortality in the neonatal period. The most important neonatal factor predisposing to infection is prematurity or LBW. The purpose in this retrospective study was to identify the bacterial microorganisms caused neonatal infectious diseases in newborns hospitalized in the Center of Neonatology during the period of 2002, 2003 and 2004.

Methods: We used clinical, microbiological, laboratory and radiology methods.

Results: 2086 newborn infants were treated at the Center of Neonatology in Podgorica during the period 2002-2004. 1391 were full term newborn (TNB) and 682 preterm newborn (PTNB). In 626 of all them were proven infections, 528 TNB and 98 PTNB. In the PTNB the most frequent infections were: omphalitis (36,7%), sepsis (30,6%), pneumonia (15,3%), cutaneous infections (12,2%), diarrhea (2,0%), conjunctivitis (2,0%), urinary tract infection (1,0%). Dominant pathogens were *Staphylococcus spp.* and *Klebsiella pneumoniae*. The bacterial agents responsible for sepsis and/or meningitis were: *Staphylococcus aureus* (26,6%), *Coagulase-Negative Staphylococcus* (20,0%), *Klebsiella pneumoniae* (20,0%), *Serratia marscescens* (13,3%),

In 528 TNB were proven infectious diseases. Most frequent infectious diseases were: omphalitis (44,9%), pneumonia (18,5%), sepsis and/or meningitis (10,9%), cutaneous infections (8,7%), ITU (5,3%), conjunctivitis (5,5%), **otitis media** (3,8%), **mastitis** (1,7%) and diarrhea (0,7%). Dominant pathogens were *Staphylococcus spp.* and *E.coli*. The bacterial agents responsible for sepsis and/or meningitis were: *Staphylococcus aureus* (19%), *Coagulase-Negative Staphylococcus* (41,3%), *E.coli* (5,3%), SGB, *Streptococcus pneumoniae*, *L. Monocytogenes*, *Klebsiella pneumoniae*, *Acinetobacter*, *Serratia marscescens*, *Pseudomonas* and *Klebsiella/Enterobacter* (each one 1,7%).

Conclusions: Preterm infants have a 3 fold higher incidence of sepsis than full-term, normal birthweight infants do.

PARAPNEUMONIC EMPYEMA IN CHILDREN IN GERMANY - FIRST RESULTS ON MICROBIOLOGICAL DIAGNOSIS FROM A NATIONWIDE SURVEILLANCE STUDY

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Introduction: An increase in the incidence of paediatric parapneumonic empyema (PPE) has been observed in several countries. We aim to determine incidence, etiology, complications, treatment and influence of pneumococcal conjugate vaccines (PCVs) in children with PPE in Germany.

Methods: Since October 2010, surveillance has been conducted in all 472 German paediatric departments using the German Surveillance System for Rare Paediatric Diseases (ESPED). Children < 18 years of age with diagnosis of pneumonia accompanied by pleural effusion persisting for ≥ 7 days or necessitating pleural drainage were included. Molecular pathogen detection from pleural fluid by broad-spectrum eubacterial 16S-rDNA PCR and pneumococcal serotyping was offered.

Results: Until June 2011, 155 patients (48% males) aged 5.0 years (median, IQR 3.4-9.2) were analysed. 116 blood cultures, 97 pleural fluid cultures and 42 PCRs were taken from 136 (88%) children; 60 of these 255 microbiological analyses (24%) were positive. Pathogens were detected in 46 of 136 children (34%), five of them with double infections. *Streptococcus pneumoniae* was detected in 27 (20%) children, *Staphylococcus hominis* and *Streptococcus pyogenes* in 3 (2%) children each. Of 27 children with confirmed *S.pneumoniae* infections, 7 (26%) had received PCV. Sequelae were documented in 30% of children with *S.pneumoniae* PPE compared to 21% of children with PPE due to other pathogens.

Discussion: *S.pneumoniae* was the most frequently identified pathogen in children with PPE. PCR of pleural fluid increased the overall bacterial detection rate from 25% to 34% especially for *S.pneumoniae*. Ongoing pneumococcal serotyping will reveal coverage by available PCVs.

AN UNUSUAL CASE OF CO-INFECTION BY *BORDETELLA PERTUSSIS* AND *STREPTOCOCCUS PNEUMONIAE* IN A NEWBORN

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Universal vaccination has greatly reduced the mortality and morbidity of pertussis in children. It represents an emerging pathogen in adolescents and adults. This increases the risk of transmission to infants too young to be immunized.

A 28-day-old infant presented at the outpatient clinic for nose obstruction. At physical examination, he showed minor respiratory symptoms without fever. He was hospitalized for surveillance. At day 1, he developed several episodes of apnea followed by bradycardia. At day 2, he presented a septic shock. Cardiopulmonary resuscitation was performed. He developed an acute respiratory distress syndrome and pulmonary hypertension. At day 6, he died from multi-organ failure despite extra corporal membrane oxygenation and hemodialysis. Day 2 biology showed an hyperleukocytosis of 62.920/mm³, with lymphocytosis (31.305/mm³), and a C - reactive protein of 14, 21 mg/dl. *Streptococcus pneumoniae* was isolated in the blood. Chest X-ray showed pneumonia of the right lung. *Bordetella pertussis* was detected by PCR in the nasopharyngeal aspiration.

Co-infection by *S. pneumoniae* and *Influenza* is a well-described phenomenon. We report here the first case of a pertussis and pneumococcal co-infection in a non-immunized infant. The emergence of pertussis infection is multifactorial. Several interventions like a booster dose administrated in young adults and the vaccination of pregnant women are proposed to prevent neonatal infections, which present a bad prognosis and eventually a fatal outcome in this risk population. Pertussis could trigger the occurrence of bacterial co-infection although pneumococcus is not a pathogen classically described in the neonatal period.

DNA FRAGMENTATION ASSAY ON J774.2 CELLS IN PRESENCE OF CYAA OF B.PERTUSSIS**N. Hosseini***Microbiology & Immunology, Yasuj University of Medical Science, Yasuj, Afghanistan*

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. The cells were treated with either CyaA or CyaA* at 0.039 mg protein/ml final concentration for 12 h. This was chosen as the concentration that gave maximum induction of caspase 3/7 activity by CyaA and CyaA* in J774.2 mouse macrophage-like cells after incubation at 37°C with 5% CO₂ for 6 h.

Results: For DNA fragmentation, all cells were treated with the same concentration of urea as was present in the toxin samples as a negative control. As a positive control, cells were grown without foetal calf serum (FCS) for 24 h, a condition known to induce apoptosis. DNA from J774.2 cells treated with CyaA showed a necrotic smear possibly because of the onset of necrosis after 12 h. The results indicated that AC enzymic activity is necessary for the induction of DNA fragmentation.

Conclusion: The remarkable effect of CyaA on J774.2 cells was seen. However, the incubation time of treatment of toxin (6 h and 12 h) may play an important role in this matter.

ADENYLATE CYCLASE OF TOXIN OF B. PERTUSSIS (CYAA) FORMULATED AS PROTEIN-COATED MICROCRYSTALS (PCMCS)

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Introduction: 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). CyaA was formulated as protein-coated microcrystals (PCMCS) on the surface of microcrystals of DL-valine. The aims of this formulation were to remove the urea, normally used to stabilize the protein, and to determine the stability of the enzymic and cytotoxic activities of the protein in this form, as a dry powder and when the PCMCS were redissolved in aqueous solution.

Materials and methods: Many different types of PCMC formulation were prepared in attempts to increase solubility of PCMCS in aqueous solution. PCMCS were made with CyaA coprecipitated with different combination of CaM, BSA, CaCl₂ or ATP and crystals were dissolved in different buffers at various pHs.

Results: The CyaA in the PCMCS was shown not to be readily soluble in aqueous buffers, but could be resolubilised in urea buffer and retained high AC and cytotoxic activity. The most promising results were obtained with CyaA-CaM-BSA-PCMCS where the highest levels of both AC enzymic and cytotoxic activities were seen when the PCMCS were dissolved in 100mM Bicine (pH 8).

Conclusions: CaM alone preserved only the AC enzymic activity of PCMCS when coprecipitated with CyaA and DL-valine. AC and cytotoxic activities of CyaA were stable in PCMCS for up to a week at 37°C.

MENINGOCOCCAL INFECTIONS IN CHILDREN - CLINICAL PRESENTATION, TREATMENT AND OUTCOME

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Background and aims: Meningococcal infections (MI) cause substantial morbidity and mortality. Previous studies from Slovenia reported stable and low incidence compared to some other European countries.

Methods: A retrospective analysis all invasive MI cases in children < 15 years of age admitted to Department of Infectious Diseases, University Medical Centre Ljubljana from 2000 to 2010 was performed. Serotyping and antibiotic susceptibility testing was done at the Institute of Public Health.

Results: There were 31 cases, 14 boys and 17 girls with a mean age of 2,2 years. 87% of all cases were in children < 5 years and 38% in infants. Twenty-two children were admitted within the first 24 hours of illness. There were 12 meningitis, 9 meningococemia and 10 mixed cases. Rash was present in 17 (55%) patients. Classical signs of meningitis were present in only 4 (13%) cases. Other presenting features were diarrhea in 29%, rhinopharyngitis in 19%, myalgias in 10%, febrile seizures in 7% and ARDS in 3%. Eight (26%) children required admission to the ICU (1-8 days). Empirical treatment consisted of cefotaxime. In 10 cases therapy was switched to penicillin. One child required VP drainage placement. The mean hospital stay was 9.7 (5-32) days. One child died and one had a relapse. Twenty-six (84%) of cases were due to serogroup B.

Conclusions: The incidence of MI in children in Slovenia remains low and stable. The majority of infections are caused by group B meningococci.

INVASIVE B-HEMOLYTIC STREPTOCOCCUS GROUP A INFECTION MIMICS SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background and aims: β -hemolytic streptococcus of Lancefield group-A (β HSA) is common infection that can cause post-streptococcal reactive ployarthritis (PSRA). Leucopenia may predispose patient to invasive bacterial infection. PSRA with invasive β HSA infection superimpose leucopenia can mimic SLE. Needs for multidisciplinary approach.

Methods: 12- year old girl presented with 4-days history of left knee and non-migratory symmetric small joint arthritis, fever (38.5 C) and malar rash. Over 2-months she manifested fatigability, weight loss, hepatitis and cytopenia; however, bone marrow biopsy ruled out malignancy.

Results: Leucocytes $3.2 \times 10^9/l$, lymphocytes $1.1 \times 10^9/l$, haemoglobin 10.7 g/dl and thrombocytes $82 \times 10^9/l$). CRP was 129mg/l, AST 348 IU/L and ALT 124 IU/L. Knee joint fluid analysis showed: leucocytes 32,000 cell/cmm (95% PMNC) and erythrocytes 280 cell/cmm. Blood and joint's fluid cultures grew β HSA. Anti-strepolysine-O titer 1470 IU/ml. Immunologic work up and echocardiogram were normal. She was treated by IV Floxacillin for 6-weeks, Ibuprofen and tramadol for arthritis then slowly improved over 4-weeks. Leucopenia of unknown cause resolved.

Her manifestations mimic SLE. Normal immunologic work up and documented invasive β HSA with high ASO titer confirmed the diagnosis of PSRA. Unlike the arthritis of rheumatic fever, PSRA is non-migratory symmetric of small joints and asymmetric of large joints that respond slowly to non-steroid anti-inflammatories. SLE often indolent that needs Immunosuppressant.

Conclusion: β HSA is common infection during childhood and can be invasive. PSRA needs high index of suspension epically if it is associated with invasive β HSA that superimposed prolonged leucopenia. Multi-systemic disease needs multi disciplinary approach to avoid complications from unnecessary therapy.

CHRONIC MENINGOCOCCEMIA: CASE REPORT IN AN IMMUNOCOMPETENT CHILD

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Chronic meningococemia is an uncommon manifestation of meningococcal disease characterised by recurrent fever, inflammatory joint manifestations and diffuse maculo-papules secondary centred by petechiae. It is rare in children with 10% of reported patients being under 18 years of age.

We report the case of chronic meningococemia in a 22-month-old immunocompetent child. She had an 18-day history of fever accompanied with widespread erythematous and brownish papules with palmar-plantar affection, myalgia, arthralgia and fatigue, in the absence of meningeal irritation or severe sepsis manifestation. She was initially thought to suffer from spotted Mediterranean fever and treated with a macrolide antibiotic. Blood cultures were positive for group B *Neisseria meningitides* and she was treated for 7 days with a third-generation cephalosporin. Immunology studies revealed low CH50 113 U Eq/ml (normal >190) and low Mannose-binding lectin serum levels 514 ng/ml (normal >1300ng/ml) during acute infection and is awaiting confirmation. She made a full clinical recovery and remained subsequently asymptomatic.

Clinical manifestation of chronic meningococemia can be confused with other infectious processes and auto-inflammatory disorders and should be considered in children with prolonged and recurrent fever, cutaneous and joint manifestations even or importantly in the absence of positive blood cultures. This will help to avoid a delayed diagnosis and/or inappropriate treatment. Positive blood culture or PCR remains the diagnostic sine qua non. The reason why some patients develop chronic meningococemia whereas other suffer from severe and disseminated disease remains to be established; microbial and host factors may predispose to this form of meningococcal disease.

ATYPICAL PATHOGENS CAUSING INFECTIVE ENDOCARDITIS IN A CHILD WITH CONGENITAL HEART DISEASE: *HAEMOPHILUS APHROPHILUS* AND *STAPHYLOCOCCUS LUGDUNENSIS*

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Background: The incidence of infective endocarditis (IE) has increased over the past years as survival rates of patients with congenital heart disease (CHD) improve. There are increasing reports of new or atypical pathogens causing IE, including those that are resistant to standard antibiotic therapy.

Case report: 4-year old female with corrected CHD (transposition of great arteries and pulmonary stenosis) was admitted in 2009 with a 3 week history of fever. Cardiac auscultation revealed mitral-related holosystolic murmur. A FBC revealed anemia (Hb 7.4 g/dL), leukocytes of 12520/mm³, platelets of 257000/mm³; CRP 221mg/L. Echocardiogram was suggestive of endocarditis with vegetation on the Contegra bioprosthesis and antibiotic therapy was started with penicillin plus gentamicin. On day 3 of treatment, *Haemophilus aphrophilus* (HACEK group bacteria) was identified in blood culture and treatment was switched to ceftriaxone to complete 8 weeks. She was readmitted in 2011 with a 16-day history of fever. Repeated blood cultures identified *Staphylococcus lugdunensis* MS and treatment consisted of 2 weeks with gentamicin, penicillin and rifampicin followed by 4 weeks with penicillin and rifampicin. 2 weeks after hospital discharge she suffered from recurrence BC negative endocarditis, underwent prosthetic tube replacement and remains asymptomatic at 6 months follow-up

Conclusion: Unusual pathogens such as *H.aphrophilus* and *S. lugdunensis* can cause IE in children, the later being generally associated with aggressive and severe disease, similar to those caused by *S.aureus*. This is the 2nd patient reported only with *S.lugdunensis* endocarditis at such young age.

SEVERE COMPLICATIONS OF PANSINUSITIS IN A CHILD HOSPITALISED IN PICU

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Background: Five -year old boy was admitted to our Pediatric Intensive Care Unit, due to a short history of headache, forehead and left eyelid swelling, fever, one episode of focal seizures and a deteriorating Glasgow scale. CT brain scan revealed superior saggital sinus thrombosis.

Methods: Thus he was intubated and intraparenchymatical catheters for Intracranial Pressure monitoring, and Cerebral Blood Flow measurement were placed. The transcranial Doppler had evidence of elevated intracranial pressure. Due to high ICP values,the patient was placed on the ICP protocol (sedation with midazolam, bolus infusions with i.v. hypertonic saline 7,5% and mannitol). Acetazolamide was also given in order to reduce CSF production. Persistence of high ICP resulting from sinus thrombosis led to the decision of making CSF drainages by lumbar puncture, on day 1 and day 3. ICP stabilized on day 5.

The patient received anticoagulants (tadroparine), from day 1 to day 10, with gradual transition to warfarin p.os, triple antibiotic regimen and levetiracetame as prophylaxis.

Results: MRI -MRV on day 9 , showed evidence of recanalization of the sinus. He was discharged home on day 15. Screening did not reveal a prothrombotic disorder.

Conclusions: In children with unusual acute headache, venous thrombosis should be included in the differential diagnosis. New MRI techniques can contribute to the early diagnosis and treatment. Early administration of antibiotics in head infections with such complications is crucial. Elevated intracranial pressure should be managed according to protocols.

THE BURDEN OF CHILDHOOD INVASIVE BACTERIAL INFECTIONS IN A DISTRICT GENERAL HOSPITAL IN THE UNITED KINGDOM

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Background and Aims: Invasive bacterial infections remain a major preventable cause of morbidity and mortality in children and account for 20% of childhood deaths in the UK. Little is known about children who develop invasive bacterial infections in an era when most are immunised against important pathogens. This objective of this study was to describe the aetiology, risk factors and outcome of invasive bacterial infections in children admitted to a district general hospital in London over a 12-month period

Methods: The case notes of children aged 1 month to 15 years with positive blood cultures who were admitted to Kingston Hospital between January and December 2010 were reviewed and data were extracted using a standardised questionnaire

Results: Of the 1,350 paediatric blood cultures taken over the 12-month period, 114 (8%) were positive, including 33 (29%) in infants aged 1-11 months, 43 (38%) among 1-5 year-olds and 38 (33%) among >5 year-olds. Case notes were reviewed for 87 positive cultures (76%) relating to 70 distinct episodes of infection, of which 31 (44%) were clinically significant and included 17 (55%) central line-related infections, mainly among those with haematolo-oncological conditions (n=10). Positive cultures in previously healthy children (n=11) included *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Salmonella typhi*. There were no recorded deaths and only one child required admission to intensive care

Conclusions: Invasive bacterial infections continue to occur, particularly in immunocompromised children with indwelling catheters, but serious morbidity and mortality appear to be uncommon, suggesting that current management strategies are effective.

TEN YEARS OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS [MRSA] DISEASE IN A PEDIATRICS DEPARTMENT OF A TERTIARY CARE HOSPITAL IN LISBOA

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Background and aims: MRSA is the most commonly isolated antibiotic-resistant pathogen in European hospitals. The reported prevalence of nosocomial MRSA in Portugal (2009) is among the highest in Europe (53%) but Portuguese paediatric population specific data is scarce. The aim of this study was to determine the prevalence of *Staphylococcus aureus* [SA] and MRSA isolates in our Paediatrics Department (PD) in the last decade.

Methods. Review of SA isolates from children admitted in the PD by the hospital Microbiology-Laboratory and their susceptibility to methicillin, vancomycin and linezolid between 01-01-2002 and 30-11-2011. Total number of admissions to the department was obtained, excluding newborns.

Results: The PD registered 27365 admittances. SA was identified in 1208 samples (860 admittances, 435 patients); 158 strains were methicillin-resistant (89 admittances, 68 patients). MRSA strains represent 13.0% of SA isolates, 10.3% of SA admittances and 15.6% of SA infected patients. Number of isolates-per-year were stable except for a peak in 2010. Samples were from respiratory tract (58%), skin/mucosal exudates (34%), blood or catheter tips (6.3%) and cerebral spinal fluid (1.3%). All strains were susceptible to vancomycin and linezolid.

Conclusions: MRSA were identified in 0.3% of admittances to the PD, corresponding to 15.6% of all SA infected children admitted in the last decade. The majority of isolates were collected from the respiratory tract of chronic lung disease patients. We intend to review the clinical files of MRSA infected patients to identify risk factors, distinguish healthcare associated MRSA from community acquired MRSA and start a prospective surveillance program.

ORBITAL CELLULITIS: A 17-YEAR REVIEW OF HOSPITALIZED CHILDREN

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Background and aims: Orbital cellulitis (OC) is a serious infection that requires prompt diagnosis and treatment. The aim of the study was to evaluate the epidemiology, accuracy of clinical diagnosis, management and complications in a paediatric referral centre.

Methods: Retrospective study of patients admitted with OC, confirmed by computed tomography (CT), between January-1995 and December-2011. Telephone inquiry was performed to assess recurrences and long term complications.

Results: 134 patients were identified. 56% were boys, median age of 48-months and 45% younger than 3 years-old. There was winter-spring season predominance (69%). As predisposing factors, 79% had sinusitis, 65% recurrent upper respiratory tract (URT) infections/allergy, 7% skin infection and 4% local trauma. Prior antibiotic therapy was present in 27%. and 70% had fever. Absence of OC clinical signs was found in 65 versus 28 % respectively in children < 3 year-old and >3 year-old. Microbiological diagnosis was made in five cases (4%). CT identified complications in 62 children (47%): 52 subperosteal abscesses, 5 orbital abscesses, 1 venous sinus thrombosis. The majority (94%) were treated with amoxicillin-clavulanate, 33% had short-course corticosteroid therapy and 14 % required surgery. The mean length of admission was 6,9 (\pm 3) days. Telephone inquiry in 70 cases: nine had recurrence periorbital/OC, all with chronic URT disease. There were no sequelae.

Conclusions: Albeight the limitations of retrospective study, clinical signs of postseptal involvement may be difficult to assess in children less than three year-old. Amoxicillin-clavulanate remains an efficacious first-line therapy. Recurrence may occur in non treated chronic URT disease.

PREVENTION OF GROUP B STREPTOCOCCUS INFECTION BY PERPARTUM SCREENING IN THE DELIVERY ROOM. USE OF XPRT GBS TEST IN POC

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Introduction: In France, *Streptococcus agalactiae* (Group B *Streptococcus*: GBS) is the most common organism in severe neonatal infection, it may lead to sepsis and death of the newborn, or cause severe neurologic sequelae.

The female genital tract colonization by GBS is intermittent, the mother's prevalence during pregnancy is between 10% and 30%.

Since 2001, antenatal screening for GBS of all pregnant women is recommended by ANAES. In case of positive, an intravenous penicillin antibiotic is prescribed at the time of delivery.

Screening performed between 34 and 38 weeks has been shown to be unreliable for predicting the status of intrapartum carriage. A high proportion of women positive during antenatal screening is negative at birth and receives an excessive antibiotic treatment; conversely, negative women are carriers during childbirth.

Objectives: Our approach aimed to prevent GBS infection by intrapartum screening for an optimal management of mothers at risk and children.

Materials and methods: We used the Xpert GBS test (Cepheid, France) at the time of delivery. All required standard procedures (repeatability, reproducibility,) were performed. A vaginal swab was kept to confirm the PCR results by conventional bacteriological techniques, look for the presence of other pathogens and perform an antibiogram in case of penicillins allergy.

Conclusions: The innovative Xpert GBS test, routinely used since 2011, enabled us to identify 155 positive women (12.7%) and to treat properly the positive mothers at the time of delivery. The better efficiency of antibiotic treatment convinced the patients to accept these new screening and prevention terms.

NEUTROPHIL RECEPTOR EXPRESSION AFTER STIMULATION WITH FMLP IS HIGHER AND MORE DIVERSE IN NEWBORN INFANTS THAN IN ADULTS

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Background: In response to infectious exposure, newborn infants are at risk of developing tissue injury and chronic inflammation due to prolonged and exaggerated activity of leukocytes.

Aim: To investigate neutrophil receptor expression, involved in adhesion and migration, in newborn infants after stimulation with intermediate (IL-8) or end target (fMLP) chemoattractants.

Method: Blood was collected from healthy adults (n = 8) and healthy, term newborn infants (n = 8, umbilical cord; caesarean section; spinal anaesthesia). Leukocytes in blood were stimulated with IL-8 or fMLP. The expression of 11 different cell surface receptors was analysed with flow cytometry.

Results: Neutrophils from newborn infants displayed higher basal expression of CD35, CD64 and CD65 than neutrophils from adults ($p < 0.05$). fMLP up regulated neutrophil expression of CD11b, CD35 and CD64 and down regulated CD181, CD182, CD88, CD162 and CD44 in newborn infants ($p < 0.05$). IL-8 down regulated neutrophil expression of CD181, CD182, CD15S, CD162 and CD44 in newborn infants ($p < 0.05$). In contrast fMLP up/down regulated five cell surface receptors on neutrophils from adults, while IL-8 up/down regulated the expression of eight receptors.

Conclusions: Neutrophils from newborn infants express a higher and more diverse receptor activity in response to fMLP than to IL-8, when compared to adults, suggesting a higher level of responsiveness to infectious stimuli.

MENINGITEC^R-BASED VACCINATION CAMPAIGN FOLLOWING A CLUSTER OF SEROGROUP-C INVASIVE MENINGOCOCCAL DISEASE IN FRANCE: RESULTS FROM THE 2002-2009 SURVEILLANCE PROGRAM

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Background and aims: 12 cases of severe invasive meningococcal disease (IMD), due to hypervirulent strains of *N. meningitidis* serogroupC-serotype2a, subtypes P1-5, P1-2, or P1-2.5 (ET-37 clonal complex), affected infants and teenagers in the fall of 2001 in a restricted area in and around Clermont-Ferrand, France: incidence rate: 2/10⁵ versus 0,25/10⁵ in France, purpura fulminans: 67% (8/12), case fatality rate: 25%(3/12). The National Health Authorities decided a vaccination program using a monovalent conjugate C meningococcal vaccine (Meningitec^R, Pfizer). We report the long-term impact of this intervention over the period 2002-2009.

Methods: The target population was all people < 21y living or attending school in the restricted area defined by the geographic origin of the patients. The vaccination involved pediatricians, GPs and school physicians from 16th January to 9th February 2002. We reviewed, from 2002 to 2009, all notifications of IMD and all bacteriological identifications of *N. meningitidis* from the Hospital of Clermont-Ferrand, which serves the targeted population.

Results: The vaccine coverage (CV) was 78.1% (65 536/83 928), higher (85%) in the (10-14y) age group. Around 7000 additional children received the meningo A+C vaccine (Aventis-Pasteur-MSD) leading to a **VC > 80%**. 7 cases of serogroup-C IMD occurred further on, but none among vaccinees with Meningitec^R. One case occurred in a teenager vaccinated with the Meningo A+C vaccine. No increase in other meningococcal serogroups during the 8y period.

Conclusion: For the first time in France, a mass vaccination campaign using Meningitec^R was successfully implemented and stopped the transmission of virulent serogroupC meningococci.

TRANSCRIPTIONAL BIOMARKERS DISTINGUISH CHILDREN WITH ACTIVE TUBERCULOSIS FROM THOSE WITH LATENT TUBERCULOSIS AND TB-LIKE DISEASES

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Background and aims: Childhood tuberculosis (TB) is a major cause of death globally. Traditional diagnostic methods, such as sputum culture and chest x-rays tend to be less reliable in pediatric TB cases. Furthermore, co-infection with HIV enhances the progression to the active form of the disease, hindering TB diagnosis and increasing mortality. The aim of this study is to elucidate the host transcriptional response to childhood TB and select biomarkers to discriminate TB from other phenotypes using host gene expression profiling.

Methods: Illumina HT-12 arrays were used to examine whole blood RNA from 334 children including TB HIV+/- (111), other diseases (OD) HIV+/- (169) and latent TB infection (LTBI) HIV- (54), collected from two different sites in Africa representing urban and rural populations (South Africa/Malawi). A logistic regression model was employed to detect differences between the groups, and a variable selection method was used to identify the smallest set of "best discriminator" probes. To avoid overfitting of the signatures we used different training and testing sets.

Results: We identified distinct subsets of genes differentially expressed when comparing TB to LTBI, TB to OD, and TB to both LTBI and OD. The variable selection provided with signatures (the smallest but most informative probe set for every comparison of interest), which were used for classification of the testing cohort.

Conclusions: A minimal probe set is able to discriminate between different phenotypes and can be used as a robust signature for potential pediatric TB diagnosis, regardless HIV status and location of the population.

EFFECT OF EARLY TOOTH EXTRACTION ON THE DURATION OF HOSPITALIZATION IN FACIAL CELLULITIS OF ODONTOGENIC ORIGIN IN CHILDREN

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Objective: The aims of this retrospective study were to investigate the clinical characteristics of pediatric facial cellulitis of odontogenic origin and the impact of early tooth extraction on the length of hospitalization in children.

Patients and methods: Medical records of all patients with discharge diagnosis of facial cellulitis of odontogenic origin or buccal cellulitis were reviewed. Clinical characteristics including age, sex, symptoms of infection, location of infection, type of tooth involved, the length of hospitalization, and the timing of dental interventions were gleaned. Variables were correlated to length of hospitalization.

Results: One hundred-six children (62 boys and 44 girls) diagnosed with facial cellulitis of odontogenic origin. Early tooth extraction (within 48 hours) and the count of white blood cell at the admission had a significant relationship to length of hospitalization, $p: 0.007$ and $p: 0.03$, respectively. The length of hospitalization in the upper face infections was significantly different from that of lower face infections ($p:0.01$) as well as left face infections was significantly different from that of right face infections ($p:0.01$). There was also a significant correlation between length of hospitalization and type of tooth involved ($p:0.01$). Patients who had a infection of primary first molar teeth had a shorter length of hospitalization.

Conclusion: In the management of pediatric facial cellulitis of odontogenic origin, early tooth extraction may decrease the length of hospitalization. Count of white blood cell, site of infection and also the type of tooth involved at admission had a significant impact on length of hospitalization.

AN EXPERIMENTAL ANIMAL MODEL FOR KINGELLA KINGAE PATHOGENESIS**N. Balashova***University Medicine and Dentistry of New Jersey, Newark, NJ, USA*

Kingella kingae, a Gram negative coccobacillus of the *Neisseriaceae* family, is a normal inhabitant of the human oropharyngeal flora and an emerging pathogen. *K. kingae* is recognized as a leading cause of septic arthritis and osteomyelitis in children younger than two years old. The bacterium is also a cardiovascular pathogen causing infective endocarditis. *K. kingae* produces a potent protein toxin of the RTX-group, RtxA. Cohorts of rats were injected intraperitoneally with different doses of septic arthritis isolate PYKK081, 50% lethal dose (LD₅₀) was 1.3×10^8 cells/animal. To develop a model of septic arthritis, rat knee joints were injected intraarticularly with PYKK081. Thirty one percent of animals injected with 1×10^5 and 1×10^4 bacterial cells demonstrated features of acute inflammation in the infected joint for first 72 h. Histopathological examination of the joint and adjacent bones 7 days after infection revealed the signs of chronic inflammation. The secreted RtxA (>1 µg/ml) had toxic effect on human, rat, rabbit and mouse white blood cells. When tested at high concentrations (>40 µg/ml), the toxicity of RtxA was also detected on other cell types including human synovial cells and osteoblasts. The toxic effect of the isogenic *rtxA* mutant on the mammalian cells under the same conditions was not detected.

Conclusions: The bacterium is shown to cause infections in rat offspring. A rat model of knee septic arthritis due to *K. kingae* is proposed. RtxA primarily affects multiple types of leukocytes suggesting the toxin role in host immune response evasion.

INGUINAL AND PUBIC NECROTIZING FASCIITIS (NF) WITH SEPTIC SHOCK BY STREPTOCOCCUS AGALACTIAE (GBS) IN A 35-DAY-OLD COSTA RICAN (CR) INFANT

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Background: NF produces significant morbidity and mortality in newborns and young infants. GBS is an extremely rare cause of NF in infants < 90 days, with very few published cases and none from Latin America.

Case: A 35-day-old girl was admitted to our children's hospital with a 2-day history of fever, irritability, poor feeding, and lethargy; and left inguinal erythema and edema during the last few hours. Mom's pregnancy was uneventful; however, she was not screened for GBS. On admission, she was febrile, irritable, and had a painful, indurated, and erythematous left inguinal area. Intravenous ampicillin and amikacin were started. Over the next 15 hours, the area turned violaceous and inflammation extended to the upper thigh, lower abdominal wall, and genital area. She deteriorated clinically, developed septic shock, and required intubation. Antibiotics were switched to vancomycin, cefotaxime, amikacin, clindamycin, and metronidazole. On surgery room, a NF was confirmed, and she required debridement of necrotic tissue and vacuum assisted closure (VAC) therapy. She required 6 days in the PICU, and ventilation for 3 days. Blood and tissue cultures grew penicillin-susceptible GBS; therefore antibiotics were changed to intravenous ampicillin (total 3 weeks). Multiple surgical interventions including grafts were subsequently needed. She went home 1 month after admission.

Conclusions: Although the impact of perinatal antibiotic prophylaxis is higher for preventing early rather than late-onset GBS sepsis, this case illustrates the importance of prenatal maternal screening, not routinely performed in CR. Although rare, GBS should be included among the etiologies of NF.

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) INFECTIONS AMONG CHILDREN IN CENTRAL GREECE: A PROSPECTIVE STUDY DURING 2010-2011

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Background and aims: In Central Greece during 2003-2009, 58.3% of community-associated staphylococcal infections among children were caused by an MRSA isolate. MRSA isolates belonged to sequence types ST80, ST30, ST377, and ST22. The present study investigated the recent trends in the prevalence of infections caused by a community-associated MRSA (CA-MRSA).

Methods: From January 2010 to December 2011, we performed a prospective study of children examined at the outpatient clinics or admitted to the pediatric wards of the University General Hospital of Larissa, Central Greece, with community-associated staphylococcal infections. The findings were compared with those of a retrospective study that covered the period January 2003 and December 2009.

Results: Of 90 children (0-14 years old) with staphylococcal infections, 8 (8.9%) had invasive disease (ID) and 82 (91.1%) skin and soft tissue infections (SSTIs). Eleven (12.2%) of the 90 patients were aged < 60 days. The proportion of staphylococcal infections caused by a CA-MRSA isolate in ID was 62.5% in 2010-2011 versus 57.1% in 2003-2009, whereas in SSTIs was 64.6% in 2010-2011 versus 58.3% in 2003-2009. The overall rates of resistant (R) and multidrug-R (MDR) isolates appear in the following table:

Time period	no. of isolates	MRSA	Clindamycin-R	Fusidic acid-R	Tetracycline-R	Ciprofloxacin-R	MRSA-MDR
2010-2011	90	58(64.4%)	21(23.3%)	58(64.4%)	45(50%)	1(1.1%)	14(24.1%)
2003-2009	309	180(58.3%)	61(19.7%)	189(61.2%)	165(53.6%)	1(0.3%)	38(21.1%)

[Table 1]

Conclusions:

1. In Central Greece, there is a sustained high prevalence of ID and SSTIs due to CA-MRSA.
2. Clindamycin-R isolates are relatively common.

INGUINAL MASS IN A 10-YEAR-OLD BOY MIMICKING A LYMPHOMA**M.K. Docx¹**, D. Vervloessem²*¹Paediatrics, ²Paediatric Surgery, Queen Paola Children's Hospital, Antwerpen, Belgium*

Cat scratch disease is mostly an infectious self-limiting disease caused by *Bartonella Henselae* with in the majority of the patients a self-limiting regional adenopathy.

This report describes the case of a 10-year-old boy who presented with general malaise, fever and pain in his left leg since 1 month. An inguinal left lymph node was observed. An ultrasound was performed, which showed no signs of abscedation. Because of positive serological tests for *B. Henselae*, he was treated with clarithromycin for 5 days. Despite his treatment, there was no relief .

On clinical examination a deep mass was felt in his left inguinal region.

Abdominal MRI together with views of the upper region of the left leg showed giant lymph nodes in the left inguinal region and left fossa iliaca. The lymph nodes had a necrotic aspect with abscedation. Serologic tests showed a recent *B Henselae* infection (IgM > 1/100, IgG > 1/1280). Treatment with rifampicin and azithromycin was started.

Surgical treatment was no option, because of probability of chronic fistulisation.

A few days after initiation of the antibiotic treatment, an involution of the glands was seen.

Two weeks later, the boy was seen on a follow-up consultation with a tender, superficial, fluctuating mass in his left groin.

A surgical drainage with biopsy was performed and the PCR for *B Henselae* was positive on the biopsy material. 1 month postoperatively, there was no longer pus evacuation and the first signs of granulation were noticed.

Ultrasound showed decreasing lymph nodes and antibiotic treatment was stopped after 6 weeks.

FATAL NECROTIZING CELLULITIS (NC) AND FASCIITIS (NF) AS A COMPLICATION OF ACUTE OMPHALITIS (AO): ARE WE CONSIDERING THE DIAGNOSIS PROMPTLY?

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Background: AO is well recognized by most pediatricians. However, the diagnosis of serious complications such as NF and NC is usually delayed. We describe two fatal cases referred to Costa Rica's only pediatric tertiary referral hospital in which early clinical suspicion and surgical intervention was delayed. NC and NF were confirmed on autopsies, respectively.

Case 1: An 8-day-old boy was admitted with a 24-hour history of fever and abdominal distention. On admission, his abdominal wall was indurated and had periumbilical erythema. Ampicillin, clindamycin and amikacin were started and then the spectrum was increased. He worsened, and developed periumbilical violaceous coloration that extended to the scrotum. He required mechanical ventilation in PICU, developed septic shock, acute renal failure, and abdominal compartment syndrome, among other complications. He died 31 hours after admission. Blood cultures grew *Streptococcus pyogenes*.

Case 2: A 9-day-old girl was admitted with a 2-day history of periumbilical erythema and induration. On admission, she had a painful abdomen with periumbilical violaceous coloration that extended to genitalia. Vancomycin, metronidazol and ceftazidime were started. She developed septic shock and multiorgan failure, among other complications. A NC was documented during surgery and NF in autopsy. She died in PICU 22 hours after admission. Tissue cultures grew *Citrobacter koseri*, *Staphylococcus haemolyticus*, and *Enterobacter cloacae*.

Conclusions: Abdominal wall induration, pain, and particularly ecchymosis or violaceous skin coloration following AO should alert about possible NF or NC. Early broad spectrum antibiotics against Gram (+), Gram (-), anaerobes and early surgical intervention are key features during management.

IMPETIGO - TREATMENT AND EVOLUTION IN A PAEDIATRIC EMERGENCY SERVICE**C. Cancelinha**¹, D. Martins¹, M.M. Zarcos²*¹Paediatric Department, Hospital Pediátrico Carmona da Mota, Coimbra, ²Paediatric Department, Centro Hospitalar Leiria-Pombal, Leiria, Portugal*

Introduction: Impetigo is the most common skin infection in children. Uncertainty exists as to the most effective treatment, or even if it is necessary. In 2011 flucloxacillin oral suspension, the first choice in cases of widespread disease, was not available in Portugal.

Aim: To compare the effectiveness of oral flucloxacillin, first generation cephalosporins and amoxicillin/clavulanate and analyze differences between 2010-2011.

Methods: Retrospective study with consultation of processes of children/adolescents with diagnosis of impetigo, treated with systemic antibiotic, observed in a secondary hospital emergency service, from 1st January 2010 to 31st December 2011. Exclusion criteria: age \leq 28 days. Treatment failure was defined as persistence/recurrence of impetigo within 15 days after starting oral/topical antibiotic.

Results: A total of 215 children were included (2 months - 17 years; median 4 years), with epidemiological context in 11.6%. Most cases (70.2%) occurred between July-September.

There were 119 cases in 2010, 92.4% treated with oral flucloxacillin. In 2011 (n=96) the majority was treated with first generation cephalosporins (37.5%), flucloxacillin (29.2%) and amoxicillin/clavulanate (15.6%). Hospitalization for intravenous therapy with flucloxacillin occurred in 2.3%, all cases with favorable clinical outcome.

Treatment failure occurred in 27%, being 65.5% previously treated with topical fusidic acid, 13.8% with amoxicillin/clavulanate, 10.3% with oral flucloxacillin, and 5.2% with first generation cephalosporins.

Discussion: Topical fusidic acid is related with high percentage of treatment failure, which may be correlated with widespread disease. First generation cephalosporins is an effective treatment for impetigo and can be considered the first choice when oral flucloxacillin is not available.

BONE AND JOINT INFECTIONS IN CHILDHOOD: EVALUATION OF NEW FRENCH RECOMMENDATIONS IN ONE UNIVERSITARY HOSPITAL CENTER

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Background and aims: In case of bone and joint infections, the paediatric surgery department of university hospital of Rennes (France) used as first line of treatment cefotaxim/cefepime for children aged under 2 years and cloxacillin/gentamycin for children aged over 2 years. In 2011, the department chose to use amoxicillin-clavulanic acid for children aged under 2 years and cloxacillin for children over 2 years according to new French recommendations. In 2 cases, antibiotherapy is accorded to infectious agent and its sensitivity.

Methods: The study population is all children hospitalized for bone and joint infections during 2010 and 2011 in the pediatric surgery department of university hospital of Rennes. In this study, we compare the data in terms of duration of treatment, normalization of the CRP, adverse evolution with antibiotic strategy change between 2010 and 2011. For comparison, we use Student and Fischer tests.

Results: 17 patients in 2010 and 14 patients in 2011 were treated as bone and joint infections. Mean duration of intravenous treatment for 2010 and 2011 was respectively 5.3 days and 5.4 days. The processing time for normalization of CRP for 2010 and 2011 was respectively 4.9 days and 5.1 days. One child in 2010 versus 2 children in 2011 had adverse evolution requiring a change in treatment. The observed difference are not statistically significant.

Conclusions: We don't find any significant difference between old and new strategy in terms of duration of treatment, normalization of CRP, adverse evolution. Study on largest population must be conducted.

STAPHYLOCOCCUS AUREUS OSTEOARTICULAR INFECTIONS IN CHILDREN

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Background and aims: The incidence of Staphylococcus aureus (SA) osteoarticular infections (OAI) is increasing. Recent evidence suggests shorter antibiotic treatment is safe and effective.

Methods: A retrospective review of children < 15 years of age hospitalized with SA OAI at the Department of Infectious Diseases, University Medical Centre Ljubljana from 2006 to 2011 was performed.

Results: There were 35 children, 23 boys and 12 girls with a mean age of 8.75 years. The mean duration of symptoms was 3.7 (1-28) days. 17 (49%) children had history of trauma and 7 (20%) had antecedent skin infection. There were 17 osteomyelitis, 8 septic arthritis and 10 OM osteomyelitis with adjacent arthritis cases. In 91% of patients the infection was localized to lower body. Three children had necrotizing pneumonia and required intensive care, all had Panton Valentine leukocidin (PVL)-positive SA infections. One child with SA bacteremia had mitral valve endocarditis. All SA isolates were methicillin-sensitive. 34 children received empirical treatment with flucloxacillin, only one received clindamycin. Treatment was changed in 4 patients, in 3 due to allergy and in one due to other reasons. Mean duration of treatment was 45 (28-84) days. Surgery was required in 63% of children. Two patients had a relapse - both isolates were PVL positive - and recovered completely. One child (also PVL positive) had permanent sequelae.

Conclusions: The incidence of SA OAI in children is increasing with all SA isolates remaining methicillin-sensitive. PVL positive infections have a more severe course with a tendency to relapse.

CLINICAL PROFILES IN CHILDREN WITH ACUTE OSTEOMYELITIS IN SINGLE CENTER IN KOREA FROM 1989 TO 2010

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Purpose: Most cases of osteomyelitis in children arise hematogenously, occurring in the metaphysis of long bones, such as the femur, tibia, and humerus. We retrospectively reviewed the clinical characteristics, pathogen, diagnosis, treatment, and complication in children below 15 years old in a single center.

Methods: A retrospective analysis was made of 87 children with osteomyelitis and/or septic arthritis who underwent antibiotic management or operation between Jan 1989 and Dec 2010 for acute osteomyelitis at Kyung Hee University Hospital.

Results: The study group was composed of 57 boys and 30 girls, and mean age was 7.3 ± 5.2 years old. The most common affected age groups were 6-10 yr (n=29, 30%), and 11-15 yr (n=37, 38%), respectively. Femur (n=29, 30%) and tibia (n=29, 30%) were the most common infected site. The chief complaints were pain, swelling and fever. By far the most common bacterial pathogen is *Staphylococcus aureus* in all age groups. *Mycobacterium tuberculosis* was isolated (n=3, 3.1%). Most of patients were treated with operation and concomitant antibiotics (n=65, 67%). Route of hospitalization is through orthopedics department (n=73), through pediatrics (n=11), and miscellaneous ways (n=3). The number of admission is definitely decreased from 1989 to 2010.

Conclusion: Over the past two decade, there are tend to decrease the annual incidence of admission, increasing microbial virulence, diminishing antibiotic sensitivity, and advances in diagnostic molecular microbiology and imaging techniques, those have led to changes in the diagnosis and clinical management.

OSTEOMYELITIS IN CHILDREN: PRESENTATION OF 25 CASES**C.L. Faria**¹, G. Rubino¹, G. Rocha²¹*Children's Hospital, Coimbra University and Hospital Center,* ²*Infectious Diseases, Children's Hospital, Coimbra University and Hospital Center, Coimbra, Portugal*

Background and aim: Osteomyelitis is a common disease that affects previously healthy children of all age groups. The aim of this study was to describe its etiology, clinical presentation, laboratory findings, treatment and outcome.

Methods: Retrospective analysis of the medical records of children hospitalized with osteomyelitis between January 2006 and September 2011 (n=25).

Results: Our group had a median age of 8.4 years and 56% were male. The most common manifestations were severe local tenderness and pain (80%) and swelling (60%). Long bones and the foot accounted for the majority of cases: femur (24%), tibia (19%), radius (14%) and foot (14%). Almost all cases (96%) presented with high erythrocyte sedimentation rate, median 75.5 mm/hour; C-reactive protein was elevated in 54% and white blood cell count in 36% of patients. The etiological agent was determined in 12 patients (48%). The most common microorganism was *Staphylococcus aureus* (33%), 25% methicillin-resistant. Antibiotic monotherapy was started in 80% (mostly Flucloxacilin) and 20% required combined therapy. Half of the patients required surgical procedures. Three patients (8%) had disease recurrence and 5 (20%) developed chronic osteomyelitis.

Conclusions: This study confirms reports concerning the characteristics of osteomyelitis in children. Clinicians should be aware to allow for early diagnosis in order to rule out an infection which can progress to permanent disability.

SPONDYLODISCITIS - REPORT OF TWO CASES**S. Bacalhau**¹, M. Cassiano Neves², H. Neves¹, A. Serrão Neto¹¹*Unidade Funcional de Pediatria e Neonatologia*, ²*Unidade de Ortopedia Infantil, Hospital Cuf Descobertas, Lisbon, Portugal***Background and aims:** Spondylodiscitis is uncommon in children and correct diagnosis is often delayed due to unspecific clinical symptoms.**Methods:** Presentation of clinical cases.**Results:**

Case 1 - A previously healthy 2 year-old boy complained of back pain and progressive limp for 3 weeks. At admission, he was limping and presented loss of lumbar lordosis. Lumbar spine X-ray was normal. Erythrocyte sedimentation rate (ESR) was elevated. Magnetic resonance imaging (MRI) revealed spondylodiscitis in L5-S1, with contiguous epidural empyema and prevertebral abscess. No agent was isolated in hemoculture or aspirative puncture. Therapy with parenteral Cefotaxime (21 days), Flucloxacilin (21 days) and Metronidazole (7 days) was instituted. He fully recovered but with L5-S1 fusion.

Case 2 - A previously healthy 14 months-old girl was admitted with a 10 days history of night crying and refusal to walk. At admission, she presented inability to walk. Lumbar spine X-ray was normal. ESR was elevated. Bone scintigraphy showed increased uptake in L5-S1 and MRI revealed spondylodiscitis in L5-S1. Parenteral Flucloxacilin was instituted (7 days) followed by oral amoxicillin + clavulanic acid (10 days). Hemoculture was negative. She had an uncomplicated recovery.

Conclusions: As described in literature, laboratory findings were unspecific and hemocultures were negative in both cases. MRI has the best capacity to distinguish discitis from vertebral osteomyelitis. Bone scintigraphy is useful in workup of unknown location pain. Specific nucleic amplification assays should be routinely used in order to improve agent identification. Duration of antimicrobial therapy was different in those cases due to different severity.

CHRONIC SUPPURATIVE OSTEOMYELITIS OF THE MANDIBLE - A CASE REPORT

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Background: Chronic osteomyelitis (CO) is a rare entity especially in children. The mandible is one of the most affected bones and, due to its immaturity in childhood, the inflammatory process quickly spreads to surrounding areas.

Case report: A 10-year-old boy, with history of dental caries was referred to our outpatient clinics with an 1-month history of a soft and painless right mandibular swelling. Initially, he was treated with anti-inflammatory drugs with clinical improvement. Four months later, he presented a sero-hematic discharging from a cutaneous sinus present on the border of the mandible. The face magnetic resonance imaging (MRI) revealed CO of the mandible. Laboratory studies showed normal white blood cell count, C-reactive protein and erythrocyte sedimentation rate. On admission, bone biopsy, surgical debridement and resection of the cutaneous sinus tract were done. Orthopantomogram revealed apical reaction of the 46, which was removed. The patient was empirically treated with intravenous cefuroxime and clindamycin. After the identification of *Prevotella buccae* (resistant to clindamycin) in the bone cultures, the antibiotherapy was changed to metronidazole. After four weeks of treatment he was discharged. At 9th week of treatment, he was symptom-free and the MRI revealed only residual inflammatory changes.

Conclusions: Although CO of the mandible is rare, this entity should be considered in children with mandibular swelling, especially in those with previous history of dental caries. The duration of antibiotic therapy is not well defined in the literature. In our case, thirteen week course of antibiotics in combination with surgical debridement were successful.

DIAGNOSIS AND MANAGEMENT OF ACUTE HAEMATOGENOUS OSTEOMYELITIS (AHO) IN CHILDREN: A RETROSPECTIVE STUDY

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Background and aims: Acute haematogenous osteomyelitis (AHO) use to be a fatal or devastating disease and is traditionally treated with long courses of antimicrobial therapy. The aim of this study is to describe clinical presentation, management and organisms responsible for AHO and to evaluate current antibiotic treatments in our Hospital.

Methods: We performed a retrospective review of medical records of children presenting to "Bambino Gesù Hospital" with AHO during a 36month period. The assessed data were: age, gender, symptoms, risk factors, bones involved, investigations, causative agents, sensitivity to antibiotics, treatments, complications and length of hospitalization.

Results: During the 3-years of the study we observed 22cases of AHO, aged from 1month to 14years. The most common symptoms were tenderness and adjacent joint hypomobility(77%), fever(64%), local swelling(27%). Just one patient presented the three classic symptoms simultaneously. The most frequent localizations were femur (n=9) and tibia (n=7). Blood and/or tissue cultures were taken from all patients. Microbial diagnosis was established in 8/22 and S.Aureus was the most common organism. Our analysis revealed that55% of patients received intravenous combined therapy for a mean duration of 30 days (range7-60 days) without significant difference among patients with severe or uncomplicated infection.

Conclusions: Our data revealed a trend to administer prolonged antibiotic treatments in most patients, despite recent studies documented the efficacy and safety of a considerably shorter duration, especially for uncomplicated AHO. Prospective studies are necessary to identify early indicators of response to therapy to establish the appropriate timing of antibiotic therapy, to reduce drug toxicity and length of hospitalization.

CHRONIC NON-BACTERIAL OSTEOMYELITIS - A CASE OF MANDIBLE, UNIFOCAL PRESENTATION

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Introduction: Chronic non-bacterial osteomyelitis is a rare auto-inflammatory disorder which typically occurs during childhood. Most frequently has multifocal bone involvement. Cases with unifocal involvement have been reported, making it necessary to exclude malignancy and infection. It affects mainly the metaphysis of the long bones and mandibular involvement is uncommon.

Case report: A 12-year-old boy previously diagnosed with Dandy-Walker Syndrome presented with pain and swelling in his left mandible starting two months before without dental foci. Despite two antibiotic courses (oral and intravenous) bony enlargement showed progressive worsening. Erythrocyte sedimentation rate was 39mm/h, CT scan revealed lytic and sclerotic lesions of the cortical bone and tc-99 bone scintigraphy increase of bone turnover both in the left side of mandible without additional bone foci suggesting neoplastic or infectious disease. Histopathologic findings of the involved bone were consistent with chronic osteomyelitis. Extensive microbial investigation (blood and biopsy tissue) was negative. Antituberculous treatment was started without improvement and stopped after negative bone PCR for *Mycobacterium tuberculosis* and Lowenstein culture. With exclusion of infection and malignancy the patient was started on indometacin resulting in impressive clinical and laboratory improvement.

Discussion: At initial presentation, chronic non-bacterial osteomyelitis may mimic acute hematogenous osteomyelitis or malignancy. The definite diagnosis is made after excluding these conditions especially if it presents in an unusual bone and with a single lesion. Prompt diagnosis of chronic non-bacterial osteomyelitis will allow patients to avoid the risks associated with lengthy courses of antibiotic therapy and repeated bone biopsies, which can delay the appropriate therapy.

CANDIDA OSTEOMYELITIS IN PEDIATRIC PATIENTS

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Background and aims: *Candida* osteomyelitis is an uncommon and debilitating form of invasive candidiasis. Little is known about this infection in pediatric patients.

Methods: We analyzed the epidemiology, pathogenesis, clinical manifestations, diagnosis, and treatment of 39 cases (26 neonates/infants; 13 children/adolescents) of *Candida* osteomyelitis in patients ≤18 years from the English literature.

Results: Among the mechanisms of infection, hematogenous dissemination developed in 30 cases (77%), contiguous infection in 5 (13%) and direct inoculation in 4 (10%). Reflecting the predominantly hematogenous mechanism of infection, 59% had *Candida* osteomyelitis in ≥2 bones. *Candida* osteomyelitis was diagnosed predominantly via direct culture and less frequently by histopathology with or without culture through percutaneous closed guided biopsy or by open biopsy. The femoral and humeral metaphyses were the most frequently infected sites in 23 (59%) and 17 (44%) cases. Concomitant *Candida* septic arthritis also developed in association with epiphyseal infection. Local symptoms and signs were present in 82%. However, biomarkers of inflammation, including ESR, CRP and WBC count were only minimally elevated or within normal limits in some patients. Antifungal therapy included single agents and combination therapy. Antifungal therapy and/or surgery achieved a complete response in 17 (44%), partial response in 17 (44%), and failure in 5 (12%) patients.

Conclusion: *Candida* osteomyelitis in pediatric patients occurs most frequently as a multifocal infection arising from hematogenous dissemination to femoral or humeral bones. Most children have localized symptoms and signs. Accurate diagnosis and timely initiation of antifungal therapy are associated with a favorable response.

LINEAR GROWTH AND BODY MASS INDEX IN YOUNG CHILDREN AFTER ACUTE MENINGITIS: A CONTROLLED STUDY

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Background: Meningitis that occur during periods of rapid growth may adversely affect growth and nutritional status of children.

Aim and methods: We recorded and analyzed the growth data of 40 children with acute meningitis (age 5.8 +/- 3.1 years) for a year or more after adequate treatment and compared them with normal age-matched children.

Results: None of the patients had underweight and/or stunting for one year or more after treatment. The height standard deviation scores (HtSDS) of patients decreased significantly from -0.06 +/- 0.95 at the onset of meningitis to -0.46 +/- 1 after a year or more of follow-up and were significantly lower than those for normal controls (0.31 +/- 0.5) . Fifteen out of the 40 patients had decreased HtSDS > -0.5, while 3 had decreased HtSDS > -1 after > 1 year of follow-up. The BMI of patients significantly increased after 1 year or more of the acute attack but did not differ from the BMI for the controls. One patient and none of the controls had BMISDS > 2 at presentation. 5/40 patients and 2/100 children from the control group had BMISDS > 2 after 1 year or more of follow-up.

Conclusion: Impairment of linear growth and tendency to weight gain appear to be important sequel of acute meningitis affecting young children that necessitates close and long-term monitoring of growth in these children.

EBV ENCEPHALITIS IN INFANCY: A REPORT OF A VERY YOUNG CASEF. Gurbuz¹, H. Tezer¹, **G. Kalkan**²*¹Pediatric Infectious Diseases, Republic of Turkey Ministry of Health, Ankara Diskapi Children's Training and Research Hospital, ²Pediatrics, Gazi University, Ankara, Turkey*

Epstein - Barr virus (EBV) infection causes a wide spectrum of illness in humans including subclinical infection, infectious mononucleosis (IM), and is associated with some malignancies. Although EBV is known to cause neurologic disease in pediatric population, it is extremely rare during infancy. This report presents an unusual case of EBV encephalitis in a 10 months old infant with a febrile infection and seizures. The clinical manifestations, a serologic study, and a dynamic change of EBV DNA in cerebrospinal fluid with spontaneous recovery confirmed the diagnosis of EBV infection of the nervous system. To our knowledge this is one of the youngest ever reported cases of EBV encephalitis. EBV has to be considered in a variety of acute neurologic illnesses even in the infancy and the clinicians should take advantage of potential benefit from acyclovir treatment.

AN UNUSUAL CASE OF BRAIN ABSCESS BY GEMELLA

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An immunocompetent 2-year-old infant with acute onset of drowsiness and irritability was admitted to our hospital. Parents reported a 2-week history of episodic vomiting with low grade fever. A comprehensive history was unremarkable. The baby had an ill-appearance and neurological examination revealed neck stiffness. Blood count showed: 14840/mm³ white cells, 67% neutrophils; C-reactive protein was 96,9 mg/l. A CT scan showed a right-sided parietal round lesion with ring enhancement and perilesional oedema with shift of the brain midline to the left. A differential diagnosis included both brain tumor and infectious aetiology. Corticosteroid and mannitol were started. A MRI highlighted the presence of a simil-cystic lesion. The child was taken into surgery for removal of the mass. Due to the identification of Gram + cocci on the extemporary analysis, intravenous linezolid was empirically started. The culture identified *Gemella spp.* and the diagnosis was a brain abscess. Intravenous antibiotic therapy was continued for 3 weeks, followed by oral administration of linezolid for 3 weeks. The child's status progressively improved and the CT scan showed complete resolution.



[Brain MRI]

Discussion: The most frequent implicated organism in cerebral abscesses is streptococcus and multiple organism are identified in different percentage according to the series.

Gemella is a rare pathogen but the prevalence is probably underdiagnosed. Linezolid has an excellent bioavailability both intravenously and orally. Treating serious Gram+ infections with this antibiotic offers the opportunity to start oral therapy once patients are stabilized, rather than prolonged hospitalization.

MOLECULAR DETECTION OF ECHOVIRUS 30 IN A CHILD WITH MENINGITIS IN SUMMER 2010, GREECE

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Background and aims: A large outbreak of West Nile virus (WNV) infections occurred in 2010 in Northern Greece, with 171 neuroinvasive cases reported. The first WNV case was diagnosed on 5 August. On August 27, a 7.5-year old boy was admitted to the hospital with fever, headache, vomiting, abdominal pain, and stiff neck. CSF testing revealed 550 cells/mm³, 80% lymphocytes. Cultures for common bacteria and serological testing for WNV were negative. After 4-day hospitalization the patient was discharged without sequelae. Aim of the present study was to check for a probable enterovirus infection.

Methods: Viral RNA was extracted from a CSF sample taken from the child upon admission. An RT-nested PCR was applied and phylogenetic analysis of the obtained sequence was performed.

Results: A PCR product of the expected size was obtained and sequenced. Phylogenetic analysis revealed that the causative agent was echovirus 30 (E30).

Discussion: E30 is one of the most common enteroviral serotypes causing meningitis outbreaks. In summer 2010 large E30 outbreaks occurred in Novi Sad in Vojvodina, Serbia, and in Latvia. It has to be noted that one week before the present case, one additional E30 case was observed in Greece, in a child coming from Serbia. Although the two cases were not epidemiologically linked, it cannot be excluded that a certain E30 strain was circulating this period in Europe causing meningitis mainly in children. Further molecular studies will give insight into the E30 epidemiology in 2010 in Europe.

FREQUENCY OF SINUSITIS (CT SCAN) IN HOSPITALIZED CHILDREN WITH MENINGITIS: A CROSS SECTION STUDY; TEHRAN, IRAN**S. Noorbakhsh¹, V. Zarabi¹, M. Farhadi², A. Tabatabaei¹***¹Research Center of Pediatric Infectious Diseases, Tehran University of Medical Sciences, ²Research Center for Diseases of Ear, Nose, TUMS, Tehran, Iran*

Background: Paranasal sinuses are a common place for infection in Iranian children. Careful search for sinusitis and appropriate treatment is needed to decrease the risk of bacteremia and subsequent invasive infections (eg meningitis, subdural empyema, brain abscess).

Objective: Determine the frequency of sinusitis (CT scan) in children with meningitis.

Methods and materials: A prospective, cross sectional study done in pediatric infectious ward of Rasul Akram Hospital in Tehran, Iran (2010-2011). Exclusion criteria: We excluded all cases diagnosed as concomitant or nosocomial infection (eg; pneumonia, osteomyelitis; UTI etc).

Results: 65 cases with meningitis had full criteria for following the sinusitis. Paranasal sinus CT performed in 65 cases; 1 month-16 years; mean =4.2 year, septic meningitis 53.6% (36/65); aseptic meningitis: 46.4%(29/65). Undeveloped sinus 7.6% (n=5) < 4 months). Sinusitis 32%(20/ 65); including: Maxillary sinusitis in 16/60(64%); Pan sinusitis(12%); sphenoiditis: 8%; ethmoiditis:16%; frontal sinusitis =0; Chronic sinusitis: 50% (n=33) cases.

Conclusion: Physicians treating hospitalized cases with sinusitis should be aware of the risk of meningitis (septic & aseptic meningitis) in 31% of cases. Meningeal manifestations or CSF changes might be due to bacterial sinusitis. The diagnosis of initial site of infection; cause or confection in meninges or sinus tract is very difficult. We recommend sinus tract evaluation in every case with meningitis (septic; or aseptic), adequate treatment in chronic sinusitis would be helpful in preventing of readmission.

ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM) AND DISSEMINATED INTRAVASCULAR COAGULATION

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The Acute Disseminated Encephalomyelitis (ADEM) is an acute disease characterized by multifocal inflammatory demyelinating lesions that typically affect the white matter of the CNS.

Clinical case: A two years old girl was admitted with alteration of consciousness, lower limbs hypertonia, upper limbs hypotonia, "setting sun" eyes, red dermatographism, greyish skin, rigor nuchalis and seizures. The child was intubated and ventilated. CT brain and fundus oculi were normal. Blood tests showed a CID and MRI showed the characteristic lesions of ADEM. We started therapy with antibiotics, activated protein C, acyclovir, mannitol, furosemide and corticosteroids. It was administered plasma and AT III with normalization of coagulation value and resolution of hypertransaminasemia. HHV-6 DNA was detected in blood and liquor. During the hospitalization seizures disappeared with gradual and mild improvement in the state of consciousness. After 5 months of rehabilitation, the child showed a complete resolution of the neurologic status.

Discussion: The ADEM is a immunomediata disease and usually occurs after a viral infection (measles, chickenpox, rubella, HSV) or vaccinations. The autoimmune event is directed against the myelin basic protein with axonal demyelination. The diagnosis is clinical, laboratoristic and radiologic. The MR image shows widespread, multifocal, or extensive white matter lesions and occasionally involvement of deep gray matter, of the thalamus or the basal ganglia. ADEM and CID are rarely associated. Treatment usually involves corticosteroids iv, antiaedemic and anti-inflammatory drugs. At the moment the use of Ig is controverse. The prognosis is generally good. A small group of patients have neurological disorders.

IMPACT OF MACROPHAGES ON *BALAMUTHIA MANDRILLARIS* VIRULENCE PROPERTIES USING HUMAN BRAIN MICROVASCULAR ENDOTHELIAL CELLS *IN VITRO*

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Background and aims: Balamuthia amoebic encephalitis (BAE) is a serious human disease almost always leading to death. An important step in BAE is amoebae invasion of the bloodstream, followed by their haematogenous spread. Balamuthia entry into the central nervous system (CNS) most likely occurs at the blood-brain barrier (BBB) sites. The objective of the present study was to determine the impact of cytokines and macrophages on the virulence characteristics of Balamuthia in vitro.

Methods: Using human brain microvascular endothelial cells (HBMEC), which constitutes the BBB, adhesion and cytotoxicity assays were performed in the presence of cytokines and macrophages. To investigate the engulfing property and proteolytic activity of the amoeba, phagocytosis and zymography assays were performed respectively.

Results: It was observed Balamuthia exhibited >90 % binding and >70 % cytotoxicity to HBMEC which was further enhanced in the presence of cytokines and macrophages. Furthermore it has also been observed that cytokines TNF- α and TGF- β significantly increased the *Balamuthia* numbers in the presence of macrophages. Balamuthia numbers were more than doubled in the presence of cytokines and macrophages within 24h. The bacterial uptake by Balamuthia is limited which is further significantly decreased in the presence of cytokines. Zymography assays revealed cytokines and macrophages have no inhibitory effect on proteolytic activity of Balamuthia. Furthermore the activated macrophages also could not show any vital effects on amoebic virulence properties.

Conclusions: Overall we described for the first time that cytokines and macrophages have no inhibitory effects on the virulence properties of Balamuthia in vitro.

ARE CHILDREN WITH MENINGITIS AND MENINGOCOCCAL SEPTICAEMIA RECEIVING THE CORRECT CARE?

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Background and aims: Bacterial meningitis (BM) and meningococcal septicaemia (MS) are both serious illnesses that affect many children in Europe. Evidence shows that children who are treated effectively and quickly have significantly better outcomes compared to children who do not.⁽¹⁾ NICE updated guidelines in June 2010 for the management and treatment of BM and MS in children.⁽¹⁾ Our aim is to assess whether children presenting with suspected meningitis are receiving the correct care in accordance with NICE guidelines and to identify weaknesses in aspect of management and introduce improvements.

Method: We audited all cases of suspected meningitis in children ages 29 days to 16 years over a 1 year period across the Worcestershire Acute Trust. Data was collected retrospectively from patients' notes and electronic systems.

Results: 78% had a lumbar puncture. 100% had blood cultures. 86% were given the correct antibiotics. 80% of patients with confirmed bacterial meningitis received the correct length of course of antibiotics. 0% received the correct type of maintenance fluid. Of patients who received fluid boluses, 100% received the correct type of fluid and 25% received the correct amount. 21% had follow-up and 21% had hearing tests within the recommended timeframe. Only 7% (n=1) had both.

Conclusion: Meningitis is a potentially life-threatening condition which overall is being diagnosed, investigated and treated well within the Trust.

(1) National Collaborating Centre for Women's and Children's Health. Management of bacterial meningitis and meningococcal septicaemia in children and young people younger than 16 years in primary and secondary care. London, 2010.

TUBERCULOUS MENINGITIS IN CHILDREN: THE ATTRIBUTION OF LABORATORY AND IMAGING FINDINGS IN DIAGNOSIS

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Background and aims: Tuberculous meningitis (TBM) may be a rare disease but still carries significant morbidity and mortality. Our aim was to approach the attribution of laboratory and imaging findings in early diagnosis of TBM because of its great importance for treatment and prognosis.

Methods: We analyzed data from 43 children, aged 7 months to 13 years, hospitalized in our department, with the diagnosis of TBM, during a 25-year period (1984-2008).

Results: CSF examination revealed a clear fluid with high cell counts (mean 200/mm³, range 32-1200), mostly lymphocytes, high protein (mean 94mg%, range 11-628) and low sugar levels (38.35±16.31mg%) in most of cases. Only 15 patients had a positive CSF culture (35%). Positive gastric aspirate culture was found in 3 patients (7%). Blood cultures were negative in all patients. No specific elevated values of bacterial infection markers were found.

Chest X-rays were abnormal (mostly consolidation) in only 15 patients. Computed tomography (CT) and magnetic resonance imaging (MRI) had a higher percentage of abnormal findings (25/33 of patients had abnormal CT scans and 8/9 of patients abnormal MRI scans, mainly hydrocephalus).

Conclusions: Despite the great advances in medicine, clinical suspicion still remains of greatest importance for the diagnosis of TBM. Laboratory tests fail to identify the majority of cases and cultures still have low accuracy. CT and MRI offer significant help. Until better diagnostic methods become available, laboratory and imaging tests should be used to confirm the clinical diagnosis based on clinical findings and a careful medical history.

INCIDENCE AND AETIOLOGY OF ACUTE BACTERIAL MENINGITIS IN A BUSY LONDON TEACHING HOSPITAL

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Background: The aetiology of acute bacterial meningitis (ABM) is continually changing with the introduction of new vaccines into national immunisation programmes.

Objectives: This study aims to estimate the incidence and aetiology of culture-confirmed acute bacterial meningitis (ABM) in a London teaching hospital over a 3-year period.

Methods: Croydon University Hospital currently participates in the south London Childhood Acute Bacterial Infection Network (CABIN) surveillance. For this study, microbiological data for all children aged 1 month to 15 years admitted to our hospital between 01/01/2009 and 31/12/2011 were retrieved and a standardised questionnaire was used to extract data from case notes of those with a positive cerebrospinal fluid culture.

Results: A total of 5,874 children were admitted over the 3 year-period, of whom 2,954 (50%) had suspected sepsis. Lumbar puncture was performed in 516 children (8%) and cerebrospinal fluid culture was positive in 10 cases, of which 5 (0.9/1,000 admissions) were considered clinically significant and required antimicrobial therapy. These included Group B streptococcus in 2 young infants aged 1-3 months, and 3 cases in toddlers aged 1-4 years, including *Salmonella* sp. in a child with sickle cell disease, *S. aureus* in a child with neuroblastoma and *N. meningitidis* in a previously healthy child. All children survived, but two had long-term neurological sequelae.

Conclusions: Lumbar punctures are infrequently performed in children and the yield of CSF culture remains low. ABM is rare but must be considered in all children presenting with infection because of its potentially devastating consequences.

CHANGES OF HYPOTHALAMUS CORTICOTROPHIN RELEASING FACTOR LEVELS IN ILL CHILDREN WITH ACUTE BRAIN INJURY

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Objective: To explore the changes of corticotrophin releasing factor (CRF) levels secreted by hypothalamus neuron in ill children with acute brain injury.

Methods: Fifty-one intracranial-infection ill children with brain injury and eleven intracranial-noninfection ill children with brain injury were chosen as the researched objects from pediatric intensive care unit of our hospital, severities of their brain damage were evaluated by Glasgow Coma Scale Score, and CRF levels in cerebrospinal fluid and serum TNF- α and IL-6 level were measured by radioimmunoassay.

Results: There was no significant difference of Glasgow Coma Scale Scores between the intracranial infection group and intracranial-noninfection group ($P = 0.3026$), CRF concentration of intracranial infection group in cerebrospinal fluid was significantly lower than that of intracranial noninfection group ($P < 0.01$), serum TNF- α and IL-6 levels of intracranial infection group were significantly higher than those of intracranial-noninfection group ($P < 0.001$, $P < 0.01$). As comparing to the CSF CRF and serum TNF- α and IL-6 in the children with 6~7 score of Glasgow Coma Scale Scores, those in the children with 4~5 score significantly increased ($P < 0.05$, $P < 0.001$ and $P < 0.05$).

Conclusions: CSF CRF levels of the children with acute brain injury are increased, which may be concerned with the secretion of hypothalamus CRF neuron stimulated by TNF- α and IL-6 and hypoxia stress in ill children with brain injury.

TWO CASES OF SUCCESSFUL TREATMENT OF INFANTS WITH GRAM-NEGATIVE VENTRICULO-PERITONEAL SHUNT INFECTIONS OF THE CNS WITH CIPROFLOXACIN

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Background: Ventriculo-peritoneal shunt (VP) is a common procedure in neurosurgical practice. 2.2% - 39% of infants with VP shunt develop shunt infection. Gram-negative bacteria are responsible for 19 - 22% of cases. Therapeutic failures are common. The object of the present research is the clinical and laboratory follow up of two cases of CNS shunt infections, caused by Gram-negative bacteria successfully treated with i.v. ciprofloxacin.

Case presentation:

Case 1: A 5 months old infant with severe head trauma, internal hydrocephaly and VP shunt. Two months after surgery clinical symptoms of CNS infection developed. *Enterobacter cloacae*, *Acinetobacter baumannii* and *E.coli* were consequently isolated from the spinal fluid. Treatment with various antibiotics failed. Ciprofloxacin i.v. 10 mg/kg/24hr twice a day was started and in 21 days spinal fluid was normalized.

Case 2: A 5 months old infant with a Dandy-Walker syndrome suffered bacterial meningitis caused by *S. agalactiae* at the age of two months. Later internal hydrocephaly developed requiring VP shunt. Ten days after surgery clinical symptoms of CNS bacterial infection developed. *Stenotrophomonas maltophilia* was isolated from the spinal fluid. A 12 days course with Cephtazidim failed despite sensitivity of the agent in vitro and *Stenotrophomonas maltophilia* was isolated again from the spinal fluid. A 14 days course with i.v. ciprofloxacin 20 mg/kg/24hr twice a day normalized the spinal fluid.

Conclusion: Intravenous ciprofloxacin in a dose 10 - 20 mg/kg/24hr twice a day can be used successfully for treatment of problematic Gram-negative VP shunt infections in infants.

ACUTE DISSEMINATED ENCEPHALOMYELITIS: LITERATURE REVIEW AND CASE REPORT

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The purpose of this study is the literature review of acute disseminated encephalomyelitis (ADEM) as well as the presentation of a case report. A previously well 7-year-old girl was admitted to hospital with symptoms of lower respiratory tract infection. Due to persistent low grade fever and frontal headache fundoscopy and MRI of brain were performed without pathological findings. Because of recurrent headache accompanying with diplopia and strabismus was held new fundoscopy which revealed papilledema. New MRI revealed lesions suggestive of ADEM. The child was treated with corticosteroids and showed dramatic improvement.

ADEM is a rare demyelinating disease of the central nervous system (CNS) that typically presents as a monophasic disorder associated with multifocal neurologic symptoms and encephalopathy. ADEM is considered an autoimmune disorder that is triggered by an environmental stimulus in genetically susceptible individuals. Alves-Leon et al have found that the alleles HLA DQB1*0602, DRB1*1501, and DRB1*1503 confer genetic susceptibility to acute disseminated encephalomyelitis. ADEM usually develops in the wake of a wide variety of infectious illnesses or immunizations. More than 80% of childhood cases occur in patients younger than 10 years. Characteristic ADEM lesions on magnetic tomography of CNS are found in 80 to 90 percent of patients. ADEM should particularly be distinguished from multiple sclerosis. It is often treated with corticosteroids and intravenous immunoglobulin. The outlook for recovery is generally excellent even in children with serious neurological signs.

Acute disseminated encephalomyelitis should be considered in the differential diagnosis of acute encephalomyelopathy especially after an infectious illnesses or immunization.

HEALTH-RELATED QUALITY OF LIFE IN CHILDREN AFTER BACTERIAL MENINGITIS

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Background and aims: Bacterial meningitis is not only a potentially life-threatening but also causes neuropsychological sequelae in survivors and impacts on many aspects of children's development. This study aims to measure health-related quality of life of survivors of childhood meningitis and to identify factors associated with quality of life after meningitis.

Methods: Among 114 survivors after bacterial-confirmed meningitis who were admitted to Vietnam National hospital of Pediatrics (2007 - 2010), we could only track down 56 patients and 24 parents agreed to participate. One matched control per case was recruited. Control was either a same-sex sibling closest in age to the case or a similarly-aged same-sex child in the neighbourhood. Health-related quality of life of cases and controls were measured using PedsQL™ Generic Core scales. Neuropsychological examination and hearing tests were done in each case.

Results: Mean age of cases was 39.0 ± 18.6 months. On average 25.6 months after meningitis, patients had significantly lower mean physical function score ($p=0.012$), emotional function score ($p=0.006$), social function score ($p=0.042$), school function score ($p=0.029$) and general score ($p=0.001$) compare to controls. The negative effects on quality of life were not significantly influenced by causative organisms, surgical intervention, or presence of hearing impairment. 75% patients had hyperactivity disorder and there was a significantly association between this disorder and psychosocial health summary score on the PedsQL™ ($p=0.05$).

Conclusions: Children with bacterial meningitis have poorer health-related quality of life. Our findings support screening for hyperactivity disorder during follow-up after meningitis.

LUMBAR PUNCTURE AMONG 6-18 MONTHS OLD WITH FIRST SIMPLE FEBRILE SEIZURE IN TERTIARY PEDIATRIC GOVERNMENT HOSPITAL IN QUEZON CITY, 2010-2011

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Background and aims: This study aims to determine the association of negative lumbar puncture (LP) with first simple febrile seizure (FSFS) among 6 - 18 months old in a tertiary pediatric government hospital in Quezon City.

Methods: This is a retrospective cohort review conducted among patients with FSFS aged 6 - 18 months admitted in a tertiary pediatric government hospital January 2010 - November 2011. Results of LP were categorized as negative or positive based on American Academy of Pediatrics (AAP) Practice Parameters. Those patients who had previous seizures, underlying illness (e.g. ventriculoperitoneal shunt, or chronic medication use), history of trauma prior to the seizure and with presenting signs and symptoms of bacterial meningitis were excluded. Data were analyzed using frequency and Bayesian confidence interval and proportion at 95% level of confidence.

Results: Out of the 253 patients admitted for simple febrile seizure, only 171 presented as first episode. 62.57% were infants 6 - 12 months old, and 37.43 % were 13 -18 months old. Majority showed negative LP results (94.74%, confidence 95%, CI = 0.9029 - 0.9717, proportion = 0.9490). Only 5.26% (confidence 95%, CI = 0.0282 - 0.0970, proportion = 0.0526) had positive LP results.

Conclusion: In this study, there is a low probability of positive lumbar puncture among those with first simple febrile seizure episode hence the risk of bacterial meningitis presenting as FSFS at ages 6 to 18 months is very low. Use of LP among those with FSFS among 6-18 months old may be reconsidered.

CHILDHOOD BACTERIAL MENINGITIS IN CRETE, 1991-2010

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Background and aims: Bacterial meningitis remains a threatening infection in childhood, despite the availability of vaccines against *Haemophilus influenzae* type b, *Streptococcus pneumoniae*, and *Neisseria meningitidis*. The purpose of this study was to analyze the long-term incidence trends of bacterial meningitis in children aged 1 month to 14 years in the island of Crete.

Methods: The study included all children with culture- or PCR-proven meningitis hospitalized in the Paediatric Departments of the two major General Hospitals from 1991 through 2010.

Results: A total of 133 cases were identified. *N meningitidis* was responsible for 77 (57.9%) of all, followed by *S pneumoniae* for 36 (27.1%) and Hib for 11 (8.3%) patients. Nine cases (6.8%) were caused by other bacterial pathogens. *N meningitidis* cases (serogroup B, 58%) were seen all during the study period with two outbreaks in 1999 and 2002. *S pneumoniae* cases were also seen all during the study period. By contrast, all Hib cases were seen in the first 5 years of the study, before the vaccine introduction. Children younger than 2 and 5 years represented 48% and 75.2% of the cases, respectively. The case fatality rate was 5.3%. All fatal cases were related to *N meningitidis*.

Conclusions: Bacterial meningitis is still related to considerable morbidity and mortality in the study area. Vaccination has eliminated *H influenzae* cases and similar success may be anticipated with the vaccination against *N meningitidis* and *S pneumoniae*.

HERPES ENCEPHALITIS WITH SEVERE DISABILITY DESPITE SPECIFIC ANTIVIRAL THERAPY

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Aims: We present two HSV encephalitis (HSE) cases ended with severe disability despite spesific antiviral therapy.

Case 1: A 16-months-old girl presented with fever, vomiting, altered consciousness and generalized seizures. Analysis of CSF revealed high protein levels and pleocytosis, HSV PCR was positive. Cranial MRI showed hyperintense signals on right temporal lobe and right thalamus. After 12 days of acyclovir therapy, she was discharged with minor neurological sequelae. One week later she presented with refractory seizures, choreoathetosis and ballistic movements. EEG showed high amplitude rhythmic spike and waves over the right central and temporal areas. Acyclovir treatment was started again to fulfill 21 days. Repeated CSF analysis revealed negative HSV DNA. No new lesions were found at cranial MRI. She was discharged with severe neurological sequelae.

Case 2: A 16-years-old boy was presented with fever, headache, vomiting and behavioral changes. CSF findings revealed no pleocytosis and a mild increase in protein, . HSV PCR was positive. Brain MRI suggested bilateral limbic encephalitis. Acyclovir treatment was given for 21 days. He developed acute upper gastrointestinal hemorrhage and was admitted to intensive care unit with diagnosis of superior mesenteric artery syndrome. Repeat CSF sampling was negative for HSV. Repeat brain MRI showed diffuse cortical injury. EEG revealed generalized suppression at background electrical activity. He was transferred to an inpatient rehabilitation program.

Conclusion: Although it could not be possible to confirm drug resistance due to technical difficulties, treatment failures in our cases might be a result of clinical and virological resistance phenomenon.

CLINICAL PROFILE AND OUTCOME OF CULTURE PROVEN NEONATAL MENINGITIS IN A LEVEL III NICU DELHI

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Background and aims: The clinical presentations of neonatal meningitis are subtle, but its consequences are fatal if misdiagnosed. Etiological profile of neonatal meningitis varies in different parts of world. Present study was undertaken to study the etiological profiles and immediate clinical outcome of culture proven meningitis in Indian neonates.

Methods: This was a retrospective chart review of all culture proven neonatal meningitis patients admitted in neonatal intensive care unit from 1st June, 2011 to 31st December 2011. Demographic profiles, risk factors, haematological and microbiological investigations of patients were recorded.

Results: A total of 9 babies (7 male, 2 female) had culture proven neonatal meningitis. Four babies were pre-term. Five babies had normal birth weight, while 2, 1 and 1 were low, very low and extremely low birth weight, respectively. Six babies had early onset sepsis with meningitis, while 3 had late onset neonatal sepsis. Organisms grown on CSF culture and their sensitivity pattern are presented in Table 1. Seven patients were discharged after appropriate antibiotic therapy, while 1 expired and 1 left against medical advice. Among survivors, 1 patient had post meningitis hydrocephalous and required ventriculoperitoneal shunt, while others were neurologically normal at discharge.

Table 1: Organisms isolated from CSF and their sensitivity pattern

Organism	Sensitivity Pattern*
E. coli (3)	Meropenem (3/3), Amikacin (3/3) Gentamycin (3/3), Ceftriaxone (2/3) Amoxycillin (1/3), Ciprofloxacin (1/3)
Klebsiella (2)	Meropenem (2/2), Gentamycin (2/2) Ciprofloxacin (2/2), Amikacin (1/2) Ceftriaxone (0/2)
Enterococcus (2)	Vanc omycin (2/2), Gentamycin (2/2) Ciprofloxacin (2/2), Ceftriaxone (1/2) Amoxycillin (1/2), Linezolid (1/2)
Acinetobacter (1)	Imipenem (1/1), Amikacin (1/1) Gentamycin (1/1), Ciprofloxacin (1/1) Amoxycillin (0/1)
Staphylococcus aureus (1)	Vanc omycin (1/1), Amikacin (1/1) Gentamycin (0/1), Amoxycillin (0/1) Ciprofloxacin (0/1)

*numbers in parenthesis are number of sensitive organism out of total isolated organisms.

[Organisms Isolated and Sensitivity Patterns]

Conclusion: Gram-negative organisms are predominant cause of neonatal meningitis in Indian neonates. Early detection and institution of appropriate antibiotic therapy is associated with better neurological outcome.

FOCAL PYOGENIC CNS INFECTIONS IN CHILDREN: ANALYSIS OF 18 CASES PRESENTING IN A TERTIARY PEDIATRIC MEDICAL CENTER

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Background and aims: Focal CNS infections are rare in pediatric population but continue to have high morbidity and mortality rates. They have an incidence of 4 cases per million. 25% occur in children, mostly from 4 to 7 years of age. We aim to characterize children with focal pyogenic CNS infections diagnosed in our hospital and reassess clinical presentation, predisposing factors, treatment and short-term outcome.

Methods: Retrospective case series of children diagnosed with focal pyogenic CNS infections from 2000 to 2011. We analyzed medical records for gender, age, clinical presentation, predisposing factors, laboratory tests, imaging, microbiology results, management and outcome.

Results: Eighteen patients were identified, of which 72% were male; mean age of 5 years. We did not register mortality and 61% of our patients presented complications. Intracranial parenchymal abscesses were identified in 51% of patients. Other patients presented subdural empyema and epidural abscesses. Predisposing factors were found in all patients, 44% arose from otogenic infections. Main symptoms and signs included fever (66%), nausea and vomiting (50%). All patients received antibiotic therapy and 61% required a surgical procedure. 47% of patients treated initially with cefotaxime combinations had a poor response to the antibiotic treatment, having to be submitted to a surgery and to a change in the antibiotic regime to meropenem combinations.

Conclusions: Focal CNS infections may have subtle manifestations. An early diagnosis is crucial. The main predisposing factor is an otogenic infection. Meropenem may be an alternative to traditional antibiotic therapies. Morbidity continues to be important in pediatric population.

PEDIATRIC CENTRAL NERVOUS SYSTEM TUBERCULOSIS (CNS-TB) IN EMILIA ROMAGNA REGION, 1996-2006

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Introduction: Central nervous system tuberculosis (CNS) is the most severe presentation of active tuberculosis (TB): globally, it is noted in 5 to 10% of extra-pulmonary TB (EP-TB) and accounts for about 1% of cases (1.5% in Italy).

Methods: A retrospective study was conducted, by analyzing Regional Database of Emilia Romagna Region (Italy), and evaluating all cases of TB identified in ERR from 1996-2006. An estimate for main risk factors for EP-TB cases was performed through calculation of Odds Ratio (OR) and relative 95% Confidence Interval (95%CI).

Results: In total, 5,377 TB cases were reported and 37 CNS-TB cases identified (4 of them, 10.8%, at autopsy), with an annual notification of 3.36 (SD±1.43) cases. Standardized notification rate was calculated in 0.85 cases (min. 0.23 - max 1.53)/1,000,000 inhabitants/year, and in 3.85 cases for foreign-born peoples. CNS-TB were the 0.7% of total TB cases and 2.57% of EP-TB: when age groups were considered, CNS-TB were identified in the 5.88% of 0-14 EP-TB cases and in the 2.49% of cases older than 14 years. Twelve cases (32.4%) were new diagnoses (OR=0.484 95%CI:0.241-0.971). Finally, five cases (13.5%; OR=3.557 95%CI:1.338-9.457) had a previous diagnosis of immunodeficiency and 4 cases were HIV+ (10.8%; OR=4.236 95%CI:1.431-12.542).

Discussion: Incidence of CNS-TB cases was lower than expected (1-1.5% and 1.0 case/1,000,000 inh./y): also pediatric CNS-TB incidence was unexpectedly low. A possible cause could be found in the general under-reporting of foreign-born cases. On the other hand, it is possible that several cases missed the correct etiologic identification.

PREDICTION OF BACTERIAL MENINGITIS BASED ON CEREBROSPINAL FLUID PLEOCYTOSIS IN CHILDREN

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Background: Children with cerebrospinal fluid (CSF) pleocytosis are sometimes treated with parenteral antibiotics, but only few have bacterial meningitis. Although some clinical prediction rules, such as Bacterial Meningitis Score, are of well known value, the CSF white blood cells (WBC) count could be the initial available information.

Aim: To establish a cutoff point of CSF WBC count that distinguished bacterial from viral and aseptic meningitis.

Methods: Retrospective study of children aged 29 days-17 years who were admitted between 2005-2009, with CSF pleocytosis ($WBC \geq 7/\text{microL}$). Cases of traumatic lumbar puncture (LP) and of antibiotic treatment before LP were excluded.

Results: There were 295 patients with CSF pleocytosis, 60.3% females, medium age 5.0 ± 4.3 years distributed as: 12.2% 1-3 months; 10.5% 3-12 months; 29.8% 12 months-5 years; 47.5% >5 years. 31 children (10.5%) had bacterial meningitis, 156 (52.9%) viral meningitis and 108 (36.6%) aseptic meningitis. Bacterial meningitis was caused by *Neisseria meningitidis* (48.4%), *Streptococcus pneumoniae* (32.3%), other *Streptococcus* species (9.7%) and other agents (9.7%). CSF WBC count was significantly higher in patients with bacterial meningitis (mean, 4839cells/microL) compared to patients with viral meningitis (mean, 159cells/microL, $p < 0.001$), with those with aseptic meningitis (mean, 577cells/microL, $p < 0.001$) and with both ($p < 0.001$). A cutoff value of 321 WBC/microL showed the best combination of sensitivity (80.6%) and specificity (81.4%) for the diagnosis of bacterial meningitis (area under ROC curve 0.837).

Conclusion: The value of CSF WBC count was found to be a useful and rapid diagnostic test to distinguish between bacterial and nonbacterial meningitis in children.

MOLECULAR-VIROLOGICAL INVESTIGATION OF ENTEROVIRUSES IN BULGARIA AND FIRST DETECTION OF ENTEROVIRUS 71**A. Dikowa¹, A. Stoyanova^{1,2}, Z. Mladenova²***¹Virology, Faculty of Biology, Sofia University 'St. Kliment Ochridski', ²Virology, NCIPD, Sofia, Bulgaria*

Non-polio enteroviruses (EVs)(Picornaviridae family) are one of the most important pathogens of human health as they cause broad spectrum of clinical manifestations. The aim of the study was molecular detection and strain identification of EVs in patients with non-specific febrile illness or neurological symptoms. In 2011, stools and cerebrospinal fluid samples of 188 patients were tested for presence of EVs with RT-PCR followed by type-identification using PCR toward EV group A, B, C and EV71 and sequencing. A total of 35 patients (18.6%) were EV-positive. Among them, males (male:female ratio 1.5:1.0) and children less than 5 years old were most affected. Nine EVs were sequenced and the results revealed that most prevalent were EVs group B with detection of E6 in 3 samples and single cases of E4, E11, CA9 and CB. EVs group A - EV71 and CA16 were also found in 2 samples from patients with neuroinfections. None EV group C was detected. EV71 strain was detected for the first time in Bulgaria and sequencing of it's partial VP1 gene and phylogenetic analysis have shown 98% nucleotide identity with the isolate GB05/Ab/W/10. The present study indicated great strain diversity of EVs circulating in Bulgaria during one-year period.

MENINGITIS BY REACTIVATION OF VARICELLA-ZOSTER VIRUS IN AN IMMUNOCOMPETENT 7-YEAR-OLD BOY

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Background: The neurologic complications in herpes zoster are considered to be rare. Although children with cellular immunodeficiency are expected to be more susceptible to neurologic complications, these have also been described in immunocompetent children.

Case report: A previously healthy 7-year-old boy, not vaccinated for varicella-zoster virus (VZV), born to non-consanguineous parents, with history of uncomplicated varicella at the age of two, was admitted in our hospital. He had a 5-day history of frontal headache, a 2-day history of vomiting, photophobia and vesicular rash in his left scapular region; and an 1-day history of somnolence. On admission, he was afebrile, hemodynamically stable, drowsy but easily aroused without meningeal or focal neurological signs and presented vesicular skin eruption in his left scapular region. Laboratory studies showed peripheral white blood cells count (WBC) of 6 000/mm³ with 90.2% neutrophils and normal C-Reactive protein. Brain computerized tomography was normal. The cerebrospinal fluid (CSF) revealed 480/mm³ WBC (96.7% mononuclear cells), protein 90 mg/dl and glucose 41 mg/dl. The CSF bacterial culture was negative. VZV was detected in CSF by polymerase chain reaction. Immune investigations were normal. The patient was treated with intravenous acyclovir (10 mg/kg/day) during 14 days with clinical improvement. Three weeks after discharge, he was asymptomatic with residual lesions of shingles.

Discussion: Although involvement of the central nervous system is rare in immunocompetent children, we must consider this entity as a possible cause of meningitis, when we have a child with vesicular rash and history of varicella in early childhood.

ETIOLOGY AND NEUROLOGIC COMPLICATIONS OF BACTERIAL MENINGITIS IN CHILDREN WITH SPECIAL EMPHASIS TO SUBDURAL COLLECTIONS

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Despite the progress in medicine, bacterial meningitis causes substantial morbidity and mortality in children. The aim of the study was to determine etiology and neurologic complications of bacterial meningitis in children with special attention to subdural collections.

Methods: This observational and prospective study included 277 children (aged 0-16 years, 162 boys), treated for bacterial meningitis at the Clinic of Infectious Diseases in Prishtina (Kosovo) in years 1997-2002.

Results: Of the 277 children treated for bacterial meningitis, 60 children developed neurologic complications (22%) and 15 died (5%). The etiology was confirmed by culture in 124 cases (45%); 71 meningococcus, 22 H.influenzae, 17 pneumococcus and 11 Gram negative bacilli isolates were found. The most common neurologic complications during the acute phase of bacterial meningitis were subdural collections in 38 children (14%): subdural effusion in 35 children, two cases of subdural empyema and a single case of subdural hematoma. Most of cases (29/38) underwent medication treatment, while 9 children (24%) underwent neurosurgical treatment (mean time, day 5). Other diagnosed acute structural neurologic complications include: 7 cases of hydrocephalus and single cases of spinal abscess, cerebritis and intracerebral hemorrhage. The causative pathogens of cases complicated with subdural collections were found to be S. pneumoniae (6/17), H. Influenzae (6/22), N. meningitidis (11/71), S. aureus 2/2 and gram negative bacilli (2/11).

Conclusions: Meningococcus, H. Influenzae and pneumococcus were found to be the most common pathogens of bacterial meningitis cases in children. Subdural collections were the most frequent neurologic complications with good outcomes based on long-term follow-up.

INVASIVE MENINGOCOCCAL DISEASE IN POLISH CHILDREN, 2009-2011

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The aim of this study was to describe the characteristics of invasive meningococcal disease (IMD) among patients under 20 years of age in Poland.

Methods: The study was performed on all invasive *Neisseria meningitidis* isolates responsible for IMD in Poland, collected between 2009 and 2011 in the National Reference Centre for Bacterial Meningitis. The isolates were identified and serotyped. MICs were determined by the Etest method. A PCR technique was used for identification of the etiological agent directly from clinical materials in the case of a negative culture.

Results: Among 771 IMD cases notified, 75.6% affected patients aged 0-19, including 20.9% children under one. The average incidence rate in patients aged 0-19 was 2.33, was higher under 5 (6.64) and the highest in children under one (12.95/100000). Serogroup was defined for 90.0% of cases. Majority of cases were caused by meningococci of serogroup B (MenB, n=309; 59.5%), followed by serogroup C (MenC, n=199; 38.3%), Y (n=8, 1.5%) and W-135 (n=3; 0.6%). In children under 2 years of age more than 72% of cases were caused by MenB, whereas above 10 most common was MenC (55%). Case fatality ratios for MenB and MenC cases were similar, 10.4 and 9.0%, respectively. Decreased susceptibility to penicillin (MIC>0.06mg/L) characterised 20.9% of isolates.

Conclusions: Although in age group less than 20, MenB predominated, MenC cases are widely present, especially in patients above 10. These cases could be reduced by the wider use of MenC vaccination in Poland.

PAEDIATRIC TRANSVERSE MYELITIS - INFECTIOUS ETIOLOGY?**V.M. Machado**¹, M.J. Brito¹, J.P. Vieira²¹*Paediatric Infectious Diseases Unit, ²Neurology Paediatric Department, Hospital Dona Estefânia, CHLC, EPE, Lisbon, Portugal*

Background: Acute transverse myelitis (ATM) is a rare disease in children, characterized by a spinal cord inflammatory lesion. Infectious, autoimmune, demyelinating diseases and immunizations may be associated.

Aims and methods: We report three patients with ATM and describe the clinical, radiologic, therapeutic and evolution data and investigation results of our patients.

Results: The medium age was 3 years. Two patients had a previous viral respiratory infection. No recent immunization was reported. They had acute loss of spinal cord function with plegia of the lower limbs (2) and the upper limbs (1), muscle weakness in the lower limbs (2). Bladder disturbance (2) and bowel disturbance (1) were described. No sensory loss was reported but the patients' age precluded a confident assessment. CSF examination was abnormal in one patient. No intrathecal IgG synthesis was found; one patient displayed identical oligoclonal bands in serum and CSF (mirror pattern). MRI made the diagnosis with lesions at the cervico-thoracic spinal cord in all cases. *Mycoplasma pneumonia* was identified in one case and *Borrelia burgdorferi* in another and antibiotic therapy was given to these patients. All patients received methylprednisolone pulse therapy, and one was also treated with plasmapheresis and intravenous immune globulin. One patient had neurogenic bladder dysfunction and one had sequelae 1.5 years after the occurrence.

Conclusions: Post or parainfectious inflammation is thought to be a frequent cause of ATM. Even though, all potential etiologies should be excluded. Besides the small number of cases, the lack of paediatric series makes every report of great value.

EPIDEMIOLOGY OF TUBERCULOUS MENINGITIS IN PEDIATRIC POPULATION IN GREECE DURING THE LAST DECADE

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Background: Tuberculous meningitis (TBM) represents the most severe extrapulmonary manifestation of TB infection and is associated with considerable mortality and high rate of complications among survivors. Greece is low-prevalence country for TB, however the incidence of the disease is notable in non-native Greeks (immigrants and minority populations).

Methods: The aim of this study was to evaluate the epidemiology of the pediatric patients who were diagnosed with TBM in Greece. A multicenter, retrospective study was performed, reviewing the records of patients < 14 years of age, who had been diagnosed with TBM during 2001 - 2010 in the whole country. Patients who fulfilled criteria for diagnosis of TBM (Marais BJ reference) were included in the study.

Results: 23 patients (74% females) were identified and their medical records were evaluated. Mean age was 3.8 (0.2 - 11.5) years. Of all patients 52% were native Greeks, however, this percentage was reduced to 35% in the subgroup of children < 5 years of age. The outcome was good in 76% and neurological sequelae was recorded in 14.5% of the patients. Two patients (9.5%) died.

Conclusion: TBM remains a rare complication of TB in native Greek population, nevertheless the outcome is equal to other low-risk countries. The national vaccination schedule includes the BCG in children; however, the annual notification rate of the disease in native Greek children under 5 year of age is 0.58 / 1,000,000 general population / year for the last five years, which could fulfill the criteria for BCG discontinuation.

STREPTOCOCCUS AGALACTIAE MENINGITIS WITH SUBDURAL EMPYEMA ON A 4 MONTHS OLD INFANT

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Background: In spite of recent advances in maternal chemoprophylaxis strategies, that led to a decline in the incidence of neonatal disease, *Streptococcus agalactiae* (GBS) stills colonizes 25-40% women in reproductive age and remains a major pathogen for neonates, pregnant women and immunocompromised patients. GBS infection in neonates and young infants is classified by age at onset into early-onset (< 7 days of age), late-onset (7 to 89 days), and late-late onset infection (≥90 days).

Case report: The authors present a 4 months old infant, with mother streptococcus B+, birth by caesarean at 38 weeks, with ampicillin prophylaxis, Apgar score 10/10. Neonatal period without complications. Well until 3 days before admission, when he presented high fever and grunting. He had bulging fontanel, tachycardia and prolonged capillary refill. Leukopenia ($2,83 \times 10^3 / \mu\text{l}$) and CRP 1.36mg/dl. Biochemical CRF unable to be performed because of hematic content. Started ceftriaxone and vancomycin. On day 3 ceftriaxone susceptible GBS was identified in CRF. On day 9, he restarts fever and irritability. CT and MRI showed subdural fronto-temporal empyema. Surgical drainage was performed, with good clinical outcome. Dismissed on day 21, after 3 weeks of ceftriaxone and 10 days of vancomycin. In follow-up we found normalization of white cells. Immunology test showed hypo-IgG, without further defects.

Conclusion: Late late-onset GBS infections are most common in prematures and immunocompromised infants. Meningitis accounts for about 30 percent of cases of late late-onset GBS infection. It is necessary to consider this agent in CNS infections after the neonatal period.

TUBERCULOUS MENINGITIS: A CASE REPORT

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Background: Tuberculous meningitis is the most severe complication of extrapulmonary tuberculosis and practically the only cause of death from this infection in childhood. It has a low incidence in developed countries.

Method: We report the case of a 2-year old girl from Eastern Europe with Tuberculous meningitis.

Results: The child was admitted to our department due to fever (twice a day), vomiting (5-6 episodes daily) and irritability that started 15 days prior to admission. Low appetite was reported in the last two days. The symptoms persisted despite the oral antibiotic treatment that she received in the first 9 days. Physical examination revealed sleepiness and mild dehydration. Signs of meningitis were not present. Mantoux test was positive (12mm). Blood test results: WBC: 8180/mm³ (neutrophile 42% - lymphocytes 45%), HCT: 35,8%, HGB: 11,7 g/dl, PLT: 476000/mm³, ESR: 71 mm, CRP: 0.16mg/dl. Chest X-ray and other diagnostic blood and urine tests were normal. CSF collected during lumbar puncture showed the following results: 455 WBC (neutrophile 2% - lymphocytes 98%), protein 256mg/dl, glucose 21mg/dl (blood glucose 112mg/dl), Negative Gram stain and positive Zeihl-Neelsen stain. The positive Mantoux test and CSF findings lead to the tuberculous meningitis diagnosis. The child was transferred to a tertiary Children's Hospital for specialised treatment. Later it was revealed that other family members had been treated for tuberculosis in the last year.

Conclusion: In this case report we try to point out the necessity of Mantoux test in every child suffering from prolonged fever for an early tuberculous meningitis diagnosis.

FIRST FATAL SEROTYPE 3 PNEUMOCOCCAL (S3P) MENINGITIS IN A 5-WEEK-OLD COSTA RICAN (CR) INFANT

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Background: Culture-proven *S.pneumoniae* meningitis is associated with 16% mortality in CR children. Universal PCV7 vaccination for children < 2 years was introduced in our national immunization program (NIP) in January 2009 and was replaced by PCV13 in August 2011. Serotype 3 represents 7.5% of all invasive pneumococcal isolates at our institution. We describe the first fatal pediatric case due to S3P in CR.

Case: A 42-day-old girl presented to a regional hospital with a 5-day history of fever, irritability, poor feeding, and during the last day she developed pallor, grunting, lethargy, and left palpebral ptosis. On admission, she was received on septic shock and had neurological deterioration; therefore she was intubated and transferred to our institution. A turbid CSF revealed 5,950 leukocytes/mm³, glucose 12 mg/dL, proteins 306 mg/dL, and abundant Gram + diplococci. On admission to our center, she had a tense bulging fontanelle, was hypotensive, and developed seizures. She required treatment with cefotaxime, vancomycin, fluid therapy, vasopressors, hydrocortisone, multiple blood products, and management in PICU. CSF and two blood cultures had a rapid growth of penicillin/cefotaxime susceptible serotype 3 *Streptococcus pneumoniae*. A cerebral ultrasound revealed severe edema and subdural effusion. Her condition worsened, and she progressed to brain death on day 3 of admission.

Conclusions: This case illustrates the importance of expanding pneumococcal serotype coverage among NIP's. For infants too young to be vaccinated as this patient, herd immunity achieved through universal conjugate vaccination may decrease the risk of acquiring pneumococcal infections in this group.

UNUSUAL INFECTION OF CNS DUE TO LISTERIA MONOCYTOGENES

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Background: A previously healthy, completely unvaccinated 3-year-old boy, was transferred to our PICU with clinical signs of meningitis and hyponatremic seizures. Prior to admission, he presented fever, dizziness and confusion. He was started on Ceftriaxone and vancomycin.

Methods: On admission he was dizzy, with no focal neurologic signs. Transcranial Doppler showed no evidence of elevated intracranial pressure. His hyponatremia was attributed to SIADH, and was corrected appropriately.

Lumbar puncture on day 2, revealed 2680 cells/ μ l with polymorphonuclear pleiocytosis, low Glucose and increased protein.

Results: Gram-positive bacillus was identified in CSF and blood. CSF PCR isolated *Listeria monocytogenes*.

The antibiotic regimen was changed to ampicillin plus gentamicin. The patient became afebrile after 2 days.

According to the patient's history the boy has consumed expired butter.

Lumbar puncture was repeated at day 8 in order to decide on the duration of therapy. It showed 320 cells/ μ l, with normal protein and glucose. Culture was negative and gentamycin was stopped.

Testing of immunity that failed to confirm any immunological abnormalities, included: negative HIV test, normal quantification of serum immunoglobulins, C3 and C4, flow cytometry of lymphocyte subgroups and protein electrophoresis. After 8 days he was transferred to the general ward to complete 21 days of ampicillin.

MRI imaging after completion of the antibiotic regimen showed no evidence of calcifications or abscesses.

Conclusions: Clinicians must bear in mind *Listeria* infection according to positive clinical history. The result is determined by the immune status and early diagnosis and therapy.

CYTOMEGALOVIRUS INFECTION AND GUILLAIN BARRÉ SYNDROME

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Introduction: Guillain-Barré syndrome (GBS) is an acute, paralysing, inflammatory peripheral nerve disorder, preceding in 60% of cases by a nonspecific infectious episode. It is a rare syndrome in children throughout the world, with a median annual incidence of 1.3 cases per population of 100 000. Males were more affected than females. *Campylobacter jejuni*, Cytomegalovirus (CMV), Epstein-Barr virus and *Mycoplasma pneumoniae* are commonly identified as antecedent pathogens. There is a broad clinical spectrum and variable severity making diagnosis difficult.

Cases report: Two children with 2 and 2.5 years old were admitted for acute muscular pain and weakness of the legs one week and three weeks respectively after an upper respiratory tract infection. Initial clinical examination showed symmetrically reduced leg's muscle, ataxia and absence of deep-tendon reflexes of the lower limbs. There were no blood inflammatory markers, and creatine phosphate kinase level was normal. Medical imaging study was also normal. However, cerebrospinal fluid showed albuminocytological dissociation. Clinical and laboratory features suggested the diagnosis of GBS. Further investigations found recent CMV infection by serological tests. Intravenous immunoglobulin was given. Both fully recovered within 36 days and 10 days respectively.

Conclusion: GBS, an autoimmune disease, is rare in children under 3 years old. It is a common cause of acute neuromuscular paralysis and should be suspected in all patients with unexplained motor weakness. Among the infectious agents involved, CMV represents 10-20% of cases of GBS. Specific management strategies such as intravenous immunoglobulin are more effective if given early in the course of the disease.

TUBERCULOUS MENINGITIS IN CHILDREN STILL A DIAGNOSTIC DILEMMA IN DEVELOPING WORLD

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Background and aims: Clinical and investigational variables indicators of early diagnosis suffering from tuberculous meningitis in children.

Design: Case control prospective study.

Place and duration of study: Department of Neurology Children's Hospital, Lahore from March 1, 2010 to August 30, 2011.

Methods: Clinical data of 300 patients being treated as TBM (group A) admitted in the Neurology department, and another 300 patients with diagnosis of meningitis, encephalitis or cerebral malaria (group B) were evaluated. History, clinical examination and relevant investigations were evaluated and Kenneth Jones criteria were applied to both groups. All children were followed and their outcome was also studied.

Results: Data of 300 patients with TBM and controls was analyzed. Clinically 77% children were in TBM stage III and 22% were in TBM stage II and only one child was in TBM stage I.

Hydrocephalus was seen in 67 Children and 47 children develop basal meningial enhancement. 26 children had brain Tuberculoma. Above 50 ESR was seen in 43 children. Twenty children lost their lives during the first admission (period varies from 10 day to 38 days) while another 7 children expired subsequently.

Conclusion: Tuberculous meningitis remains a serious health threat in developing countries. The variable, natural history and accompanying clinical features of TBM had significant capacity for the early diagnosis and prognosis. There is a need to educate primary care pediatricians about early diagnosis of Primary TB and TBM.

CLINICAL AND LABORATORY PROFILE OF BLOOD CULTURE POSITIVE SEPSIS

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Objective: The aim of study was determine the clinical and laboratory profile of blood culture positive sepsis in newborn admitted to NICU.

Methods: In a cross- sectional study one hundred document of newborn with sepsis blood culture positive were elected. The data about clinical and result of laboratory test recorded and analyzed.

Results: In this one hundred document 75% were low birth weight, 57% were male, and 83% preterm, 56% delivered by cesarean section. Sixty seven percent were symptomatic in day one. The most common organism include coagulates negative staphylococci, coagulates positive staphylococci, klebsiela pneumonia, antrobacter, Ecoli and entrococci. There were 64% cases with gram positive and 36% gram negative bacteria. Eight percent had urinary tract infection with male predominance. In plate late count 24% had thrombocytopenia (PLT< 100000) .It was significantly more common in gram negative than gram positive culture (P=0.000). Decreasing hemoglobin was observed in 42%. In leukocyte count 11% had leucytosis, 4% leucopenia and 85% had normal count. Erythrocyte sedimentation rates (ESR) have been done in only 38% cases, from each 7 cases have high ESR. The most common clinical symptoms were respiratory distress syndrome, cyanosis, lethargy and poor feeding.

Conclusion: This study showed culture positive sepsis was more common in low birth weight preterm, male newborn and gram positive sepsis was more common than gram negative. Thrombocytopenia was more common in gram negative sepsis and leucosytosis was observed in about 10%. Respiratory symptom was more common feature of clinical profile.

STUDY OF DEVICES, SOLUTIONS AND PERSONAL HANDS CULTURES RESULT AT NICU EMAMREZA HOSPITAL NORTHEAST IRAN

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Introduction: Infection is a common cause of neonatal death, nosocomial infection may increase neonatal death at NICU, as we know the nosocomial infection is more than 11% at NICU, We decide to study the result of contamination of devices solutions and personal hands at NICU and based on the type of bacteria and the device which is contaminated we take the serious steps for prevention of contaminating and its disinfection.

Method: All devices and solutions which were related to neonates studied with culture during 2005 - 2006 at NICU of Emamreza hospital Mashhad. Two samples were taken by head nurse weekly. If the culture was positive, after disinfection of devices another's culture was taken.

Result: From 155 samples, 66 samples were sterile (42/6%) and 89 (57/4%) contaminated. Common organisms were gram positive non pathogen (25/8%), staph. Coagulase negative (12/9%) and staph. Aureus (6/5%).

Conclusion: This study shows that the common contaminable organisms are same as nosocomial organisms at NICU and common contaminated places are incubator and personal hands.

Recommendation: To recommend the disinfection of incubator and hands at NICU.

AN AUDIT AGAINST CURRENT GUIDELINE FOR THE MANAGEMENT OF CHILDREN BORN TO VDRL+ MOTHERS

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Background and aims: Untreated maternal syphilis results in perinatal loss/morbidity. Congenital infection results in deafness, bone, teeth and eye abnormalities. Children have serology at birth (maternal pairing) and are followed up at intervals until all serology is negative.

Hypothesis: Better clinic compliance and reduced follow up duration may be achieved by discharging children once VDRL negative and TPPA titres are decreasing, without adversely affecting outcome.

Methods: Retrospective case note audit. 67 cases over a 2 year period (January 2009-January 2011). Criteria assessed included demographics, gestation at booking/referral/delivery, serology, clinic attendance, treatment and mean length of follow-up.

Results: 82% of mothers were aged 16-35 years. 67% of patients were Asian/Afro-Caribbean. Co-infection present in 15%, Chlamydia most prevalent. Treatment required at birth in 3%. 20% defaulted clinic follow-up (risk factors: maternal late booker, drug abuse and antenatal clinic defaulter). At birth 75% babies were VDRL negative, and 30% were TPPA negative. Of the 25% of babies found to be VDRL positive at birth (n=9), 90% were negative by 3 months (n=8). 27% of total patients (n=18) were still being seen at 6 months as not all TPPA titres had fallen to zero, however all had reduced. No child with a negative VDRL and falling TPPA titre subsequently required treatment.

Conclusions: *Based on the information available, a reduced number of appointments, dependent on results of investigations, could be incorporated into future guidelines, therefore reducing costs and potentially improving clinic attendance.*

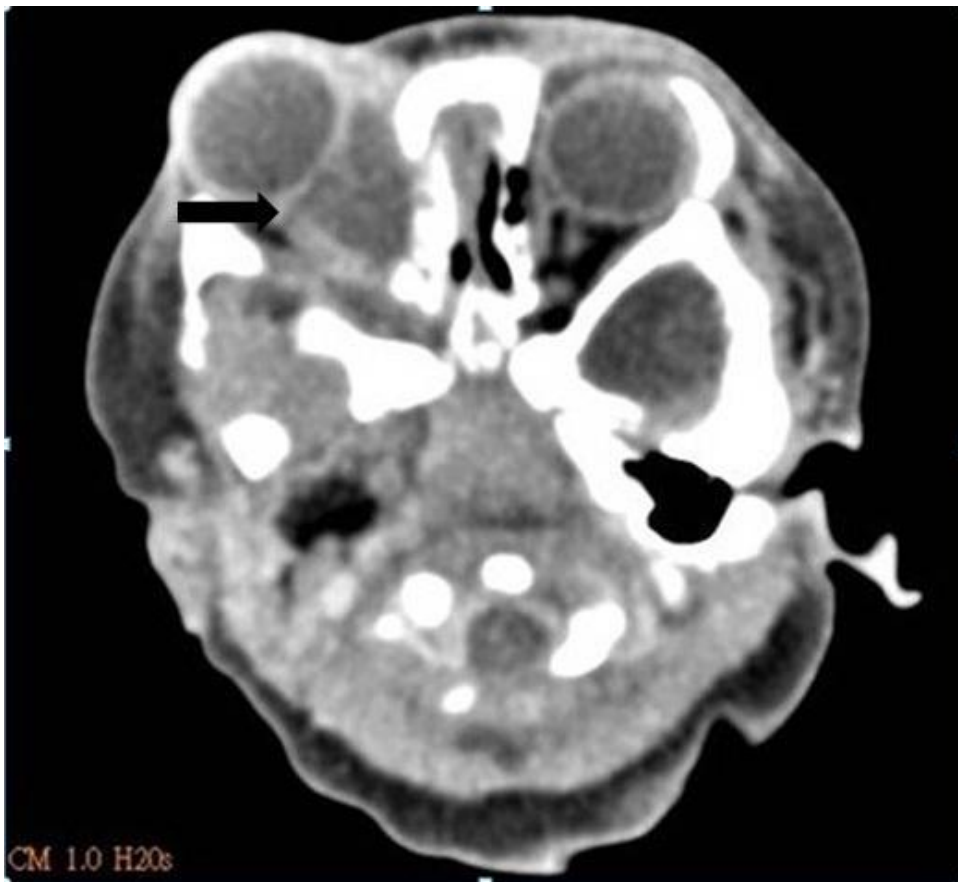
NEONATAL ORBITAL ABSCESS

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Background and aims: Orbital abscess is life-threatening and rare in children. Neonatal orbital abscess is extremely rare and prompt diagnosis and early treatment are mandatory.

Methods: We report a term male neonate with Methicillin-resistant *Staphylococcus aureus* orbital abscess and provide a literature review of this disease (Figure)



[Figure]

Results: 11 neonates diagnosed with neonatal orbital abscess are reported in the literature (Table).

Author ^o	Sex	Fever ^o	os/od ^o	Leukocyte count (10 ⁹ /L) ^o	Ethmoiditis	Sepsis	Pathogen ^o	Surgery	Outcome ^o
<u>Burnard^o</u>	F ^o	Yes ^o	od ^o	24 ^o	No ^o	No ^o	S.A. ^o	Yes ^o	Cure ^o
<u>Burnard^o</u>	M ^o	ND ^o	ou, od>os ^o	3.5 ^o	No ^o	Yes ^o	S.A. ^o	No ^o	Death ^o
<u>Burnard^o</u>	F ^o	No ^o	od ^o	11.3 ^o	ND ^o	No ^o	No ^o	No ^o	Cure ^o
<u>Maruszczak^o</u>	M ^o	Yes ^o	os ^o	normal ^o	No ^o	No ^o	S.A. ^o	Yes ^o	Cure ^o
<u>Maruszczak^o</u>	F ^o	No ^o	os ^o	elevated ^o	No ^o	No ^o	Diplo. Pneumoniae ^o	Yes ^o	Cure ^o
<u>Saunders & Jones^o</u>	F ^o	No ^o	os ^o	ND ^o	Yes ^o	No ^o	S.A. ^o	No ^o	Cure ^o
<u>Reddy^o</u>	M ^o	Yes ^o	os ^o	26.1 ^o	Yes ^o	No ^o	MSSA, Aspergillus ^o	Yes ^o	Cure ^o
<u>Cruz, A^o</u>	F ^o	No ^o	od ^o	normal ^o	Yes ^o	No ^o	ND ^o	Yes ^o	Cure ^o
<u>Cruz, A^o</u>	F ^o	Yes ^o	od ^o	9 ^o	Yes ^o	Yes ^o	S.A. ^o	Yes ^o	Cure ^o
<u>Anari^o</u>	M ^o	Yes ^o	od ^o	8.49 ^o	Yes ^o	Yes ^o	MRSA ^o	Yes ^o	Cure ^o
<u>Present^o</u>	M ^o	Yes ^o	od ^o	12.3 ^o	Yes ^o	Yes ^o	MRSA ^o	Yes ^o	Cure ^o

ND: not described^o

S.A.: *Staphylococcus aureus*^o

MRSA: Methicillin-resistant *Staphylococcus aureus*^o

[Table]

There is no sexual predilection and one neonate is delivered prematurely. Leukocytosis, fever, ethmoiditis and associated URI are found in about half of them. 4 neonates have sepsis and 8 patients undergo surgical intervention. 1 patient expired. *Staphylococcus aureus* is identified in 8 out of 11 patients.

Conclusions: Neonatal orbital abscess is rarely encountered but may be fatal. Timely diagnosis and intervention are required to ensure a favorable outcome. Appropriate antimicrobial agent against *Staphylococcal aureus* is essential in treating neonatal orbital abscess.

NEONATAL LISTERIOSIS: A CASE OF FAVORABLE PROGNOSIS

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Infection with *Listeria monocytogenes* (LM) in pregnant women can lead to abortion, stillbirth or premature birth of infants with neonatal sepsis and meningitis. The infection is associated with high perinatal mortality rate (20-45%). A 36 weeks pregnant patient was admitted in the Emergency Room by fever with 1 day of evolution. She had a normal delivery of a male newborn with meconium in amniotic fluid and cord circular requiring prior ligation. Apgar Score: 1 '7, 5'8 and 10'9. Immediate weeping, marked pallor and hypotonia were observed. His weight was 2425g. He maintained pallor, difficulty breathing and groaning and was transferred to the NICU. Hypoxemia and respiratory acidosis were also observed. Assisted ventilation was maintained until day 3 (D3). Hemodynamic instability was reported and he started inotropic support with dopamine and dobutamine till D5. The blood exams performed revealed an increased C- reactive Protein (126 mg / L), hypoglycemia, and thrombocytopenia (30000/ul). On suspicion of neonatal sepsis treatment with ampicillin and gentamicin were initiated. Blood cultures revealed LM. Cerebrospinal fluid analysis showed meningitis . Treatment with Ampicillin was maintained for 21 days. Histology of the placenta revealed acute chorioamnionitis and funisitis. He was discharged on D22. Transplacental transmission and infected meconium aspiration were recognized as transmission routes of infection. Early diagnosis of perinatal infection is dependent on a high index of clinical suspicion and early antibiotic therapy is essential when there is infection of the CNS, as exemplified by this case and certainly contributed to the favorable evolution observed.

EARLY-ONSET SEPSIS: 14-YEAR EXPERIENCE

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Background and aims: Early-onset sepsis (EOS) remains an important cause of morbidity and mortality amongst newborns. GBS and *E. coli* are the most frequent pathogens. Our aim was to evaluate trends and clinical data of newborns with EOS.

Methods: Retrospective analysis of the medical records of all newborns with EOS from January 1998 to December 2011, defined by clinical signs and symptoms compatible with laboratory studies suggestive of infection (CRP >2mg/dL; WBC >30000/uL or < 5000/uL, with or without isolated organism).

Results: During the 14 year period, among a total of 44105 live births (LBs), 119 newborns developed EOS (2,7 cases per 1000 LBs). Hyporeactivity and grunting were the most frequent symptoms. CRP was >2mg/dL in 75%. A total of 48 cases had positive blood cultures (1,1 per 1000 LBs). The most frequently isolated bacteria were GBS (19; 0,43 per 1000 LBs) and *E. coli* (10; 0,23 per 1000 LBs). Most newborns with GBS were term (74%; median 38 weeks); 90% with *E. coli* were preterm (median 31 weeks). When comparing the incidence of GBS and *E. coli* infection in 1998-2004 and 2005-2011, these remained similar (GBS 0,4 and 0,46 per 1000 LBs; *E. coli* 0,18 and 0,28 per 1000 LBs, respectively). Seven newborns with EOS died, 57% with *E. coli* infection.

Conclusions: GBS is the most frequent pathogen in term newborns and *E. coli* in preterm newborns, in agreement with literature. During the 14 years we did not find a substantial difference in the number of infections by these microorganisms.

PREVENTION OF PERINATAL GROUP B STREPTOCOCCUS (GBS) DISEASE: EFFECTIVENESS AND COST OF GBS INTRAPARTUM PCR SCREENING STRATEGY

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Background: GBS intrapartum PCR screening has been implemented routinely 24/7 for term deliveries in a Paris hospital. Our objective was to estimate the effectiveness and cost of intrapartum PCR screening on early-onset GBS disease compared with the antenatal lower-vagina culture screening recommended in France.

Methods: This was a single-institution study, comparing the intrapartum PCR screening strategy implemented in 2010 with antenatal culture strategy in place in 2009. Early-onset GBS disease in newborns was exhaustively monitored. We estimated direct costs, including screening test costs and hospital costs, for deliveries of healthy versus GBS-infected newborns. Costs in 2009 and 2010 were compared on an intention-to-treat basis.

Results: Term deliveries were 2,761 and 2,814 in 2009 and 2010, respectively. Among the screened mothers, the vaginal GBS colonization rate was 11.7% based upon antenatal GBS culture screening in 2009 vs. 16.7% in 2010 using the intrapartum PCR testing. The overall probabilities of neonatal GBS disease were 0.9% vs. 0.5%, and the average total cost per delivery €1,390+/-955 in 2009 vs €1,386+/-665 in 2010 (p=0.9) in antenatal and intrapartum screening strategies, respectively. The number and severity of early-onset GBS disease and the resulting hospital costs were higher in 2009.

Conclusions: In our hospital, PCR intrapartum screening strategy used 24/7 in routine clinical situations for term deliveries in 2010, was cost-neutral when compared to the 2009 antenatal lower-vagina culture screening, with a significant decrease in early-onset GBS disease.

THE DETECTING ALGORITHM FOR CANDIDATE OF THE SYMPTOMATIC CONGENITAL CYTOMEGALOVIRUS INFECTION USING MATERNAL SEROLOGICAL TESTS AND FETAL ULTRASONOGRAPHY

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Objective: The purpose of this study was to establish the effective detecting method for candidate of the symptomatic congenital cytomegalovirus infection (CMV) using maternal IgM and IgG avidity, and fetal ultrasonography.

Methods: Prospective study was conducted in 1151 pregnant women managed at primary hospitals. IgM and IgG avidity index (AI) were measured until 12 weeks of gestation. Abnormal Ultrasonography (US) such as ventricular dilatation, ascites, hepatomegaly, hyperechogenic bowel and placental enlargement were examined at 20-21 weeks of gestation. CMV infection was confirmed by polymerase chain reaction using neonatal urine. All neonates were followed their neurological development.

Results: All pregnant women were divided into 4 group according to IgG and IgM test; IgG(+)/IgM(±) (n=17, 1.5%), IgG(+)/IgM(+)(n=36, 3.1%), IgG(+)/IgM(-)(n=905, 78.6%), IgG(-)/IgM(-)(n=193, 16.8%). In IgG(+)/IgM(+) group, 9 women had low AI, in which 1 showed abnormal US and had symptomatic infected baby. The remaining 8 showed normal US and 1 had hemi-lateral hearing impairment. On the other hand, 27 women had high AI and normal US, but 1 had asymptomatic infected baby. In IgG(+)/IgM(-) group, 69 women had low AI and normal US, but 1 had asymptomatic infected baby. In IgG(-)/IgM(-) group, one showed seroconversion and had asymptomatic infected baby.

Conclusion: It was useful to detect congenital infected neonate with severe sequelae using the combination of US, IgM and AI. However, it could not detect congenital infected neonate with hearing impairment.

NEONATAL THROMBOCYTOPENIA AND INTERFERON ADMINISTRATION IN MOTHER WITH HEPATITIS

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Background: We report two babies born from a woman on interferon-alpha treatment for chronic hepatitis C and review the literature regarding the fetal and neonatal effects of interferon during pregnancy.

Case report: Two preterm, IUGR babies, were delivered to this mother. Were tested for hepatitis C and also for platelets values in the abnormal range (50000 e 90000/mmc) in boths without sepsis and other clinical signs. Platelets values were normal after two weeks without treatment.

Discussions: There are no reports of interferon acting as an abortifacient in humans. However, no formal studies have been performed evaluating large numbers of pregnant patients receiving interferon therapy. The effects on pregnancy of exogenously administered interferon in animals are variable. Teratogenicity has not been convincingly linked to interferon use in animals or humans. The safety of interferon administration during conception and pregnancy is uncertain but there are no controlled studies in women and in newborns. A theoretical risk exists of interferon's ability to inhibit both cellular proliferation and protein synthesis. In terms of fetal risk, interferon is classified as category C by the Food and Drug Administration. It's difficult a correlation with IFN administration in pregnancy and neonatal thrombocytopenia, perhaps it inhibit megacariocytes proliferation. In conclusion as the number of patients treated with interferon alpha is increasing, all doctors should know its undesirable effects also in neonates.

THE PREVALENCE AND ADVERSE EFFECTS OF GROUP B STREPTOCOCCAL COLONIZATION DURING PREGNANCY

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Background and aims: This study was done to evaluate the prevalence of rectovaginal colonization with Group B Streptococcal (GBS) among pregnant women who delivered in our center. Maternal and neonatal complications were compared between colonized and noncolonized groups.

Methods: Rectovaginal cultures were obtained from 1197 pregnant women with gestational ages (GA) greater than 24 weeks who were admitted to the labor room. All of the neonates had surface cultures after birth. The GBS carrier and noncarrier groups were compared for maternal and neonatal complications that occurred in the first week after delivery.

Results: Out of the 1197 pregnant women, 110 (9.1%) had rectovaginal colonization (group1) and 1087 women were not colonized (group2). 66 neonates had positive GBS cultures after birth with a transmission rate of 60%. One neonate developed early-onset GBS sepsis. Out of the 110 women who had positive GBS culture, 40 (36.3%) developed preterm labor as compared with 155 (14.3%) out of the 1087 in group2 (P=0.001). The mean GA of newborns in (group1) was 32.8±11 weeks compared with 36.2±7.9 for group2 (P=0.001). Eighteen women (16.3%) in group1 developed preterm rupture of membranes (ROM) compared with 65 (6.0%) in group2 (P=0.001).

Prolonged ROM was observed in 6.3% of women with GBS carrier states as compared with 0.5% in the group2 (P=0.001). Intrapartum antibiotics were initiated primarily on the risk based strategy for 34 (30.9%) women in group1 as compared with 12 (1.1%) in group2 (P=0.001). Maternal complications were not different between the groups.

Conclusions: 9.1% of the women had positive rectovaginal GBS cultures with a 60%

transmission rate to their neonates. Also preterm birth, prolonged (ROM), and

preterm premature (ROM) had a higher incidence among GBS colonized

mothers.

CORRELATION BETWEEN UREAPLASMA BIOVARS DETECTED BY REAL-TIME PCR FROM A SINGLE VAGINAL SMEAR AND PRETERM DELIVERY: PRELIMINARY RESULTS

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Background and aims: Although numerous studies have associated *Ureaplasma* spp with preterm delivery and adverse outcome for preterm infants, the proof of a causal relation between vaginal isolation of *Ureaplasma* species and adverse pregnancy outcome is missing. We hypothesize that it is important to differentiate between *Ureaplasma* biovars with potentially high and low pathogenicity and that pregnant women with isolation of vaginal *Ureaplasma parvum* (Biovar 1) are at increased risk for preterm delivery compared to women with isolation of *Ureaplasma urealyticum* (Biovar 2) or negative results. We report on preliminary results of our ongoing multicenter study.

Methods: Vaginal swabs are obtained during routine nuchal translucency screening and are analyzed for *Ureaplasma* biovars by real-time PCR. PCR results are correlated with pregnancy outcome. It is planned to include 4000 pregnant women in the study.

Results: Until January 2012, PCR results were available from 1840 women. 1003 swabs revealed negative PCR results. *Ureaplasma parvum* was found in 742 (40,33%) whereas *Ureaplasma urealyticum* was found in 140 (7,61%) women. 45 women had a concurrent infection with *Ureaplasma parvum* and *Ureaplasma urealyticum*. Pregnancy outcome is available for 886 women. Preterm delivery occurred in 66 (13,7%) pregnancies with negative culture results, in 55 (15,10%) pregnancies with isolation of *Ureaplasma parvum* and in 10 (14,7%) pregnancies with isolation of *Ureaplasma urealyticum* ($p>0,05$).

Conclusions: These preliminary data show no statistically significant correlation between rates of preterm delivery and isolation of *Ureaplasma* biovars in vaginal swabs during first-trimester pregnancy.

SEPTICAEMIA-RISK FACTORS FOR EVOLUTION OF NECROTISING ENTEROCOLITIS (NEC) IN EXTREMELY PRETERM INFANTS

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Background and aims: NEC is one of the most unpredictable diseases in premature infants. The pathophysiology of NEC is considered to be multifactorial. We investigated the incidence of NEC in relation to the septicaemia in preterm infants during a nine year period in the neonatal intensive care units (NICU).

Material and methods: Retrospective study of 161 infants born before 28 weeks of gestational age (GA) and hospitalized in the NICU in Lund between 2002-2010. Criteria for septicaemia were positive blood cultures or U-Arabinitol quota >5 (Candida). Septicaemia onset was registered as early (< 72 hours of life) or late (>72 hours of life). The diagnostic criteria for NEC was clinical or radiographic criteria (defined by Bell staging criteria) or findings in surgery or at post-mortem examination.

Results: Out of 161 infants 37,9% (95%CI 30,8-45,5%) were identified as cases of septicaemia and 8,1% (95%CI 4,9-13,1%) of NEC. The median of GA and of birth weight (BW) were 25 weeks and 735g respectively. Incidence of early septicaemia was 9% (95%CI 5,4-13%) and late 29,2% (95%CI 22,8-36,6%). Out of 61 infants with septicaemia 21,3% (95%CI 13,3-27,3%) developed NEC and out of 100 infants without septicaemia 3% (95%CI 1,5-7,6%) developed NEC. In relation to the early and late septicaemia NEC was diagnosed in 14,3% (95%CI 7,1-36,8%) and 17% (95%CI 9,5-29,5%) respectively.

Conclusion: The incidence of NEC in this patient group was 8,1%. NEC was highly associated with septicaemia. The most frequently identified bacterias were coagulase negative staphylococci.

BLOOD VOLUMES DURING ROUTINE VENESECTION FOR BLOOD CULTURES: A STUDY HIGHLIGHTING VARIABLE PRACTICES

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Background and aims: Blood culture is the gold standard for detecting bacteraemia in clinically septic neonates. There is limited information about the optimal volume for blood culture in neonates but volumes of 0.5-1 ml have been recommended.

Methods: The volume of blood submitted for culture was measured by weighing each blood culture bottle (BacT/ALERT® bioMérieux, France) before and after inoculation. Measurements were taken using a top loading precision balance (Sartorius, Germany).

Results: Forty blood culture samples from different babies were evaluated. Ninety percent were obtained from a peripheral vein. The median gestational age was 31+5 weeks ; median birth weight was 2490 g .The bottles contained a median volume of 0.48 mL blood. No samples contained 1ml or more. Blood sample volumes were not statistically different across the birth weight groups (< 1kg, 1-2 kg and > 2 kg). Two of four samples taken from a central line were of inadequate volume. Three blood cultures were positive and all had more than 0.5 mL of blood. The more senior practitioners had a tendency to take higher volume samples.

Conclusions: In our routine practice half of neonatal blood cultures contained less than 0.5 mL. Until there is a reliable blood culture system with acceptable yields using volumes of blood < 0.5ml clinicians will need to focus on blood culture acquisition to ensure adequate sampling. Additionally, lower volume inoculations are likely to result in possible false negative results under standard culture conditions.

CONGENITAL CYTOMEGALOVIRUS INFECTION: LOST OPPORTUNITIES

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Background and aims: Cytomegalovirus infection (CMVi) is the most common congenital infection in Europe. 10% of infected children present symptoms at birth and up to 30-40% have some degree of hearing loss. Delay in diagnosis may limit treatment opportunities. Our aim is to review the cases of congenital CMVi diagnosed out of the neonatal period and to assess the causes of the delay in the diagnosis.

Methods: We conducted a retrospective study selecting all children diagnosed of congenital CMVi in the past two years in our hospital. We included those diagnosed out of the neonatal period (i.e. diagnosed via dried blood spots) and evaluated the causes of such delay.

Results: Among 10 children with congenital CMVi, 5 were diagnosed using dried blood spots. The reasons for studying CMVi were hearing loss, microcephaly and neurological impairment (2 patients), hearing loss alone (2) and born to HIV-positive mother (1). 2/5 had relevant gestational history (fever, elevated liver enzymes and contact with CMV-infected relative) and 3/5 had a pathologic hearing screening-test. In none of them congenital CMVi was confirmed before 3 months of age (mean 196, SD=80 days) thus retarding initiation of specific treatment.

Conclusions: Congenital CMVi may be asymptomatic at birth or present as hearing loss and neurological impairment in infancy. In our centre, 50% of children were diagnosed outside the neonatal period. Therefore, a high degree of suspicion is necessary, especially if risk factors are present, in order to make an accurate diagnosis and start specific treatment to improve the outcome.

NEONATAL DENGUE IN PERU

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We present the case of a full-term female newborn, whose mother died seven days postpartum from multi-organ failure due to severe dengue confirmed by NS1 antigen detection and positive IgM. The newborn did not have any complication, but at the fourth day of life she developed fever, jaundice, signs of plasma leakage, thrombocytopenia, hepatomegaly, ascitis and other signs of systemic inflammation response syndrome. She fully recovered with supportive treatment. The RT-PCR test of a peripheral blood sample revealed a positive result for the dengue virus serotype two, confirming the first case of neonatal dengue reported in Peru.

IS CUTANEOUS ANTISEPSIS INADEQUATE IN PREVENTING CENTRAL VENOUS CATHETER-RELATED COLONISATION AND SEPSIS?

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Background: Despite local skin disinfection at insertion, indwelling percutaneous central venous catheters (PCVCs) become colonised with skin bacteria and predispose to catheter-related sepsis (CRS). Our hypothesis was that bacterial colonisation of the PCVC insertion site is an important risk factor for PCVC colonisation and CRS.

Methods: At each PCVC removal, a skin swab from the insertion site, and three PCVC segments were sent for bacteriological cultures. An additional peripheral blood culture was obtained from neonates with clinical features of sepsis. PCVC colonisation was defined as a positive growth in any PCVC segment from a well neonate. Definite CRS was defined as positive growths with the same organism in both any PCVC segment and blood culture in a clinically septic neonate.

Results: In a prospective study over 14 months, 39(21%) of skin swabs were culture-positive from 187 PCVC removals. The table shows culture-positive skin swabs according to subgroups.

Subgroup	culture-positive skin swabs n(%)	culture-positive skin swabs with same organism n(%)
Well baby, colonised line, n=36	16(44%)	16(100%) †
Well baby, sterile line, n=104	9(9%)	0(0%)
Unwell baby, definite CRS, n=15	10(67%)	8*(80%) ‡
Clinically septic, without definite CRS, n=32	4(13%)	1(25%)

*one had 'mixed growth' and another 'skin flora'; † Colonised vs. Sterile, P<0.0001; ‡ Definite CRS vs. Clinical sepsis, P<0.01

[Culture-positive skin swabs in various subgroups]

Conclusion: Positive insertion site skin swabs are strongly associated with both PCVC-colonisation and definite CRS. These data support the extraluminal route of PCVC colonisation and subsequent CRS. Current methods and/or agents of topical skin antiseptics appear inadequate for preventing this mode of bacterial spread.

VERTICAL TRANSMISSION OF HEPATITIS C VIRUS - PROSPECTIVE STUDY**C. Machado**¹, S. Carvalho¹, H. Antunes², I. Cunha³

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Background and aims: Vertical transmission of hepatitis C virus (HCV) is a rare condition. Presence of anti-HCV antibodies in pregnant women occurs in 0-4%; these can be detected in the majority of newborns. Risk of transmission is higher in HIV-positive women. About 5% newborns of HCV-positive mothers may acquire infection. The aim of this study is to determine vertical transmission rate of HCV in a Portuguese population, since there is only one published Portuguese study.

Methods: Prospective study between 1990 and 2011 including newborns of HCV-positive women followed in Neonatology consultation. Children with persistent positive HCV-antibodies were referred to Pediatric Gastroenterology, Hepatology and Nutrition (PGHN) unit.

Results: We had 55 children (60% male), 9 abandoned the consultation. There was intravenous drug use in 69.1%, and maternal hepatitis C was diagnosed before pregnancy in 90.9%. HIV co-infection has occurred in 20% (11) and HBV co-infection in 1.8% (1) cases. There was no association between HIV and HBV infection in the mother and HCV infection in infants. Were not breastfed 90.9%. One child (2.2%) (n=46) became HCV-carrier and was referred to PGHN unit. There are 2 more children in PGHN unit that were not included in this coorte but both had HCV vertical transmission (4a genotype; 1a genotype).

Conclusions: In this study the rate of vertical transmission of HCV obtained was lower than the one on the only Portuguese study published.

NEONATAL MENINGITIS WITH OSTEOMYELITIS AND EPIDURAL EMPYEMA: A CASE REPORT**B. Maia Vale**, I. Nunes Vicente, S. Morais, C. Resende, A. Taborda, C. Lemos*Serviço de Neonatologia, Maternidade Bissaya Barreto, Coimbra, Portugal*

Introduction: Neonatal meningitis is a serious disease that is associated with significant mortality and morbidity. In the neonate, the signs and symptoms are subtle, nonspecific, atypical or absent. Cephalohematoma is frequent in newborns and complications are uncommon and include infection after hematogenous spread in the setting of bacteremia or meningitis with possibility of osteomyelitis, epidural abscess and subdural empyema. We report the case of a 5-day-old newborn with *E. coli* meningitis, parietal cephalohematoma with osteomyelitis and epidural empyema.

Case report: Pre-term neonate (36 weeks), unremarkable pregnancy, born by vacuum-assisted vaginal delivery. On physical examination she had a parietal cephalohematoma. Discharged at 3 days of life. Twelve hours later she presented with irritability, fever (38°C), grunting and pale and was admitted to the NICU. WBC $1.9 \times 10^3/\text{ml}$, CRP 17,1mg/dl, CSF protein concentration >900 mg/dl, glycorrachia < 1 mmol/L. She started ampicilin, gentamicin and cefotaxime. Neurologic deterioration with seizures and opisthotonus occurred and phenobarbital was started. CSF and blood cultures were positive for *E. coli*, β -lactamic resistant. After 14 days therapy brain MRI was performed that revealed a right parietal epidural empyema communicating with a subcutaneous abscess associated with osteomyelitis and moderate supratentorial hydrocephalus. The culture of abscess material was positive for *E.coli*. She completed 6 weeks of antibiotic. She has neurological sequelae with cerebral palsy.

Discussion: The case reported associates meningitis, osteomyelitis, epidural abscess and cephalohematoma. We believe that hematogenous seeding of the cephalohematoma occurred, but the questions persists if bacteremia is the cause or consequence of an infected cephalohematoma.

COMAMONAS TESTOSTERONI SEPSIS IN A NEWBORN: CASE REPORT FROM LEVEL III NICU DELHI

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Comamonas testosteroni is an aerobic gram negative bacillus. This species, known as *Pseudomonas testosteroni* before its reclassification, metabolizes testosterone. It is ubiquitous found in water, soil, and plants. It is infrequently recognized as a human pathogen.

A preterm (32 weeks), 1750gm female baby born to a primigravida, unbooked mother was admitted in neonatal intensive care for respiratory distress. There was history of leaking per vaginum for more than 24 hrs in mother. Respiratory distress settled in 3 hours and gavage feeds were started. At 26 hours of life patient had abdominal distension and regurgitation of feeds. At 50 hours of life the baby started having upper GI bleed and there was increase in abdominal distension. Baby was started on Injection Piperacillin- Tazobactam, Amikacin and Metrogyl as sepsis screen was positive. Blood culture grew gram negative bacilli. Pending identification sensitivity report was available and the organism was sensitive to Ciprofloxacin, Gentamicin, Amikacin and Trimethopram-Sulfamethoxazole. The organism was subsequently identified by BacT/Alert 3D 120 Vitek-2 (bioMerieux France) as *Comamonas testosteroni*. The baby responded to supportive therapy and antibiotics. Cultures of the maternal stool, urine and high vaginal swabs were negative for *Comamonas testosteroni*. Environmental cultures did not grow *Comamonas testosteroni*.

Only 30 patients have been reported in World Literature. Among the 7 cases reported with bacteremia two were neonates. In 1 case, the child was stillborn and the other premature. In both there was history of maternal intravenous drug abuse. This is the first neonate who has been successfully treated.

CONGENITAL TUBERCULOSIS: A CASE REPORT

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Congenital tuberculosis is rare with only 300 cases reported in literature till now. Diagnosis is often delayed because of the nonspecific clinical manifestations. The early diagnosis of congenital tuberculosis is important because the outcome is invariably poor in the absence of early institution of antitubercular therapy.

We hereby report a preterm male newborn with congenital tuberculosis. Present baby was born through a normal vaginal delivery at 35 weeks of gestation and weighed 2170 grams. Baby was transferred to neonatal intensive care unit due to respiratory distress (Silverman Score 3/10) and hepato-splenomegaly. Military tuberculosis was diagnosed in mother in postpartum period based on chest X-ray and positive Mantoux test and anti-tubercular therapy was started. Chest X-ray of baby revealed diffuse infiltrates in both lung fields. Mantoux test was negative and CSF examination was normal. Ultrasound skull was also normal. CT abdomen revealed hepatosplenomegaly with coarse attenuation pattern of liver parenchyma and multiple hypodense lesions in spleen with retroperitoneal lymph nodes suggestive of diffuse Granulomatous pathology. Liver biopsy specimen showed multiple granulomas with central necrosis and positive acid fast bacilli staining. HIV serology was negative in both baby and parents.

Child was started on 4 drug anti-tubercular therapy (Isoniazide, Rifampicin, Pyrazinamide and Ethambutol) and showed gradual improvement. He was discharged on day 40 life and till last follow up at 12 weeks, is doing well.

High index of suspicion for congenital tuberculosis should be kept in newborns diagnosed with congenital pneumonia, especially in tuberculosis endemic regions.

CMV CONGENITAL INFECTION - THREE DIFFERENT CASE REPORTS

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Introduction: CMV is the most common congenital infection. Although most newborns are asymptomatic, it represents a major cause of sensorineural hearing loss and neurological disability in children.

Case reports: Three cases are presented. The first two had prenatal surveillance with maternal CMV seroconversion during the first trimester and positive PCR in amniotic fluid. In case 3, the pregnancy was unsupervised with positive IgM for CMV at delivery. The three cases were confirmed by positive postnatal CMV culture in urine. All had normal blood tests. No treatment was started.

Case 1: (2 years old): Fetal sonography detected intrauterine growth restriction and exuberant periventricular calcifications. Born hypotonic at 35 weeks needing neonatal resuscitation. Microcephaly at physical examination. Postnatal brain sonography/MRI showed multiple calcifications, ventriculomegaly, polymicrogyric cortex, enlarged cistern magna and cerebellar vermis hypoplasia. The child progressed to cerebral palsy. Retinal scarring was diagnosed and audiological assessment was normal.

Case 2: (2 months): Fetal sonography showed bilateral subependymal cysts. Term delivery with normal physical examination. Neonatal brain sonography confirmed parafrontal pseudocysts of the lateral ventricles. Follow-up is in progress.

Case 3: (5 years old): Delivery without complications. Normal physical examination. Postnatal evaluation showed stable periventricular microcalcifications on brain sonography and retinal scarring. Development and audiological assessment were normal.

Discussion: The clinical spectrum of CMV congenital infection is broad and progressive, therefore long-term follow-up is essential. These three children had CNS abnormalities, but their severity was very different.

THE CONSEQUENCES OF CONGENITAL CYTOMEGALOVIRUS INFECTION

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Background and aims: Cytomegalovirus (CMV) is the leading cause of congenital infection in developed countries, occurring in 0.3-2% of all live births and the most common cause of deafness and disabilities such as mental and motor retardation, hearing loss and vision loss.

Aim: To determine the outcomes of congenital CMV infection.

Methods: We examined 37 children with congenital CMV infection which was identified by the presence of DNA CMV in saliva, blood, urine, cerebrospinal fluid. We suggested the program of dynamic observation which included: laboratory tests (blood, urine, and biochemical blood analysis), ultrasound studies of salivary glands, thymus gland, abdominal cavity and brain, hearing screening, ophthalmologic and neurological exams.

Results: Median age of children is Me (P25-P75) 4 ± 2 months. Of these 25 (67.6%) - boys and 12 (32.4%) - girls.

Dynamic observation of children during 12 months and more has determined that 20 (54%) children had no abnormalities, 15 (46%) had long-term complications of congenital CMV infection such as CMV-associated hearing loss - 4 (11%) cases, chorioretinitis and optic nerve hypoplasia - 3 (8%), epilepsy- 2 (5.5%), cerebral palsy - 3 (8%), the combination of optic nerve atrophy with cerebral palsy, hearing loss and epilepsy - 3 (8%), chronic hepatitis in 2 (5.5%) children. All children with damage of central nervous system had psychomotor delay.

Conclusion: Congenital CMV infection threatens with the development of serious disabilities in children, remaining both medical and social problem.

RISKS OF OCULAR LESIONS IN CHILDREN WITH CONGENITAL TOXOPLASMA INFECTION TREATED PRE AND POSTNATALLY

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Background and aims: It is broadly believed that ocular lesions due to congenital toxoplasmosis (CT) seldom appear after the first years of life. Consequently, extended follow up is deemed not necessary. Our aim was to describe the age at presentation with new chorioretinitis in a large series of French children with CT treated pre- and postnatally.

Methods: The study draws on a consecutive cohort of cases with CT diagnosed between 1987 and 2008 at the Lyon reference centre and managed according to a standardised protocol.

Results: 480 children with CT had received treatment with pyrimethamine and sulphonamides for 12 months on average and been followed for a median time of 10 years (0.5-22 years). Ten percent had intracranial calcifications (n=45) and/or hydrocephalus (n=8) and 135 (30 %) had at least one chorioretinal lesion which caused unilateral blindness in 12 (no bilateral vision loss). First lesions were diagnosed between birth and 22 years of age, in 57% after 5 years and in 13% after 10 years of age. First macular lesions, observed in 50 children, were detected in 25% after 7 years of age. In 37% of children with retinal lesions, one or more recurrences and/or new lesions were observed up to 12 years after the initial event.

Discussion: Overall, the ocular prognosis in CT is satisfactory in children diagnosed early and treated. But, because of a significant risk of late occurrence of ocular lesions after more than 7 years of age, follow-up on a yearly basis without limitation seems rationale.

CONGENITAL SYPHILIS: A 7-YEAR RETROSPECTIVE STUDY

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Background and aims: Despite widespread antenatal screening, congenital syphilis appears to be increasing in Europe. Our aim was to review our experience in the last 7 years.

Methods: Retrospective analysis of the medical records of all newborns at risk of congenital syphilis, admitted to our Neonatology Unit, from January 2005 to December 2011 (7 years). The inclusion criteria was the presence of reactive maternal serologic tests for syphilis (treponemal and non-treponemal tests).

Results: During this period there were 22 747 live births in our centre, with 13 newborns presenting criteria for inclusion in this study, representing a prevalence of risk for congenital syphilis of 57 per 100 000 live births. The majority of these mothers (54%) did not receive adequate treatment during pregnancy or treatment was not effective; 38% had other associated risk factors (social status, previous history of syphilis). One newborn was symptomatic at birth. Other newborn presented a positive *T. pallidum* CSF PCR despite mother's adequate treatment. Six newborns (46%) were treated with penicillin at birth. Two cases (15%) had complications: one was admitted in the first month of life with congenital syphilis and was treated with penicillin without sequelae; another is now 12 months old and has cerebral palsy.

Conclusions: The prevalence of risk for congenital syphilis was superior to that described in literature. Unexpectedly, only a small proportion of mothers had associated risk factors. Most newborns were asymptomatic, but CNS involvement occurred despite mother's adequate treatment.

CLINICAL CHARACTERISTICS OF MOTHERS WITH REACTIVE SEROLOGY FOR SYPHILIS AND THEIR NEONATES IN THREE INSTITUTIONS IN SOUTH KOREA

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Background: Congenital syphilis(CS) occurs when the spirochetes, *Treponema pallidum*, is transmitted from a pregnant woman via her fetus. Transmission can occur at any stage of pregnancy and vertical transmission rate is 100%. Although CS is a serious health priority, limited data are available to address this problem in Korea. This study aims to evaluate the pattern and presentation congenital syphilis over a 10-year period as seen in three institutions in Korea.

Method: We retrospectively reviewed 20 medical records of women and neonates that have been detected with reactive syphilis serology from January 2000 to December 2010 at Kyung Hee University Hospital, Kyung Hee University Hospital at Gangdong, and Han-Il General Hospital.

Results: 20 cases were diagnosed as CS, and 38% (5/13) of their mothers had symptomatic syphilis infection during the first trimester of pregnancy. Among 13 mothers, 4 (31%) were foreign born immigrants, 2 (15%) were unmarried women.

The 62% (8/13) and 38% (5/13) of mothers were positive in non-treponemal test and treponemal test, respectively, whereas 60% (12/20) and 95% (19/20) of infants were positive in non-treponemal test, and treponemal test respectively. The 19 infants were asymptomatic, and one infant showed hepatosplenomegaly and jaundice. But 2 out of 19 had VDRL positive in CSF and one of 19 had bony changes in X-ray.

Conclusion: Only few CS babies were born to mothers who are with symptomatic syphilis infections and promoting awareness about the extents and gravity of CS and mounting effective surveillance is necessary in South Korea.

A RARE CASE OF SEPSIS IN NEWBORN: *STREPTOCOCCUS PNEUMONIAE* SEPTICEMIA AND MENINGITIS

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Introduction: Streptococcus pneumoniae is an important pathogen; However, neonatal infections due to this organism are rare. We report on an early-onset pneumococcal septicemia.

Case report: The newborn of a 17-year old mother with an APGAR score of 9/10 was hospitalized at the postnatal 36 hours due to hypotonia and a septic appearance. He was tachypneic and dyspneic with normal respiratory sounds by auscultation and without other systemic signs. The chest X-ray was normal and the PCT value was 13.24 mg/dl. The laboratory values revealed: WBC 2,310 mm³. The color of CSF was clear, protein was 1434 mg/dl and blood glucose/CSF glucose was 63/36 mg/dl with 2 cells . He developed seizures and required Phenobarbital and midazolam to control it. Administration of ampicillin plus gentamicyn was begun. Blood was drawn for culture and mechanical ventilation was needed. After 24 hours incubation *S. pneumoniae* was identified. It was also isolated from specimens taken from the mother's cervix and vagina. The mother had no clinical signs of genital tract infection. All the isolates were sensitive to penicillin. The specimen from the newborn and his mother were identified as serotype 5. The baby improved slowly with therapy. Mechanical ventilation was stopped after 4 days and antibiotic therapy after 21 days. He was discharged 23 days after admission with a brain CT scan and EEG without abnormalities.

Commentary: This case demonstrates the sporadic occurrence of pneumococcal neonatal sepsis. Colonization of the maternal genital tract by *S. pneumoniae* may lead to septicemia of the newborn.

PREVALENCE OF BACTERAEMIA PATHOGENS AND PATTERN OF ANTIBIOTIC RESISTANCE PROFILE, OVER 5 YEARS IN A TERTIARY SURGICAL NEONATAL CENTRE

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Background: Neonatal sepsis with bacteraemia causes high morbidity and mortality. Early empirical antibiotics are essential to reduce this. Antibiotic policies are made, based on local epidemiological data of pathogens and resistance profiles.

Objective: Identify bacteraemia pathogens and antibiotic resistance rates including incidence of Extended Spectrum Beta Lactamase producing Enterobacteriaceae, thus informing policy.

Compare pathogen profile in Medical versus Surgical admissions.

Methods: All positive blood cultures from January 2006 to December 2010 were obtained from Microbiology database and analysed. False positives were excluded using concurrent laboratory results (from date of positive culture to 10 days after) if CRP < 10, WCC < 22 & Platelets > 100, along with clinical data from electronic database (SEND) for secondary outcomes.

Results:

	2006	2007	2008	2009	2010	Average (5years)
Admissions (n=)	523	536	540	525	634	551
Bacteraemia episodes (excluding contaminants)	85	101	76	75	83	
(as % of admissions)	16.3	18.8	14.1	14.3	13.1	15.3%
CoNS (clinically significant/total)	88/70	88/52	89/52	44/61	47/62	
(% clinically significant)	54.3	63.5	75	72.1	75.8	68.1%
(% of + cultures)	44.7	32.7	51.3	58.7	56.6	48.8%
Enterobacteriaceae	23	30	15	11	15	
(% of + blood cultures)	27.1	29.7	19.7	14.7	18.1	21.8%
Group B Streptococcus	2	1	3	2	4	
(% of +cultures)	2.3	0.9	3.9	2.6	4.8	2.9%
Enterococcus, S Aureus & others	22	37	19	18	17	
(% of +cultures)	25.8	36.6	25	24	20.4	
<i>(Resistance - as % of Enterobacteriaceae)</i>						
Cefotaxime (ESBL positive)	26.1	20	13.3	18.2	20	18.9%
Tazocin	43.5	53.3	26.7	35.4	26.7	36.7%
Gentamycin	4	0	6.6	0	0	2.1%

[Pathogens and Antibiotic resistance]

Commonest pathogens in early onset sepsis (< 48 hours age) n=28 (6.6%), were Group B Streptococcus (35%) & coliforms (23%), and in late onset sepsis (n=392) CoNS (48%), Enterococcus (9.1%) and Klebsiella (6.8%). No candidaemia seen in 2009-10, despite surgical antibiotics.

There was no significant differences in pathogens between surgical (n=232) and medical (n=188) infants. In 5 years, 11 babies died during episodes of sepsis and 2 term babies had cerebral bleed, reflecting the bane of sepsis.

Conclusion: Pathogens and resistance patterns were stable with a decreasing trend in Tazocin resistance. Tazocin with Gentamicin (resistance 2.1%) is a reasonable 2nd line for late onset sepsis. ESBL rate was 18.9% compared with BSPI National surveillance data (26%), probably attributable to low Cephalosporin use. Since pathogen profiles change, it is important to review epidemiology periodically, to inform antibiotic guidelines.

EVALUATION OF A SYSTEMATIC CONGENITAL CYTOMEGALOVIRUS INFECTION SCREENING PROGRAM IN PREMATURE NEWBORNS

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Background and aims: Up to 35% of congenital cytomegalovirus (CMV) infected infants are born prematurely and 50% are small for gestational age. We evaluated a urine screening in premature newborns to optimize future screening strategies.

Methods: Prospective study of premature infants (< 37 weeks) born in a tertiary care children's hospital from December 2009 to December 2010. Congenital CMV infection screening was performed using shell vial urine culture assay (Vircel®) during first week of life. Premature newborns were classified according to gestational age and birth weight. We considered small for gestational age those infants with birth weight below 10th percentile for gestational age.

Results: A total of 418 premature newborns (53.2% male, median gestational age 32.7 weeks, median birth weight 1820 g) were included. Thirty-two (7.6%) were < 27 weeks' gestation, 191 (45.7%) were born between 27-34 weeks and 195 (46.7%) were born between 34-37 weeks. Forty-five (10.7%) were small for gestational age. Congenital CMV infection was detected in only one asymptomatic 35 week born infant, small for gestational age. Two very low birth weight infants developed symptomatic acquired CMV infection during follow-up. Prevalence of congenital CMV infection among preterm infants was 0.24%, reaching 2.2% in those small for gestational age. During study period, an additional 49 small for gestational age full-term infants were screened for CMV, and two (4%) were positive.

Conclusions: A congenital CMV infection screening program in all premature newborns might not be a helpful strategy. Screening might be restricted to small for gestational age newborns.

MENACE OF GRAM NEGATIVE FLORA AND ANTIBIOTIC RESISTANCE - PROFILE OF NEONATAL SEPTICEMIA FROM A TERTIARY CARE HOSPITAL IN INDIA

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Background: Neonatal septicemia presents with myriad of clinical manifestations of variable severity. Management of these infections poses an indomitable challenge due to emergence of antibiotic resistance. Meticulous housekeeping and regular infection surveillance is important in the management of septicemia.

Methods: Retrospective chart review of the newborns admitted to a level III NICU in North India in year 2010 with clinical diagnosis of septicemia was done. Baseline clinical characteristics, time of presentation, hospital stay and final outcome were recorded. The clinical profile of septicemia with respect to various organisms was studied.

Results: During the study period, 707 blood cultures from 688 newborns were evaluated for bacterial growth. Of these, 511 were sterile and 7 showed contamination. One hundred and eighty nine (27%) blood cultures which showed bacterial growth were further analysed. Three fourths of the affected newborns were preterm and 85% were LBW. Majority of isolates were gram negative (65%), with *Acinetobacter* (24%) being the commonest followed by *Klebsiella* (16%) and *E.Coli* (15%). Newborns with *Enterococcus* septicemia were significantly more premature (30 ± 2 vs 32 ± 2 weeks), had lower birth weight (1193 ± 329 vs 1586 ± 661 grams) and a longer hospital stay (31.3 ± 15.6 vs 18.13 ± 14.6 days). Mortality was highest with *Klebsiella* (66%) followed by *Pseudomonas* sepsis (55%). Resistance to commonly used antibiotics like Ampicillin, Gentamycin and Cefotaxime was high (88-100%).

Conclusions: Gram negative septicemia continues to be a major concern in developing countries like India. Prematurity and LBW are significant risk factors for culture proven sepsis. Universal resistance to firstline antibiotics is a cause for concern.

USE OF COLISTIN FOR THE TREATMENT OF MULTI DRUG RESISTANT ISOLATES IN NEONATES**E.A. Khan¹**, S. Choudhry¹, B. Hussain², A. Batool¹¹*Paediatrics, Shifa International Hospital, Islamabad, ²Medical Student, Aga Khan University Hospital, Karachi, Pakistan*

Background and aims: Experience of using colistin for multi drug resistant organisms (MDRO) in neonates remains limited. We conducted this study to report our experience of using low dose colistin in neonates with MDRO.

Methods: It is a retrospective study at neonatal intensive care unit (NICU) of Shifa International Hospital (SIH), Islamabad, Pakistan. The hospital records of neonates admitted from January 2009-October 2011 were reviewed. Neonates who received colistin were analyzed for tolerability and side effects (fever, rash, seizures, nephrotoxicity and bronchospasm).

Results: Thirty neonates (80% males) received colistin therapy. More than half (53.3%) were preterm babies (\leq 37 weeks gestation). About half (44%) had risk factors for MDRO that included mechanical ventilation (87% cases) and prolonged antibiotics (23%). The commonest pathogens isolated were *Acinetobacter* (73% cases) and *Pseudomonas* (23%). All isolates were susceptible to colistin but panresistant to cephalosporins, amikacin, meropenem and piperacillin- tazobactem. Colistin therapy was used for bacteremia (7% cases), clinical sepsis (60%), pneumonia (7%) and probable colonization (26%). Majority (50%) received both intravenous (IV) and inhaled colistin, 30% received inhalation therapy only. The average doses were 250,000 units/kg/day and 25,000 units/kg/day for inhalation and IV therapy respectively. None of the neonates had any side effects including neurotoxicity, nephrotoxicity, bronchospasm, urticaria or fever. The mean duration of therapy was 5 ± 4 days. Crude mortality was 16.7% with no difference between routes of administration ($p=0.24$).

Conclusion: Low dose colistin therapy is well tolerated in neonates for treatment of MDRO.

MEAN PLATELET VOLUME (MPV) IN NEONATAL PNEUMONIA

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Aim: Neonatal pneumonia is still the most frequent cause of infant (0-1 years) mortality in Türkiye. We aimed to evaluate the value of mean platelet volume (MPV) as well as CRP levels for diagnosis and in the course of treatment in neonatal pneumonia.

Material and methods: We reviewed the hospital records of neonates(n=156) in NICU hospitalised for neonatal pneumonia. The control group consisted of 81 healthy neonates. Complete blood counts and CRP were evaluated. SPSS 11.5 package program is used for statistical analysis.

Results: There was no significant difference in gender distribution, type of delivery between two groups. Neonates with pneumonia had higher hemoglobin ($13,89 \pm 2,2$ g/dl), MPV($8,13 \pm 0,8$ fl) and serum CRP levels ($1,0 \pm 1,6$ mg/dl) at administration ($p < 0,001$). At the discharge CRP and MPV levels decreased with treatment. ($p < 0,001$ and $p = 0,032$, respectively).

Conclusion: Mean platelet volume is one of the laboratory parameters in neonatal pneumonia which may be helpful for diagnosis and in the course of treatment.

IMMIGRATION AND CONGENITAL SYPHILIS

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Objectives: Knowing the demographic characteristics, clinical situation and follow up of paediatric patients, with positive syphilis serology, in Children's Hospital La Paz (Madrid).

Patients and methods: We conducted a retrospective observational study of newborns and children with positive serology for syphilis, between January 2008 and August 2010 (32 months). Syphilis screening at pregnancy followed "inverse screening" strategy, starting with IgG EIA and validating positive results with APTT and RPR.

Results: Of the 66 patients included, 53% were boys and 47% girls. 94% of patients with positive serology for syphilis were born from foreign mothers. Latin America being the predominant origin (61%), Eastern Europe (22%), Maghreb (4%) and Asia (4%). Spanish mothers were only 6%. Main reason for checking infants for syphilis was positive syphilis-test during pregnancy (92%) or uncontrolled pregnancy (8%). 65% of patients asked to return for follow up testing failed to do so. Of those starting up follow up, only 26% completed it. Most of the cases studied could be classified as unlikely syphilis (71%) or very unlikely (9%). Only 3 patients (5%) suffered from congenital syphilis.

Conclusions: Majority of children with positive serology for syphilis were born from foreign mothers. Latin America and Eastern Europe were the most common countries of origin. Gestational screening detected most neonates at risk for congenital syphilis. Many patients were lost to follow up.

CYTOMEGALOVIRUS: VERTICAL TRANSMISSION AND DISEASE. THE REALITY OF A HOSPITAL

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Background: Cytomegalovirus (CMV) is one of the main agents of congenital infection; the risk of transmission is particularly high in primary infection. The incidence of intrauterine infection varies between 0.2 and 2.4%. Most newborns are asymptomatic. Routine prenatal screening is not systematically done in our country. However, the new therapies in research seem promising, raising the discussion of the need of its implementation.

Aims: Improve the knowledge of the reality of maternal-fetal transmission and evolution of congenital CMV infection in our hospital.

Methods: Retrospective analysis of the clinical records of newborns with suspected congenital CMV infection, from January 2006 to December 2010.

The parameters evaluated included aspects related to pregnancy, childbirth and newborn. In infected newborns we also analysed clinical presentation at birth and its evolution in terms of psycho-motor development and hearing/ophthalmological sequelae.

Results: We reviewed the cases of newborns with suspected infection, a total of 47, and a history of maternal seroconversion during pregnancy was found in 45 cases. The transmission rate was 31%. At birth 79% were asymptomatic. Clinical findings included: fetal growth restriction, prematurity, microcephaly, jaundice, cytomegalic inclusion disease. During the follow-up, one child had delayed psychomotor development, with persistent clastic lesions on MRI. There was no case of sensorineural hearing loss.

Conclusions: As the sample was small we can't take conclusions. So, the knowledge of the reality of each medical centre may help evaluating the importance of perinatal screening.

ANTENATAL SCREENING FOR T.PALLIDUM IN IRELAND: YIELD, NEONATAL OUTCOMES AND THE ROLE OF PERINATAL ID EVALUATION

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Background: Prevalence of T.pallidum is increasing in Europe. Universal antenatal screening is in place in Ireland. International policy makers aim to eliminate Congenital Syphilis by 2015.

Aims: To audit antenatal screening yield and perinatal assessment practice with existing guidelines. To compare results between two tertiary referral maternity hospitals, one of which has an onsite ID service.

Methods: Laboratory surveillance data (2006-2010) identified positive screening serologies. 18,000 screening tests are performed annually in these institutions. Mothers not returning for delivery, miscarriages and neonatal deaths not attributed to T.pallidum were excluded. Retrospective chart review obtained maternal and infant data. Data was analyzed using SPSS 14.0 .

Results: There were 134 confirmed positive maternal serologies. 88 pregnancies were included. 95.5% were first generation immigrants. Infant evaluation and follow is based on a management algorithm. 28(31%) of infants were incompletely evaluated. Despite similar maternal profiles between hospitals, the rate of appropriate perinatal care was significantly improved by presence of an onsite ID service.

	Previous Treatment	Treatment current pregnancy	Incomplete Infant Assessment
Hospital 1 (ID service)	17 (36.2%)	22 (46.8%)	9 (19.1%)
Hospital 2 (No ID service)	22 (62.9%)	19 (59.4%)	19 (46.3%)
P value	0.017	0.27	0.006

[Impact of Perinatal ID team. ($p < 0.05$)]

Conclusions: Incomplete perinatal assessment of infants born to mothers with positive T.pallidum serology remains high. An onsite perinatal ID service improves outcomes.

LATE ONSET SEPSIS AND 5-YEAR NEURODEVELOPMENTAL OUTCOMES OF VERY PRETERM INFANTS: THE EPIPAGE STUDY

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Background and aim: Neonatal infections are frequent complications of very preterm infants receiving intensive care. To determine if late onset sepsis are associated with increased risks of adverse neurodevelopment at 5 years of age in a population-based cohort of very preterm children.

Methods: We included all live births between 22 and 32 weeks of gestation from 9 regions in France in 1997 (EPIPAGE study). Of the 2665 live-births, 2193 were eligible for follow-up evaluation at 5 years of age, 1769 had a medical examination and 1495 a cognitive assessment. Cerebral palsy and cognitive impairment were studied according to number of episode of late onset sepsis (LOS) and pathogen type after adjustment for potential confounding variables using multivariate logistic regression models.

Results: In total, 591 (22%) of the 2665 live births included had one episode of LOS and 225 (8%) two episodes of LOS. At 5 years, the rate of cerebral palsy was 9% (157/1769) and cognitive impairment 12% (177/1495). Compared with uninfected infants, cerebral palsy was increased in the group of one episode of LOS (OR = 1.42, 95% CI: 0.91-2.23), in the group of two episodes of LOS (OR = 1.54, 95% CI: 0.85-2.77), and in the group of coagulase-negative staphylococci (OR = 1.32, 95% CI: 0.72-2.39). There was no association between late onset sepsis and cognitive impairment.

Conclusion: Late onset sepsis among very preterm infants are associated with an increased risk of cerebral palsy at 5 years of age.

CURRENT MANAGEMENT OF LATE ONSET NEONATAL SEPSIS (LOS) IN SELECTED EUROPEAN COUNTRIES AND PERFORMANCE OF NEW DIAGNOSTIC CRITERIA

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Background and aims: Clinical trials of treatment of LOS are urgently required but few validated definitions of sepsis are available. We evaluated appropriateness of new expert panel-derived criteria defining LOS and described the current management of LOS.

Methods: Prospective observational study performed between July 2010 and September 2011 recruited infants < 3 months with suspected LOS, based on clinical and laboratory criteria of sepsis (Lutsar et al. 2011 or Goldstein et al. 2005) depending on age.

Results: Of 166 screened patients from 15 centres in 5 countries 113 fulfilled enrolment criteria. Median age at onset of LOS was 14 days, median birth weight 1190g, and 62% were male. 61% had culture proven sepsis (41% CoNS, 35% Enterobacteriaceae, 16% other Gram positive and 9% non-fermentative Gram negative organisms). In infants \leq 44 weeks of corrected age of 21 clinical criteria, mottled skin, impaired peripheral perfusion and increased oxygen requirement were the most commonly observed (approximately 40% each). Of laboratory markers, CRP > 15 mg/L and platelet count < 100×10^9 cells/L were the most frequent, occurring in 85% and 42% of subjects respectively. Overall 18 antibiotics in 49 treatment regimens were used for empiric therapy. Meropenem +/- vancomycin or vancomycin + amikacin were the most frequent, used in 9% of patients each. All-cause mortality was 8%.

Conclusions: The expert panel - derived diagnostic criteria performed well in this study identifying a high rate of culture proven sepsis. Future studies should address the significant variability of empiric treatment regimens for LOS in Europe.

GENETIC RELATEDNESS OF COAGULASE-NEGATIVE STAPHYLOCOCCI (CONS) FROM GASTROINTESTINAL TRACT (GIT) AND BLOOD OF NEONATES WITH LATE-ONSET SEPSIS (LOS)

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Background and aims: In neonates CONS are the first colonizers of GIT and the most common causative agents of LOS. Skin is considered the primary source; translocation from gut has been suggested but not unequivocally proven. We aimed to assess genetic relatedness of CONS isolated from blood and GIT in neonates with LOS.

Methods: From August 2006 to November 2007 22 neonates with CONS LOS with available blood isolates were included. Rectal swabs were collected twice weekly from birth. CONS were identified to species level by *tuf* gene sequencing. For genetic relatedness, *Staphylococcus epidermidis* (SE) was typed by multilocus variable number of tandem repeats analysis and multilocus sequence typing, *Staphylococcus haemolyticus* (SH) by pulsed field gel electrophoresis.

Results: In 22 neonates (median gestational age 26.5w) LOS (median age at onset 10d) was caused by SH in 13, SE in 7 and *Staphylococcus hominis* in 2. Prior GIT colonization with CONS was present in 21 but three did not harbour CONS of same species. Typing of CONS was performed thus in the remaining 18 patients. Blood isolate and ≥ 1 antecedent colonizing isolates were genotypically similar in 3/7 and 10/11 patients with SE and SH infection, respectively. Concordant GIT strain was present 0-7 days prior to positive blood culture.

Conclusions: Genetic relatedness between bloodstream and GIT isolates supports the hypothesis of the gut origin of CONS sepsis, at least in some cases of LOS. Considering the ubiquity of CONS our results should be interpreted with caution with regard to translocation.

HUMAN BETA DEFENSIN 2 (HBD2) SERUM LEVELS MAY PREDICT SUSCEPTIBILITY TO INFECTIONS IN PRETERM NEONATES

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Background: Preterm neonates (gestation age (GA) < 37 weeks) are particularly susceptible to infections in the first month of life. Antimicrobial peptides (AMPs) such as HBD2 being part of the innate immunity are known to have activity against a variety of microorganisms and may play an important role in the above setting. No data exist regarding HBD2 levels in cord blood.

Objective: Observational study to determine HBD2 levels in cord blood and to relate HBD2 levels to infections in neonates.

Methods: Determination of HBD2 serum levels in cord blood of 31 preterm neonates using ELISA-Kit (PhoenixPharmaceuticals). Clinical and laboratory data were collected and analyzed retrospectively.

Results: 31 preterm neonates with a median GA of 30 weeks (IQR 29-31) and a birth weight (BW) of 1328g (IQR 1049-1580) were enrolled. 11 out of 31 preterm neonates suffered from late-onset sepsis. Organisms were isolated in 7/11 patients: *S.epidermidis* (4); *K.pneumonia* (2); *E.faecalis* (1). HBD2 serum levels were significantly lower in patients suffering from late-onset sepsis (median 556 pg/ml, IQR 391-880) compared to those neonates who did not suffer from the above (median 1552 pg/ml, IQR 633-2775; p=0.01). This observation was not related to birth weight, gestational age, chorioamnionitis or the use of corticosteroids before birth. Two patients with very low HBD2 levels (98 and 54pg/ml respectively) suffered from *K.pneumonia* sepsis, the latter being fatal.

Conclusion: Low HBD2 levels at birth might be a predictor of increased susceptibility to neonatal infections in preterm neonates. Prospective studies are needed to confirm our observations.

NOSOCOMIAL INFECTIONS IN NEONATAL INTENSIVE CARE UNIT: EPIDEMIOLOGY AND PATHOGENS

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This paper presents an epidemiological profile of nosocomial infections (NIs) diagnosed in a neonatal intensive care unit (NICU) from a Brazilian hospital.

Methods: Prospective surveillance of NI according to National Healthcare Safety Network (NHSN) protocols for events occurred between oct/2008 and sep/2011.

Results: 337 infections were diagnosed in three years; 83% refer only to three major sites: 169 (50%) primary bloodstream infections (BSI); 80 (24%) ear, eyes, nose, and throat infections and 30 (9%) pneumonia. BSI are the major infections in all weight categories, but we observed significant differences in other types of infections according to birth weight (p -value = 0.011). We collected data from 1,603 patients (PTs) of 5 birth weight categories: 92 PTs ≤ 750 g, 213 PTs 751-1,000g, 357 PTs 1,001-1,500g, 586 PTs 1,501-2,500g, and 355 PTs $> 2,500$ g. The risk of infection decreases significantly with increasing birth weight (p -value < 0.001): ≤ 750 g = 34%, 751-1,000g = 35%, 1,001-1,500g = 22%, 1,501-2,500g = 18%, and $> 2,500$ g = 13%. Incidence of ventilator-associated pneumonia (VAP), calculated by #VAPs/1,000 ventilator-days, stratified by weight categories: ≤ 750 g = 8.1, 751-1,000g = 4.2, 1,001-1,500g = 2.3, 1,501-2,500g = 4.4, and $> 2,500$ g = 6.1. Central line-associated primary bloodstream infections (CLABSIs), calculated by # CLABSIs/1,000 central line-days: ≤ 750 g = 16.2, 751-1,000g = 12.3, 1,001-1,500g = 11.6, 1,501-2,500g = 10.6, and $> 2,500$ g = 6.4. Only 4 microorganisms caused 50% of NIs: MRSE, *K. pneumoniae*, *A. baumannii* and *P. aeruginosa*.

Conclusion: In this NICU, BSI was the most common NI. Types of infection and pathogens differed with birth weight.

LONG TERM IMPACT OF TREATED CONGENITAL TOXOPLASMOSIS: VISUAL PERFORMANCE AND QUALITY OF LIFE IN FRENCH YOUNG ADULTS FOLLOWED-UP SINCE BIRTH

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Background and aims: Little is known concerning the long-term impact of congenital toxoplasmosis on the life-quality and visual function of patients treated ante- and postnatally. The benefit of systematic postnatal follow-up is also debated. We present data based on a cohort of young adults who were regularly monitored since birth at a French centre.

Methods: A questionnaire study was conducted on 126 adults with congenital toxoplasmosis (mean age: 22 years; range: 18-31). The main outcomes were measured using a quality of life (Psychological General Well-Being Index: PGWBI) and a visual function (VF14) questionnaires and correlated with disease-specific factors.

Results: Of the 102 patients (81%) who responded, 12 (12%) suffered from neurological effects and 60 (59%) manifested ocular lesions leading to reduced visual function in 13 (13%). The overall global quality of life score (75 ± 14) lay close to the expected normal range for the general population (74 ± 15) and was not influenced by the clinical characteristics of congenital toxoplasmosis. Overall, visual function was only slightly impaired ($M = 97$ on a 0-100 scale [95% confidence interval, 96-99]). Neurological pathologies, reduced visual acuity, the foveal location of the retinal lesion and squinting contributed to decreased visual function. Follow-up was perceived as useful by 98% and reassuring by 92%.

Conclusions: Congenital toxoplasmosis has very little impact on the quality of life and visual function of individuals treated pre- and postnatally. Follow up is however perceived as useful by patients. These findings may help paediatricians to inform parents and to manage children with congenital toxoplasmosis.

BACTERIAL MENINGITIS IN BABIES 0-90 DAYS OF AGE: A UK AND REPUBLIC OF IRELAND PROSPECTIVE STUDY

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Background and aims: Meningitis in the first 3 months of life is associated with significant mortality and morbidity. Previous UK studies were conducted in the 1980s and 1990s. It is important to define the current burden of disease in order to prioritise treatment and prevention strategies.

Methods: Cases were identified prospectively by active surveillance through the British Paediatric Surveillance Unit, routine microbiological surveillance through the Health Protection Agency and via parents of cases through meningitis and Group B streptococcus (GBS) support charities. The surveillance period was July 2010 - July 2011.

Results: From all sources, 863 reports were received and 300 met the case definition. 261 (87 %, preliminary incidence 0.36/1000 livebirths) were from England, 14 (4.7%) from Wales and 11 (3.7%), 7 (2.3%) and 7 (2.3%) were from Scotland, Northern Ireland and the Republic of Ireland respectively. 170 (57%) were male and the median age of disease was 13.5 days (range 0-88). 238 bacterial isolates were obtained from cerebrospinal fluid and / or blood cultures: GBS (119, 50%) was the most common isolate followed by *Escherichia coli* (30, 13%) *Streptococcus pneumoniae* (21, 9%), *Neisseria meningitidis B* (16, 7%), *Listeria monocytogenes* (9, 4%) and other Gram negative bacteria (21, 9%). The case fatality ratio was 7.4%.

Conclusion: There remains a significant burden of bacterial meningitis in the first 3 months of life but the mortality appears to have declined over the last 2 decades. GBS is the most common causative bacteria. New strategies for prevention are required.

EVALUATION OF THE EFFECTIVENESS OF ZINC SULFATE IN DURATION OF COMMON COLDS SYMPTOMS IN CHILDREN

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Background and objectives: Common cold is the most common disease in children. Young children have an average of 6 to 7 colds each year. Some complications of common cold include: secondary bacterial infections, school absence and excessive cost for treatment.

Methods: This was a clinical trial study. The subjects were children between 1 - 7 years old with common cold that attended to pediatrics clinic of Arak Amir Kabir Hospital. The study included 112 patients randomized in 2 groups. One group received zinc sulfate within 10 days and other group didn't receive this drug. Using a researcher made questionnaire duration of symptoms: rhinorhea and nasal obstruction, cough, sneezing, fever and duration of illness, in both groups were evaluated.

Results: Consumption of zinc sulfate significantly reduced the mean duration of rhinorhea and nasal obstruction in children with common cold ($p < 0.05$). Also the mean duration of cough in zinc group was lower than the control group ($p < 0.05$). Compared to the group that didn't receive zinc sulfate, the zinc group had shorter mean duration of sneezing ($p < 0.05$).

Also the mean duration of fever in zinc group was shorter than the other group ($p < 0.05$). The mean duration of illness in patients who had received the zinc sulfate was significantly less than the other group ($p < 0.05$). No side effect was observed in subjects received zinc sulfate.

Conclusion: According to the results zinc sulfate can be administered with other supportive treatments of common cold, for reduction of symptoms duration and complications in children.

PROCALCITONIN - RAPID DIAGNOSTIC MARKER OF NEONATAL INFECTION

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Leak of a specific early marker of infection in suspected neonatal infection may be partially responsible for delayed diagnostic or use of unnecessary treatment in uncertain cases.

Aim: to evaluate correlation between procalcitonin (PCT) and neonatal infection and outcome.

Methods: by BRAHMS test (immunochromatography for semiquantitative dosage of procalcitonin) we evaluated two groups of neonates (group I - 127 subjects with suspected sepsis and group II - 32 cases of confirmed sepsis by positive hemoculture), between 2008-2010, born in a level III maternity hospital. The determinations were performed during the first 72 hours of life. Values between 0,5 - 2 ng/ml were interpreted as possible severe systemic infection, values between 2-10 ng/ml as higher probability of systemic infection and values higher than 10 ng/ml as high probability of sepsis.

Results: In both groups prematurity was better correlated with significant positive levels of PCT. Respiratory distress secondary to infection was significantly correlated with PCT ($r = 0,488$ and $p < 0,05$). PCT is a better marker of infection than fibrinogen. In first 24-72 hours of life, PCT has 88,98% specificity and 87,5% sensitivity. Positive C reactive protein (CRP) and positive PCT are highly correlated ($r = 0,87$, $p < 0,05$, 95% CI), but PCT increases faster than CRP in neonatal infection ($r = 0,56$, $p = 0,0067$, 95% CI).

Conclusion: PCT may be a faster method of diagnostic for neonatal infection than CRP, and can be an alternative in suspected cases where hemoculture may be late or false negative.

SPECTRUM AND INOCULUM SIZE EFFECT OF A RAPID ANTIGEN DETECTION TEST FOR STREPTOCOCCAL PHARYNGITIS IN CHILDREN

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Objectives: We aimed to assess whether the performance of a rapid antigen detection test (RADT) for group A streptococcus (GAS) is affected by the clinical spectrum and/or bacterial inoculum size.

Methods: Double throat swabs were collected from 785 children with pharyngitis in an office-based, prospective, multicenter study (2009-2010). We analyzed the effect of clinical spectrum (i.e., Mclsaac score and its components) and inoculum size (light or heavy GAS growth) on the diagnostic accuracy of a RADT, with laboratory throat culture as the reference test.

Results: GAS prevalence was 36% (95CI: 33%-40%). The inoculum was heavy for 85% of GAS-positive cases (81%-89%). We found a significant spectrum effect on sensitivity, specificity, likelihood ratios and positive predictive value ($p < 0.05$) but not negative predictive value, which was stable at about 93%. RADT sensitivity was greater for children with heavy than light inoculum (95% vs. 40%, $p < 0.001$). After stratification by inoculum size, the effect of clinical spectrum on RADT sensitivity was significant only in patients with light inocula ($p < 0.05$), on univariate as well as multivariate analysis.

Spectrum effect analysis: diagnostic accuracy by clinical spectrum

Clinical variable (N)	GAS (%)	Se (%)	Sp (%)	LR+	LR-	PPV (%)	NPV (%)
Mclsaac score							
≤2 (115)	24***	75*	98*	33	0.3	91	92
3 (262)	34	84	96	21	0.2	91	92
≥4 (408)	41	90	92	12	0.1	89	93
Age, y							
3-8 (663)	38**	89***	94	15	0.1***	90	93
9-14 (122)	25	67	97	20	0.3	87	90
Lack of cough							
Yes (428)	44***	90*	94	15	0.1*	92	92
No (357)	27	80	95	16	0.2	85	93
Anterior cervical adenopathy							
No (407)	35	83	98***	37**	0.2	95*	91
Yes (378)	38	90	91	10	0.1	86	94
Tonsillar swelling or exudate							
No (157)	42	83	96	19	0.2	93	89
Yes (628)	35	88	94	16	0.1	89	93
Fever							
No (246)	31*	88	93	14	0.1	86	95
Yes (539)	39	86	95	18	0.1	92	92
Total (785)	36	87	95	16	0.1	90	93

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

[Spectrum effect analysis]

Conclusions: Significant variations in RADT sensitivity are only observed in patients with light bacterial inocula who are more likely to be GAS carriers rather than true GAS infections. Because the spectrum effect does not affect the negative predictive value of the test, clinicians who want to rule out GAS can rely on negative RADT results, regardless of clinical features.

SENSITIVITY OF A RAPID TEST FOR GROUP A STREPTOCOCCUS IN CHILDREN WITH PHARYNGITIS AND HEALTHY CONTROLS: A MULTI-LEVEL APPROACH

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Objectives: To identify patient-level factors associated with variations of the sensitivity of a rapid antigen detection test (RADT) for group A streptococcus (GAS), taking into account a possible physician effect.

Methods: Throat swabs were collected from 1,482 children with pharyngitis and 294 healthy controls in a prospective, office-based, multicenter study. Factors affecting RADT sensitivity were studied in univariate and multi-level analyses, with laboratory culture as the reference test.

Results: In children with pharyngitis and in healthy controls, the prevalence of GAS was 38% (95CI 36%-41%), and 11% (8%-15%); 14% and 66%, respectively, showed light bacterial inoculum ($p < 0.001$). On stratified and multi-level analysis, sensitivity was higher for patients with than without pharyngitis (89% vs. 41%), those with heavy than light inoculum (94% vs. 53%) and children < 9 than ≥ 9 years (88% vs. 79%). For the same inoculum, sensitivity was higher in children with pharyngitis than in controls ($p < 0.05$). There was a significant physician effect (sensitivity range: 56%-96%; $p=0.01$); 32% of the physician-level variance was explained by the number of patients included by the physician.

Factors affecting the sensitivity of the RADT

	N	Univariate analysis		Multivariate multi-level analysis	
		Sensitivity (95CI), %	Crude OR	aOR [†]	aOR ^{††}
Patient-level factors					
Clinical Status					
Healthy	32	41 (25-61)	1	1	1
Pharyngitis	570	89 (87-92)	12.4 ***	6.0***	6.3***
Bacterial inoculum					
Light	101	53 (44-63)	1	1	1
Heavy	501	94 (91-96)	12.8***	10.6***	10.7***
Age, y					
3-8	534	88 (85-91)	1.9	2.4*	2.3*
9-14	68	79 (70-89)	1	1	1
Physician-level factors					
Number of patients included					
$n \leq 21^{\ddagger}$	32	72 (55-88)	1	-	1
$n > 21$	570	88 (85-90)	2.8*	-	3.8*
Proportional change in variance, % ^{§§}	-	-	-	0	32

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

[†]Model 1: adjusted on status, inoculum, age (level 1)

^{††}Model 2: adjusted on status, inoculum, age (level 1) and the number of patients included by the investigator (level 2)

[‡]21 was the 25th percentile of the distribution; ^{§§}The level 2 variance of the empty model was 0.19 ($p=0.03$)

[factors affecting RADT sensitivity]

Conclusions: Because the RADT does not perform equally in children with pharyngitis and in controls, we could not estimate the extent to which carriers explain RADT false-negative results in case of pharyngitis. There are important variations in sensitivity by the physician performing the test. Therefore, physicians who use RADTs without backup culture should consider diagnostic accuracy monitoring.

CONTRAST-ENHANCED-VOIDING-UROSONOGRAPHY AS A FIRST STEP STUDY FOR THE DIAGNOSIS AND GRADING OF VESICoureTERIC REFLUX IN CHILDREN WITH URINARY TRACT INFECTION

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Purpose: To assess the efficacy of contrast-enhanced Voiding Urosonography (ce-VUS) as a first step study for the diagnosis and grading of Vesicoureteric Reflux (VUR) in children.

Patients and methods: Two hundred ten consecutive children (86 boys, 124 girls, mean age 33.4 m) with 421 kidney-ureter-units (KUU) were evaluated with VUS to rule out VUR. In all children VUS was performed with a contrast-specific-harmonic-imaging-mode and 1ml of a second generation contrast agent (Sonovue, Bracco, Milan), according to ESPR working group recommendations. Ce-VUS was recorded on digital clips and read twice in a blind manner by two radiologists. The diagnosis in discordant cases was reached by consensus. The intraobserver and interobserver reproducibility was calculated by kappa coefficient.

Results: VUR was diagnosed in 178 KUU (42%) from 87 (41%) patients (34/84 boys and 53/126 girls). The rate of reflux was not significantly correlated with the sex, age, clinical indications and the presence or side of dilated pelvis. VUR was significantly more common in duplex than in single kidneys ($p < 0.001$). The intraobserver and interobserver reproducibility was excellent for the detection of VUR ($k > 0.85$) and moderate to excellent for the grading of VUR ($k = 0.75-0.84$).

Conclusion: ce-VUS with a second generation CA is an efficient first step study for the diagnosis and grading of VUR in children with UTI and it can reliably be used as an alternative radiation-free imaging method for VUR detection.

A PROTEIN PATTERN IN SERUM AS A BIOMARKER TO DIAGNOSE ACTIVE TUBERCULOSIS IRRESPECTIVE OF HIV STATUS

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Background and aims: A major impediment in controlling TB is the lack of a fast and reliable diagnostic test which would improve case detection. In the presence of HIV, the clinical and radiological features of TB do not discriminate TB from a range of other HIV associated opportunistic infections. Thus, an effective diagnostic test is urgently needed.

The aim of this study is to examine the serum protein profiles of systematically collected patients with (1) active TB, (2) latent TB and (3) other infections with clinical features resembling TB and to identify a protein pattern that uniquely characterizes active disease from any other condition, irrespective of HIV infection.

Methods: Serum samples were collected from children (n=600) and adults (n=600) with active TB (culture confirmed), latent TB (IGRA+ and TST+) and other infections, all equally including HIV+/- cases. Patients were recruited from two sub-Saharan Africa regions with differing patterns of HIV and TB prevalence. SELDI-TOF MS technology was used to define the proteomic profiles. An advanced bioinformatics analysis pipeline was designed to identify the most-predictive protein set to characterize active TB.

Results: SELDI analysis generated over 10,000 protein profiles. Approximately 700 proteins were differentially expressed between patients with active TB from those with latent and other infections regardless of HIV status. The minimal set of proteins that achieves prediction with very high accuracy (>85%) is selected using advanced statistical approaches.

Conclusions: SELDI proteomic profiling has identified serum biomarkers of active TB, which will be used as a diagnostic signature of disease.

UTILITY OF NT-PROBNP FOR DIAGNOSIS OF KAWASAKI DISEASE

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Introduction: Kawasaki disease (KD) is a systemic vasculitis of unknown aetiology. KD diagnosis is based on a combination of clinical, analytical and cardiac ultrasound findings. Recently NT-ProBNP has been proposed as a diagnostic marker of KS. Most published studies were carried out in Asian population. Objective was to confirm the usefulness of NT-ProBNP in diagnosis of KD in our patients.

Methods: We reviewed determinations of NT-proBNP (Roche Diagnostics Elecsys® proBNP) in paediatric patients from 2010 to 2012. Patients with NT-proBNP determinations due to clinical suspicion of KD were selected. Patient excluded were those with known heart diseases, patients with suspicion of myocarditis but not KD, patients with more than 15 days of symptoms.

Results: Maximum values of NT-proBNP in 25 patients diagnosed with complete or incomplete KD and in 22 controls. Controls does not fulfil the criteria for incomplete KD or have another confirmed diagnosis. Maximum values of NT-proBNP in patients with KD ranged from 40 to 33465 pg/ml (median 528 pg/ml) and values in controls ranged from 14 to 756 pg/ml (median 181 pg/ml). The cut off value most adequate to discriminate both groups of patients was 433 pg/ml with a sensibility of 64% (42-82%) and specificity of 95% (76-100%). Area under the ROC curve (AUC): 0.8 (0.65-0.90).

Conclusions: Determination of NT-ProBNP has proved to be useful in the diagnosis of KS. Values above 433 pg/ml have high specificity for diagnosis of KS. However sensitivity is low and lower values do not exclude KS.

LEVELS OF INTERLEUKIN-6(IL6) AS PREDICTORS OF EARLY TERM NEONATAL SEPSIS DURING 2010-11

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Rate of hospital admission of neonates suspicious to systemic infections are more than sepsis prevalence, due to nonspecific sign and symptoms of neonatal sepsis. This study was conducted interleukin 6(IL6) plasma level as a marker for early detection of neonatal infection.

Objective: Level of plasma IL6 and blood culture were checked in all term neonates who were admitted with suspicious of sepsis in neonatal intensive care unite . Positive blood culture was considered as definit sepsis and negative blood culture as suspicious sepsis. Then level of IL6 compare with blood culture states.

Results: A total of 142 hospitalized neonates were checked for plasma level of IL6 .10 cases of them were healthy neonate who were admitted due to physiologic jaundice . Others had signs and symptoms of infection and Bactec blood culture was obtained. 74 cases were male and 68 cases female. The prevalence of early neonatal sepsis was 7% .The most etiologic bacterial agents were SGB and SE . The most common symptoms of patients was tachypnea (35.9%). The average level of IL6 in first group (admitted with sepsis signs and symptoms and positive blood culture)was 1545.65pg/ml and in second group(admitted with sepsis signs and symptoms and negative blood culture)was 14.79pg/ml and in control group was 11.04pg/ml.

Conclusion: Plasma level of IL6 as an inflammatory factor is a good predictive marker for detection of sepsis in neonates who are admitted with nonspecific sign and symptom of infections and sepsis.

SERUM CALGRANULIN (S100 PROTEIN) AS A NEW DIAGNOSTIC MARKER OF SEPSIS IN NEONATAL AGE

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Background: Despite the crucial role during response to pathogens early in the life, mediators of innate immunity have not been investigated as a markers of neonatal sepsis.

Objective: Determining the diagnostic power of serum (s-) calgranulin (Clg), an S100 protein that represent the main antimicrobial peptide secreted by innate immunity cells, in neonatal sepsis. Methods. Multicenter study involving very low birth weight (VLBW) newborns with a postnatal age > 72 hours of life. Accuracy of s-Clg for sepsis diagnosis was compared with the most commonly used markers of neonatal sepsis (white blood cell count, immature-to-total neutrophils ratio, platelet count, C-reactive protein).

Results: 62 newborns with confirmed sepsis showed significantly higher s-Clg concentration (3.1 ± 1.0 mg/ml) compared to 110 healthy controls (0.91 ± 0.58 mg/ml) and 29 non-infected subjects (1.1 ± 0.3 mg/ml) ($p < 0.001$). Serum calgranulin has the best diagnostic accuracy (sensitivity 89%, specificity 96%) when compared with traditional markers of neonatal sepsis.

Conclusions: Serum calgranulin is an accurate marker of sepsis in VLBW newborns. It is a simple and inexpensive method to explore rapidly the presence of the disease.

SERUM CALPROTECTIN AS A NEW MARKER FOR EARLY DIAGNOSIS OF NECROTIZING ENTEROCOLITIS

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Background: The “fecal” calprotectin (Clp) has been proposed as marker of necrotizing enterocolitis (NEC), but a wide overlap between normal and pathologic values limits their use in the neonatal clinical practice.

Aim: To evaluate the diagnostic utility of “serum” (s-)Clp in NEC.

Methods: Multicenter study enrolling neonates with gestational age (GA) < 32 weeks with suspected NEC. Clinical details were collected at the enrollment, together with a blood sample to determine s-Clp concentrations (by ELISA technique). We evaluated if s-Clp is able to predict development of definite NEC (Bell stage ≥ 2) within 72h from the enrollment.

Results: Out of 72 newborns with suspect of NEC (male 42; GA 28.9 w, 95%CI 28.4-29.4), 16 developed definite NEC (Bell stage ≥ 2), 11 culture-proven sepsis, 4 intestinal obstruction and 41 remain stable (Bell stage 1) or showed a resolution of symptoms and were considered as controls. Of the 16 neonates with definite NEC, 10 evolved in advanced disease (Bell stage 3) requiring surgery. The s-Clp level was significantly ($p < 0.001$) higher in newborns with NEC (4.04 mcg/ml; 95%CI 3.7-4.3) compared with those affected by sepsis (2.7 mcg/ml, 95%CI 2.5-2.8), intestinal obstruction (1.2 mcg/ml, 95%CI 0.81-1.59) and controls (0.68 mcg/ml; 95%CI 0.58-0.78). We calculate the accuracy of s-Clp (sensitivity 100%, specificity 96.4%, positive predictive value 88.9%, negative predictive value 100%) with an optimal cut-off value of 3.0 mcg/ml for diagnosis of NEC.

Conclusions: s-Clp is useful in the diagnostic approach of newborns with suspected NEC.

IMPACT OF THE USE OF RAPID ANTIGEN DETECTION TEST IN THE DIAGNOSIS AND TREATMENT OF ACUTE PHARYNGITIS IN PEDIATRIC EMERGENCY ROOM

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Background and aims: Sore throat is a common disease in the pediatric emergency room. The most common etiology is viral. Only 20-30% of cases are caused by Group A beta-hemolytic Streptococcus. Based only on the clinical findings the use of antimicrobials is often unnecessary. The main objective of this study was to evaluate the impact of routine performance of rapid antigen detection test (RADT) in the diagnosis and treatment of acute pharyngitis in children treated at an academic hospital.

Methods: This is a prospective, observational, protocol compliance, established at the Emergency of Hospital Universitário da Universidade de São Paulo, in Brazil, for the care of children and adolescents diagnosed with acute pharyngotonsillitis.

Results: We studied 650 children and adolescents. Based on clinical findings, antibiotic was prescribed in 389 patients (59.8%) and using the RADT was prescribed in 286 patients (44%). Of the 261 children who did not receive antibiotics for the clinical, 111 (42.5%) had positive RADT. The diagnosis based on clinical sensitivity was 61.1%, specificity 47.7%, positive predictive value of 44.9% and negative predictive value of 57.5%.

Conclusions: The clinical diagnosis of streptococcal pharyngitis has low sensitivity and specificity. The routine use of rapid test for streptococcal research led to a reduction of antibiotic use. On the other hand, in 42.5% of cases would not receive the antibiotic if rapid test was positive, which can identify a risk group for complications of streptococcal infection.

DIAGNOSIS OF PAEDIATRIC COMMUNITY- ACQUIRED LOWER RESPIRATORY TRACT INFECTION CAUSED BY *MYCOPLASMA PNEUMONIAE*

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Background: *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.

Aims: To detect IgM and IgG antibodies to *M. pneumoniae* by enzyme immunoassay, *Mycoplasma pneumoniae* DNA in nasopharyngeal aspirates by polymerase chain reaction (PCR) and to correlate clinical, serological and PCR findings for establishing diagnosis of *Mycoplasma pneumoniae* 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 infection. The detection must be performed by a combination of serology and PCR.

RAPID DIAGNOSIS TEST FOR SEMI - QUANTITATIVE DETECTION OF CRP USING BIONEXIA® CRPPLUS

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Background and aim: C-reactive protein (CRP) is a classical marker used to detect an inflammatory reaction in the body. CRP can also be used to monitor the therapeutic effect of antibiotic treatment.

We evaluated the specificity and sensitivity performances of the semi-quantitative rapid bioNexia® CRPplus (bioMérieux SA), in comparison to two Rapid Diagnostic Tests : NycoCard CRP and Olympus CrP Latex.

Methods: The analytical sensitivity study was performed using the WHO international human CRP reference standard 85/506.

The qualitative and semi-quantitative agreement study (bioNexia® CRPplus versus NycoCard CrP, and bioNexia® CRPplus versus Olympus CrP Latex) was conducted using 109 fresh samples representative of the different CrP levels.

Results: The analytical sensitivity was estimated at 10mg/L: a concentration of 10 mg/L in whole blood sample produces one red positive test line. If the specimen contains between 40-80 mg/L of CRP, two test lines appear (T1,T2). With concentrations higher than 80 mg/L, three test lines appear (T1,T2,T3).

The qualitative comparison between bioNexia® CRPplus and NycoCard CrP showed a global agreement at 93.58% IC [87.22-97.38].

The qualitative comparison between bioNexia® CRPplus and Olympus CrP Latex showed a global agreement at 80.73% IC [72.07-87.66].

The semi-quantitative comparison including the 3 semi-quantitative areas (10-40 mg/L, 40-80 mg/L, > 80 mg/L), showed a global agreement between bioNexia® CRPplus and NycoCard at 77.98% IC [69.03-85.35], and between bioNexia® CRPplus and Olympus CrP Latex at 80.73% IC [72.07-87.66].

Conclusion: The bioNexia® CRPplus results show performances comparable to two quantitative commercially available devices.

THE PREDICTIVE VALUE OF IMMATURE GRANULOCYTES AND IMMATURE MYELOID INFORMATION IN THE DIAGNOSIS OF NEONATAL SEPSIS

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Aim: To determine the predictive value of the immature granulocyte number and the immature myeloid information in neonatal early-onset sepsis (EOS) we examined 133 blood samples of patients admitted to our neonatal intensive care unit.

Methods: Measurements were performed using the Sysmex XE-2100, an automated hematological analyzer. Patients were divided into two groups (1) symptomatic neonates with diagnosis of EOS and (2) controls including asymptomatic neonates who were admitted because of prematurity, low birth weight, or delayed postnatal adaptation.

Results: The number of immature granulocytes and the immature myeloid information were significantly elevated in neonates with EOS compared to controls (median 0.28 vs. 0.05 x 10⁹/L, p=0.049 and 639 vs. 89, p< 0.0001, respectively).

Conclusion: Automated determinations of immature granulocytes and immature myeloid information seem to be useful adjunctive parameters in the diagnosis of EOS.

TUBERCULIN SKIN TEST IN MALNOURISHED CHILDREN. HOW SHOULD WE INTERPRET THE RESULTS?

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Background and aims: The tuberculin skin test (TST) is the most useful method for classification of tuberculosis (TB). Malnutrition could be a cause of a TST false negative result. Published articles in this regard are contradictory. The main objective was to evaluate TST results in a population of immigrants and adopted children; to analyze whether the nutritional status, as measured by McLaren index, may modify or not the TST results.

Methods: Cross-sectional observational study. Adopted children or immigrants evaluated in our hospital between January 2003 and December 2008 were included. Children diagnosed with TB, or live attenuated virus vaccinated with two months earlier, HIV-infected, chronically ill or under treatment with immunosuppressive agents, were excluded. TST was considered as dependent variable. Independent variables were: gender, age, national origin, BCG scar, nutritional status, immune status and intestinal parasitism.

Results: 1074 children were included, 69.6% girls. BCG scar in 79%. Mantoux = 0 mm in 84.4%, < 10 in 4.1%, and ≥ 10 in 11.4%. McLaren index was normal ($\geq 90\%$) in 26.7%, mild malnutrition (80-89%) in 36%, moderate (70-79%) in 23.2% and severe ($\leq 69\%$) in 14.1%. There were no differences in TST result between different nutritional status of children.

Conclusions: The nutritional status, as measured by McLaren index, does not change the results of TST. McLaren index only grade protein-calorie malnutrition. Further studies are needed, so other malnutrition index, in order to determine whether nutritional status should be taken into account or not when interpreting TST results.

DENGUE DIAGNOSTIC TOOL: A DESIGN AND CONSTRUCTION OF AUTOMATIC DEVICE FOR TOURNIQUET TEST**W. Waowaeo***Biomedical Instrument Research and Development, Mahidol University, Phuttamonthon, Thailand*

Dengue fever is an emerging arboviral infection with major public health consequences in many tropical and sub-tropical countries including Thailand. In dengue endemic area, positive tourniquet test helps in making early diagnosis of dengue infection with a high positive predictive value. Other laboratory findings during an acute dengue fever episode of illness are total white blood cell count, platelet count and haematocrit count.

For tourniquet test, the Wintrobe method is popular and has been used for several decades. In order to provide accurate diagnosis and minimize variations, it is found that there are several issues of the Wintrobe method needed further standardization.

This prompts me to design and construct a new instrument call Dengue Automatic Device (DAD) for performing tourniquet test. The system consists of Data Acquisition, pressure sensor, instrumentation amplifier, solenoid valve and relayed board for control pressure and time. There is system for capturing image created. LabVIEW programme consists of pressure control and tourniquet image is included in the operation system. Fifteen clinically confirmed dengue patients were included in the study. Petichiae counts using Automatic Device and the Wintrobe Method were compared in several groups of patient using several parameters, namely, mild v/s severe subjects, haemoconcentration level, platelet depletion level and leukopenia. Data obtained clearly demonstrated that more abundant petichial counts from Automatic Device were obtained as compared with the Wintrobe method. This preliminary investigation revealed possible predict value of the Automatic Device in discrimination of mild and severe dengue subjects.

HIGH PERFORMANCE OF QUANTIFERON®-TB GOLD *IN-TUBE* ASSAY FOR DIAGNOSIS OF TUBERCULOSIS INFECTION IN CHILDREN SINCE 1 YEAR OF AGE

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Background and aims: IFN γ -Release Assays offer benefits in tuberculosis (TB) infection diagnosis yet in adults. Controversial data in young children limit however their applications to clinical paediatric practice. Here, the performance of the QuantiFERON®-TB Gold *In-Tube* (QFT-IT) assay was evaluated in 127 immunocompetent children stratified into < 1year and 1-4y old groups.

Methods: All consecutive children below 5 years of age with Tuberculin-Skin Test (TST) available and evaluated for QFT-IT reactivity from November 2007 to December 2011 in a single center were considered. 26 with known or suspected immunodeficiency were excluded. The 127 remaining had clinical suspicion of TB disease or recent contact with TB. TST positivity was defined by ≥ 10 mm in BCG-vaccinated or ≥ 5 mm induration diameter in non-vaccinated children.

Results:

- 1) Indeterminate results were observed in 8/50 (16%) infants and 9/77 (11.7%) 1y-4y children of whom most suffered from acute inflammatory diseases unrelated to TB.
- 2) No children with TB infection excluded evidenced QFT-IT positivity.
- 3) QFT-IT sensitivity as assessed in children with TB disease [clinical symptoms and TST positivity (n=20) with bacteriological confirmation in 11/20] was 4/10 (40%) in infants but 10/10 (100%) in children over 1 year of age (median age: 3y8m)
- 4) In latent TB (TB contact with no clinical symptoms but TST positivity) 0/4 infants but 4/11 children ≥ 1 y evidenced QFT-IT positivity.

Conclusions: High sensitivity in addition to high specificity of QFT-IT was observed in children ≥ 1 year old, with indeterminate results mostly related to ongoing acute inflammation unrelated to TB.

RAPID ANTIGEN DIAGNOSIS TEST FOR THE DETECTION OF GROUP A STREPTOCOCCAL ANTIGEN USING BIONEXIA STREP A PLUS

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Background and aim: The use of Rapid antigen detection tests (RADTs) to identify group A beta-haemolytic Streptococci (GABHS) pharyngitis offers an alternative to culture. RADT have the potential to reduce unnecessary antibiotic treatment and eliminate laboratory involvement. The purpose of this study was to evaluate the analytical sensitivity and the cross-reactivity of the rapid diagnosis device, bioNexia Strep A plus (bioMérieux SA).

Methods: The limit detection (LoD) was determined using *Streptococcus pyogenes* ATCC 19615. A dilution range was tested. Each dilution was tested 72 times using 2 lots of reagents, 2 operators, 3 readers. The LoD was also verified on 9 other GABHS.

The analytical sensitivity of the device was evaluated using 12 GABHS serially diluted from 20 up to 2×10^8 CFU/mL and tested in duplicate according to a protocol validated by AFSSAPS during the evaluation of different TDR. The cross-reactivity of bioNexia Strep A plus regarding 15 respiratory pathogens likely to be found in the respiratory tractus was evaluated.

Results: The LoD was estimated at 8×10^4 organisms/test. The LoD at 8×10^4 organisms/test was confirmed on 8 strains among 9 tested. One strains has been detected at 10^5 organisms/test.

The 12 GABHS were detected by bioNexia Strep A plus from 10^5 organisms/test. No-cross-reactivity was observed with respiratory pathogens tested.

Conclusion: The bioNexia® Strep A plus RADT shows very good performances in terms of analytical sensitivity and specificity. It is therefore a valuable test which can be used for the detection of GABHS in pharyngitis.

ACCURACY OF RAPID INFLUENZA DETECTION DB DIRECTIGEN EZ FLU A+B IN DIAGNOSIS OF INFLUENZA A AND B IN CHILDREN

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Background: Rapid influenza diagnostic tests (RIDTs) may be helpful in early diagnosis of the disease but their results should be interpreted carefully.

The aim of our study was to estimate the accuracy of the rapid influenza detection test BD Directigen™ EZ Flu A+B (Becton, Dickinson and Company, Sparks, MD, USA) used among children with influenza-like illness (ILI) consulted in the ambulatory care clinics.

Materials and methods: The total number of 150 patients were enrolled into the study. Inclusion criteria were: age of the child less than 59 months, presentation of ILI according to CDC definition (fever > 37,8°C, cough and/or sore throat in the absence of another known cause of illness), duration of symptoms shorter than 96 hours.

In all patients two nasal swabs and one pharyngeal swab were obtained and tested by RIDT, RT-PCR and real time RT-PCR.

Results: For influenza A (H1N1)2009 virus sensitivity of RIDT was 62,2% (95% CI 53,4-66,5%), specificity 97,1% (95% CI 93,4-99%), PPV 90,3% (95% CI 77,5-96,5%), NPV 85,7% (95% CI 82,4-87,3%). For influenza B virus sensitivity was 36,8% (95% CI 23,3-41,1%), specificity 99,2% (95% CI 97,3-99,9%), PPV 87,5% (95% CI 55,4-97,7%), NPV 91,5% (95% CI 89,7 - 92,1%).

Conclusions: The chosen RIDT immunoassay is a very specific but moderate sensitive method in diagnosis of influenza.

PROCALCITONIN TEST IN THE DIAGNOSIS OF URINARY TRACT INFECTIONS IN CHILDREN

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Background: High prevalence of urinary tract infection (UTI) and difficulties in differential diagnosis of upper and lower UTI determine the need for new sensitive laboratory markers that can be helpful in early diagnostics. Procalcitonin test (PCT) is one of the modern markers of bacterial inflammation that can be used as an indicator of the severity of inflammation in children with UTI.

Methods: 74 children aged from 1 month to 14 years we recruited in study. Group 1 included 54 children with acute pyelonephritis, group 2 - 20 children with lower urinary tract infection. Blood count with ESR evaluation, urine testing, CRP evaluation, doppler ultrasound were performed in all children. Procalcitonin test was performed on the day of admission to clinic, 5th and 10th day of therapy.

Results: Blood counts didn't differ significantly between groups at the time of admission. Leukocytosis in patients from group 1 consists $17,37 \cdot 10^9 \pm 1,1$, from group 2 - $16,0 \cdot 10^9 \pm 0,7$ ($p > .05$). There was no significant difference in leukocytosis between groups on the 5th and 10th days of treatment. The mean ESR in patients with pyelonephritis at the day of admission was $21,09 \pm 2,13$ mm/h, in children with lower UTI - $21,2 \pm 3,2$ mm/h ($p > .05$). CRP was found to be a sensitive indicator of upper UTI at admission, being 2,5 times higher in 1st group children. As well as CRP, PCT at admission was significantly higher in children with pyelonephritis ($4,56 \pm 1,3$ ng/ml and $0,17 \pm 0,02$ ng/ml, $p < .04$).

Conclusion: PCT can be an early sensitive indicator of pyelonephritis in children.

OPTIMAL POSITIONING OF INFANTS IN THE NEONATAL INTENSIVE CARE UNIT FOR LUMBAR PUNCTURE AS DETERMINED BY BEDSIDE ULTRASONOGRAPHY

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Objective: To standardize the optimal position for lumbar puncture in hospitalized neonates.

Design: A prospective and observational study.

Setting: A university hospital.

Patients: Infants hospitalized in the neonatal intensive care unit, for whom lumbar puncture was not indicated.

Interventions: The infants were placed in two lateral recumbent and two upright positions (lateral recumbent without flexing the hips, lateral recumbent with maximal hip flexion, sitting without flexing the hips, and sitting with maximal hip flexion) with concomitant heart rate, transcutaneous PO₂, and interspinous distance (with ultrasonography) measurements.

Main outcome measures: Maximum interspinous distance, minimum change in heart rate and transcutaneous oxygen saturation.

Results: Having the patient sit with maximal hip flexion provided the largest interspinous space for the grand majority of the infants. Sitting positions with/without flexion have resulted in significant increases in heart rate with respect to lateral recumbent position without flexion. Although statistically significant drops in oxygen saturations have been observed between lateral recumbent and sitting with flexion, lateral recumbent with flexion and sitting without flexion, and lateral recumbent with flexion and sitting with flexion positions; no adverse hypoxic events occurred during positioning.

Conclusions: Sitting flexed position, which seems to be sufficiently safe and serve to enhance the success rate of a lumbar puncture should be favored for sick neonates whenever the infant's condition permit a spinal tap.

MARKERS OF EARLY DIAGNOSIS AND PROGNOSIS IN PEDIATRIC SEPSIS (MARS): RATIONAL OF OUR PROSPECTIVE STUDY

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Background: A prompt diagnosis plays a key-role in improving outcome in septic children. Moreover, an early identification of septic patients could lead to a better use of antibiotics decreasing toxicity, cost and rise of resistant bacterial strains. We performed a literature review about diagnostic/prognostic markers of sepsis in order to determine the most useful ones in pediatrics.

Methods: Four search issues related to sepsis, markers, diagnosis and prognosis in English language have been combined using Pubmed database until June 2011.

Results: Nowadays, the most widely used serum markers are PCT and CRP in association with WBC. A lot of pro- and anti-inflammatory cytokines, as IL-6, IL-10, TNF- α , IL-1b, IL-8 and IL1R- α , have been investigated. Among them, IL-6 resulted the most promising one because of its early increase in infections, high both sensitivity and specificity but, unfortunately, extremely short half-life. Surface cell markers have also been studied, and in particular neutrophils CD64 showed very high sensitivity but poor specificity, requiring high laboratory expertise. New promising markers recently described are sTREM-1 (soluble receptor of triggering receptor expressed on myeloid cells), IL-33 and its soluble receptor sST2. On preliminary adult data, they seem to have high sensitivity/specificity in both diagnosis and prognosis of sepsis combined with a suitable half-life.

Conclusions: Using "multimarkers strategy" we designed a prospective study to investigate the role of PCT, sTREM-1 and sST2 in diagnosis and prognosis of pediatric sepsis. On June 2011 we received local ethical committee approval for MARS study and started enrollment.

DIAGNOSIS OF VARICELLA-ZOSTER VIRUS (VZV) INFECTIONS BY DETECTION OF VZV DNA IN SALIVA**A. Gershon¹, M. Gershon², J. Chen², S. Steinberg¹, P. La Russa¹***¹Pediatrics, ²Pathology, Columbia University Medical Center, New York, NY, USA*

Non-infectious VZV DNA can be detected in saliva using PCR in individuals with varicella and herpes zoster (HZ). DNA genotyping reveals whether the virus is wild (WT) or vaccine (VT) type. We analyzed salivary VZV DNA in 7 subjects. VZV DNA was detected in saliva and rash (face, shoulder, or arm) in 4/4 adults with HZ. VZV DNA was present in saliva during illness but disappeared afterwards. Analysis of VZV ORFs 38 and 62 revealed all were WT. WT DNA was also detected in saliva of 1/1 adult with chickenpox and in 2/2 subjects with atypical, occult HZ. One, a 72 year old male experienced severe pain and allodynia without rash on the right side of his chest and arm. After VZV WT DNA was found in saliva, he was treated with valacyclovir. Pain disappeared after 1 week and, following clinical recovery, VZV DNA was no longer detected in saliva. The other, a previously healthy adolescent male had been vaccinated against varicella. Severe abdominal pain and blood loss developed requiring surgical resection of a gastric ulcer. There was no rash. VZV DNA was detected in his saliva 3 weeks after onset of pain. PCR analysis of resected tissue revealed VZV ORFs 38 and 62 and immunocytochemistry revealed VZV gE and ORF63 in the gastric mucosa. VZV DNA disappeared from saliva after recovery, when a repeat gastric biopsy was normal. Analysis of saliva for VZV DNA is a useful diagnostic test.

ARTERIAL AND CAPILLARY BLOOD SUGAR AMONG PATIENTS FOR LUMBAR PUNCTURE IN PEDIATRIC TERTIARY GOVERNMENT HOSPITAL IN QUEZON CITY, 2011

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Background and aims: For patient economics this study is done to determine if there is correlation between arterial and capillary blood sugar (HGT) among patients for lumbar puncture in pediatric tertiary government hospital in Quezon City from March to October 2011.

Methods: This is a method comparison design done in a pediatric tertiary government hospital in Quezon City. 40 patients aged 6 months to 19 years admitted for lumbar puncture were included. 40 in-patients with viral illnesses who prior to discharge were clinically asymptomatic with normal CBC values comprised the control group. Before lumbar tap, arterial blood (brachial) was extracted for serum glucose and capillary blood sugar or HGT (finger) was determined with a glucometer simultaneously from each patient. CSF/arterial blood sugar and CSF/capillary blood sugar ratios were also compared. For the control group, glucose determinations were performed on the day of discharge. Scatter plot diagram was used to evaluate the correlation between arterial and capillary blood sugar for both groups. Same method was used between CSF/arterial blood sugar and CSF/capillary blood sugar ratios.

Results: Strong correlation was seen between arterial and capillary blood sugar in experimental group ($R^2=0.6577$, $R=0.811$) but not in control group ($R^2=0.1111$, $R=0.333$). Strong correlation was seen between CSF/arterial blood sugar and CSF/capillary blood sugar ratios ($R^2=0.7591$, $R=0.871$).

Conclusion: Arterial and capillary blood sugar were comparable in experimental group hence can be reliable for CSF/serum glucose ratio. Similar studies however should be done to establish stronger correlation between the two values in the pediatric population.

COMPARING THE TUBERCULIN SKIN TEST AND QUANTIFERON-TB GOLD IN-TUBE IN DIAGNOSING LATENT TUBERCULOSIS INFECTION IN BCG-VACCINATED CHILDREN

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Background and aims: The QuantiFERON-TB Gold In-Tube test (Cellestis, Carnegie Victoria, Australia) was approved for the diagnosis of latent tuberculosis infection. Although it has been shown to be sensitive and specific in adults, limited data are available on its performance in children.

Methods: This was a retrospective study of BCG-vaccinated children younger than 15 years of age in Seongnam, South Korea. We compared the tuberculin skin test (TST) and QuantiFERON-TB In-Tube test results in children who had exposed to household with contagious pulmonary tuberculosis disease within the past 3 months.

Results: Among the 36 children with a history of exposure to a household with contagious pulmonary tuberculosis disease, 21 (58%) had positive results for the tuberculin skin test, whereas 10 (28%) had positive results for the QuantiFERON-TB In-Tube test. Concordance between the TST and QuantiFERON-TB In-Tube test results was 69% ($\kappa = 0.43$).

Conclusions: The QuantiFERON-TB In-Tube test is a specific test for diagnosis of latent tuberculosis infection in children whose household contact has contagious pulmonary tuberculosis disease. Additional studies are needed to further assess the utility of the QuantiFERON-TB In-Tube test in the children with high risks of exposure to M tuberculosis.

DIAGNOSTIC VALUE OF EOSINOPENIA IN CHILDREN WITH BACTERIAL INFECTIONS

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Objective: To determine the role of eosinopenia in diagnosis bacterial infections in childhood and its comparison with other acute phase reactants.

Methods: The study was conducted among 0-14 years old children admitted to the Pediatric Emergency Service and Pediatric Outpatient Clinics between January 2008-December 2008. Patients with bacterial infections, viral infections and control group without any infection sign enrolled in the study.

Results: Among 2144 patients, 519 (24.2 %) were diagnosed as bacterial infection, 356 (16.6%) as viral infection, 282 (13.1%) as systemic diseases, and 972 (45.4%) as other diseases. In bacterial infection group and viral infection group the absolute eosinophil count (aEC) were 103.7 ± 176.9 and 192.8 ± 229.3 respectively and this is statistically significant. In bacterial infection group, patients with fever had statistically lower aEC than patients without fever and patients who were hospitalized had statistically lower aEC than who were not hospitalized. We found the sensitivity of white blood cell count (WBC), absolute neutrophil count (aNC), aEC, CRP and erythrocyte sedimentation rate (ESR) in diagnosis of bacterial infections as 59.2%, 63.5%, 61.4%, 71.1% and 62.7% and specificity as 68.9%, 70.2%, 82.4%, 77.1 % and 71.8% respectively. The cut off point for aEC was 50 /mm³. The two greatest area were CRP and aEC in ROC analysis performed to estimate the diagnostic value in bacterial infection ((CRP: 0,791 unit² ; mES: 0,753 unit²).

Conclusion: In diagnosing childhood bacterial infectious diseases, aEC is as sensitive and specific as ANC and CRP and it can be used easily in daily practice.

CEPHEID XPRT C. DIFFICILE ASSAY: RAPID DIAGNOSIS OF CLOSTRIDIUM DIFFICILE INFECTION IN PEDIATRIC PATIENTS

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Background and aims: The aim of this study is to evaluate the utility of a PCR-based tool (Cepheid Xpert C. difficile assay) in the rapid diagnosis of *Clostridium difficile* infection (CDI) in a pediatric hospital.

Methods: Between June and December 2011 a total of 81 soft or liquid stool specimens, collected from pediatric patients affected by diarrhea (45 from Surgery Department and 36 from Pediatric Emergency Care Unit), were tested for routine CDI diagnosis. Specimens were tested daily or stored at 4°C and tested within 24 h. A multiplex real-time PCR that detects the toxin B gene (*tcdB*), the binary toxin gene (*cdt*), and the *tcdC* gene deletion (Cepheid Xpert C. difficile assay) was performed according to the manufacturer's instructions. All samples were also investigated for adenovirus, rotavirus, norovirus, *salmonella* spp. and *shigella* spp.

Results: Of 81 samples tested, the toxin B target (*tcdB*) was detected in 5 (11.1%) surgical patients and in 5 (16.1%) pediatric patients. None of them were positive for the binary toxin gene (*cdt*), and the *tcdC* gene deletion. Only one patient (pediatric emergency care unit) resulted also affected by *Salmonella* spp. infection.

Conclusions: Laboratory diagnosis of CDI continues to be an important issue specially if a PCR tool with a TAT of 45' is available. Intestinal tract of children is often colonized by *C. difficile* as reported in literature. Our results suggest that only one patient was colonized because suffering by salmonella enteritis, while the other 9 cases were CDI following the antibiotic treatments.

CHEST RADIOGRAGY VALUE IN FEBRILE CHILDREN

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Background and aim: The routine use of chest X-Ray (CXR) in all infants and children with fever increases health cost and can often unnecessarily expose the patients to radiation. We aimed to evaluate the association between the clinical findings and the CXR in febrile children presenting in the Emergency Department of a District Children's Hospital.

Methods: We examined 1120 febrile children $>38^{\circ}\text{C}$, aged 1 month to 14 years old during 2009-2010, 59.6% males and 40.4% females and were divided in two groups: Group A 66.8% without cough or any other symptom of lower respiratory tract infection (LRTI), and Group B (33.2%) with cough.

Results: CXR was performed in 38.4% of children, in 16% of Group A and in 83.1% of Group B. Children presented with fever $>24\text{h}$ in Group A was 72.8% and with fever $>3\text{days}$ was 48.3%, while in Group B was 38.7% and 19.3% respectively. Pneumonia was diagnosed in 4% of patients of Group A and in 29% of Group B. In total we diagnosed pneumonia in 138 patients (8.2%). Clinical signs of LRTI (crackles in lungs, or tachypnea, or wheezing, or oxygen saturation $\leq 95\%$) were found in 69% of Group A and 98% of Group B. Almost all patients 99% had nasal flaring (mucous production).

Conclusions: CXR was performed in one third of febrile children examined. The percentage of positive CXR is increased when the fever is prolonged more than 3 days or when it is combined with cough or any other symptom of LRTI.

A RECENT INCREASE IN PERTUSSIS IN ENGLAND AND WALES (2011)**G. Amirthalingam**¹, H. Campbell¹, N. Fry², T. Harrison²*¹Immunisation, Hepatitis and Blood Safety Department, ²Respiratory and Systemic Infection Laboratory, Health Protection Agency, London, UK*

Background and aims: Since the introduction of an accelerated infant schedule (1990) and pre-school booster (2001), pertussis incidence in children under 10 years has declined. Despite high vaccine coverage, pertussis remains the most common vaccine-preventable cause of hospitalization and death in infants in England and Wales (E&W) with continued 3-4 yearly cyclical peaks in activity; the last peak year was recorded in 2008. Following a period of low incidence (2009-2010), laboratory confirmed cases increased in 2011 and we describe this recent increase.

Methods: Four routine surveillance sources were analysed for 2011 and compared with previous years: notifications of clinically suspected cases; laboratory confirmed cases (culture, serology and PCR); hospital admissions and certified deaths.

Results: Provisionally 1120 pertussis cases were confirmed in E&W in 2011 compared with 902 cases in 2008. The highest incidence of laboratory-confirmed cases was in infants under 3 months (108 per 100,000). Incidence in older infants and children under 10 years has declined. In those ≥ 15 years however, incidence was almost 50% higher in 2011 compared with 2008. In 2011, there were 7 reported deaths, all in unvaccinated infants under 2 months.

Conclusions: The disproportionate burden of pertussis continues in infants too young to be vaccinated. An increasing number of cases are being confirmed in teenagers and adults. Routine availability of serological testing since 2002 has contributed; the true incidence in older age groups is unknown and needs to be better defined to inform a review of an adolescent pertussis booster vaccination programme in the UK.

EPIDEMIOLOGY OF PERTUSSIS IN CHILDREN ATTENDED TO A PAEDIATRIC REFERRAL HOSPITAL IN BRAZIL, 2007-2011

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Background: Pertussis is a highly contagious disease that may occur at any age. Humans are the only pertussis reservoir and it has re-emerging in the recent years. Most cases of serious diseases are observed in early infancy. The aim of the present study was to assess the incidence of pertussis among children admitted to a Paediatric Quaternary Hospital (Hospital Pequeno Principe- HPP) in Curitiba city, Brazil.

Methods: Between 2007 and 2011 all pertussis suspected cases were investigated by the Epidemiology and Infection Control Service of HPP. Lab tests to confirm pertussis are made in IAL, until 2010 and in 2011 PCR was implanted. We analysed confirmed pertussis cases, age, year and outcomes.

Results: In this 5 years of surveillance, 219 suspected cases were investigated, 62 cases (28.31%) were confirmed, with a increase proportion of confirmed cases in 2011(40.74%). The mean age was 3.67months, 55.70%(122) female and a one death was observed in 2011.

Conclusions: pertussis in early infancy showed high morbidity and mortality and we observed an increase of pertussis incidence in 2011. Certainly under diagnosed and underreporting cases of pertussis occurred, due to low raising awareness of pediatricians about the re-emerging of this infection.

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) OR MOSCHCOWITZ SYNDROME IN A CHILD WITH INFLUENZA VIRUS A (H1N1) INFECTION

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Background and aim: Infection with influenza A (H1N1) manifests with symptoms similar to seasonal influenza. Thrombotic thrombocytopenic purpura (TTP) or Moschcowitz syndrome is defined as a syndrome of microangiopathic hemolytic anemia with thrombocytopenia, neurological abnormalities, renal dysfunction and fever. TTP is associated with infections, drugs, autoimmune diseases, and malignancies. We describe the case of a 12-year old boy with influenza A (H1N1) virus infection who gradually developed Moschcowitz syndrome.

Methods: A twelve-year old boy presented with high fever (39,4°C), cough, malaise, abdominal pain, vomiting and macroscopic hematuria. PCR for Influenza A (H1N1) virus was positive and he was treated with oseltamivir. Over the next few days, he developed purpuric rash, acute renal failure and microangiopathic hemolytic anemia (anemia, thrombocytopenia, elevated reticulocyte count, LDH and indirect bilirubin, schistocytes) and severe neurologic symptoms leading to coma.

Results: Plasmapheresis was started immediately (9 sessions in all) with complete remission of TTP. The patient remained intubated for one week in the ICU. Neurological symptoms improved gradually over the next 2 weeks and the patient was discharged in good general health. Over a 2-year follow up period, there was no relapse of TTP.

Conclusions: To our knowledge, this is the first case of TTP associated with Influenza A (H1N1) virus infection in children. TTP is an hematologic emergency and prompt diagnosis and treatment are crucial for the outcome.

RE-EMERGING OF PERTUSSIS IN IRANIAN SCHOOL-AGE CHILDREN

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Infections caused by *Bordetella pertussis*, have recently been reported increasingly even in highly immunized populations. In these populations adolescents and adults now constitute the main source of infection in infants.

This problem may be caused by waning of immunity induced by vaccination, heterogeneity of bacteria, inefficiency of the available vaccines or improving the surveillance system. Frequency data of the disease in different age groups will lighten the epidemiologic trends of pertussis in different populations

Methods and Material: In this population-based, descriptive study, nasopharyngeal sampling obtained from school children between 6-14 years old with coughing for two weeks were examined for *Bordetella pertussis* and *Bordetella parapertussis* by Polymerase chain reaction and culture.

Results: Out of 6601 students, 328(4.97 %) had cough for at least 2 weeks. The mean duration of cough was 20 days. Among them 182(55.5%) had whooping, 194 (59.1%) and 73 (22.3%) had paroxysms and post-tussive vomiting respectively. A total of 21 (6.40%,) children were found to be positive by polymerase chain reaction assay for *Bordetella pertussis* and 6 (2.43%) children had this test positive for *Bordetella parapertussis*.

Bordetella Pertussis was detected in the culture of 4(1.22%) specimens (all culture positive cases were positive for Polymerase chain reaction too) and *Bordetella parapertussis* culture was not found positive at all. The estimated frequency of *Bordetella pertussis* in this age group was 318/100000 and for *Bordetella parapertussis* was 2/100000.

Conclusion: Pertussis is still one of the common etiologies of prolonged cough in children and adolescents even in highly immunized countries.

PERSISTENT ENDEMICITY OF INVASIVE MENINGOCOCCAL DISEASE IN NORTHERN MEXICO: A SEVERE, PREVENTABLE AND UNRESOLVED HEALTH PROBLEM

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Background and aims: Invasive meningococcal disease (IMD) is underreported in Mexico, and is based on passive surveillance. The Tijuana, Mexico - San Diego, CA border is the most transited internationally. We looked for all IMD pediatric cases based on an active surveillance system.

Methods: Between October - 2005 and September - 2011, all patients < 16 years old with confirmed IMD were prospectively admitted at Tijuana General Hospital (TGH). Following blood and/or cerebrospinal isolation, serogroup identification was performed using Latex-agglutination method (Pastorex®). Both clinical and microbiological data was analyzed.

Results: A total of 30 IMD cases were admitted. Avg age was 4.3 years old (20 days - 15 years), from which 50% were ≤ 2 years old. 9 patients had clinical purpura fulminans (CPF) (33%) and 27 (90%) had meningitis with/without CPF. Overall mortality was of 23.3% (7 patients). Serogroup distribution was as follows: "C" - 57%, "Y" - 23%, "B" - 13%, and ignored - 7%. *Neisseria meningitidis* was the leading cause of bacterial meningitis (60%). Based on the population-coverage of TGH, estimated rates of IMD are of 3.3/100,000 population in < 16 years old, 6.9/100,000 in children < 5 years old, and 11.7/100,000 in children < 2 years old, respectively.

Conclusions: IMD in the northern Mexican border is much higher than what is Nationally reported, with rates even higher than in countries where vaccination is mandatory. Serogroup "C" is the most prevalent. Vaccination is mandatory in our region, and a National Surveillance System is ongoing based on these results.

CHRONIC CNS INFECTIONS IN DEVELOPING COUNTRIES: SUBACUTE SCLEROSING PANENCEPHALITIS IN PAKISTAN

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Objective: To find out the role of electroencephalography in the early diagnosis of subacute sclerosing panencephalitis.

Design: Cross sectional observational study.

Place and duration of study: Department of Neurology Children's Hospital, Lahore from April 15, 2009 to September 15, 2011.

Subjects and methods: Children between the ages of 4 to 18 years (n=100) with myoclonic jerks were admitted in Neurology department. History and clinical examination was carried out and EEG and CSF antimeasles antibodies were performed. Children may have EEG findings consistent with SSPE (EEG abnormalities having burst suppression in high amplitude slow and sharp waves recur at 3-5 second interval on slow background) or other EEG findings like myoclonic epilepsy with normal background, normal EEG etc. CSF of all children was sent for antimeasles antibodies for further confirmation which was considered diagnostic. Brain imaging was done in all children to exclude other possible diagnosis.

Results: Total of 79 patients with EEG findings of subacute sclerosing panencephalitis were further confirmed with CSF anti measles antibodies. It was positive in 57 children. (P value < 0.05). While thirteen children had negative EEG findings and all of them had negative results for CSF antimeasles antibodies. Male to female ratio was 1.4:1. Age range was six to fifteen years.

Conclusion: Subacute sclerosing panencephalitis is one of the common chronic CNS infection in children in developing countries. Clinical presentation varies in different stages of the disease, which makes the diagnosis difficult. Electroencephalography has significant value in early, cost effective and reliable diagnosis.

MEASLES EPIDEMIC IN BELGIUM, 2011: REASONS FOR NON-VACCINATION**M. Sabbe**¹, D. Hue¹, V. Hutse², P. Goubau³*¹Public Health and Surveillance, ²Viral Diseases, Scientific Institute of Public Health, ³Departement of Virology, Université Catholique de Louvain, Brussel, Belgium***Background:** The WHO Europe set a target of eliminating measles in the Region by 2015. Since the beginning of 2011, Belgium has seen an increase in the number of measles cases.**Methods:** Cases were reported through the health systems of the communities and Brussels region. Additionally, cases were observed through the National Reference Centre for measles and rubella and the paediatric surveillance unit "PediSurv". Data on reasons for non-vaccination were collected through the reporting physician.**Results:** Between 1 January and 20th December 2011, a total of 553 cases were reported, compared to 40 cases in 2010. Measles resurgence began in anthroposophical schools in Flanders but outbreaks were reported elsewhere in the country, especially in Brussels and Wallonia. Vaccination status was known for 310 cases (56%). Of these, 239 had not been vaccinated with the measles-mumps-rubella vaccine (MMR). In the cases older than one year, and thus old enough to be vaccinated, reason for non-vaccination was given in 136 cases. Main reasons were their parents' anthroposophical or philosophical beliefs (76%), oblivion to vaccinate (10%) or vaccination could not be carried out due to circumstances such as illness at time of vaccination, travelling or allergy (14%).**Conclusions:** Our findings draw attention to the need to sensitise health professionals and raise their awareness of the issues through medical education. Convincing parents and health professionals reluctant to vaccinate children with MMR vaccine will be a challenge for years to come.

HAND, FOOT AND MOUTH DISEASE: CHALLENGES FOR CHINA**Q.J. Feng**¹, S.J. Chen¹, L. Xiang¹, J.H. Lu¹, Z.M. Guo²¹*School of Public Health, ²Pharmaceutical College, Sun Yat-Sen University, Guangzhou, China***Background:** Ever since hand-foot-and-mouth disease (HFMD) gripped the Linyi City, Shandong Province in 2007, the disease has swept over 31 Chinese provinces and cities.**Methods:** The monthly reported cases based on Chinese HFMD Surveillance System from 2007 to November 2011 were analyzed. The descriptive methods and systematic review analysis were performed to present the epidemic and etiologic characteristic of HFMD.**Results:** From 2007 to 2010, the incidence of HFMD increased by degrees: 32.5, 194.3, 468.5, 797.7 per 100,000, respectively, with the fatality rate creeping up from 0.02% (2007) to 0.05% (2010). There were 1,496,048 HFMD cases reported to November in this year, including 17,775 severe cases and 467 deaths. The disease spread more rapidly, induced more serious symptoms in rural-urban fringe. Children under the age of 3, particularly boys, are at higher risk. The epidemic peak appears during May to July. The alternated or simultaneous spread of EV71 and CA16 caused HFMD local outbreaks and repeated prevalence. The first three causes of HFMD deaths were central nervous system damage, heart failure and pulmonary edema, which were often induced by EV71. The C4a was the most prominent EV71 subgenotype, while for CA16 was B genetic group. Homologous recombination has been proved to play a role in generating genetic diversity during the outbreak of EV71 and CA16. Besides, increase of cases infected by other enteric viruses should be taken seriously.**Conclusions:** HFMD is posing a major threat to children's health in China. Effective treatments and specific vaccines are needed urgently.

NON-BLANCHING RASHES IN PAEDIATRIC PRACTICE: THINK *MENINGOCOCCUS* BUT DO NOT FORGET ROTAVIRUS**S.P. Paul**^{1,2}, D.C. Candy²¹*Paediatrics, Great Western Hospital, Swindon*, ²*Paediatrics, St Richard's Hospital, Chichester, UK*

Background and aims: Since 1970s, rotavirus recognised as systemic disease. Isolated associations such as encephalopathy, cutaneous vasculitis have been reported previously. We report a new association in systemic rotavirus illness: encephalopathy with vasculitis. The aim of the case series is to make clinicians aware that rotavirus can mimic serious bacterial pathologies.

Methods: Three children aged 6months to 3years presented to the emergency department with irritability/drowsiness, fever, non-blanching petechial spots (non-SVC distribution), diarrhoea, vomiting and looking unwell.

Results: In view of fever and non-blanching rashes, all the 3 children were initially treated as suspected meningococcal disease. Two of the children were acidotic which resolved within 12hours. Blood inflammatory markers were reported within normal limits in all 3 cases. The children recovered within 48 to 72 hours and blood culture and meningococcal PCR were reported as negative. One child needed transfer to the PICU for 24 hours; all 3 suffered significant morbidity. Stool ELISA were reported positive for rotavirus in all 3 cases. The final diagnosis was systemic rotavirus illness with encephalopathy and vasculitis.

Discussion:

- 1) Encephalopathy previously reported with rotavirus; demonstrated in CSF,
- 2) Fluid resuscitation and replacement necessary,
- 3) Vasculitis demonstrated in laboratory studies and following rotavirus immunisation,
- 4) Previous studies showed only 11% of non-blanching rashes were due to meningococcal disease, and
- 5) Oral rotavirus vaccines will prevent morbidity and mortality.

Conclusion: This case series demonstrated a new dimension in systemic rotavirus illness. Stool samples should be sent if a child presents with encephalopathy, non-blanching rashes and gastroenteritis.

PERTUSSIS RE-EMERGENCY IN 2011 CAUSED 18 DEATHS IN YOUNG BABIES IN SÃO PAULO STATE, BRAZIL

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Background and objectives: In Brazil, the majority of Pertussis reported cases comes from São Paulo state, where there are 33 reference centers for pertussis surveillance. Even with low incidence rate in comparison with other regions, in 2011, the number of cases and deaths by pertussis in São Paulo state grew substantially, pointing to a hyper endemic situation.

Methods: We analysed confirmed Pertussis cases and deaths registered in São Paulo by reporting center (included or not in surveillance net), age and year of notification from 2000-2011.

Results: The number of pertussis cases varied from 57 (2001) to 578 (2011), and the number of deaths, from 9 (2002) to 18 (2011). During this period, the majority of cases and all deaths were registered in children < 6 month of age. In 2011, 299 cases and 16 deaths were registered in children < 2 months of age, and the CFR was very high (6%).

Discussion: Even considering that the recent introduction of RT-PCR could have improved pertussis diagnosis, the high number of pertussis deaths in São Paulo state in 2011 points to the re-emergency of pertussis. Most of cases were diagnosed in reference centers, showing the need to improve the surveillance of pertussis in other regions. Considering that human beings are the only Pertussis reservoir and the difficulties to establish the diagnosis and to control the transmission of pertussis in healthy facilities, the immunization of contacts of young children, including health care workers, should be considered.

CRYPTOSPORIDIOSIS AND IMMUNOLOGICAL STATUS AMONG CHILDREN WITH MALIGNANT DISEASES

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Background and objective: Cryptosporidiosis is one of the emerging disease specially in the immunocompromised patients. Thus the aim of this study is to investigate the relationship of *Cryptosporidium* and immunological parameters among children with malignant diseases.

Methods: Stool samples were collected from 101 children with malignant disease and 107 apparently healthy children. Direct smear method and then formalin-ether sedimentation method were done for all stool samples to identify intestinal parasites. Fecal smears were prepared from the sediment and stained by the modified Ziehl-Neelsen method for the recovery of acid-fast oocysts of *Cryptosporidium*. Phagocytic activity, complement C3 and C4 estimation, immunoglobulin levels and CD3, CD4, CD8, CD19 marking and phenotyping were carried out for 30 patients and 20 control groups.

Results: ALL was the major type (47.52%) of malignant cases in the studied subjects. The other type ranged from 0.99% to 10.9%. Out of the 101 patients, 50 (49.5%) were found to be positive for intestinal parasites compared to 13 (12.15%) of the control group ($P < 0.01$). *Cryptosporidium* oocysts were found to be excreted by 10 (9.0%) patients and 1 (0.93%) of the control group ($P < 0.01$). The phagocytic activity, levels of IgM, IgA, IgG and CD3, CD4 cell numbers were lower in patients than in control group while higher in case of C3, C4, CD8 and CD19.

Conclusion: *Cryptosporidium* and other intestinal parasites must be considered in the differential diagnosis in this immunocompromised group in order to reduce the suffering often faced by those children.

ASYMPTOMATIC INFECTION WITH BORRELIA BURGDOFERI IN CHILDREN LIVING IN AN URBAN NOT ENDEMIC AREA

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Background and aims: Despite considered possible, asymptomatic *Borrelia burgdorferi* infection has never been exactly quantified. Such information could be useful to evaluate the real need for a specific vaccine. This study was planned to evaluate the incidence of asymptomatic borreliosis in children living in an urban not endemic area.

Methods: Children requiring laboratory blood tests for minor surgery in Milan, Italy, were enrolled. A small amount of blood was used to perform ELISA test for IgM and IgG antibodies to *B. burgdorferi* sensu lato. Positive cases were retested by Western Immunoblot (WI) for confirmation. Results were interpreted according to CDC suggestions for both IgM and IgG bands.

Results: A total of 555 children with a negative history for symptoms of borreliosis were enrolled. ELISA test was positive in 27% of the cases. WI confirmed infection in 7 cases (1.26%), with IgM positive in 6 and IgG in one. Positivity was not found in any of the 101 children aged < 2 yrs, 1/107 aged 2-3 yrs, 2/113 aged 4-6 yrs, 1/89 aged 7-9 yrs and 3/144 aged 10-18 years.

Conclusions: Asymptomatic *B. burgdorferi* infection seems possible in children living in an urban not endemic area. However, because the specificity of serologic criteria for the diagnosis of asymptomatic infection is not known as it is its natural history, further studies on positive cases are needed. These could clarify whether these results are the consequence of false positivity, of infection due to non-pathogenic strains or can later evolve in Lyme disease.

ABDOMINAL ACTINOMYCOSIS MIMICKING LYMPHOMA

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Background: Actinomycosis is rare granulomatous infection involving cervicofacial, thoracic and abdomen. The symptomatology is not specific and diagnosis usually is confirmed following suspicion of tumour.

5 month old Chinese boy presented with recurrent abdominal pain since early 2011. At initial presentation, he had fever with loss of appetite and loss of weight but resolved after 2 weeks leaving only abdominal pain with recur intermittently. There was no history of preceding trauma. He presented acutely with abdominal pain, fever in October 2011 to a district hospital and following diagnosis of acute appendicitis, laparotomy was performed.

Result: Accidental finding of tumour was found. The mass was arising from splenic flexure, yellow in colour with nodule noted at omental wall. Computed tomography of Abdomen/pelvis showed enhancing lesion involving ascending colon from hepatic flexure to midway of transverse colon, encasing it with no intraabdominal lymphadenopathy or ascites.

Case was referred as bowel lymphoma to tertiary hospital and laparotomy with limited left hemicolectomy and excision of omental mass done. Histopathological examination of the mass showed it was indeed actinomycosis with no evidence of malignancy.

Ultrasound abdomen following surgery showed no residual lesion with full blood count and CRP of almost normal. He was commenced with intravenous penicillin and plan to complete for 6 weeks followed by oral antibiotic.

Conclusion: To improve diagnosis, actinomycosis needs early diagnosis and should be included in the differential diagnosis of infiltrative neoplastic abdominal masses especially if clinical appearance of yellow (sulphur granules), sinus producing tumour.

THE PEDIATRIC EARLY WARNING SCORE PREDICTS HOSPITALISATION AND SERIOUS BACTERIAL INFECTIONS IN FEBRILE CHILDREN

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Background: The pediatric early warning score (PEWS) is a severity of illness score based on vital signs, oxygen therapy, and fluid therapy.¹ It was developed for children admitted to hospital wards and may be useful as triage tool in emergency departments (EDs). The study aim was to assess the predicted value of the PEWS for hospitalisation and serious bacterial infections (SBIs) in febrile children at the ED.

Methods: We performed a prospective observational study among febrile children (< 16 years) who visited the ED of a university-affiliated hospital in the Netherlands (2009-2010). The PEWS (range 0-19) was validated for the use in the ED by hospitalisation and serious bacterial infections. Sensitivity, specificity, and c-statistics were calculated as measure for performance. A PEWS threshold of five was used for sensitivity and specificity calculations.

Results: Among 1,574 febrile children (44% female, median age 2.2 years), 24% (N=383) were hospitalised and 11% (N=173) were diagnosed with a SBI. The sensitivity of PEWS to predict hospitalisation was 65% (95%CI 60-70%) and specificity was 71% (95%CI 68-73%). The c-statistic of PEWS for hospitalisation was 0.74 (95%CI 0.71-0.77). The sensitivity to predict SBIs was 66% (95%CI 54-76%) and the specificity 65% (95%CI 60-68%). The c-statistic of PEWS for SBIs was 0.70 (95%CI 0.62-0.77)

Conclusion: The discriminative ability of PEWS to predict hospitalisation and SBIs in febrile children was moderate.

1. Duncan H, et al. The Pediatric Early Warning System score: a severity of illness score to predict urgent medical need in hospitalized children.

CRITICALLY ILL CHILDREN WITH INFLUENZA A H1N1 INFECTION IN NORTH GREECE**S. Stabouli**¹, E. Volakli¹, A. Violaki¹, E. Roilides², M. Sdougka¹¹*Pediatric Intensive Care Unit, Hippokration Hospital, ²Third Department of Pediatrics, Hippokration Hospital, Aristotle University, Thessaloniki, Greece***Background:** During the Influenza A H1N1 pandemic aggressive manifestations of the disease were observed. We aimed to describe the clinical features and outcomes of children with H1N1-related critical illness.**Methods:** Clinical and epidemiologic characteristics, treatment, and outcomes of all children with H1N1 infection, admitted to a Pediatric Intensive Care Unit (PICU) in a tertiary-care hospital from 01-11-09 to 31-03-11, were recorded.**Results:** The study population was consisted of 9 girls and 6 boys, age range 0.5-14.0 years. 73.3% of the patients had pre-existing chronic health conditions. 93.3% of the patients presented with fever, 86.6% with respiratory distress and 33.3% with convulsions. The mean time from symptom onset to PICU admission was 5.4±3.8 days. All patients required mechanical ventilation. 33.3% of the children presented ARDS, 20% shock, 20% renal failure, 13.3% multiple organ dysfunction, and 13.3% myocarditis. Five patients (33.3%) and 3 patients (20%) presented ventilator-associated and catheter-associated infections, respectively. One patient presented acute hepatitis and one virus-associated hemophagocytic syndrome. Oseltamivir was administered to all patients. Mean duration of PICU stay and mechanical ventilation were 36.80±31.46 and 33.27±28.02 days, respectively. Multivariate regression analysis showed that pH, pO₂ at admission to PICU and bacterial superinfections were independently associated with duration of PICU stay (R²=0.78, P< 0.05). Mortality (20%) was observed only during 2009-2010 season. 66.7% of the children who died, had comorbid conditions.**Conclusions:** Critical illness due to influenza A H1N1 was associated with hypoxemia, prolonged mechanical ventilation, and bacterial superinfections. Mortality rate was higher in cases with pre-existing chronic disease.

ANTIBIOTIC RESISTANCE OF *STENOTROPHOMONAS MALTOPHILIA* ISOLATED FROM BLOODSTREAM OF PEDIATRIC PATIENTS

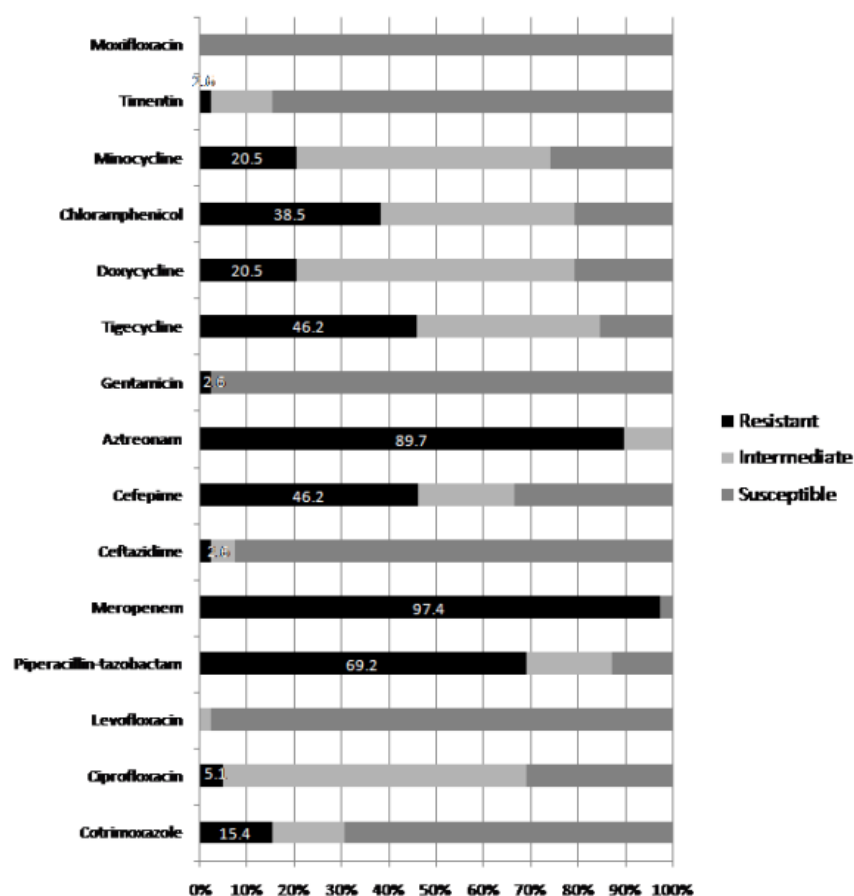
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Background and aims: Infection due to *Stenotrophomonas maltophilia* (SM) has emerged as an important nosocomial infection in immunocompromised patients in many regions, causing bacteremia, endocarditis, etc. Hospitalized children are extremely vulnerable to infections caused by SM. Information regarding the susceptibility patterns of SM is of prime importance for determining the active antibiotics.

Methods: This study assessed admitted children between June 2010 and September 2011. All blood cultures were screened for SM using biochemical tests. The drug susceptibility of SM isolates was determined using disk diffusion method and interpreted according to CLSI guidelines.

Results: A total of 39 isolates were identified as SM in monomicrobial culture. The resistance profile is shown in figure 1. More than half (69.2%) of strains were susceptible to Cotrimoxazole and 15.4% were resistant.



[Antibiotic profile]

Conclusion: This study demonstrated the emergence of Cotrimoxazole resistant strains of SM. Cotrimoxazole is recommended as the first choice for the treatment of SM bacteremia in children; the high rate of resistance to Cotrimoxazole should be regarded in therapy approaches and it should be administered with precaution in children.

MEASLES EPIDEMIC TO BE EXPECTED IN THE NETHERLANDS?

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Background and aims: Recently, resurgence of measles was observed in Europe. However, measles transmission in the Netherlands has remained limited. We assessed the immunity against measles in the general Dutch population and studied changes in this over the past 10 years.

Methods: Two population-based seroepidemiological studies were carried out in the Netherlands: Pienter-1 (1995/6) and Pienter-2 (2006/7) with 9856 and 7900 participants, respectively. In Pienter-1 serum samples were analyzed by an in-house ELISA and in Pienter-2 by a bead-based multiplex immunoassay. IgG levels ≥ 0.2 IU/ml were considered protective.

Results: Measles IgG seroprevalence in the general population was high in both studies (95.3% and 95.7%, respectively). For those twice vaccinated and not exposed to natural measles in Pienter-2, the IgG GMC decreased from 1.2 IU/ml to 0.6 IU/ml from 10 to 28 years of age. The IgG GMC among those vaccinated (0.9 IU/ml at 29-31 years) was much lower than among cohorts exposed to natural measles (3.6 IU/ml at 40-44 years; $p < 0.0001$). Participants up to age 9 years in Pienter-2 from religious communities (partly) refusing vaccination had a low seroprevalence (63.3% at 5-9 years).

Conclusions: The general Dutch population is well-protected against measles. In vaccinated cohorts a declining antibody level over time was observed. However, antibody levels remained well above the cut-off for protection. Considering the high measles incidence in other European countries and the large susceptible group among children from religious communities refusing vaccination, there is a high risk of a large measles outbreak in the Netherlands.

NEUROLOGICAL COMPLICATIONS IN RUBELLA-INFECTED CHILDREN: IS IT REALLY RARE ONE?**N.T.T. Do**, T.A. Ho, A.N. Pham, L.V. Nguyen, H.T. Do*Infectious Diseases Department, National Hospital of Pediatrics, Hanoi, Vietnam*

Background and aims: Rubella is a mild viral illness, and rarely causes complications. However, in a non-vaccination population like Viet Nam, widespread outbreaks usually occurred and its complications are not very rare. This study's aim was to describe the clinical, investigational characteristics and outcome of neurological complications in children with rubella.

Subject: 85 children infected with rubella who had neurological complications admitted to Vietnam National Hospital of Pediatrics from December, 2010 to November 2011 were enrolled for this study.

Methods: Cross-sectional study.

Results: Mean age was 8.4 ± 3.3 years; the disease was seen mainly from February to June, peak prevalence occurred in April.

76/85 children had mild and moderate symptoms, 9 (10.6%) children had severe symptoms requiring mechanical ventilation. Symptoms as rash, fever and lymph node were seen in 100%, 85.9% and 8.2%, respectively. Neurological complications could occur from day 1 to day 8, mean 3.7 ± 1.3 days. The most frequent neurological manifestations were coma (100%), seizures (91.8%), meningeal signs (58.8%).

In cerebral spinal fluid, 53.9% cases had mild pleocytosis (5 - 300 cells/mm³), and 60% cases had increased protein value (>0.45 g/l). Images of cerebral lesion in CT-scanner were seen in 35% cases, most of them were brain edema.

Most cases made a full recovery (96.4%), mean duration for recovery is 6.9 ± 2.9 days. Sequelae prevalence was 2.4%.

Conclusions: It is important to take notice of neurological complications in a children infected with Rubella. A vaccination program should be promoted to prevent these life-threatening complications.

PERTUSSIS BURDEN IN YOUNG INFANTS: A WORRYING TREND

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Background: Pertussis is still responsible for considerable childhood morbidity. Of several possible control strategies, Israel implemented booster vaccine doses in schoolchildren, leading to an incidence decline. However, in 2011 a worrying rise was observed among young infants.

Methods: Population-based epidemiologic study in the Jerusalem district, focusing on children, and a case-control study exploring risk markers.

Results: 2125 pertussis cases were reported from 1998 to November 2011. Children under 1, 5 and 14 years comprised 14.3% (n=303), 27% (n=573) and 62% (n=1321), respectively. The proportion of under 5 year-olds increased from 27% in 2010 to 39% in 2011 (p=0.007). Infants under one year had the highest average incidence rate (87/100,000); rising from 62/100,000 in 2009 to 360 in 2011 (OR=5.8). The median age of infants was 2.9 months; 78.5% being under 6 months. Their vaccination status (age-appropriate) was: unvaccinated -54.8%, partially vaccinated - 17.5%, fully vaccinated - 27.7%. The overall hospitalization rate was 6.7%; infants - 37.1%, under 6 months 44.7%. The main clinical signs in hospitalized infants were cough (94%), desaturation/cyanosis (72%) and apnea (33%). Low birthweight (13% vs. 7%) and higher birth order (5.1 vs. 3.2) were significantly more frequent among pertussis cases vs. controls. Predisposing conditions included congenital anomalies and genetic disorders (e.g. Down syndrome). Household transmission occurred in 22% and 12% of households with/without a case in a child under 14 years (OR=2).

Conclusions: Pertussis in young infants constitutes a significant disease burden. Identifying specific risk markers can expedite the adoption of tailored control strategies such as cocooning.

PLASMODIUM VIVAX CAUSING CEREBRAL MALARIA AND MULTIORGAN DYSFUNCTION IN CHILDREN: AN OBSERVATIONAL STUDY FROM BIKANER (NORTHWESTERN INDIA)

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Background and aims: Epidemiological studies and clinical description of *P.vivax* cerebral malaria in children are rare and more attention is needed to understand the dynamics and its interaction with the immune system.

Methods: This prospective study was done on 388 admitted children of malaria. The diagnosis was done by peripheral smear and rapid diagnostic test and further confirmation of severe *P.vivax* mono-infection was done by polymerase chain reaction with their prior informed consent.

Results: Severe disease was present in 43.8% children, with the risk greatest among *P.vivax* (55.2%) compared with *P.falciparum* and mixed infections (OR=2.1 [95% CI=1.3-3.3], p=0.001). In children < 5 years age, the proportion of severe malaria attributable to *P.vivax* rose to 67.4% compared with 30.4% of *P.falciparum* (OR=4.7 [95% CI=2.6-8.6], p< 0.0001). We encountered 18 children of *P.vivax* cerebral malaria categorized as per WHO (2000) criteria for *P.falciparum*, out of which 55.6% had multiorgan dysfunction. The other associated severe manifestations included severe anemia in 55.6%, hepatic dysfunction in 22.2%, renal dysfunction in 22.2%, bleeding manifestation in 22.2%, respiratory distress in 11.1%, metabolic acidosis in 11.1%, shock in 11.1% and hemoglobinuria in 11.1% children. Hypoglycemia was not observed in any child. There was no evidence of neurological sequelae in any child. The case fatality rate of severe *P.vivax* was 2.8% versus 2.6% of severe *P.falciparum* malaria (p=1.0). Mortality due to cerebral malaria alone was 12.5% which increased to 20% when concomitant multiorgan dysfunction was present.

Conclusions: *P.vivax* mono-infection can cause cerebral malaria, multiorgan dysfunction and mortality in children.

SURVEILLANCE OF INFLUENZA AND INFLUENZA LIKE ILLNESS IN CHILDREN AGED 6 MONTHS TO 17 YEARS IN UGANDA

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Background and aims: Following outbreaks of influenza virus H5N1 in 2006 and Pandemic Influenza A(H1N1) in 2009, Makerere University Walter Reed Project (MUWRP) , Ministry of Health and partners undertook surveillance for influenza and influenza-like illnesses (ILIs) in humans in Uganda to detect potential pandemic influenza threats and control them. Objective of this study was to conduct surveillance of influenza and ILIs in children.

Methods: From October 2008 to May 2011, children aged 6 months to 17 years presenting with fever ($> 38^{\circ}$ Celsius) plus cough and/or cold and/or sore-throat within 72 hrs were enrolled at 5 outpatient clinics. Exposure history and a physical examination were done. Throat and/ or nasopharyngeal swab was collected for virus isolation and typing using RT-PCR for flu A and B .

Results: 3182 children were enrolled in the study. 2875 (90.4%) and 307 (9.6%) were < 5 yrs and 5 -17 respectively. Majority, 2917 / 3182 (91.7%) tested negative on screening for Flu A & B , while 221(6.9%) tested positive for Flu A. 179/221(81%) were < 5 while 42 (19%) were aged 5-17yrs. On subtyping for Flu A, 2 (1 %) were H1, 79 (35.7 %) were H3 and 3 (1.4 %) had co-infections of H3 and H1N1,76 (34.4 %) had H1N1 , 43 (19.5 %) had H3N2 while 18 (8.9%) were untypable.

Conclusion: Influenza virus was not commonly isolated from children presenting with influenza/ILIs. Influenza A virus H1N1 followed H3N2 were the main virus subtypes being isolated.

IMPORTED FULMINATING SUBACUTE SCLEROSING PANENCEPHALITIS

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A 13 year old girl was transferred from Kosovo to our hospital for neurosurgical workup.

Recent onset of fatigue, ataxia, difficult gait, slight fluid dysphagia and dysarthria. MRI evidence of pons lesion extending through the middle cerebellar peduncles interpreted as a possible glioma..

Previous medical history uneventful. Neither Measles nor vaccination reported.

On admission awake and responsive although delayed, scarce verbal response; sustained gait, slight leftside pyramidal signs, prompt peripheral reflexes.

Further MRI scan showed a progressed lesion, non surgically accessible, preferably evocating (also on spectroscopy basis) a demyelinating rather than glial process involving subcortical white matter .

EEGs showed continuous delta slowing, progressing along with gradual worsening of her neurological and mental status.

IVIg, Prednisolone, Ceftriaxone, Claritromycin, plasmapheresis gave no results. Extended search for viral and bacterial antibody titers, autoimmune diseases, thyroid hormones, metabolic disease proved negative. A very high Measles serum IgG (IgM negative) while negative in CSF with presence of oligoclonal bands.

Subsequent CT scan showed total white matter disruption.

A cerebral biopsy showed aggressive encephalitis with perivascular lymphocytic infiltrates and intracellular inclusion bodies.

The child got constantly worse and died within two months from admission.

PCR for Measles RNA was negative but neurohistochemistry analysis of bioptic tissue eventually proved positive for Measles virus confirming the diagnosis of Subacute Sclerosing Panencephalitis. Such disease is now rarely reported in developed countries so that an occasional case, exspecially with fulminating course and peculiar features, may create diagnostic pitfalls.

PeBenito R. Fulminating Subacute Sclerosing Panencephalitis. Clin Pediatr (Phila) 1997; 36(3):149

MEASLES OUTBREAK IN ROMA POPULATION IN SPAIN

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Background: Despite available safe and effective vaccines, measles continues to be a public health threat around the world, with a current re-emergence in Europe. Current data suggests that Roma population is disproportionately affected by measles and other vaccine-preventable diseases.

Aims: The objective of this study is to describe the epidemiological, demographic and clinical characteristics of the pediatric measles outbreak in a tertiary hospital in Madrid (Spain), focused on Roma children.

Methods: We prospectively included all suspected pediatric (0-14 years) measles cases seen in the pediatric emergency department between the October-1 to December-31, 2011. Laboratory confirmation was established with positive IgM and/or positive PCR in pharyngeal exudate. Epidemiological data was obtained through personal interviews and verified through official public health registries.

Results: Out of 39 suspected cases, 32 were laboratory-confirmed, 5 were non-measles confirmed, and 2 were probable cases.

Ethnics and demographics		Clinical		Microbiology	
Romani: n (%)	30 (88,2%)	Age (years): Median (range)	3.2 (0.25- 14.8)	Positive IgM	27/32 (84,4%)
Vaccination lost opportunities (%)	26/34 (76.5%)	Complications: n(%)	9 (26.5%)	Positive PCR (pharyngeal exudate)	5/5 (100%)

[Outbreak main characteristics]

None of the patients were vaccinated against measles and 26 of them (76.5%) were vaccination lost opportunities (children ≥ 12 months of age who should have received the first dose of measles vaccine according to the Spanish schedule).

Conclusions: The majority of cases were Roma children and the highest incidence was seen in patients over 12 months. The large proportion of vaccination lost opportunities seen in this study highlights the need for improvement in vaccination coverage among Roma population.

MENINGOCOCCAL C SEROPREVALENCE STUDY. VALENCIA, SPAIN

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Background and aims: Population-based seroprevalence studies provide important data on susceptible groups and the potential for future outbreaks or need of change in vaccination schedules.

MenC Vaccine programs: 1997 one dose of plain polysaccharide vaccine in subjects 18 months to 19 years (coverage 85%). In 2000, conjugated vaccines were scheduled at infants and a progressive catch up until 19 years (coverage over 90% in children less than 6 years, and decreased in older ages). In 2006 a booster dose was added to children born from 2005.

The objective of the study was to estimate the seroprotection level against meningococcal C on the population of Valencia by age group.

Methods: Seroprevalence study. Samples were obtained, after getting the informed consent. Exclusion criteria included: immunosuppression, severe medical illness, previous meningococcal disease and organ transplants.

The serum bactericidal activity (SBA) was measured using rabbit complement at the Spanish National reference laboratory for Meningococci. Seroprotection was considered with SBA titres equal or higher than 1:8.

Results: This preliminary report includes 417 subjects.

Of the 27 children aged 3-7, 81.5% (61.9-93.7%) were seropositive; 17.1% (7.2-32.1%) of the 41 children aged 8-12; 48.1% (34.3-62.2%) of the 54 adolescents 13-18 years; 32.8% (21.9-45.4%) of the 67 subjects 19-29 years and 9.21% (5.8-13.7%) of the 228 aged 30-65 not included in any vaccine program.

Conclusions: Seroprotection of subjects who were vaccinated in the first year of life is lower than those who received a booster or a catch up dose after 1 year of age.

EPIDEMIOLOGY OF THE HOSPITALIZATIONS DUE TO ROTAVIRUS INFECTION IN SPAIN (2005-2009)

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Background: This epidemiological survey was undertaken to estimate the burden of hospital admissions for rotavirus in children under 5 in Spain during a five year period (2005-2009). Rotavirus vaccines were introduced in Spain between late 2006 and early 2007. The vaccination coverage was 17% in 2007, 35% in 2008 and 38% in 2009.

Methods: Retrospective survey reviewing data of the National Spanish Surveillance System for Hospital Data. Codes for infectious gastroenteritis due to rotavirus were selected by using the 9th International Classification of Diseases. The annual rate of hospital admissions was calculated by using census-derived population estimates. Results were gathered by age.

Results: A total of 26,500 hospital discharges for acute gastroenteritis due to rotavirus were reported during the study period. The overall annual rate of hospitalization was 235 cases per 100,000. The higher hospitalization rate was observed among children < 12 months (692.3 per 100,000) and it decreased with increasing age to 17.5 per 100,000 in 4-year-old children. Among the study period the hospitalization rate decreased from 300.3 to 174.1 per 100,000. This decrease was more marked in children < 2 years of age. For children up to 12 months the hospitalization rate reduced from 906.1 to 477.1 per 100,000 and in the second year of life from 416.5 to 251.3 per 100,000.

Conclusions: Hospital burden of rotavirus infections has decreased in young children during the last years in Spain. These data can contribute to evaluate the impact in hospitalization rates of non-systematic use of rotavirus vaccine in Spain.

IMPLEMENTATION SURGICAL SAFETY CHECK-LIST IN A PAEDIATRIC HOSPITAL

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Background and aims: The surgical procedures are susceptible to many adverse events, including bleeding, wrong site surgery, wrong patient, failure in equipment and surgical site infection and even death. The WHO designed a program to avoid complications and deaths by improving perioperative care, denominated: Safe Surgery Saves Lives. The Hospital Pequeno Príncipe (HPP), a quaternary referral paediatric hospital, with an average of 1300 surgeries/month, started the implantation of checklist for safe surgery in 2010. The aim of this study is to evaluate the effectiveness of the implementation of the protocol of Safe Surgery after 1 year of activity.

Methods: Meetings were held with the Clinical Director, Infection Control Service, teams of Anesthesiology, Surgical and Nursing. It created a model checklist, conducted internal disclosure, dissemination posters in the operating room and monitoring the process in some surgeries.

Results: We analyzed 2.914 checklists from June/2010 to October/2011. The surgical specialties with higher rates of check-list were: Urology (41.7%) and Paediatric Surgery (36.2%). There was observed a reduction in the rate of surgical site infection in some specialties, as greater adherence to the checklist. Comparing the deaths before and after implementation of the protocol we observed reduction of 7%.

Conclusions: Preliminary data show a reduction in infection and mortality rates, however, adherence to the protocol needs to be improved.

COMPARATIVE STUDY OF CASES OF THE NOVEL INFLUENZA A(H1N1) DURING THE WINTRY PERIOD 2009-2010 AND 2010-2011

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Introduction: In 2009, the novel influenza virus A(H1N1) expanded rapidly, including the pediatric population. The virus caused pandemic in 2009-2010 while in 2010-2011 remained the prevailing virus of seasonal flu.

Aim: Comparative study of children affected by the influenza virus A(H1N1) during the pandemic period 2009-2010 and the post-pandemic 2010-2011.

Methods: The recorded cases were of children 30days-14years old with hyperpyrexia, prolonged fever and severe respiratory symptoms. They were distributed according to age, clinical presentations and seasonal prevalence. The virus was detected by molecular control(RT-PCR) of the pharyngeal swabs.

Results:

<i>Seasonal prevalence</i>	2009-2010	2010-2011	<i>Age</i>	2009-2010	2010-2011	<i>Clinical presentation</i>	2009-2010	2010-2011
September	2	-	< 1 year	2	2	Pneumonia	14	0
October	14	-				Sore throat	15	4
November	43	-	1-5 years	12	3	Gastroenteritis	3	0
December	21	-				Bronchitis	-	3
January	11	4	5-10 years	12	4	Benign Myositis	3	0
February	9	11				Encephalitis	2	1
March	-	0	10-14 years	8	1	Febrile Seizures	1	2
April	-	0						
<i>Specimen</i>	Total 238 Positive 38	Total 74 Positive 15	<i>Admission</i>	38	10	<i>Home</i>	66	5

[Results]

Conclusions: During 2009-2010 the epidemic wave began in July climaxing in November, while in 2010-2011 it began January and was culminated in February. The most frequent clinical presentations in both periods were from the respiratory system and the most serious from the CNS. The activity of influenza A(H1N1) amongst children during the 2010-2011 period was inferior than in 2009-2010.

CD64 AS A DIAGNOSTIC MARKER OF A SERIOUS BACTERIAL INFECTION IN CHILDREN WITH FEVER PRESENTING TO THE EMERGENCY DEPARTMENT

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Background and aims: Expression of neutrophil CD64 is elevated in presence of a bacterial infection. Studies on its diagnostic value show good results in adults, and diverse results in neonates and children admitted to the ICU with sepsis. One study at the emergency department (ED) showed a sensitivity of 94.7% and a specificity of 46.5%. We aimed to determine the diagnostic value of CD64 in children presenting with fever at the ED, to detect a serious bacterial infection (SBI).

Methods: We performed a prospective observational study including children aged 1 month-16 years with fever, who presented at the ED of a large teaching hospital in the Netherlands. Patients with chronic conditions or presenting with a viral upper airway infection, were excluded. CD64 was determined using flowcytometry. An SBI was determined by a combination of a positive culture, radiology or consensus diagnosis. Follow up was based on an inpatient visit or telephonic follow up.

Results: During 6 months in 2011 we included 208 children of whom CD64 was determined in 137 patients (66%). Twenty eight children (20.4%) had an SBI. The area under the curve of the receiver operator curve was 0.65 (95% CI 0.53-0.77). (Preliminary results)

Conclusion: The diagnostic value of CD64 as marker of a SBI at the emergency department was moderate. Further analysis will focus on the added value of CD64 in comparison to clinical signs and other diagnostic markers such as CRP and procalcitonin.

PASSIVE SMOKING AND BRONCHIOLITIS' MANIFESTATION

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Introduction and aim: According to WHO's data, children's 50% worldwide, are passively exposed to cigarette's smoke, while passive smoking's consequences are manifested by increased lower respiratory's system, morbidity. Possible relation infants' passive smoking (at least one parent smoker) and bronchiolitis' manifestation is investigated.

Methods: 267 infants with bronchiolitis' episodes from our institutes ER's data were recorded. Infants were divided into exposed and not to passive smoking, while the morbidity's frequency of each group was investigated. The research is retrospective and concerns years 2010-2011.

Results: The statistic results are presented at the following table:

	BRONCHIOLITIS	NO BRONCHIOLITIS	TOTAL
PASSIVE SMOKING	22 15,1%	124 84,9%	146 100,0%
NO PASSIVE SMOKING	8 6,6%	113 93,4%	121 100,0%
TOTAL	30 11,2%	237 88,8%	267 100,0%

[table 1]

Conclusions: There is correlation between bronchiolitis and passive smoking as babies exposed to passive smoking have higher morbidity's possibility than those that were no exposed (percentages 15,1% and 6,6% respectively).

PERTUSSIS SURVEILLANCE IN THE FRENCH HOSPITALS: RESULTS FROM 1996 TO 2010

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This study presents the 15 years results of the French paediatrician hospital-based network surveillance (Renacoq) set up in 1996 to monitor the trend of pertussis (whooping cough) in infants and the impact of vaccination strategies.

Microbiologists from 42 hospitals participating on a voluntary basis notify pertussis diagnosis and paediatricians fill in a questionnaire for infants less than 6 months of age that fulfil the microbiological, clinical or epidemiological case definition. The network covers about 30% of pertussis paediatric cases seen in French hospitals.

Since March 1996, the network has described 2070 cases of pertussis less than 6 months of age which represent around 150 cases annually. Four peaks occurred. The male-female ratio was 1.0. The estimated national average incidence rate for the 0-2 months-old children is 244/100 000, among which 16% were admitted in intensive care units. The average case fatality ratio was 1%. Vaccination status was confirmed through medical records for 87% of infants and 99% were not yet fully vaccinated. The source of contamination was identified for 54% of cases and was in majority the parents.

Renacoq data confirmed the risk for young children and the need of a timely pertussis vaccination. The proportion of parents as contaminators increased over the study period despite a vaccination recommendation for adults since 2004 whereas the proportion of siblings as contaminators decreased, probably as a consequence of the adolescent booster recommendations since 1998. Improving vaccination coverage in adults in contact with infants too young to be protected is needed.

BURDEN OF ROTAVIRUS GASTROENTERITIS AMONG CHILDREN AGED < 5 YEARS IN SAUDI ARABIA: A HOSPITAL-BASED PROSPECTIVE SURVEILLANCE (2007-2008)

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Background and aims: Globally, rotavirus (RV) is the leading cause of severe gastroenteritis (GE) in children aged < 5years. Recently published epidemiological data for RVGE in Saudi Arabia is limited. This active hospital-based prospective study aimed to estimate the disease burden of RVGE and dominant RV-serotypes in children aged < 5years in Saudi Arabia during a 12-month period.

Methods: 1007 children hospitalized due to GE were enrolled from four study centers in Saudi Arabia (February 2007-March 2008) using WHO's generic protocol for RVGE-based surveillance. Stool samples were tested for RV using ELISA and RV-positive samples were serotyped by PCR. Vesikari scale (severe RVGE=Vesikari score \geq 11) was used to assess the severity of RVGE.

Results: 970 children were included in the according-to-protocol analyses; 395 were RV-positive, 568 were RV-negative and 7 had an unknown RV status. The proportion of RVGE among GE hospitalizations was 40.7% (95%CI:37.6, 43.9). The percentage of RVGE hospitalizations seen in children aged < 2years was 83.0%. While RVGE occurred year-round, peak in RV cases was seen in June 2007 (57.1%). The most common RV types detected were G1P[8] (33.7%), G2P[4] (3.3%) and G9P[8] (0.5%). Severe RVGE episodes were reported in 88.1% of RV-positive and 79.6% of RV-negative children before hospitalization.

Conclusion: These results show that RV was responsible for a high proportion of GE hospitalizations in children aged < 5years. Routine RV vaccination in children may reduce RVGE-associated morbidity, mortality and disease burden in Saudi Arabia.

MEASLES OUTBREAKS IN THE CANARIES, IN THE CONTEXT OF ELIMINATION PLAN 2001-2011

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Background and aims: It presents an assessment of measles outbreaks in the Canaries verified after implementation of the Elimination Plan, to the present

Methods: We analyzed disease outbreaks reported to the Epidemiological Surveillance Network Canaria from 0 hours of January 1, 2001 at 24 am on December 31, 2011. The information analyzed was obtained from a specific epidemiological tab provided in the Plan.

Results: We checked five outbreaks, two in 2006, one in the island of Gran Canaria with 14 confirmed cases and a compatible, which could bind to 93% of patients, many of them isolated in measles virus Genotype B3 and another family in the island of Tenerife, with three brothers, German tourists, affected. Two others occurred in April 2010, one on the island of Fuerteventura with three cases linked epidemiologically and one in the family area of Lanzarote, with two cases (mother and child). The fifth outbreak was observed from March to July of 2012.en Tenerife. In the same were studied a total of 97 cases of which 47 were discarded (48%) and 46 (47%) cases were confirmed, of which 40 (87%) were serologically and 6 (13%) for link epidemiological. In 10 patients became virus isolation detected in all of them, measles virus genotype D

Conclusions: The low number of verified outbreak syndicates the correctness of and measures taken against this disease there, a good herd immunity in the Canaries.

WHOOPIING COUGH IN GRAN CANARIA HEALTH AREA, 1999-OCTOBER 2011. CASES INCREASE

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Background: We propose a descriptive epidemiological study on the evolution of pertussis in the island of Gran Canaria during the time period 1999-October 2011, analyzing in detail the increase in cases verified that year.

Methods: We studied the cases of laboratory-confirmed pertussis and reported in the Canary Island Network of Epidemiological Surveillance, from 0 hours of January 1, 1999, at 24 am on October 30 2011. The information was obtained through the established epidemiological tab for the declaration of a suspected case, and supplied by the Microbiological Information System Canarias (SIMCA) studied all the processes, reporting year.

Results: During 1999-2010 105 confirmed cases were reported (58% of all cases reported during the study period), while from January to October 2011 found 76 confirmed cases (42% of total cases reported in the period). Of these, 24% were under 1 year old, 18% between 1 and 4, and 21% between 5 and 9. 20% had between 10 and 29, and 17%, 30 and over. The number of processes started to increase in 2011, from epidemiological week 17. During the period 1999-2010, the bulk of reported cases occurred in 2006 with a total of 18 cases.

Conclusions: During 2011 there has been a significant increase in cases. We must emphasize the importance of monitoring of these processes, if necessary to establish new strategies for prevention.

SEASONAL VARIATION OF RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN HOSPITALISED WITH LOWER RESPIRATORY TRACT INFECTIONS IN MALTA

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Background and aims: The majority of children < 2 years of age hospitalised with an acute respiratory illness during winter and spring are infected with Respiratory Syncytial Virus (RSV). We studied the prevalence of RSV in children hospitalised with bronchiolitis or viral-induced wheeze in Malta, a small island in southern Europe.

Methods: A prospective observational study was performed in children < 24 months hospitalised with a lower respiratory-tract infection (LRTI) from October 2009 to September 2011. Nasopharyngeal swabs were used for specimen collection and RSV was cultured using a shell vial assay.

Results: From October 2009 to September 2010, 134 children were hospitalised with a LRTI. RSV was detected in 30 children (22%; mean age 8.2 months) hospitalised from November till May, with the highest number of RSV positive swabs (10/30; 33.3%) collected in April. Subsequently, from October 2010 to September 2011, 49 of the 144 children hospitalised with LRTI (34%; mean age 7.4 months) had positive RSV cultures from November through March. The peak of RSV cultures was recorded in January (16/49; 32.6%). A comparison of the two seasons showed that a significantly higher number of children with RSV disease were hospitalised from March to May 2009/10 (weeks 22 to 35; $p=0.04$) whilst in 2010/11 more children were hospitalised from December till February (weeks 10 to 21, $p=0.003$).

Conclusion: The RSV season in Malta varied significantly over 2 consecutive years. This differs from the consistent annual peak of RSV activity observed in Northern European countries with temperate climates.

TUBERCULOSIS IN CHILDREN: CHARACTERISTICS, INCIDENCE AND GEOGRAPHICAL DISTRIBUTION (2000-2010)

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Introduction: Cases of tuberculosis infection (TB) continues to increase in Portugal and represent a serious public health problem.

This study aims to characterize the TB cases, estimate the incidence and represent the geographical incidence of TB (2000 to 2010).

Methods: A cross-sectional and descriptive study of children (0-18 years) with TB was conducted.

Results: There were notified 28 cases of TB disease. Eighteen (64%) children lived in the county of Braga and the remaining 10 cases belonged to the counties of Vila Verde, Amares and Póvoa de Lanhoso. The median age was 13 [0-17] years-old. About 88% of children were born in Portugal and 6% in Romania and Brazil. Fifty percent of children had pulmonary TB and 25% pleural TB. The duration of treatment (median) was 6 months for pulmonary and lymph forms and 7 months for pleural TB.

An annual incidence of 4.9 cases/100 000 children was estimated. The highest notified incidence of tuberculosis was observed, in 2001, in the county of Póvoa de Lanhoso (30.1 cases/100000children). Higher incidence for children aged ≥ 15 years was observed (5.2 cases/100000children/year).

Geographic distribution showed that TB cases lives predominantly in urban and densely populated areas.

Discussion: In the past ten years there was a very slight decrease in the incidence of TB. The largest number of TB cases occur in adolescents aged between 15-18 years, probably reflecting the entry remains active in the community where the potential for transmission. It is important to improve the efficiency of TB control policies.

EPIDEMIOLOGICAL CHARACTERISTICS OF MENINGOCOCCAL DISEASE IN VOJVODINA (SERBIA) AT THE BEGINNING OF 21ST CENTURY (2001-2010)

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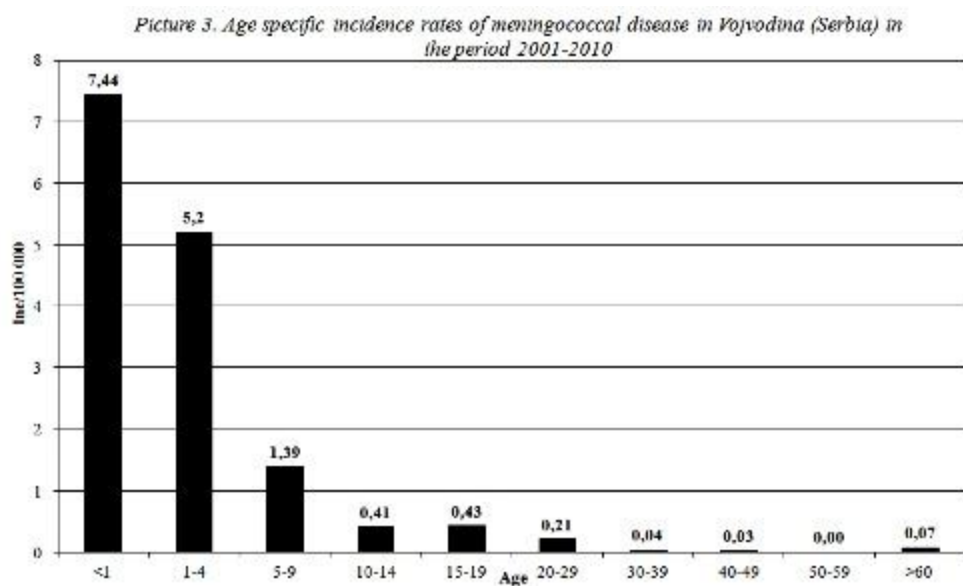
Background and aims: Meningococcal infections are ubiquitous. The aim of this study was to determine descriptive characteristics of meningococcal disease in Vojvodina (Serbia) in the period of 10 years.

Methods: The study included cases of meningococcal disease in the period from 2001-2010 in Vojvodina. We analyzed epidemiological characteristics of meningococcal disease chronologically, demographically and topographically.

Results: During the period of observation total of 89 cases were registered. Incidence rate of meningococcal disease ranged from 0.09 to 0.93 per 100.000 population with the decreasing trend. Only in one out of 45 municipalities incidence rate was higher than 2/100.000 inhabitants. Total of 31 (34.8%) cases were laboratory confirmed and serogroup B was detected in 29 (93.5%) and serogroup C in 2 (6.5%) cases.

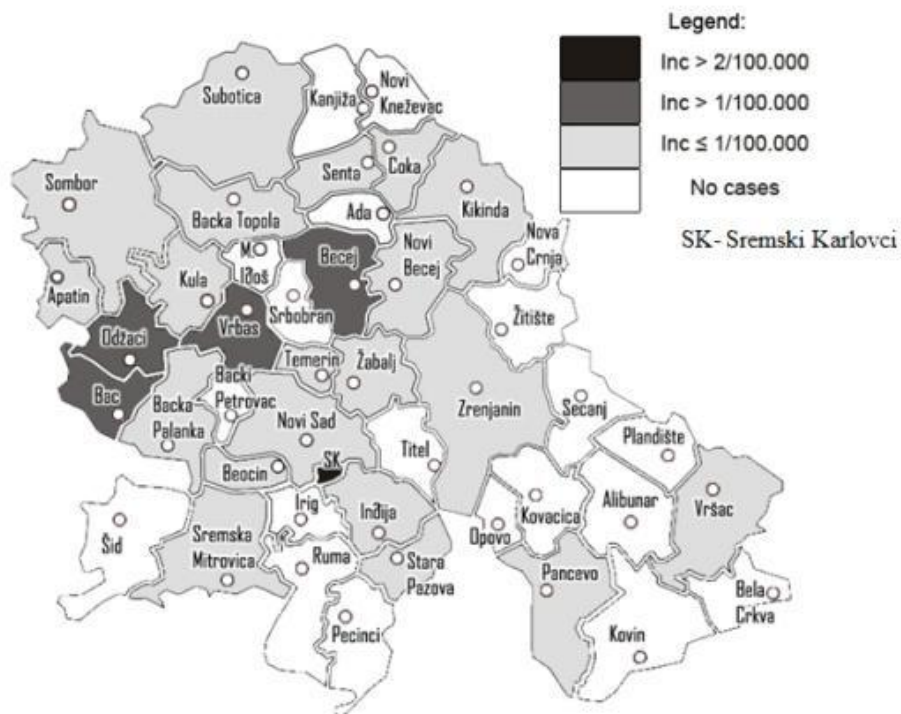
The largest number of cases was registered in children under 5 years of age (58.4%) and nearly $\frac{3}{4}$ (64/89) of cases were registered in the period from January to March. Meningitis and septicaemia were reported in about equal proportions (meningitis: 51.7%; septicaemia: 48.3%). Case fatality rate (CFR) was 14.6% (septicaemia 27.9%; meningitis 2.2%).

Conclusions: Meningococcal disease in Vojvodina represents an important clinical entity, especially if it occurs in the form of meningococcal sepsis. It is necessary to improve the disease surveillance in order to provide further relevant data on the incidence and distribution of serogroups in the population so that the prevention program and immunization strategy could be created.

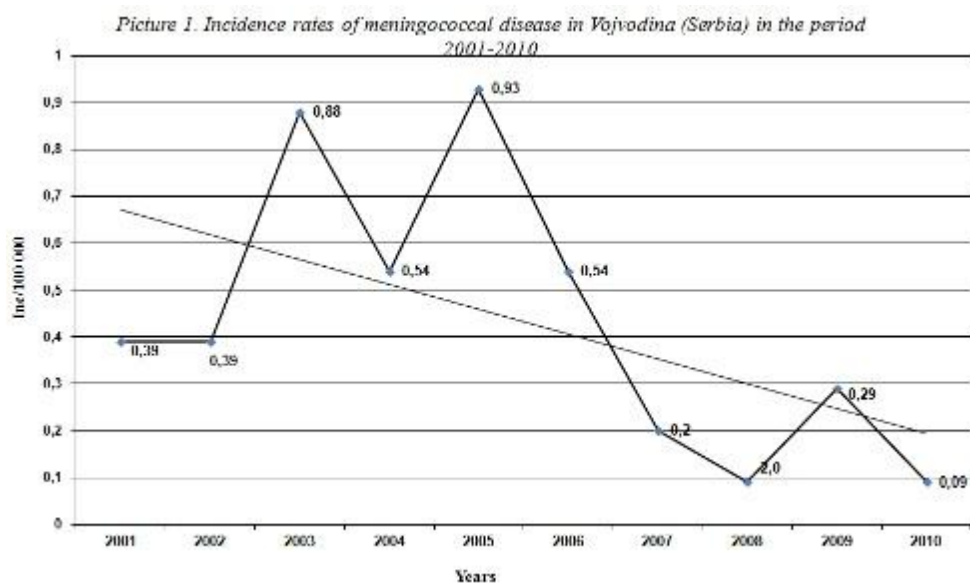


[age]

Picture 2. Topographic distribution per 100.000 population of total number of reported meningococcal disease cases in Vojvodina (Serbia) in the period 2001-2010



[topography]



[trend]

CLINICAL PREDICTION RULES FOR SERIOUS INFECTIONS: EXTERNAL VALIDATION AND POTENTIAL USE IN PRIMARY CARE

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Background and aim: Most clinical prediction rules (CPRs) for serious infections have been developed in secondary care. Only few have been externally validated, hampering broad implementation in practice. We aimed to externally validate CPRs for serious infections for use in primary care.

Methods: Observational study among children (< 16yrs) who consulted a General Practitioner Cooperative with fever between March 2008-February 2009. Clinical information was registered in a semi-structured way and manually recoded. CPRs for serious infections were selected from literature. The outcome measure was 'referral to emergency department' as proxy for 'serious infection'. Sensitivity, specificity (high vs. low risk; for CPR 2 risk-score was adjusted for low-prevalence setting) and discriminative ability (area under the receiver operating characteristic curve (AUC)) were calculated for each CPR.

(Preliminary) Results: We included 11,600 children, median age 2.2yrs (IQR 1.0-4.4), 6% were referred. CPR 1 and 2 performed less at external validation than at derivation. CPR 3 performed well, comparable with performance in the derivation setting (table).

CPR	Derivation-setting			Validation-setting		
	Sensitivity (%;(95%CI))	Specificity (%;(95%CI))	AUC (95%CI)	Sensitivity (%;(95%CI))	Specificity (%;(95%CI))	AUC (95%CI)
1. Van den Bruel et al. (Br.J.Gen.Pract.2007)	97 (83-100)	89 (88-90)	N/A	57 (53-60)	67 (66-68)	N/A
2. Brent et al. (Arch.Dis.Child.2011)	68 (55-79)	77 (75-79)	0.77 (0.71-0.83)	40 (36-44)	72 (71-73)	0.64 (0.62-0.67)
3. Bleeker et al. (Acta.Paed.2007)	76 (66-84)	63 (58-69)	0.69 (0.63-0.75)	40 (35-44)	94 (93-95)	0.71 (0.68-0.74)

[Performance of CPRs]

Conclusion: Our preliminary results show low to good validity of CPRs for serious infections in a large primary care population.

HOSPITAL ADMISSIONS FOR INFECTION IN INFANCY AND EARLY CHILDHOOD: A PROSPECTIVE STUDY

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Background: Infectious diseases are a leading cause of morbidity during childhood worldwide.

Aim: To prospectively investigate the incidence of hospital admissions for infections in infancy and early childhood and to define possible risk factors in Crete, Greece.

Methods: In a representative sample of 1,049 infants, 926 (88.3%) of infants were followed-up all during infancy and 590 (56.2%) during the first six years of life. Hospital admissions for infections, including acute otitis media (AOM), acute respiratory infection, gastroenteritis and urinary tract infection were recorded at 1, 3, 6, 9 and 12 months as well as 6 years of life.

Results: Hospital admission for infection was required for 14.5% of infants and 17.6% of children aged 1-6 years. Duration of exclusive breastfeeding (r_s -0.06), birth in winter (RR 0.33, 95% CI 0.20 to 0.55) and parental education years (r_s -0.14) were demonstrated to affect admissions for infections during infancy. Admissions for infection at the age of 1-6 years were related to non-Greek ethnicity (RR 2.25, 95% CI 1.13 to 4.49) and maternal perceived ill-health during pregnancy (RR 1.48, 95% CI 0.89-2.45). For admissions due to AOM in particular, parental smoking was found to be a significant risk factor ($r_s=0.086$).

Conclusions: This prospective study in a well-defined child population of adequate healthcare standards suggests that infections remain a leading cause for hospitalization in childhood. Factors associated with hospitalization for infection seem to differ between infants and toddlers.

MATERNAL PERCEIVED ILL HEALTH IN PREGNANCY AND RISK OF INFECTIONS IN THE OFFSPRING

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Background: Maternal ill health during pregnancy has been recently associated with increased prevalence of disease in the offspring.

Aim: To prospectively investigate the effect of maternal self-reported ill health in pregnancy on common infections in infancy and early childhood.

Methods: In a representative sample of 1,049 infants, born in Crete, Greece, 926 (88.3%) of infants were followed-up during infancy and 590 (56.2%) during the first six years of life. Ill health during pregnancy was estimated by maternal self-report at week 1 postpartum. Infectious episodes and hospital admissions for infections were recorded at 1, 3, 6, 9 and 12 months as well as 6 years of life.

Results: Infants born to mothers with perceived ill health in pregnancy were more prone than their peers to present with infections (RR 2.73, 95% CI 1.29-5.77), in particular AOM (RR 1.39, 95% CI 1.13-1.71), gastroenteritis (RR 1.28, 95% CI 1.08-1.52) and thrush (RR 1.80, 95% CI 1.25-2.57), and to be hospitalized for infection (RR 1.41, 95% CI 1.02-1.95). Furthermore, the maternal feeling of a complicated pregnancy was associated with more hospital admissions in early childhood (RR 1.48, 95% CI 0.89-2.45), in particular for gastroenteritis (RR 3.29, 95% CI 1.48-7.34). Logistic regression analysis including confounding factors confirmed the impact of maternal ill health on infectious episodes.

Conclusions: The maternal feeling of a complicated pregnancy seems to be related to higher morbidity from infections in the infant/toddler, regardless of the nature and the validity of maternal complaints.

CHILDHOOD DEATHS BEYOND THE NEONATAL PERIOD FROM INFECTIONS IN A TERTIARY HOSPITAL IN NORTH-EAST NIGERIA: A DECADE REVIEW

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Background and aims: Infection accounts for two - thirds of childhood deaths globally. 99% of these occur in developing countries. Millennium Development Goals 4 and 6 are aimed at reducing child mortality and combating malaria, AIDS and TB. This study reviews the contribution of infections to childhood deaths beyond the neonatal period.

Methods: Federal Medical Centre, Gombe is a tertiary facility that commenced services in May 2000. It serves Gombe State which has a Population of 2.3million. As part of an ongoing retrospective study of all children admitted and managed between May 2000 and May 2010 , Information including age, sex, diagnoses and outcome were analyzed.

Results: 6682 children ages 1-< 18 yr were admitted; 84.5% (5646/6682) were discharged, 1.6% (106/6682) left against medical advice, 2/6682 absconded, 0.6% (40/6682) were transferred. 13.3% (889/6682) died. Surgical patients constituted 10.6% (708/6682), and accounted for 8.3% (74/889) of deaths. 89% (5974/6682) were pediatric medical cases. Infections accounted for 32.3% (1932/5974) of admissions. 27 % (219/815) of medical deaths were attributable to infections. Malaria accounted for 34 % (76/219) of these deaths. 16 % (34/219) and 15 % (33/219) were due to septicemia and PAIDS respectively. Pneumonia, diarrhea and tuberculosis contributed to 13.2% (29/219), 9.6% (21/219) and 6% (13/219) of infectious disease deaths respectively. The 7th, 8th and 9th leading causes of death were UTI and its complications, tetanus and enteric fever, accounting for 4.6 % (10/219), 3.7 % (8/219) and 1.4 % (3/219) respectively.

Conclusion: Combating childhood infections remains a top priority in the tropics.

UNDER-FIVE MORTALITY: ARE INFECTIONS A MAJOR CONTRIBUTOR? A DECADE EXPERIENCE FROM A NORTH-EAST NIGERIAN TERTIARY HEALTH FACILITY

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Background and aims: Nigeria is a major contributor to under five mortality globally. 60% of under five mortality is contributed to by infections. Maternal and child health interventions have aimed at reversing these appalling trends. Early identification and appropriate treatment of infections is critical in child survival and development. This review describes the contribution of infections to under five deaths.

Methods: The North East sub-region of Nigeria has an estimated population of 36 million. The Federal Medical Centre Gombe, a 400 bed capacity hospital, is one of the two leading tertiary health Institutions in this sub-region. Clinical service provision commenced in May 2000. Records from case files including age, sex, diagnoses and outcome from inception were retrieved and analysed.

Results: 7,940 medical cases 0-< 18years were admitted between May 2000 and May 2010. 46.9%(3709/7940) were male and 42.6% (3395/7940) female. 33.1 %(2624/7940) were 0-5years. 13.5 %(1076/7940) died. Children aged 0-5years constituted 49%(531/1076) of paediatric medical deaths. 50.5% (268/531) of these under 5 deaths were due to infections. Neonatal infections, malaria and septicaemia accounted for 31% (83/268), 20.9% (59/268) and 14.9% (40/268) of infectious under 5 deaths respectively. 2/3rds of infectious under 5 deaths were attributable to the triad of neonatal infections, malaria and septicemia. 11.5%(31/268), 10.4%(28/268), 7.6%(20/263) and 3.8%(10/263) of infectious deaths resulted from AIDS, Pneumonia, diarrhoea disease and tuberculosis respectively.

Conclusion: Urgent Improvements in obstetric and newborn care, prevention of mother to child transmission of HIV/AIDS and early identification and prompt treatment of malaria, are needed to reduce child mortality.

AGE AND TEMPERATURE SPECIFIC RESPIRATORY CENTILES CAN PREDICT LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN

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Aim: We aimed to validate the ability of age-specific and temperature dependent centile charts of respiratory rate to predict lower respiratory tract infections (LRTIs).

Methods: Respiratory rate centile charts were derived using data from 1,555 children with fever attending the paediatric emergency department (PED) of the Erasmus MC - Sophia children's university hospital, the Netherlands, in 2006 and 2008. The predictive ability of the centile charts was validated in 671 febrile children at risk of LRTI who were recruited at the PED of the Erasmus MC - Sophia (n=311, 2003 - 2005) and at the paediatric assessment unit of the University Hospitals of Coventry and Warwickshire (n=360, 2005 - 2006). We calculated diagnostic performance measures of children with 'definite bacterial LRTI', 'probable viral LRTI' and 'other infections'. We compared the diagnostic performance of the centile charts with the APLS threshold values and the continuous reference values as described by Fleming et al.

Results: The age and temperature dependent 97th centile cut-offs were more useful to rule in LRTI (specificity 0.94 (95% confidence interval (CI): 0.92-0.96), positive likelihood ratio (LR+) 3.66 (2.34-5.73)) than APLS thresholds (specificity 0.53 (0.48-0.57), LR+ 1.59 (1.41-1.80)) and the 99th centile of the reference values of Fleming et al. (specificity 0.78 (0.75-0.82), LR+ 2.13 (1.69-2.68)). None were able to differentiate between definite bacterial and probable viral LRTI.

Conclusion: The 97th centile cut-offs of the age-specific and temperature dependent centile charts outperformed existing respiratory rate thresholds to rule in presence of LRTI.

A REVIEW OF THE MEASLES OUTBREAK IN GREECE FOR THE YEARS 2010-2011

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Background: Measles is a highly contagious disease that can cause serious complications and even death. The aim was to describe the characteristics of the recent measles outbreak in Greece between January 2010-July 2011.

Methods: Measles' cases were notified through the mandatory notification system; data were collected and analyzed in the Hellenic Centre of Diseases Control and Prevention (HCDCP). Genotyping was performed by the Hellenic Pasteur Institute.

Results: Totally, 189 cases (149 in 2010; 40 in 2011; 126 laboratory confirmed) were notified to HCDCP corresponding to an annual incidence of 1.32/100,000 population for 2010 and 0.35 for 2011. The outbreak onset occurred in individuals of Bulgarian nationality who represented the majority of cases in the first 7 weeks. During the outbreak evolution, cases in Greek population were reported (mainly Greek Roma children < 14 years after the 21st week) and apparently the spreading concerned indigenous population with low vaccination coverage (85.4% unvaccinated). In 2011, after a 5 week's interval, the outbreak continued principally in Greek nationals who didn't belong to a specific subpopulation group (80%), aged ≥20 years (84.4%) with low vaccination coverage (70.4% unvaccinated). Measles' virus genotyping in pharyngeal swab and urine samples revealed 27 D4 and 1 D6.

Conclusions: Despite the existence of effective vaccines, measles outbreaks continue to occur throughout Europe. This outbreak highlights the need to ensure high vaccination coverage with 2 doses of a measles vaccine in children, adolescents and young adults taking special care in reducing pockets of undervaccinated populations as the Roma minority.

EPIDEMIOLOGY OF LOWER RESPIRATORY TRACT (LRT) ISOLATES OBTAINED FROM INTUBATED CHILDREN IN A PEDIATRIC INTENSIVE CARE UNIT (PICU)

E. Iosifidis¹, S. Stambouli², K. Skoumis², E. Gianniou², G. Kythreotou³, E. Siaka³, M. Sdougka², E. Roidides¹

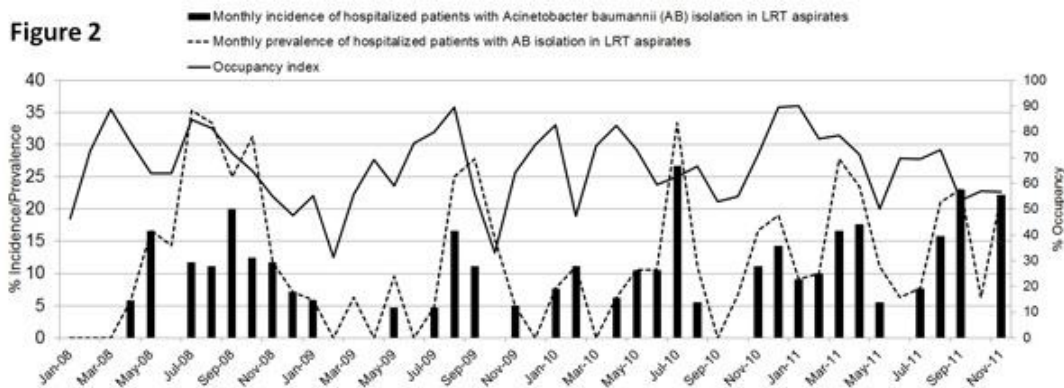
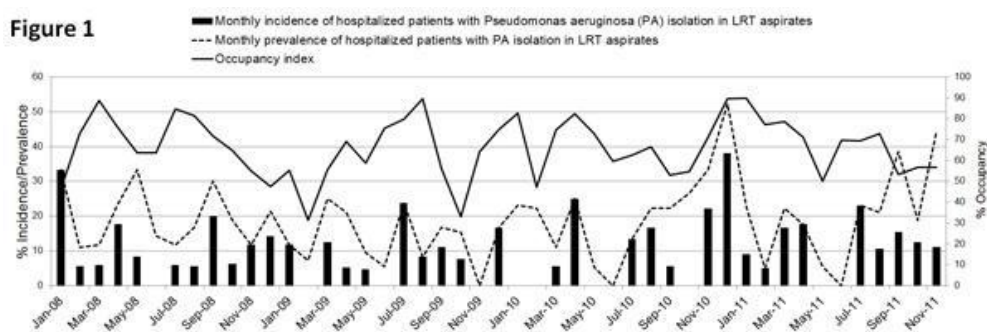
¹3rd Pediatric Department, Aristoteles University of Thessaloniki, ²Pediatric Intensive Care Unit, Hippokration General Hospital, ³Microbiology Department, Hippokration Hospital, Thessaloniki, Greece

Background and aims: LRT infections are common in PICU. We studied the epidemiology of LRT pathogens isolated from patients hospitalized in a PICU.

Methods: A retrospective analysis of LRT specimens was conducted in an 8-bed polyvalent PICU of a general university hospital from 2008 to 2011. LRT specimens were collected from intubated children on admission and thereafter routinely twice weekly or on suspicion of LRT infection.

Results: Among 424 intubated children, 144 (34%) had a positive LRT culture at least once. Of 2246 LRT specimens collected, 624 (28%) were positive for *Pseudomonas aeruginosa* (PA, 59%), *Acinetobacter baumannii* (AB, 28%), *Stenotrophomonas maltophilia* (5%), *Staphylococcus aureus* (3%) and other bacteria (5%). Isolation of PA and AB from LRT on a monthly base is shown in figures 1 and 2, respectively. Monthly incidences of PA and BA correlated to monthly prevalences of PA ($r=0.6$, $p<0.0001$) and BA ($r=0.83$, $p<0.0001$), respectively. Table 1 depicts antimicrobial resistance rates of PA and BA.

Conclusion: High incidence of LRT colonization/infection was found. Non-fermenters predominate, and high level of antimicrobial resistance is of concern.



Antimicrobial	Resistance rates (%) of <i>Pseudomonas aeruginosa</i>				Resistance rates (%) of <i>Acinetobacter baumannii</i>			
	2008	2009	2010	2011	2008	2009	2010	2011
Imipenem	54	34	49	42	96	95	97	77
Ceftazidime	54	50	34	13	100	100	93	94
Piperacillin/tazobactam	11	56	23	13	100	100	93	94

[Table 1]

FEVER WITHOUT SOURCE: AN CLINICO-ETIOLOGICAL PROFILEB.S. Sharma¹, **S.L. Kumhar**¹, P. Sharma², M. Gupta³*¹Pediatrics, SMS Medical College, ²Pediatrics, Fortis Escorts Hospital, ³Pediatrics, MGNIMS, Jaipur, India*

Fever without source accounts for 20% of fever patients in children. To determine the causes of FWS in our setting this descriptive type of observational study was conducted on 250 patients of FWS aged 1 month to 36 months in Department of Pediatrics, S.M.S. Medical College, Jaipur - INDIA) between December 2010 to November 2011. The study classifies the risk of serious bacterial infections (SBI) according to the presence or absence of toxemia, age and temperature. In our study, 58(23.2%) cases [out of 250] were diagnosed as having a bacterial infection out of them 34(58.62%) were enteric fever, 17(29.31%) UTI (E. coli), 2(3.44%) cons, 1(1.72%) enterobactor, 1(1.72%) E. coli, 1(1.72%) COPS septicemia ,1(1.72%) meningitis and 1(1.72%) pulmonary TB. Nonbacterial causes were also found in significant number in form of malaria in 26 cases (10.40%), dengue fever in 18 cases (7.20%), and other probable viral fever in 148 cases (59.20%). This is the first study done to determine the causes of FWS in India. A sizeable number of malaria and dengue as cause of FWS was a unique observation in this study which was not reported earlier in any other study worldwide. The results of this study can serve as a reference data base which can be extrapolated on children with fever without source in similar epidemiological settings.

REASONS FOR VISITING THE PAEDIATRICIAN IN THE HEALTH CENTRE OF AN ISOLATED GREEK ISLAND

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Background and aims: Alonnisos is an isolated island of Sporades in Greece with approximately 300 children population and no paediatrician until recently. The aim of the study was to record the reasons why children visit the paediatrician.

Methods: From 12/7/2010 to 14/12/2010 all reasons for visiting the paediatrician were recorded.

Results: 356 children were examined (180 girls), most of them Greek (58,74%). Most children came for a scheduled visit (vaccination 40,7%, developmental control 8,2%, school health card 4,37%). The reasons for the visit that parents recorded as most important were: cough (14,5%), fever(6%), exanthema(6%), nasal congestion (3,55%), earache (3,55%) etc. Most common symptoms found when the children were examined were: fever (20,12%), cough (19,12%), nasal congestion (10,38%), exanthema (6,28%) and earache (3,82%). The most common diagnosis in children with acute illness was virus infection (16,96%).

Conclusions: Children are the healthiest part of society. The most common reasons for children to visit their doctor, also in Alonnisos, are non pathological reasons and have to do with prevention (immunizations, developmental control). It is important that doctors who are in charge for children to be adequately educated and informed. Especially in isolated areas, such as Greek islands, where the distance from hospitals is long, it is important to plan educational programs regarding paediatric patients for doctors who work in such areas.

SEROPREVALENCE AND RISK FACTORS OF CYTOMEGALOVIRUS INFECTION IN THE NETHERLANDS

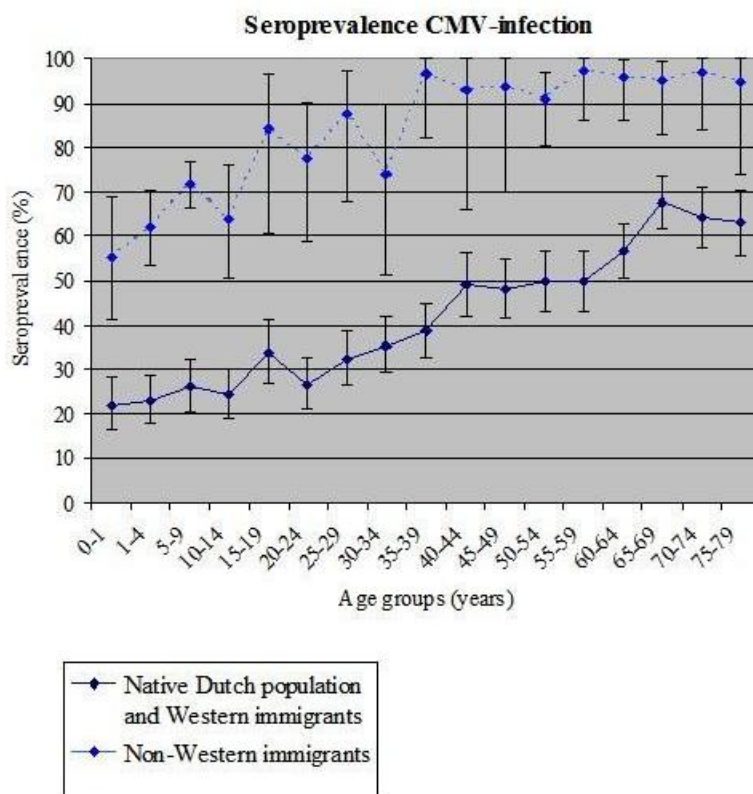
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Background and aims: Cytomegalovirus (CMV) is an endemic virus which seldom causes clinical symptoms in healthy individuals. However, in congenital CMV infection symptoms occur at birth in about 12% and long term sequelae is seen in approximately 20%. The risk of congenital CMV infection is related to the seroprevalence in future mothers. The aim of this study was to determine the seroprevalence and risk factors of CMV infection in the Netherlands.

Methods: A total of 4774 sera from individuals, participating in a population-based serum bank (PIENTER-2, 2006-2007), were tested for CMV-specific IgG antibodies using ELISA (ETI-CYTOK-G PLUS DiaSorin, Saluggia, Italy). CMV seroprevalence rates for the overall population and several subgroups were assessed using SAS.

Results: The overall seroprevalence of CMV in the general population (0-79 year) was 49%. Among native Dutch women of childbearing age (19-44 years) the seroprevalence increased from 30% to 50%. Groups with low income, low education level and non-western immigrants had higher seroprevalence.



[Seroprevalence of CMV-infection]

Conclusions: Almost half of the population showed serological evidence of prior CMV infection. In accordance with the literature CMV infection is more prevalent among non-Western immigrants and groups with lower socio-economic status. The increase of seroprevalence in women of childbearing age showed that primary infections occur frequently during this period with a risk of vertical transmission and associated sequelae for the unborn child.

ASSOCIATION BETWEEN VARIATIONS IN THE EPIDEMIOLOGY OF VARICELLA INFECTION AND CLIMATE CHANGE IN A TEMPERATE REGION

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Background and aims: The transmission rate of air-borne infectious diseases may vary secondary to climate conditions. The study assessed time trends in the seasonality of varicella infection, in relation to meteorological and biometeorological parameters, in a temperate region prior to the implementation of universal vaccination.

Methods: A retrospective cohort study was conducted among all paediatric and adolescent varicella patients (N=2366) hospitalized at the "Aghia Sophia" Children's Hospital during 1982-2003 in Athens, Greece. Date of infection was computed based on hospital admission date. Seasonal and monthly trends in the epidemiology of varicella infection were assessed with the chi-square test for linear trend. The correlation between the frequency of varicella patients and meteorological-biometeorological parameters was examined by the application of Generalized Linear Models with Poisson distribution.

Results: Prior to the implementation of universal vaccination, the incidence of varicella infection increased during summer ($p=0.001$) and decreased during autumn ($p=0.020$). Specifically, varicella incidence rates increased during June ($p<0.0001$) and decreased during October ($p=0.043$). No changes were observed during the spring and winter seasons. The occurrence of varicella infection rates was inversely associated with air temperature and relative humidity, and positively associated with wind speed. Furthermore, the probability of varicella infection was inversely associated with the Discomfort Index values, and positively associated with Cooling Power.

Conclusions: Varicella infection rates have increased during summer and decreased during autumn in the examined temperate region. Changes in varicella infection rates are associated with climatic factors, including air temperature, relative humidity, and wind speed.

COLONIZATION OF CHILDREN WITH PSYCHOMOTOR RETARDATION ON ADMISSION TO PEDIATRIC INTENSIVE CARE UNIT (PICU) AND ITS EFFECT ON HOSPITALISATION

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Aim: Patients with psychomotor retardation often require hospitalization in PICU. The aim of this study is to investigate the spectrum of preexisting colonization and the relationship with invasive infections and consecutive mortality in these patients.

Methods: A retrospective analysis of 28 patients with psychomotor retardation being admitted in PICU from 2009-2011 was performed. Demographic data, bronchial, pharyngeal and gastric swab samples on admission, data regarding developed infections and calculation of Pediatric Risk of Mortality (PRISM) score were analysed.

Results: Twenty eight patients, 17 Females and 5 Males with a mean age 4.53 years were studied. Colonization on admission was detected in 21 out of 28 patients (75%). The lower airways were colonized in 6 (21.5%) children whereas pharynx and stomach were colonized in 15 (53.55%) and 9 (32.1%) respectively. *Pseudomonas aeruginosa* was the predominant colonizer followed by *Candida albicans*, *Acinetobacter* and *Klebsiella* spp. Hospitalization >48 h prior to PICU admission and existed tracheostomy on admission did not seem to increase colonization (86.67% vs 61.54% $p=0.125$) and (25% vs 23.8% $p=0.96$) respectively. Twelve episodes of nosocomial infection were recorded, 5 of which (23.8%) were preceded by colonization. Prior colonization was not associated with the development of nosocomial infections (23.81% vs 28.57% $p=0.80$). Two deaths were recorded in which the one was associated with infection related to colonization. PRISM score was high in both cases.

Conclusions: Multisite colonisation of patients with psychomotor retardation is common on admission to PICU. However we did not conclude to have any impact on further hospitalisation.

CANDIDA COLONIZATION IN PEDIATRIC INTENSIVE CARE UNIT (PICU) SETTING: A 3-YEAR RETROSPECTIVE STUDY

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Background and aims: Candida infections are an emerging problem in PICU. Candida colonization is frequent in PICU patients and is related to the development of invasive candidiasis. The aim of our study is to record the patterns of candida colonization in PICU patients over a 3-year period.

Methods: Retrospective study of patients colonized or infected with candida spp in a multidisciplinary 8 bed PICU was conducted from 2009 to 2011. Candida isolates were retrieved from surveillance cultures (gastric and bronchial aspirates, urine, pharyngeal and anal swabs obtained twice weekly) and clinical samples including blood. Demographic and clinical data were collected from medical records.

Results: Over the period 2009-2011, 137 patients over 400 admissions (34,2%) were colonized with candida spp. Single site colonization was observed in 82 (59.8%) children, 2-site colonization in 32 (23.3%), 3-site colonization in 18 (13.1%) and 4-site colonization in 4(2.9%). Candidemia was recorded in 4 patients (2.9%). Gastrointestinal colonization was noted in the majority of patients (117/137) and was a constant and often presenting feature in multi-site colonization. PICU length of stay was significantly increased in patients colonized in >1 site ($p=0.0057$). Death occurred in 26 (18,9%) patients and did not correlate with the degree of colonization. All patients who died and most of the patients who survived (69/111) were colonized on their last day in PICU.

Conclusions: Candida colonization is persistent in PICU patients and most often arises from the gastrointestinal tract. Multi-site colonization correlates with increasing PICU stay.

THE DIAGNOSTIC VALUE OF CT-GUIDED BIOPSY IN PULMONARY INVASIVE FUNGAL INFECTIONS

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Background and aims: Despite the introduction of molecular tools such as the galactomannan enzyme immunoassay and polymerase chain reaction, diagnosis of invasive pulmonary fungal infections still remains a challenge. CT-guided percutaneous biopsy aims to improve diagnosis and allows obtaining a fungal culture, species identification and possible in vitro susceptibility.

Methods: Retrospective analysis of specimens obtained by CT-guided biopsy from evaluable high risk childhood hematologic patients with hematologic malignancies or solid tumors.

Results: In 401 patients, 16 CT-guided biopsies were carried out, because of suspected pulmonary fungal infection, according to the EORTC criteria. 81.25% were confirmed as fungal infection, in 12.5% bronchiolitis obliterans organizing pneumonia was diagnosed and in 6.25% suspicious diagnosis was ruled out. Case-fatality rates range from 14% for high-risk ALL to 20% for AML patients. Fungal culture revealed in 76.9% hyphae, including 15.3% with unseptated hyphae, 7.7% mixed hyphae plus yeast cells and 1 patient with *Saccharomyces Cervisiae*. After onset of fever biopsy was performed after 98.2 hours \pm 12.1 (average \pm SD), results were available within 12 hours, and in 46.2% patients therapy was changed after fungal culture.

Conclusion: Even in the era of advanced immunological and molecular fungal testing, lung biopsy remains a useful diagnostic tool. In nearly 50% of the patients CT-guided biopsy resulted in changes of antifungal treatment.

SPECIES BASED COMPARISON OF OUTCOMES OF INVASIVE CANDIDA INFECTIONS AMONG HOSPITALISED PAEDIATRIC PATIENTS OVER AN 8 YEAR PERIOD**J. Hawkshead III***Epidemiology, Tulane University, New Orleans, LA, USA*

Background and aims: Invasive fungal infections such as *Candida* in paediatric patients are associated with worse clinical outcomes and increased costs, yet such infections are not well represented in the current literature. Numerous *Candida* species can infect pediatric patients during the course of hospitalisation, but it is not known any particular species is associated with worse clinical outcome than others. This study aims to more clearly define which *Candida* species, if any, causes a more severe illness than others.

Methods: Inpatient records from 113 patients aged 0-18 years seen at a U.S. urban tertiary care pediatric hospital with laboratory confirmed invasive *Candida* infection over the 2003-2010 time period were reviewed for demographic and clinical data. Data were analyzed to determine whether significant ($p \leq 0.05$) differences existed among the species groups in terms of patients' lengths of stay, duration of antifungal therapy, need for ICU admission and ventilator support, deep organ involvement, hypotension, and mortality within 30 days of diagnosis of candidemia.

Results: Hospitalised paediatric patients aged 0-18 years showed significant differences in the number of antifungals prescribed ($p = 0.03$), and total antifungal days ($p = 0.04$), with *C. parapsilosis* having the highest median values. Among patients < 1 year of age, *C. albicans* was associated with a higher incidence of mortality ($p = 0.05$).

Conclusions: Overall, differences in clinical measures of disease severity associated with different *Candida* species appear slight. Significant differences may exist in the length of treatment and mortality associated with certain species.

CANDIDA HAEMULONII ISOLATED FROM BLOOD CULTURES OF THREE PATIENTS AT A PEDIATRIC HOSPITAL IN CURITIBA

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Isolation and identification of yeasts not usually found in blood cultures are a relevant and increasing preoccupation, especially in pediatric and immunocompromised patients. Some yeasts species are rare and may be resistant to conventional antifungal treatments and therefore are a concern also in ICUs.

These were the first cases of *Candida haemulonii* isolated in the Hospital Pequeno Príncipe of Curitiba between 2009 and 2010. Two patients had onco-hematological diseases (a 16 aged patient with acute myeloid leukemia and a 9 years old patient with Ewing's sarcoma). The third child has Down syndrome with heart disease and was 1.7 years old. The isolates were tested for susceptibility to: amphotericinB, fluconazole, miconazole, and anidulafungin, following the guidelines of the CLSI M27-A3 2008. The minimum inhibitory concentration (MIC) of the three isolates was 1.0 µg/mL for amphotericinB, ranged from 16-32 for Fluconazol, and 2.5 for miconazole and anidulafungin. Despite these in vitro results, two patients improved after treatment with liposomal amphotericinB and the third without antifungal treatment (considered a transient fungemia).

The phenotypic identification was not sufficient to identify the isolates; thereby two molecular methods were performed: Polymerase Chain Reaction (PCR) followed by sequencing and mass spectrometry Maldi-Tof. Both were similar to identification of *Candida haemulonii*.

This was the first isolation of this yeast species in pediatric patients with resistance to echinocandins and fluconazole.

TINEA CAPITIS SUPERINFECTED WITH CLOSTRIDIUM PERFRINGENS IN A 3 YEARS OLD CHILD

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A 3 years old Nigerian child was examined at our Emergency Department for a 8 weeks history of erythematous ovalar-shaped lesion, parieto-occipital left sided, with hair loss and serous secretion and several smaller lesions in occipital area, associated with regional adenopathies. Topical antifungal and antibiotic treatment was applied for superinfected tinea capitis without appreciating any clinical improvement.



[Tinea Capitis]

His older sister had similar lesions on the arms and was in treatment for tinea corporis.

A dermatological examination, a scalp skin and a hair sample for microbiological study were obtained. The first examination did not show the presence of septal hyphae and formation of arthrospores. The child was discharged only with topical antibiotic therapy. After a few days, due to definitive microbiological study (*Clostridium Perfringens* and *Trichophyton mentagrophytes*) and no evident clinical improvement, an hospital treatment was initiated with systemic griseofulvin (oral), penicillin (intravenous) and topical with fusidic acid.

A progressive improvement of the conditions of the scalp's lesions with disappearance of erythema and of the serous secretion and reduction of the occipital adenopathies was observed. The patient was discharged after 8 days with a close clinical control.

Tinea superinfections are often polymicrobial and broader antibiotic cover may be necessary.

This case highlights how tinea capitis could create a predisposing condition for the further infection of *Clostridium*. Superinfection of tinea capitis in children for *Clostridium* is uncommon, to our knowledge no other cases are described in literature.

FUNGAL INFECTION IN CHILDREN**H. Idrees**¹, M. Sharif², N. Sarkar³*¹Punjab Group of Colleges, Lahore, ²Chakwal College for Girls, Chakwal, ³Fatima Jinnah College, Lahore, Pakistan*

Aim: Fungal respiratory disease is associated with a high mortality in immunocompromised patients. This review aims to describe the recent advances in the aetiology, clinical presentation, diagnosis and management of fungal respiratory disease in immunocompromised patients.

Background: Fungal respiratory infection cause significant morbidity, mortality, and increased cost of care in patients. In the present study 200 children suspected with respiratory fungal infection were included.

Method: Bronchial alveolar lavage, bronchial brushing, and biopsies from chest wall, lungs and sinuses were studied. Diagnosis was made through direct fungal observation or culture.

Results: Of 200 suspected patients, 98 revealed to be infected by clinical examination. Fungi were more commonly found (54.3%) in subjects with at least one predisposing factor for fungal infection. Isolated organisms were candida albicans, candida spp., aspergillus fumigatus, aspergillus flavus, aspergillus niger, aspergillus spp. fusarium spp., and actinomyces spp.

Conclusion: Pulmonary fungal infection of community-acquired origins is becoming a serious problem. It should be taken into consideration for differential diagnosis of community-acquired pneumonia and other fungal diseases. Prevention is dependent on judicious use of antibiotics, vigorous treatment of wounds and by preventing environmental transmission.

POSACONAZOLE AS RESCUE THERAPY IN AFRICAN HISTOPLASMOSIS**D. Gonçalves, C. Ferraz, L. Vaz***Hospital São João, Porto, Portugal*

African histoplasmosis (AH) is a granulomatous disease caused by the dimorphic fungus *Histoplasma capsulatum*, var. *duboisii*. All reported cases of AH in Europe are imported from endemic areas. Its main clinical features include involvement of the skin, subcutaneous tissues, lymph nodes and bones. Treatment is usually extrapolated from american guidelines for classical histoplasmosis, and includes 2-4 weeks of amphotericin B followed by a step-down maintenance therapy with itraconazole for 12 months. Pediatric usage of posaconazole, an oral second generation azole, remains off-label, but recent surveys show that it's safe and well tolerated in children 3-17 years old.

We report a case of disseminated AH in a 12-year-old boy from Guinea-Bissau. The patient, HIV-seronegative and not otherwise immunocompromised, presented with large cervical, axillary and inguinal adenopathies with fistulas discharging a yellowish pus. Direct examination of biopsy tissue showed numerous specimens of *Histoplasma capsulatum* var. *duboisii*. Therapy with amphotericin B and itraconazole led to a progressive clinical deterioration. After approval by our hospital's ethics committee, posaconazole rescue therapy was started. A dramatic and lasting improvement was observed. At day 127 of therapy, complete cicatrization of all skin lesions was achieved. He completed 12 months of therapy with posaconazole. No relapse was noted during or 3 months after treatment.

We report that posaconazole may be a safe and efficacious drug in the salvage management of disseminated AH, either in patients with disease refractory to conventional anti-fungal therapy, or patients whose serious adverse effects of first line drugs preclude its use.

OCULAR MANIFESTATIONS OF CANDIDEMIA IN A PEDIATRIC POPULATION

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Background: *Candida* spp. are among the most frequent causes of blood stream infections and can often disseminate resulting in ocular disease and vision loss. There is a paucity of data regarding the incidence of ocular involvement in children. The aim of this study was to determine the frequency of ophthalmologic findings in children with candidemia.

Methods: We conducted a retrospective cohort study of children with candidemia from 2000 - 2009. Ophthalmology notes were reviewed. Chorioretinitis was defined as disease of the choroid or retina; endophthalmitis as disease extending to the vitreous. The analysis was restricted to patients who survived 7 days after infection diagnosis.

Results: A total of 349 children with candidemia were included. The median age was 5.7 years (IQR 0, 18.3 years). 254 (72.8%) had an ophthalmologic exam. 8 patients (2.3%), including one neonate, had ocular involvement. 4 (1.1%) had chorioretinitis and 4 (1.1%) had endophthalmitis. Of the patients with ocular involvement, 4 had *C. albicans*, 2 *C. tropicalis*, and 1 each had *C. parapsilosis* and *C. glabrata*. 1 patient diagnosed with endophthalmitis had a vitreous biopsy and culture which showed no evidence of fungus. Of the 8 patients, ocular disease resulted in retinal detachment in 2 patients and corneal perforation in 1 patient.

Conclusions: This study found that ocular candidiasis is an uncommon but serious sight-threatening complication in pediatric patients with candidemia. Future studies need to address risk factors for ocular disease in order to identify patients who should be screened.

MULTIPLE ANGIO-INVASIVE RHIZOPUS INFECTION IN A CHILD**F.-L. Huang**, P.-Y. Chen, T.-K. Chang*Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan R.O.C.*

Introduction: Zygomycosis is a rare, angiotropic infection caused by fungi in the class *Zygomycetes* of the order *Mucorales*. Herein, we report an acute myeloid leukemia case suffered from multiple vessels occlusion by *Rhizopus spp.*

Case presentation: This 7 m/o girl was a victim of AML. Chemotherapy with idarubicin and ara-c were given. Neutropenic fever developed after chemotherapy. Progressive poor activity, abdomen distension and vomiting were noted in the same time. Abdominal CT showed massive ascites, crowding of bowel loop over central portion of the abdomen. So, she received totally abdominal surgery twice and the operation found gangrene change of proximal jejunum and ischemia of splenic flexure of colon. The pathology report of intestinal specimens showed fungal infection of fungal thrombosis and hemorrhagic infarction. Mould grew progressively from operation wound and it was identified as *Rhinopus spp.* Persistent hypertension was found after surgery. Due to suspicious renal artery thrombosis, we arranged multidetector-row computed tomography for her abdominal vascular survey which showed total occlusion at left renal artery, superior mesenteric artery and splenic artery with infarction of left kidney and spleen. Multiple progressive small nodules were noted over scalp, trunk and limbs and hyperleukocytosis with blasts over peripheral blood smear were also found. She died with progressive change of leukemia and invasive fungal infection although received liposomal amphotericin-B treatment.

Conclusion: Zygomycosis is a life-threatening infection in children with leukemia in the neutropenia status. The *rhinopus spp* can cause multiple angio-invasive infection and early diagnosis, aggressive surgery and adequate treatment were suggested.

ONYCHOMYCOSIS BY *CANDIDA PARAPSILOSIS* IN A YOUNG SWIMMER CHILD

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Background: Among nail disorders in childhood Onychomycosis is one of the most common. It affects especially adolescent males and scholar aged children and is thought to be extremely rare in children younger than two years old. The prevalence of Onychomycosis is nowadays increasing in adults and is expected to rise in children also.

Case: The parents of a healthy 18-months-old child were concern because of his nails aspect. He used to go to swim twice a week in the previous months. He presented with moderate nail yellowish, brownish discoloration, subtle subungual hyperkeratosis, onycholysis and nail dystrophy, involving the first toenail in both feet. *Candida parapsilosis* was cultured from the samples collected from the nails affected. Treatment was initiated with ciclopirox 8% solution. To asses risk factors blood analysis was preformed, including glucose and VIH screening; results were normal and negative. After treatment, nails recovered properly.

Discussion: Onychomycosis accounts for 50% of nails disorders with a prevalence of 0.2-2.6 % in children. The ratio male/female is 2.2/1. Onychomycosis often affects older people. It has been reported recently an increasing in its frequency in all ages, including the pediatric group. Younger children with Onychomycosis are being reported nowadays, including newborns. Onychomycosis is due to dermatophytes, yeast and molds. *Candida parapsilosis* has been reported as a new emergent fungal pathogen. Whenever Onychomycosis is caused by this fungal agent, it is associated with large time of immersion of fingers or toes in water and with distal nail disease.

NEONATAL INVASIVE FUNGAL INFECTIONS IN ENGLAND 2004-2011

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Background and aims : Rates of invasive fungal infection are highest amongst neonates, especially those that are premature and very low birth weight (VLBW). This study aimed to describe the epidemiology, clinical presentation and current treatment of invasive neonatal fungal infections in England.

Methods : From 2004-2011 prospective multicentre surveillance was conducted by 12 neonatal intensive care units within neonIN, a neonatal infection surveillance network. Clinicians completed a standardized proforma for each positive fungal culture.

Results : From 2004 to 2011 78 cases were reported. The majority of cases (86%) occurred in babies born at < 1500g (median gestational age: 25 weeks, median birth weight: 740 g, 78% < 1000g). *C. albicans* was the most frequent pathogen isolated (69%), the median time of onset of symptoms was 13 days. 92% received at least one antibiotic course prior to the episode, 89% had ventilatory support, 95% received parenteral nutrition and 87% had a central line within 48 hours of the episode. Antifungal prophylaxis was rarely provided (22%) and although choice of treatment varied, the most commonly used was Fluconazole. The overall mortality was 31%.

Conclusions : Premature and VLBW infants are at increased risk of invasive fungal infections with a high mortality rate. The vast majority of infants in this cohort were exposed to known treatment related risk factors. Improved knowledge on the epidemiology of the disease will enable the development of better strategies to improve outcome.

EPIDEMIOLOGICAL AND CLINICAL FEATURES OF ROTAVIRUS GASTROENTERITIS (RVG) IN CHILDREN YOUNGER THAN 5 YEARS OF AGE IN WEST ATTICA

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Background and aims: Rotavirus is the leading cause of acute gastroenteritis among young children worldwide. The aims of this study were to determine and evaluate the frequency of rotavirus infections in children with acute gastroenteritis in our region, according to age, gender and seasonal features. Clinical data were also studied.

Methods: All children aged < 5 years hospitalized because of acute gastroenteritis during 2011 were enrolled for parental interview and stool collection. Rotavirus was detected by enzyme-linked immunosorbent assay.

Results: A total of 60 stool specimens from 31 female and 29 male children aged between 2-60 months, hospitalized in our department with diarrhea during 2011, were included to the study. Rotavirus antigen was detected in 28,3 % of the samples. 70,5% of children with RVG were under 2 years of age, and 47% were under 1 year. Rotavirus antigen positivity was 23,5% in 13-24 months group and 40.3% in 24-60 months group. The difference between the rates of rotavirus positivities in age groups was found statistically significant ($p = 0.016$). The difference between sexes was statistically insignificant ($p > 0.05$). RVG occurred between December and May, while 53% of the cases were detected in January. Children with RVG received IV fluids for an average of 2 days, while the rest needed an average of 24hour hydration. None of the children were vaccinated against rotavirus.

Conclusions: Rotavirus accounts for a significant proportion of acute gastroenteritis cases in children less than 24 months, causing more severe dehydration. Routine vaccination could reduce the burden of RVG.

ETIOLOGICAL SPECTUM OF GASTROENTERITIS DURING COLD SEASON IN A METROPOLITAN PEDIATRIC POPULATION

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Background and Aim: In temperate climate countries there is a specific seasonal distribution of gastroenteritis (GE) etiological spectrum. Our paper is aiming to demonstrate this pattern in a large urban pediatric population.

Material and method: Retrospective case-series analysis of patients presented with GE during cold season (from November till April) in three consecutive years (2009-2011) in a pediatric tertiary referral unit.

Results: 10.941 stool samples were tested (7262 cultures and 3679 rapid antigen detection tests for viruses). Average age for outpatients was 41.2 months and for inpatients was 8.3 months. The most frequent documented pathogen was rotavirus (RV) in 34.9% of tested specimens. Only 9.35% of cultures turned positive, E coli being the commonest: 74.08% of isolates. Very rare were present Salmonella 6.77%, Shigella 1.03% and Yersinia 0.74%.

Significant seasonal distribution was present in all three years for RV with a peak in February and March in all three years with a constant small increase. Bacterial isolates had a relatively constant distribution during the study.

Conclusions:

1. RV is the most common cause of gastroenteritis in small children, being documented in 1/3 of cases.
2. RV has a significant seasonal distribution with hibernal predominance in temperate climate.
3. In metropolitan areas bacterial isolates are infrequent (1/10 cultures are positive).
4. 75% of positive cultures were E coli.
5. Empiric antibiotic treatment for acute GE in children during cold months should be avoided.

GENOTYPE CONSTELLATIONS OF HUMAN P[6] ROTAVIRUSES FROM SUB-SAHARAN AFRICA AND ASIA ARE CLOSELY RELATED TO HUMAN P[4] AND P[8] ROTAVIRUSES

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Background and aims: P[6] rotaviruses in combination with a variety of G-genotypes have been circulating with a prevalence up to 31.85% in African and Asian countries, but only a few strains have been completely characterized. In Phase 3 clinical trials of RotaTeq™, conducted between March 2007 and March 2009 in Ghana, Kenya, Mali, Vietnam and Bangladesh, 24.3% of the 790 RV-positive gastroenteritis samples contained P[6] strains.

Methods: To investigate the genomic relationship between these human P[6] rotaviruses and common human rotaviruses circulating worldwide, we sequenced 39 P[6] strains collected in Ghana (n=14), Mali (n=18), Kenya (n=2), and Bangladesh (n=5) using 454™ pyrosequencing.

Results: Genetic analysis revealed that P[6] strains were associated with a wide range of G-genotypes: G2 (n=17), G3 (n=7), G8 (n=6), G12 (n=5), G1 (n=2), G9 (n=1), and Gx (n=1). Most rotaviruses possessed a complete Wa-like or DS-1-like backbone, with only a few exceptions containing both Wa- and DS-1-like genes. Several P[6] rotaviruses (in combination with G1, G2 or G9) potentially possessed 1 or 2 gene segments of bovine-like origin. However, potential bovine-like gene segments have also been encountered in co-circulating human rotaviruses carrying the P[4] and P[8] genotypes, indicating that the genetic backbone of the subset of analyzed human P[6] strains are similar to those of P[4] or P[8] strains.

Conclusions: These data confirm that P[6] strains constitute an important cause of rotavirus gastroenteritis in sub-Saharan Africa and Asia, and need to be closely monitored, especially because vaccine efficacy is lower in these countries.

ETIOLOGICAL STUDY OF ENTERIC VIRUSE AND GENETIC DIVERSITY OF NOROVIRUS, SAPOVIRUS, AND ADENOVIRUS IN CHILDREN WITH DIARRHEA IN CHONGQING, CHINA

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Background and aims: Enteric viruses are considered the major causes of diarrhea in children less than 5 years old. Identifying the viral agents is critical in developing effective preventive measures. We aim to determine the prevalence of common enteric viruses in children with diarrhea less than 5 years old in Chongqing, China.

Methods: Five hundred fecal samples from August to November of 2010 were collected from children less than 5 years old with diarrhea in Children's Hospital of Chongqing Medical University. Antigen of rotavirus A were tested with a colloidal gold device. Rotavirus B and C, norovirus GI and GII, adenovirus, sapovirus and astrovirus by RT-PCR. Sequences of PCR products were phylogenetically analyzed to determine the genotypes.

Results: Enteric viruses were detected in 282/500 samples presented with acute diarrhea 277/477(58.1%) and persistent diarrhea 5/23(21.7%). In 477 samples from acute diarrhea, rotavirus A was identified in 132 cases (27.7%) followed by norovirus GII in 130 cases (27.3%), adenovirus in 30 cases (6.3%), sapovirus in 9 cases (1.9%) and astrovirus in 1 case (0.2%). Viruses were positive in 5/23 cases with persistent diarrhea. For norovirus GII, GII/4 was the predominant genotype. Sapovirus was classified into 4 genotypes and GI/1 was predominant. For adenovirus, G41 was the predominant strain. No rotavirus B, rotavirus C or norovirus GI were found in any samples.

Conclusions: Enteric viruses are major causes of diarrhea in children younger than 5 years old in Chongqing. Rotavirus A is the most common etiological agent follow by norovirus.

HIGH VACCINE EFFICACY OF ROTATEQ™ AGAINST AFRICAN G8P[6] AND G8P[1] ROTAVIRUSES MAY BE EXPLAINED BY THEIR PARTIAL BOVINE GENETIC BACKBONE

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Background and aims: RotaTeq™ is a pentavalent rotavirus vaccine based on a bovine rotavirus genetic backbone with human rotavirus VP7 (G1-G4) or VP4 (P[8]) genes. During clinical trials of RotaTeq™ in sub-Saharan Africa, vaccine efficacy (VE) over 2-years follow-up was numerically lower against rotaviruses with genotypes contained in the vaccine (34.0%, [11.2-51.2]) than against G8 rotaviruses (87.5%, [6.5-99.7]). Complete genome analysis of these G8 rotaviruses was conducted to gain insight into this high level of cross-protection afforded by RotaTeq™.

Methods: The complete nucleotide sequences of 1 G8P[1] and 2 G8P[6] rotaviruses (Ghana), and 4 G8P[6] rotaviruses (Mali) were determined using 454™ pyrosequencing and compared with RotaTeq™ and other rotaviruses.

Results: All genes of the G8P[1] strain were closely related to bovine-like rotaviruses (G8-P[1]-I2-R2-C2-M2-A11-N2-T6-E2-H3). The Ghanaian G8P[6] strains possessed a G8-P[6]-I2-R2-C2-M2-A2-N2-T2-E2-H3 genotype constellation of which only the VP4 (P[6]), NSP1 (A2) and NSP3 (T2) genes were closely related to co-circulating human rotaviruses, whereas the other genes were often more closely related to bovine-like rotaviruses. The Malian G8P[6] strains possessed a DS-1-like background (G8-P[6]-I2-R2-C2-M2-A2-N2-T2-E2-H2) of which VP2, VP4, NSP1 and NSP3-NSP5 were closely related to human rotaviruses. However, the other genes appeared to be closer related to animal-derived strains, or only distantly related to known rotaviruses.

Conclusions: The high VE against African G8 strains, may be explained by the fact that these strains contain a complete or bovine-like rotavirus backbone. This observation supports the hypothesis that other rotavirus genes than VP7 and VP4 play an important role in vaccine-induced immunity or protection.

ROTAVIRUS GENOTYPE DISTRIBUTION IN BELGIUM: 5 YEARS AFTER VACCINE INTRODUCTION

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Background and aims: The introduction of rotavirus vaccines in national immunization programs has resulted in dramatic declines of rotavirus gastroenteritis in children under 5 years of age. In Belgium, Rotarix™ and RotaTeq™ were introduced in 2006 and 2007 respectively, but until now Rotarix™ is the most used vaccine.

Methods: At the university hospital Leuven, the genotype distribution of rotaviruses has been monitored since the 1999-2000 season. Since 2007-2008 also national surveillance has been implemented. Rotavirus positive samples were G- and P-genotyped by sequencing.

Results: In the period before vaccine introduction yearly genotype fluctuations were observed with the G2 genotype never accounting for more than 20% of all cases at the university hospital, while after vaccine introduction (2006-2007) a steady proportional increase of the G2 genotype has been observed reaching almost 60% in the 2009-2010 rotavirus season. Nationwide surveillance in Belgium started in 2007-2008 and showed a similar genotype distribution. For the 2010-2011 rotavirus season the most prevalent genotype in Belgium was G3 (31.7%), followed by G4 (22.7%), G1 (19.6%), G2 (16.9%), G9 (7.3%) and G12 (1.3%). Most of these genotypes were found in combination with P[4] or P[8] genotypes. However, we also found 3 G12P[6] strains and one G6P[14] strain.

Conclusions: This is the first season after vaccine introduction where the G2 genotype was not the most prevalent genotype. These results re-emphasize that besides the vaccine implementation in the national immunization program also other factors influence the genotype distribution.

IMPACT OF ROTAVIRUS VACCINES AND CIRCOVIRUS IN ACUTE GASTROENTERITIS HOSPITALIZATIONS IN SPAIN

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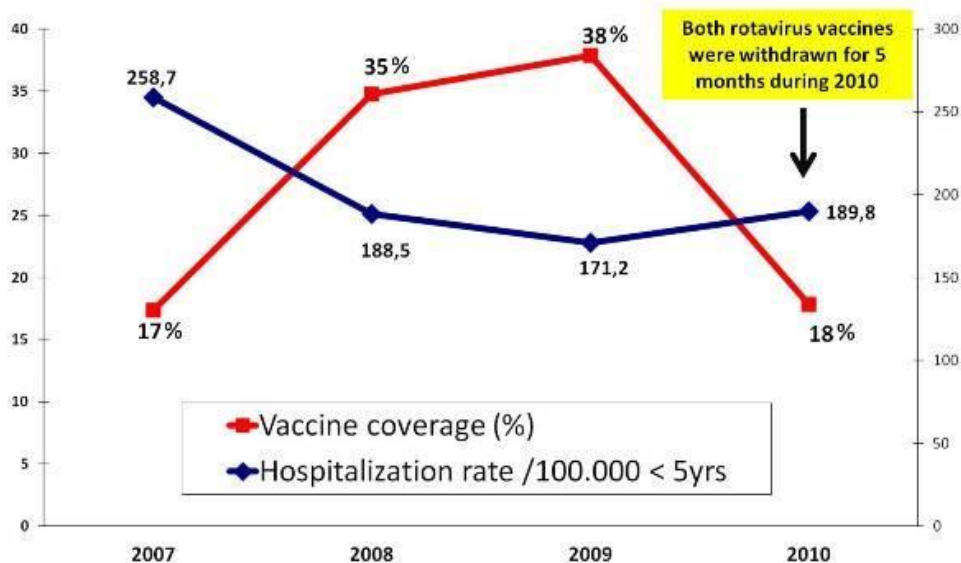
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Aim: Rotavirus vaccination is not recommended nor reimbursed by the Spanish National Health System. Significant coverage rates have not been reached however, with an average of 37% in 2009. In 2010, the Spanish Medicines and Health Products Agency did not authorize the release of new batches of both vaccines onto the Spanish market for 5 months due to circovirus detection. The objectives are: 1-to explore the eventual variations in the hospitalisations rate for rotavirus acute gastroenteritis (RAGE) among children < 5 years of age before and after vaccine introduction; and 2-to evaluate the actual impact of rotavirus vaccines temporary withdrawal -that we had previously estimated that would have led to 434 to 497 excess hospitalizations in children < 5 years.

Methods: The annual hospitalization rates (AHR) before and after rotavirus vaccine introduction for RAGE were calculated by using the national official surveillance system for hospital data.

Results: 39210 children < 5 years with RAGE were hospitalized in Spain from 2003 to 2010. The AHR for RAGE in children < 5 years of age decreased by 24% in 2008, by 31% in 2009 and by 24% in 2010 as compared with the median rate of the pre-vaccination period (2003 to 2005), correlating well with vaccine coverage (Figure).

Vaccine coverage and hospitalization rate per 100.000 children below 5 years in Spain from 2007 to 2011



[Rotefec nacional]

In 2010 there was a 11% increase (528 excess cases) in the RAGE AHR as compared to 2009.

Conclusions: Moderate rotavirus vaccine coverage may have a great impact on RAGE hospitalizations rates. Our initial estimations on the negative impact of the "circovirus affair" have been actually confirmed.

ASSESSMENT OF THE TOTAL AND VIABLE BACTERIAL AND FUNGAL COMMUNITIES COLONISING THE PRETERM GUT MICROBIOTA

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Background and aims: Illnesses related to colonisation of the preterm gut, particularly necrotising enterocolitis (NEC) and septicaemia, cause important morbidity and mortality. The bacterial community is relatively well studied, but contributions from fungi and the proportions of viable organisms within communities remain overlooked. In a large cohort of preterm infants we present data on viable bacterial and fungal colonisation of stool.

Methods: 136 stools from 32 patients were analysed by PCR-DGGE for assessment of the total (DNA) bacterial (16S rRNA) and fungal (28S rRNA) communities. Assessment of the viable (RNA) bacterial and fungal communities was analysed in 65 samples from 25 patients.

Results: Patients with NEC and septicaemia had different total bacterial communities from healthy patients. With *Sphingomonas aromaticivorans* associated with NEC. Antifungal prophylaxis significantly affected the bacterial community and was effective in treating fungal infection. Birth weight and gestational age were not significant in patients developing infection.

Meconium was not sterile containing a low diversity of bacteria with a more diverse gut established in subsequent weeks. The numbers of viable taxa detected each week, although fewer, followed a similar trend to the total community. Reduction in bacterial richness was observed in week 4, this correlates with the introduction of a more varied antibiotic regime. Treatment with metronidazole had the most significant effect.

Conclusions: Further work is needed to investigate the role of fungi in NEC pathophysiology and differences between the total and viable community warrant consideration by investigators solely exploring the total community.

THE USE OF LACTOBACILLUS GG IN CHILDREN WITH FUNCTIONAL ABDOMINAL PAIN: A DOUBLE-BLIND RANDOMIZED CONTROL TRIAL

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Objective: To determine whether oral administration of the probiotic Lactobacillus GG under randomized, double-blinded, placebo-controlled conditions would improve symptoms of recurrent abdominal pain in children.

Patients and methods: 61 children with functional abdominal pain were given Lactobacillus GG or placebo for 6 weeks and entered follow-up for 4 weeks. Children entered a randomized, double-blind, placebo-controlled trial.

Results: LGG, but not placebo, caused a significant reduction of both frequency ($P < .01$) and severity ($P < .01$) of abdominal pain. These differences still were significant at the end of follow-up ($P < .02$ and $P < .001$, respectively).

Conclusions: Lactobacillus GG was superior to placebo in the treatment of recurrent abdominal pain in children, LGG significantly reduces the frequency and severity of functional abdominal pain and may help relieve such symptoms as perceived abdominal distention.

PREVALENCE OF *HELICOBACTER PYLORI* INFECTIONS IN UPPER GASTROINTESTINAL TRACT IN ISLAMABAD, PAKISTAN

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Background and aims: Prevalence of *Helicobacter pylori* (Hp) is very high and well documented in gastroenterological disorders like gastritis, gastric carcinoma, peptic ulcer disease and non ulcer dyspepsia and gastroesophageal reflux disease. If untreated, *H. pylori* infection is lifelong. More than 50% of the world's population harbor Hp in their upper gastrointestinal tract. Infection is more prevalent in developing countries like Pakistan. The objective of the present study was to evaluate the recent Hp prevalence in gastroenterological disorders in the cosmopolitan city Islamabad, Pakistan.

Methods: Over a 24 months period, 342 patients of more than 10 years of age, with varied socioeconomic background, presented to the out patient department (OPD). All patients underwent endoscopy for the diagnosis of gastroduodenal diseases and biopsies were taken to evaluate the Hp status by histopathology and rapid urease test. For histopathological processing all the biopsies were stained with haematoxylin and eosin for further examination.

Results: Out of three hundred and forty two patients; 90 (26.31%) had chronic gastritis, 176 gastric ulcer (51.46%), 30 duodenal ulcer (8.77%) and 21 with combined gastric and duodenal ulcers (6.14%), 15 (4.38%) adenocarcinoma and 10 (2.92%) had no pathology. Overall *H. pylori* prevalence was 78.88% (71/90) in chronic gastritis, 85.79% (151/176) in gastric ulcer, 63.33% (19/30) in duodenal ulcer, 66.66% (14/21) in combined gastric and duodenal ulcers, 93.33% (14/15) in adenocarcinoma and 30.0% (3/10) with no pathology was recorded, respectively.

Conclusion: We have demonstrated that the prevalence of Hp was significantly higher in Islamabad as compared with other part of the country.

UNUSUAL EXTRA-INTESTINAL MANIFESTATION OF THE ROTAVIRUS INFECTION**A.S. Al-Makadma**, K.I. Al-Enazi*KFMC, Riyadh, Saudi Arabia*

Introduction: Rotavirus represents the single most important viral cause of gastroenteritis among children. The clinical picture may range from being asymptomatic to severe dehydration, seizures and even death. Extra-intestinal sites involvement was recognized. Associated musculoskeletal complications like myositis and rhabdomyolysis has been reported.

Objectives: To highlight Extra-intestinal manifestations and pathology, Rotavirus induces on different organs. To highlight the need for Rotavirus vaccine in the national immunization schedule.

Case report: 9 month old male with normal neonatal history, presented with fever, vomiting, diarrhea for five days. looked unwell, lethargic and dehydrated. Normal growth parameters. T:38.5; HR: 158 /min, RR: 50/min BP 95/60mmHg. WBC: of 11,700/mm³, hemoglobin 12.4 g/dL, platelets 131000/mm³, and C-reactive protein 5 mg/dL. Sodium 172 mEq/L, Potassium 3.6 mEq/L, Chloride: 146 mEq/L, Bicarbonate 13.5 mEq/L, BUN: 8.6 mmol/L, serum Creatinine: 124 μmol/L, (ALT) 103 IU/L, (AST) 2142 IU/L. serum glucose, albumin and amylase were normal. The serology for viruses were negative. stool was positive for rotavirus antigen. His blood, urine and stool cultures were negative. Urine was positive for blood and proteins. its microscopy revealed no RBCs but granulocytes. Brain CT was normal. The electroencephalogram showed mild degree of slow wave abnormalities. Brain MRI : abnormal signal intensities within the Globus Pallidus, Thalamus and the anterior limb of the Internal Capsule CPK: 41000 IU/L , LDH: 754 IU/L. The ALT peaked up.

Conclusion: Whenever diarrhea is associated with encephalopathy, rhabdomyolysis or both, Rotavirus disease should be considered. Need to consider including the Rotavirus.

MODERN SYNBIOTIC IN MEDICAL REHABILITATION PROGRAM FOR CHILDREN AND TEENAGERS WITH CHRONIC HELICOBACTER-ASSOCIATED GASTROINTESTINAL TRACT DISORDERS

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Background and aims: Gastroduodenitis, caused by *H. pylori*, can be characterized by: the high prevalence rate, disposition to chronic and recurrent courses, simultaneous damage done to the various parts of GIT, accompanied by the immune system homeostatic balance disorders, dysbiotic changes in intestinal microflora. This research is aiming to make more effective rehabilitation of children with chronic GIT disorders by introducing the synbiotic to the program.

Methods: We selected 46 patients aged 7-14 y.o., with chronic gastroduodenitis. Typical rehabilitation program included: diet-, phyto-, ballroom and kinesitherapy, trainings, gastroschool, etc. 30 children were prescribed a synbiotic containing a consortium of strains *B. bifidum*, *longum*, *breve*, *infantis*, normally prevailing in normoflora of children of this age, *L. plantarum*, *acidophilus*, *casei*, a vitamin-mineral premix, along with inulin and oligofructose.

Results: It was shown that those patients, who took the synbiotic, demonstrated more positive dynamics - they stopped complaining sooner (p -value < 0.05), dyspepsia and meteorism ceased, their stool normalized, tongue plaque and bowel sounds disappeared; the number of children with dysbacteriosis stages 2-3 decreased by 29%, whereas 35% of the patients showed complete normalization of microbiocenosis factors. The aggregate level of volatile fatty acids in patients of the main group shifted towards the median of the normal range. Significant disparity before and after the rehabilitation was detected in levels of immunoglobulins, lysozyme activity and tissue immunity balance ratio in the patients treated with the synbiotic.

Conclusions: Introduction of the synbiotic increases the effectiveness of medical rehabilitation of children with chronic GIT disorders.

HYPERTRANSAMINASAEMIA IN THE COURSE OF ACUTE DIARRHOEA IN CHILDREN

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In Poland, the most common causes of acute diarrhoea in children are viruses, especially rotaviruses. Both viruses and bacteria causing acute diarrhoea may be secondary hepatotropic factors.

The aim of this study: Was to evaluate the levels of aminotransferases in children hospitalized between 2008 and 2009 in the Department of Paediatrics in Katowice due to acute diarrhoea.

Patients and methods: The study involved 579 children, aged from 1 month to 18 years. In 226 children (41%) infection with RV virus was diagnosed; in 158 children - bacterial infection (27.3%). In all the patients AST and ALT levels were determined, in relation to age, sex, acute diarrhea etiology, inflammatory state parameters, water, electrolyte and acid-base balance, and comorbidity. The obtained results were analysed statistically.

Results: Elevated levels of AspAT were observed in 268 children (46.3%). Elevated levels of AlAT were observed in 58 children (10.1%); only in 6 children (1%) the levels of alanine aminotransferase exceeded two-fold the upper limit of normal. Among all the patients with acute rotavirus diarrhoea, elevated levels of aminotransferases (mainly AST) were detected in 189/226 (83,6%) patients. In all the children aminotransferase levels were normalised during one month's observation. Statistically, increased aminotransferase levels were significantly more frequent in children under 3 years of age, and with considerable disorders of water, electrolyte, and acid-base balance.

Conclusion: With regard to observe transient hypertransaminasemia and its quick, spontaneous normalisation, we should consider the purposefulness of routine determination of these enzymes in the course of acute diarrhoea in children.

HUMAN BOCAVIRUS TYPES 1, 2 AND 3 IN ACUTE GASTROENTERITIS OF CHILDHOOD

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Background and aims: Recently identified human bocavirus (HBoV) types 2 and 3 have been implicated as causative agents of acute gastroenteritis (AGE) in children. We studied stool specimens from children with AGE for human bocaviruses 1, 2, 3 and 4; the same specimens were also examined for known gastroenteritis viruses.

Methods: Stool specimens of 878 children with AGE and of 112 age-matched controls seen in hospital were collected in a two-year prospective study. A two step PCR method was used to detect HBoVs. Positive amplicons were sequenced to identify HBoV1, HBoV2, HBoV3 and HBoV4, respectively.

Results: HBoV of any type was found in 85 (9.7%) cases of AGE and in 6 (5.4%) controls. HBoV1 was detected in 49 (5.6%) cases and 2 (1.8%) controls, HBoV2 in 29 (3.3%) cases and 2 (1.8%) controls and HBoV3 in 8 (0.9%) cases and 2 (1.8%) controls. No HBoV4 was found. In one of the AGE cases both HBoV1 and HBoV2 were detected. In 69 (81.2%) of the HBoV positive AGE cases a known gastroenteritis virus was also found, and conversely, HBoV alone with no gastroenteritis viruses was found in 16 (1.8%) cases and in 6 (5.4%) controls. In the "pure" HBoV positive cases of AGE HBoV2 was found in 8, HBoV1 in 7 and HBoV3 in 1 patient.

Conclusions: HBoVs are rarely found alone in children with AGE, and their etiological role in gastroenteritis appears small. Further studies are warranted to confirm if HBoV2 has a minor causative role in childhood gastroenteritis.

EVALUATION OF FEVER AND LEUCOCYTOSIS IN CHILDHOOD DIARRHEA**G. Soleimani**¹, M. Parsa², A. Soleimani²*¹Department of Paediatrics, Research Center for Children and Adolescents Health, Zahedan University of Medical Sciences, Zahedan, ²Azad Islamic University, Tehran, Iran*

Background and aims: Diarrheal children who present with fever proved difficult entities. fever may be the first sign following bacteremia, instead of other symptoms of SIRS. Despite the eventual diagnosis by blood cultures, antibiotics are prescribed in majority if they had fever and leucocytosis on admission. The aim : to quantify the accuracy of fever magnitude and leucocytosis as indicators of bacteremia in childhood diarrhea.

Methods: A cross sections study was performed on childhood diarrhea admitted with fever at the pediatric ward of ali ebneabitaleb Hospital in zahedan(Iran). inclusion criteria : any episode of fever (axillar temperature >37.6C) in childhood diarrhea. Blood culture and WBC count were performed.

Result: 210 children were admitted with diarrhea among them, 95 had blood drawn for culture and WBC count. Mean ages 8.5 month (range 1-60), mean temperature 38.7oC (range 37.6-40.5C), and mean WBC counts 8000 (range 3000- 24,200). antibiotics were given to 40 patients two patients had bacteremia, with positive blood culture.

Conclusions: Increments in temperature > 39C provided no additional diagnostic specificity for bacteremia. Total WBC count combined with fever provided better information, but still cannot be used as signs for bacteremia in childhood diarrhea.

THE INFLUENCE OF APPLICATION OF FLAX-SEED OIL AND PROBIOTICS ON BIOCHEMICAL BLOOD PARAMETERS IN GNOTOBIOTIC PIGLETS INFECTED BY *E.COLI*O8:K88AB:H9

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The aim of the present work was to determine influence of administration of the probiotics and flax-seed oil on protein, energetic and enzymatic serum profiles of gnotobiotic piglets after *E.coli* infection. Animals were divided into three groups: C (control), LFA (*L.plantarum* + flax-seed oil), L (*L.plantarum*). The piglets (LFA, L) were inoculated orally each day with 2 ml of *L.plantarum* (1×10^9 CFU/ml). In addition flax-seed oil was supplemented to the animals of group LFA (0,5 ml/day). At the age of 5 days, the piglets from all groups were challenged orally with 2 ml of *E.coli* O8:K88AB:H9 strain without enterotoxin production (1×10^5 CFU/ml). The pigs from all group were sacrificed at the age at 9 days, i.e. 4 days after *E.coli* inoculation. In group L we observed a higher levels of glucose, cholesterol and LDL cholesterol against C and LFA, and higher levels of triglycerides and total lipids in group LFA against C and L. The levels of total proteins in group L were higher against C and LFA ($P < 0.001$). Also Creatinine ($P < 0.01$) and albumin levels in group L exhibited increased levels against C and LFA. Group LFA showed higher levels of lipase compared with C ($P < 0.01$) and L ($P < 0.001$). Our results demonstrated that probiotics has significant effects on the biochemical blood parameters in *E.coli* infected gnotobiotic piglets.

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THE POSSIBILITIES OF PROBIOTICS IN ACUTE INTESTINAL INFECTIONS IN YOUNG CHILDREN**A. Kharchanka***Grodno State Medical University, Grodno, Belarus*

Background and aim: The therapy with pro-and prebiotics occupies a special place in treatment of AI, both in its acute stage and during reconvalescence. To evaluate the effectiveness of probiotic-antagonist "Enterol» (*Saccharomyces boulardii*) in the treatment of acute intestinal infections in young children.

Methods: We examined 42 children aged from 1 month to 1 year with mild to moderate forms of the disease. The causative pathogen was isolated in 37 children (rotavirus - 45.2%, Salmonella - 23.8%, opportunistic flora - 19%). All patients received standard basic therapy. Depending on the ongoing correction with probiotics the children randomly were divided into two comparable groups: a main group of children (n = 20) who have received "Enterol" since the first day of hospitalization and a control group (n = 22) the children of which did not receive the drug.

Results: In children receiving the combined therapy with "Enterol" the period of diarrhea syndrome reduced, wind. After treatment normal carbohydrate content in the feces was noted in 13 (65%) children of the main group and in 7 (31.8%) children of the control group ($p < 0.05$). All these results have allowed to reduce the period of hospital stay from $11,2 \pm 0,2$ days (control group) to $6,9 \pm 0,1$ days (study group).

Conclusions: The use of probiotic - antagonist based on *Saccharomyces boulardii* is justified in the treatment of acute intestinal infections in infants, because it promotes more rapid elimination of symptoms and recovery of the gastrointestinal tract functional activity.

CHANGES IN SUSCEPTIBILITY TO ANTIBIOTICS OF ESCHERICHIA COLI STRAINS IN CONSTANTA COUNTY - ROMANIA

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Introduction: Acute diarrheal disease represents, in our geographic area, an important problem of public health, mainly during the summer months. Escherichia coli are frequently incriminated in diarrheal disease in children.

Objectives: Evaluation of clinical, laboratory and therapeutically aspects of acute diarrheal disease caused by E. coli enteropathogen, and susceptibility to antibiotics-comparison of dates between 2011, 2007 and 2003.

Material and method: Retrospective study of cases with acute enterocolitis determined by E.coli to the children hospitalized in the Clinical Hospital of Infectious Diseases Constanta during 3 different years (2011, 2007, and 2003).

Results: In 2011 there were hospitalized 237 children with E. coli, in 2007 there were hospitalized 206 patients, meanwhile in 2003 - 183 cases. Incidence was increased during the summer. Sex-ratio was: M:F= 1:1 in 2011, 1.06 in 2007, and respectively 1.23 in 2003. The majority were from urban environment (80,76% in 2011, 72.8% in 2007, respectively 72.67 in 2003). The highest incidence was at children between 1-5 years old. At this group we observed the most severe dehydrations. Regarding the susceptibility to antibiotics, according to laboratory tests, if in 2003 the majority of tested strains were keeping their susceptibility to Ampicillin (89,4%), Trimethoprim-Sulphamethoxazol (77,5%), Nalidixic acid (93,3%), in 2011 we found an important decrease of susceptibility of tested strains to these antibiotics (Ampicillin-17,6%, Trimethoprim-34,61%, Nalidixic acid- 64,5%).

Conclusions: Escherichia coli enteropathogen has thus far been identified most often in diarrheal illness in children. The susceptibility of strains of E.coli isolated by us has changed during last years.

CAMPYLOBACTER INFECTION IN CHILDREN

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In recent years Campylobacter infection has been increasingly observed in children.

The clinical presentation is dominated by diarrhoea with blood admixture, fever and abdominal pain. In most cases Campylobacter infection resolves spontaneously.

The aim of the study was a retrospective analysis of the clinical course of Campylobacter infection in children hospitalized in the period 2008-2010.

In total 71 children with Campylobacter infection were included in the retrospective analysis: 42 boys (58.3%) and 29 girls (41.7%) at the ages of 6 weeks to 10 years. 86% of infections were observed in infants and children up to 3 years of age. In all the children standard laboratory tests were performed as well as stool culture and faecal rotavirus tests.

Faeces bacteriological examination revealed in 90% patients Campylobacter jejuni infection, in 6 % Campylobacter coli, and in 4% Campylobacter sp. In 14% of the samples enteropathogenic E. coli infection was observed, in 1.5% Salmonella C, and in 15.5 % rotavirus infection.

The average duration of hospitalization was 7.24 days.

On admission, clinical symptoms included: watery diarrhoea in 48.60% , diarrhoea with blood admixture in 44.4%, vomiting in 32.4% , fever in 39.43%. Laboratory tests produced positive results for inflammatory markers in 68%, and anaemia in 23% of patients.

Infants and children up to 3 years of age were most often affected by the infection.

Duration of hospitalization of children with Campylobacter infection was relatively long; in 30 % of patients the disease was severe and required antibiotic therapy.

THE EFFECT OF FLAX-SEED OIL AND *LACTOBACILLUS PLANTARUM* ON INTESTINAL METABOLISM IN GNOTOBIOTIC PIGLETS AFTER INFECTION BY *ESCHERICHIA COLI* O8:K88AB:H9

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We investigated the influence of administration of flax-seed oil on interaction of *Lactobacillus plantarum* and *Escherichia coli* O8:K88ab:H9 and on biochemical parameters in the gut of gnotobiotic piglets. The germ-free piglets were divided into three groups: group C(control), group LFA (*L.plantarum* + flax-seed oil), group L (*L.plantarum*). The piglets from LFA and L groups were inoculated orally each day with 2ml of *L.plantarum* strain (1×10^9 CFU/ml). At the age of 5 days, the piglets from all groups were challenged orally with 2ml of *E.coli* O8:K88ab:H9 strain (1×10^5 CFU/ml). When compared to animals supplemented with *L.plantarum*, the counts of lactobacilli in the jejunal and ileal mucosa and in the intestinal content were significantly higher in LFA group ($p < 0,001$). Inter-groups comparisons of the counts of *E.coli* adhering to the jejunal and ileal mucosa revealed a significantly decreased in LFA animals ($p < 0,001$; $p < 0,05$). We observed a positive influence on intestinal metabolism of LFA piglets manifested by increased production of organic acids in the caudal sections of the digestive tract (ileum, colon), particularly with respect of acetoacetic, acetic ($p < 0,05$), lactic and succinic ($p < 0,01$) acids and the corresponding decrease in pH. The stimulatory effect of flax-seed oil on *L.plantarum* adhesion resulted in enhancement of the inhibitory effect of lactobacilli on *E.coli* in the digestive tract of piglets.

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THE BURDEN OF ROTAVIRUS GASTROENTERITIS IN THE CZECH REPUBLIC, FIRST DATA ABOUT THE COVERAGE OF VACCINATION**P. Pazdiora**¹, Č. Beneš²¹*Epidemiology, Medical Faculty Charles University, Pilsen,* ²*Unit of Biostatistics and Informatics, National Institute of Public Health, Prague, Czech Republic***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 2003-2010. Data about the vaccination against rotavirus infections was collected from pediatricians and distributors of vaccines.**Results:** There were reported 28,962 cases of rotavirus gastroenteritis. Among them 51,0% were children under 2 years, and 70,6% under 5 years. The most common among all aetiological agents of gastrointestinal disease were Campylobacters, the second frequent rotaviruses in the year 2010. 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 3,364 children under 5 years are hospitalised and another 26,908 are out-patients with more benign rotavirus gastroenteritis annually. There were reported 5 deaths on rotavirus gastroenteritis (among them 1 child). On the basis more frequent laboratory confirmation of diarrhoeal disease in last years and better reports of 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 is approximately 19% in the end of 2011. Among all pediatricians only 76% started with the vaccination against rotavirus infections.**Conclusion:** The results indicate the need of universal vaccination against rotavirus infections in the Czech Republic, too.

ROLE OF INNATE IMMUNITY IN ROTAVIRUS INFECTION AND ITS MODULATION BY VITAMIN 1,25(OH)₂D₃ IN HUMAN ENTEROCYTES

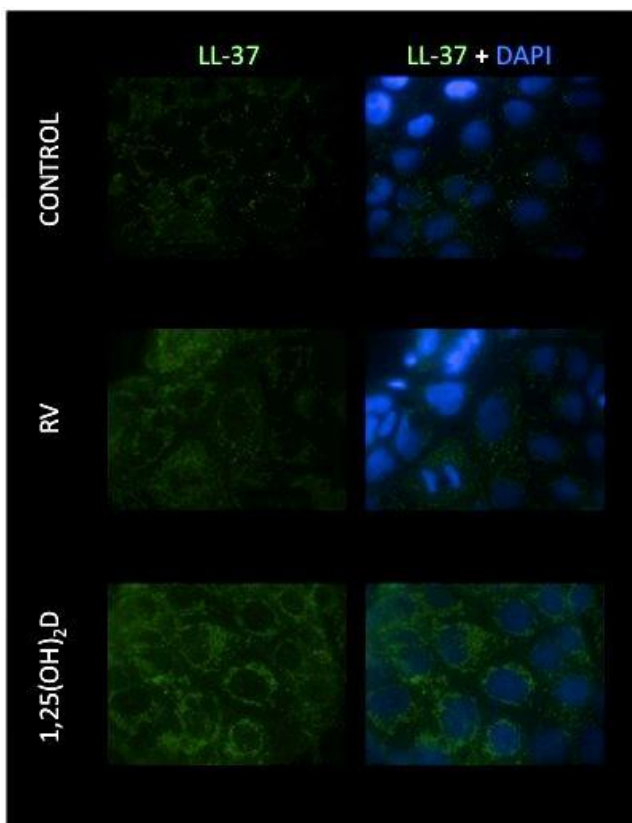
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Background and aims: The human cathelicidin LL-37 is one of the major antimicrobial peptides of the intestinal tract innate immune system. Up-regulation of LL-37 is influenced by several signalling pathways and receptors including vitamin 1,25(OH)₂D₃ (1,25D₃), and the latter induces autophagy via LL-37 in macrophages. Since autophagy is involved in the response to Rotavirus (RV), the role of 1,25D₃ and LL-37 in preventing RV-related enterocyte damage was studied.

Methods: Caco-2 cells were pretreated with different concentrations of 1,25D₃ at 37°C up to 24 hours and infected with a simian RV strain SA11. LL-37 expression was investigated by immunofluorescence. Tissue damage was estimated by transepithelial electrical resistance (TER). Apoptosis was evaluated at immunoblot with an anti-caspase-3 mAb.

Results: Caco-2 cells preincubated 12 hours with 1,25D₃ 100nM showed an evident increase of LL-37 protein expression, with a peak between 6 and 12 hours post-infection (95% LL-37+ cells with 1,25D₃ pretreatment vs 15% LL-37+ control cells, $P < .05$). In cells pretreated with 1,25D₃ and subsequently infected with RV, the cytotoxic damage was reduced as judged by TER compared to control infected cells (251 ± 6 vs $180.1 \pm 2 \Omega/\text{cm}^2$, $P < .0001$). In addition, apoptosis in response to RV infection was also reduced in cells pretreated with 1,25D₃ in comparison with non-pretreated control cells.



[Expression of LL-37 after 1,25D₃ pretreatment]

Conclusions: These data indicate that the cathelicidin LL-37 is implicated in RV pathophysiology and open a role for a use of 1,25D₃ in the rotaviral diarrhea.

THE PRETERM GUT MICROBIOTA: CHANGES ASSOCIATED WITH NECROTISING ENTEROCOLITIS AND SEPSIS

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Background and aims: The preterm gut microbiota influences important morbidity and mortality. 16S rRNA based methodologies may offer insights into microbiomic influences on infection or necrotising enterocolitis (NEC). We aimed to describe gut colonisation in infants (< 32 weeks) using both standard culture (SC) and 16S rRNA (16S) methods, exploring differences in healthy infants and those with NEC/infection.

Methods: Weekly stool collected from birth to 8 weeks was analysed by SC and 16S using PCR-DGGE. Analyses assessed the effects on gut community of gestation, sex, mode of delivery and NEC or infection. 99 stools from 38 infants, median gestation 27wks (23-32wks), and birth weight 895g (520g-1850g) were analysed by SC, 44 from 27 infants by 16S.

Results: SC identified a median of 2 organisms (0-7), DGGE median 12 (3-18). By SC commonest organisms were *Enterococcus faecalis* and coagulase negative *staphylococcus* (CONS) (40% and 39% of stools). More infants with NEC were colonised with CONS (45% vs 30%) and less with *Enterococcus faecalis* (31% vs 57%). Meconium samples were not sterile. No fungus was cultured.

By either method community structures in NEC and sepsis differed from healthy infants. SC identified *Enterococcus faecalis* associated with a reduced risk of NEC/sepsis. 16S indicated the presence of *Enterobacter*, *Flavobacterium*, *Staphylococcus* and *Propionibacterium* was associated with NEC/sepsis.

Conclusions: Important differences exist in gut community structure in preterm infants developing NEC and sepsis. The relationship of these changes to current practices in modern neonatal intensive care requires further exploration.

DISEASE BURDEN OF VIRAL GASTROENTERITIS (VGE) IN A PAEDIATRIC POPULATION IN ITALY

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Background and aims: There are limited data on the epidemiology of VGE in children. We studied the epidemiological and clinical characteristics of VGE due to Rotavirus (RVGE), Adenovirus (AVGE), Norovirus (NVGE) in Italian children < 60 months seen by family paediatricians (FPs) over a 12 months period.

Methods: Prospective cohort study using Pedianet network including children presenting with AGE to FPs in the Veneto Region. Stool samples were collected and tested by PCR for Rotavirus, Adenovirus and Norovirus.

Results: 12 FPs participated in the study accounting for 7239 p/y of follow up. 555 cases of AGE were reported with an incidence of 7,6 %. 310 out of 460 with an available stool sample (67%) were PCR positive for at least one virus with an overall VGA incidence of 4,2% (95%CI: 3,75-4,65). RVGE incidence was 1,04 (95%CI: 0,81-1,30) with the peak between 6-17 months. The seasonal peak was November and January to April. AVGE incidence was 1,74% (95%CI: 1,45-2,07), NVGE incidence was 1,51% (95% CI: 1,24-1,82) the latter with a less evident seasonality. Risk of hospitalization, hospital duration and workdays lost by parents were not different in RVGE compared to AVGE and NVGE, even if RVGE showed a trend toward a higher risk.

Conclusions: VGE represents 2/3 of all cases of AGE. Incidence of RVGE in Italian children < 5yrs presenting to FP was slightly lower than AVGE and NVGE. However it should be considered that this study didn't include the most severe cases presenting directly into the hospital.

MOLECULAR AND CLINICAL CHARACTERIZATION OF ROTAVIRUS ACUTE GASTROENTERITIS IN FRENCH INFANTS OVER 5 EPIDEMIC SEASONS, 2006-2011

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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). Prospective surveillance is required to monitor and characterize rotavirus infections, including viral and clinical data, and to detect the emergence of potentially epidemic strains.

Methods: Between 2006 and 2011, stool samples and clinical records were collected from 3843 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 P (VP4) and G (PV7) types.

Results: The genotyping of 3670 rotaviruses showed that G1 strains (59.5% [52.9-75.9]) were predominant, G9 (16.8% [7.6-25.9]) were decreasing, G2 (8.7% [1.8-18.5]) were very changing, and G3 (3.4% [2.4-4.5]) and G4 (2.5% [0.3-5.6]) circulated locally. Most strains were associated with P[8] (87.5% [76.3-94.1]). Overall, 89 uncommon strains or possible zoonotic reassortants (2.4% [1.3-4.7]) were detected including G12, G8 and P[6] strains, some being closely related to bovine strains. No difference in clinical presentation and severity was found among genotypes.

Conclusions: The relative stability of rotavirus genotypes may ensure vaccine effectiveness in the short and medium terms in France. Moreover, the likely emergence uncommon strains, especially G12 and G8 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.

PRESENCE OF ROTAVIRUS AND ADENOVIRUS ANTIGENS IN CHILDREN WITH GASTROENTERITIS IN TEKIRDAG, TURKEY

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Introduction: Viral agents are the frequent causes of infectious diarrhea in children but little is known about their epidemiology, in Turkey. With this study, we aimed to determine the incidence of gastroenteritis due to rotavirus and adenovirus, in Tekirdağ region.

Methods: Stools specimens of children with acute gastroenteritis were collected and screened for Group A rotavirus and adenovirus serotype 40-41 antigens, with the immunochromatographic test (RIDA Quick, R-Biopharm, Gemany) according to the recommendations of the manufacturer. The results of the subjects were evaluated by examining groups based on the ages: Group A (0 months to 2 years), Group B (3-6 years) and Group C (7-15 years).

Results: Of the stool samples, 2135 were tested for the presence of rotavirus and 2117 for adenovirus. Rotavirus was positive in 222(10.4%) and adenovirus in 77(3.6%) of the samples. The positivity of rotavirus was 63.7%, 27.8%, 8.5% in groups A, B and C, respectively ($\chi^2 = 104.8$, $p < 0.001$) and adenovirus was 40.3%, 36.3%, 23.4.% in groups A, B and C, respectively ($\chi^2 = 3.6$, $p = 0.16$). No statistical difference due to gender was obtained for both of the agents ($\chi^2 = 0.8$, $p = 0.38$, $\chi^2 = 1.1$, $p = 0.31$).

Conclusion: Viral agents are generally missed by routine diagnostic tests in identifying the causes of infectious diarrhea. In fact, especially in childhood stool specimens need to be tested for the presence of the viruses. Our results with 10.4% and 3.6% positivities for rotavirus and adenovirus, confirmed the importance of performing these tests in daily practice of laboratories.

AETIOLOGY OF ACUTE GASTROENTERITIS IN HOSPITALIZED CHILDREN FROM LISBON AREA

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Background: Gastroenteritis is a major cause of morbidity and mortality worldwide.

Aim: Determine the etiology of gastroenteritis in a cohort of children hospitalized.

Methods: From May 2011 to January 2012, stool samples were collected from children (4.2 ± 4.8 years). Viral agents (enteric and enterovirus) were detected by RT-PCR. Stool specimens were also tested for bacteria and parasites, by conventional methods.

Results: From the 82 stool samples, 42(51.2%) were positive for virus, 22 (26.8%) for bacteria and 35.6% (26/73) for parasites. An association between viral infection and age < 3 years (OR=4.92, p < 0.01) was observed. Distribution of viral agents was Norovirus II (33.3%), Enterovirus (31%), Rotavirus (23.8%), Adenovirus (9.5%), Norovirus I (2.4%). Simultaneous detection of two viral agents was observed in seven cases (16.7%) - Norovirus II and Enterovirus was the most frequent (57.1%); association with another agent was detected in 33.3% samples. Eight of 22 samples (36.4%) were positive for *Campylobacter jejuni*, 5 (22.7%) for *Salmonella* spp, 7 (31.8%) for *E. coli*, although always in co-infection with another agent, and 1 (4.5%) for *Shigella* spp. 38.5% of the samples were positive for *Cryptosporidium* spp., 23.1% for *Giardia* sp. and 3.8% for *Entamoeba histolytica*. 69.2% of the parasites were co-detected with other agents.

Conclusion: Results suggest that viral agents are the most common among children with acute gastroenteritis, although co-infections with bacteria and parasites are frequent. The most common viral agent associated with acute diarrhea was Norovirus II. An important percentage of cases with no infectious aetiology identified, suggesting that other emergent agents are probably implicated.

BLASTOCYSTIS HOMINIS CAUSES GASTROINTESTINAL SYMPTOMS IN CHILDREN

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In less developed countries, *Blastocystis hominis* is detected frequently in stool of children with gastrointestinal symptoms. In Germany, data on the pathogenicity of *B. hominis* are not available. Therefore, we investigated

(1) if *B. hominis* is found more frequently in children with gastrointestinal symptoms,

(2) if there exists a correlation between *B. hominis* numbers and clinical status, and

(3) if the incidence of *B. hominis* in children remains stable. Stool samples of 988 children showing gastrointestinal symptoms and 73 without symptoms were investigated microscopically using Lawless and chlorazole staining between 2006 and 2011. In 196 of the symptomatic children (22.0%) and 4 of the asymptomatic children (7.4%) *B. hominis* was found in stool specimens ($p=0.005$). No significant correlation between the quantity of the protozoons and the clinical symptoms was detected. *B. hominis* detection increased significantly ($p=0.00011$, $r=0.968$) from 2006 (13%) through 2010 (28%). Gastrointestinal symptoms in children were found significantly more frequently when the infants are colonized with *B. hominis*. Thus, there is evidence that *B. hominis* contributes to pediatric maldigestion. In consequence, standard gastrointestinal diagnostic should be extended by the detection of *B. hominis*.

CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF NOSOCOMIAL ROTAVIRUS INFECTION

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Background and aims: Along with RSV bronchiolitis rotavirus (RV) is a frequent cause of nosocomial infection.

Material and method: Retrospective analysis of consecutive RV patients in two tertiary hospitals [Institute for Mother and Child Care "Alfred Rusescu" (IMCC) and National Institute for Infectious Diseases "Matei Bals" (NIID)] during two consecutive years [2009-11] was generated. We evaluated differences in frequency, clinical features and outcome.

Results: RV accounts for 21.55% of enteritis cases in our study. ~90% of annual RV cases were present during a 7months period [November-May] in both years. 9.15% were nosocomial RV episodes. Higher values were present in IMCC compared with NIID 11.01 vs. 7.29%. Age was much younger in IMCC 84.94% being infants compared with NIID 5.06%. Most (74.77%) of NIID patients were 1 up to 5 years. Severity (Vesikari score) was comparable in both groups 14.5-13.8 IMCC vs. NIID. 0.76% and 1.49% were new episodes after a previous documented RV episode.

Discussion: Several subgroup features were different, probably generating significant differences in data: age [IMCC admits usually infants and NIID is able to admit all pediatric RV patients]; size of rooms & number of beds/room [IMCC are smaller rooms with a low nr of beds]; length of stay [IMCC 4.8d vs. 4.2d NIID].

Conclusions:

1. RV gastroenteritis is frequent (21.55%) and generates significant burden of nosocomial infection (9.15% of admitted RV cases) in a non-immunized population.
2. Severity of nosocomial RV-enteritis is similar in various age-groups and comparable with community-acquired one.
3. Risk factors were young age, in-hospital crowding and length-of-stay.

DETECTION OF GIARDIA INTESTINALIS ANTIGEN IN THE FECAL SAMPLES OF PEDIATRIC OUTPATIENTS IN TEKIRDAG REGION, TURKEY

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Background and aims: Giardiasis, is one of the major diarrheal infestation worldwide, caused by *Giardia intestinalis*. Detection of the pathogen in clinical specimens usually entails microscopy or antigen detection from stool samples. This study was planned to investigate *Giardia* antigen in patients admitted to the pediatrics outpatient clinics in Tekirdağ region.

Methods: A total of 5303 children (aged 0 months to 15 years) with the complaints of gastroenteritis, abdominal pain, nausea and vomiting were screened for *G.intestinalis* antigen. The stool specimens were collected within two years (01.01.2010-31.12.2011) and tested with RIDA Quick, r-biopharm,Germany.

Results: Of 5303 stool samples, antigen positivity was detected in 30(0.57%) samples. A total of 2548 specimens were obtained from girls and 2755 from boys. Distribution due to genders was equal (50%).

Conclusions: As a result of this study, it was shown that the incidence of giardiasis in our region was lower, when compared with other regions of Turkey.

EVALUATION OF ROTAVIRUS INFECTION IN A PAEDIATRIC POPULATION OF WEST CAMEROON: EPIDEMIOLOGICAL, CLINICAL CHARACTERISTIC AND VIRUS GENOTYPING

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Background and aims: The aim of the present study was to start the epidemiological and genotypical surveillance of rotavirus gastroenteritis in West Cameroon during the rainy season.

Methods: Patients met the following inclusion criteria: age (0-10 yrs.), acute diarrhoea, abdominal pain, vomiting, collection of stool sample in the first 48 hrs after recruitment. Each subject was clinically examined and the severity of gastroenteritis was evaluated by the Ruuska-Vesikari Scale. Each stool sample was analysed using chromatographic assay and bio-molecular techniques.

Results: Fifty-six patients were recruited. Main symptoms were fever, diarrhoea, vomiting; 21% of subjects had a Ruuska-Vesikari score ≥ 11 . rotavirus -positive samples by RT-PCR were 38% (N=19). Three different G-genotypes (G1, G2 and G8) and VP4 genotypes (P[8], P[6] and P[4]) were predominant. The main G-P combination was G1+G2P[8]. Mixed rotavirus infections have also been detected.

Conclusion: The present research represented the pilot part of a project that will be performed during 2011-2012. The identified G2P[8] genotype is an unusual emerging combination; G8 strains, associated with animals, have been sporadically recovered from humans. The untypeable P-type rotavirus strains may represent unusual rotavirus strains.

Instead of some limitations of this study, results are in line with the literature and confirm rotavirus as one of the main cause of paediatric diarrhoea in the studied areas even during the rainy season. The main perspective is to continue this surveillance, considering that this will generate data on circulating rotavirus strains that are basic to vaccine development and to vaccine effectiveness.

INVASIVE PNEUMOCOCCAL INFECTION SECONDARY TO HYPOGAMMAGLOBULINEMIA DUE TO MENETRIER DISEASE

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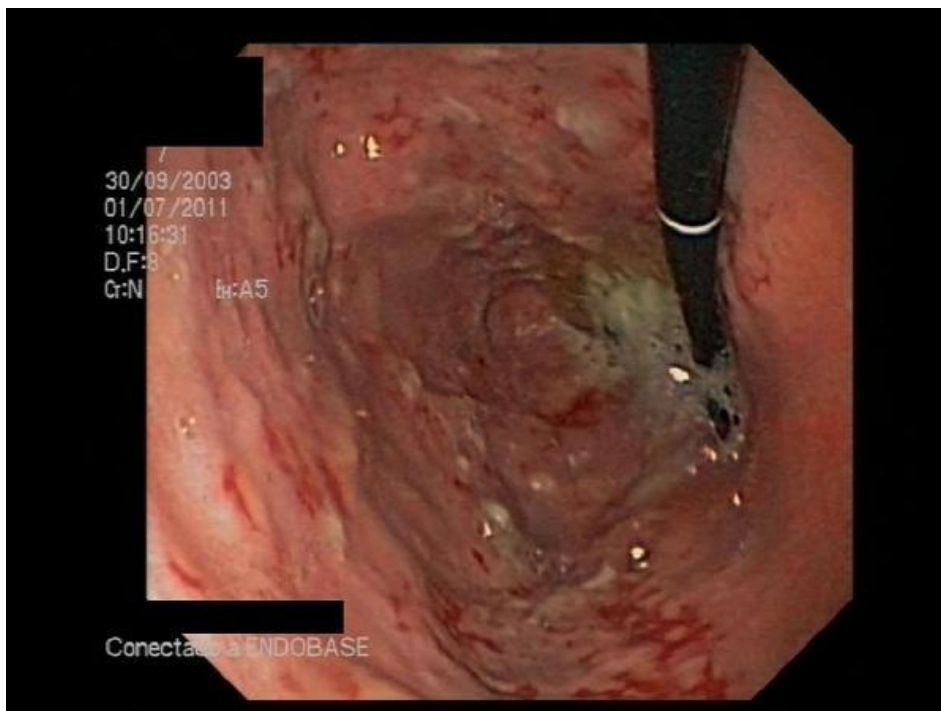
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Cytomegalovirus (CMV) infection can cause Menetrier's disease, an hypertrophic gastropathy complicated by hypoproteinemia due to gastrointestinal protein leakage. In childhood it is usually a self-limited entity, so no specific treatment is required.

Case report: A 7-year old boy with 5-day history of mild anorexia, asthenia, transient periorbital edema and progressive edema of lower extremities and scrotum. He had no fever, cough, nausea, vomiting or abdominal pain. Physical exam showed mild increased respiratory rate and skin pallor, painful edema in scrotum, 2+ pitting edema in lower extremities, abdominal distention, tenderness and moderate esplenomegaly and ascites, proved by thoracoabdominal ultrasound, as well as bilateral pleural effusion. Acute abdomen was ruled out. CBC showed leucocytes 14070/mm³ (Neutrophils 70%), Hb 11g/dl, platelets 237000/mm³; total protein 3.9g/dl, albumin 1.9g/dl; CRP 11.7mg/dl; IgG 250mg/dl. A few hours later, abdominal pain worsened, he had fever 39°C and periumbilical erythema. Antibiotherapy was started. PPD-test and HAV, HBV, HCV, HIV, *Mycoplasma* and EBV serology were negative. CMV IgG and IgM were positive. Blood culture yielded *Streptococcus pneumoniae*. Urinalysis as well as autoimmunity tests were normal. Upper endoscopy revealed diffuse erythema with hemorrhagic areas and prominent folds in the gastric mucosa with diffuse nodules. Gastric biopsy showed generalized foveolar hyperplasia, non-specific inflammatory infiltrates with some neutrophilic infiltrates suggestive of acute ulceration and positive immunostaining for CMV. CMV-culture on gastric biopsy was positive. He was treated with repeated intravenous albumin infusions and penicillin becoming afebrile within 24 hours. He recovered uneventfully at 4 weeks of discharge.

Discussion: Hypoproteinemia and hypogammaglobulinemia may predispose to invasive infections. Protein-losing enteropathy should be considered in hypoproteinemia whenever proteinuria is absent.

Conclusion: Fever in Menetrier Disease should make us consider the possibility of invasive pneumococcal infection.



[Upper endoscopy compatible with Menetrier Disease]

CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN - PRELIMINARY REPORT

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Background: Clostridium difficile (CD) is one of the main factors of nosocomial infections and the number of these infections is still growing. An increasing number of community-associated CDAD (CD antibiotic diarrhea) and CDIs with no exposure to antibiotics is observed. Tests for CD among children are not routinely conducted because of high rate of carrying (13 to 70% infants). The aim of the study was to assess the frequency CDI among children with diarrhea, analysis of the risk factors of CDI and to compare the course of infection and the response to the treatment depending on type of bacteria toxigenic profile.

Material and methods: The retrospective analysis of the clinical case record was made on 28 children with CDI at the age of 3 months to 11 years. PCR tests (Xpert C.Difficile) were used to identify CD in stool specimens.

Results: 2,4% children with diarrhea was diagnosed with CDI. It constituted 11,4 cases per 1000 admissions. All children with CDI received antibiotics before. Correlation between hospitalization and development of CDI was found in 50% children. In 68% children the toxin B-producing strains were revealed whereas in the others hiperwirulent strains NAP1/B1/027 (32%). The period of the diarrhea and the response to the treatment were comparable in both group of patients. SIRS was found in 55% cases infected by NAP1/B1/027.

Conclusion: CD is very important etiological factor of antibiotic-associated diarrhea in hospitalized children, especially with severe diseases and community-acquired CDIs. CDI should be considered in all cases of prolonged diarrhea.

SHIGELLA GASTROENTERITIS - RISK OF INTUSSUSCEPTION

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Introduction : Bacterial enteritis is a risk factor for intussusception but, in *Shigella* gastroenteritis, intestinal complications are rare (relative risk 2.5%).

Case report: Child, male, 13 months, previously healthy, hospitalized for high fever, vomiting and liquid stools with fresh blood with six days of evolution. On admission was prostrate, dehydrated and had periods that alternated between weeping and inconsolable cry. The mucous membranes were pale and the abdomen very tender. Analytically 19,900 leukocytes/mL, ESR 85 mm/h, C-reactive protein 41.7mg/L, serum sodium 129 mmol/L. He performed abdominal ultrasound that showed multiple mesenteric lymph nodes in ileocecal valve, associated with a fixed image of intestinal loops in the right abdominal quadrant. Because it was not possible to exclude intussusception an enema was performed, verifying rapid progression of the air filling the entire colon and ileum. *Shigella flexneri*, isolated in the stool culture, was resistant to ampicillin and cephalosporins 1st and 2nd generation, but sensitive to cefotaxime who was administered for 10 days. In the 2nd day of hospitalization he was afebrile with good food tolerance and progressive improvement of abdominal complaints. A posterior abdominal ultrasound revealed no changes.

Comments: The gastroenteritis may present with high fever and bloody diarrhea but associated crampy abdominal pain and inconsolable cry should raise the suspicion of intussusception. In shigellosis, the male gender, below the age of two years and hypertrophy of Peyer's patches in ileum usually 30 days after infection, are risk factors for complications. In these cases antibiotic therapy is essential to improve prognosis.

**THE ROLE OF ROTAVIRUS IN ACUTE GASTROENTERITIS A STUDY IN THE ISLAMIC HOSPITAL.
AMMAN, JORDAN**

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Objective:

1. to study the microbial pattern of AGE in Jordan.
2. to emphasize the importance of Rota virus in the etiology of AGE.

Methods: All cases of AGE admitted to our pediatric department /Islamic hospital in 2008 were retrospectively reviewed for the results of stool tests , age, sex , duration of stay in hospital and the main symptoms.

Results: A total of 1378 cases of AGE were admitted in 2008.

Confirmed diagnoses by stool testing in 570 cases (42%)

Stool tests were negative in 784 cases (58%)

Rotavirus cases = 485 (35%)

Adenovirus cases = 42 (5%)

Entameba histolytica cases =35 (1.5%)

Bacterial (shigella sp., salmonella sp.) cases = 8 (0.5%)

Rotavirus was found in 85 % of all stool +ve cases.

M/F= 1.15:1

Age: < 1year = 52%, 1-5years = 39%, > 5years = 9%

Mean hospital stay = 2.5 days.

Presentations: Fever (70%), vomiting (85%), diarrhea (96%)

Mortality: Zero%

Conclusion: AGE is a major cause of hospital admissions in Jordan.

Rotavirus is the main cause of AGE accounting for about 35 % of all causative agents. About 90 % of all cases of Rotavirus AGE occur in children under 5 years of age and

More than 50% of cases occur in infants. Vaccination against rotavirus is now the best preventive measure.

PREVALENCE OF NOROVIRUS INFECTIONS IN BULGARIA, 2011**A. Stoyanova**^{1,2}, A. Dikowa², Z. Mladenova¹¹*Virology, NCIPD,* ²*Virology, Sofia University 'St. Kl. Ochridski', Sofia, Bulgaria*

Noroviruses (NVs) are the most common cause of non-bacterial diarrheal infections in humans. They spread mainly epidemically through person-to-person contacts or contaminated food/water, but are also involved in sporadic cases of acute gastroenteritis. The study evaluated the prevalence of norovirus infections among hospitalized pediatric patients. Fecal samples from 188 children (aged 45 days to 10 years) were collected between January and December 2011. Samples were tested for the presence of NVs using real-time RT-PCR and genotype-specific primers toward NVs genogroup I and II. Genetic variation of NV strains was done by sequence and phylogenetic analysis. NV infections were found in 22.3% (42/188) of the samples tested, most often in children less than 2 years of age. Genogroup II NVs prevailed (20.2%, 38/188), but NVs genogroup I were also detected (2.1%, 4/188). Sequence analysis was performed with 17 NV strains (14 NVs genogroup II and 3 NVs genogroup I) for partial polymerase (n=12) and capsid (n=14) genome regions. Among GII NVs GII.g and GII.4/2010 variant were predominant according to polymerase sequences, and GII.1, GII.4 and GII.7 genotypes were detected according to capsid genome region. The ORF1-ORF2 gene sequences were obtained for 9 NV strains (NVs GII n=8 and GI n=1). The results revealed circulation of intergenotype recombinant forms GIIg/GII.1, GII.4 2010/GII.1 and GI.1b/GI.6. The study, presented here-in demonstrated the significant role of NVs in infantile acute diarrhea and highlights the need for continuous NV strain surveillance in Bulgaria.

THE EFFICACY OF C-REACTIVE PROTEIN IN VIRAL/BACTERIAL DISCRIMINATION OF ACUTE GASTROENTERITIS

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Aim: Acute gastroenteritis cause mortality and morbidity in childhood. The discrimination of the viral/bacterial etiology is important for infection control and rational antibiotic use. We aimed to evaluate the role of CRP levels, clinical and laboratory parameters associated with CRP which will be helpful for the etiologic discrimination.

Material and methods: We reviewed the hospital records of children (2months-14 years) (n=400) admitted with acute gastroenteritis to our emergency department. Complete blood counts, serum CRP levels, stool microscopy , stool culture, stool antigen tests for Rotavirus and Adenovirus were assessed. SPSS 11.5 package program is used for statistical analysis.

Results: Cases with fever, leucocytosis and blood in stool had higher CRP levels although no microorganism was isolated from stool culture. There was no relationship between Rotavirus/Adenovirus presence in stool and serum CRP levels. Rotavirus positive cases with fever and leucocytosis at administration had statistically significant high CRP levels.

Conclusion: Serum CRP levels are insufficient to discriminate the viral/bacterial etiology in acute gastroenteritis. Other clinical and laboratory parameters must be considered for treatment.

VITAMIN D AND VIH-INFECTED CHILDREN

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Introduction: Recent studies report a high prevalence of vitamin D (VD) deficiency as well as osteopenia in HIV-adults and children. Efavirenz (EFV) has been associated with hypovitaminosis D and tenofovir (TDF) with hypophosphatemia and low bone mineral density (BMD). The relationship of VD and calcium metabolism with inflammation is of major importance but data are scarce in children.

Methods: A cross-sectional study was done in a referral clinic (Getafe Hospital) to determine the prevalence of hypovitaminosis D, beta-cross-laps (CTX) (marker of bone reabsorption) and possible factors involved in 31 HIV-infected children.

Results: Median age was 15 years (2,5-22); Caucasian 78%; perinatally-acquired 91%; nadir CD4 310 (0-2400); CDC clinic and immunologic categorie C and 3: 28% and 74%. ART treatment 93%: TDF 45% and EFV 58%. Median VD was 35 ng/dl and 40% < 30 ng/ml. BMD done in 15 patients showed Z-score < -1 in 53%. Median time on HAART was 11y (0,8-18,7) and age at HAART initiation 31,5 months (1-175). Median treatment on TDF and EFV was 1y(0-9) and 2,5y(0-12), respectively. Calcium and phosphorus plasma levels were normal limits in all cases, whereas PTH and CTX increased in 6,4% and 58%, respectively. There was a significant correlation between VD and nadir CD4 (Spearman;0,43 p 0.013) but not with BMD Z score. No differences were observed with regard to type or duration of ART.

Conclusion: A high prevalence of hypovitaminosis D and osteopenia was observed in this cohort of HIV-infected children and adolescents. Its significance and future implications warrant further studies.

THE YOUNG AND THE RESISTANT: HIV INFECTED CANADIAN ADOLESCENTS AT THE TIME OF TRANSFER TO ADULT CARE

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Background: Paediatric HIV cohorts are aging and increasing number of adolescents will be transferred to adult care. The objective of this study was to describe clinical, immunological, virological and drug resistance (DR) profiles of HIV-infected Canadian adolescents at the time of transfer to adult services.

Methods: A Cross-sectional study based on prospectively collected data was performed at the last visit before transfer to adult care on subjects enrolled in the Mother-Child Cohort, CHU Sainte-Justine, Montreal, between 1988 and 2010 (n = 45). Clinical and socio-demographic data were reviewed, and genotypic DR testing was performed.

Results: HIV subtyping revealed class B virus in 36 of 45 subjects and in 71%, transmission was documented to be mother-to-child. At transfer, viral load (VL) was undetectable in 19 of 45 subjects, 13 of 45 subjects had CD4 counts < 200 cells/mm³ and 13 were harbouring virus resistant to at least one agent among the 3 main classes of antiretrovirals. Among the 26 subjects with detectable viremia, the median VL was 4.13 log₁₀ HIV RNA copies/ml. The median number of major mutations on the 38 tested subjects was 4. Thirty-three subjects were asymptomatic. Two had CDC stage C conditions.

Conclusions: Overall, despite universal health care access, 73.3% of transitioning adolescents were failing treatment, manifested by detectable viremia, CD4 counts < 200, triple class drug resistance, or all three. Upon transfer to adult care, these patients might face limited therapeutic alternatives and require special attention by health care personnel.

CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF HIV-INFECTED CHILDREN AT DIAGNOSIS IN EQUATORIAL GUINEA

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Background and aims: There are no previous studies describing the current situation of HIV-infected children in Equatorial Guinea. Such studies would be useful to determine patients' clinical and immunologic status and currently prescribed therapies. The objective of this study is to perform a descriptive analysis of the clinical and immunological status of HIV-infected children at diagnosis.

Methods: A cross-sectional study was performed. Data were collected from all HIV-infected children followed-up in Equatorial Guinea in the HIV Reference Unit of the Regional Hospital of Bata and in the two Ambulatory Therapeutic Centers of Bata.

Results: From January 2008 until January 2012 64 HIV-infected children who were followed were analyzed. The median age at diagnosis was 48 months (range 8-180 m) and 58% were female. At diagnosis clinical and immunological situation was as follows: 32% of the children were severely malnourished, 75% were on WHO HIV clinical stage III or IV and 73% had a CD4 number in the range of moderate to severe immunodeficiency. An 80% of the children initiated antiretroviral therapy and 81% started with a fix dose combination of NVP/3TC/d4T.

Conclusions: In Equatorial Guinea most of the diagnoses of HIV infection in children are when patients are on a clinical advanced disease and immunologically severely affected. In a high proportion of children we found severe malnutrition. Therefore most of the children at diagnosis require antiretroviral therapy. A higher index of suspicion will be needed to make a diagnosis of HIV-infection in less affected children.

MOTHER-TO-CHILD HUMAN IMMUNODEFICIENCY VIRUS (HIV) TRANSMISSION FAILING PRENATAL SCREENING

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Background and aims: Universal prenatal screening of HIV infection is crucial for prevention of mother-to-child transmission and early diagnosis of infected children. In Portugal it is recommended since 1998 and transmission rates under 2% were achieved for the last 6 years. However some HIV infected children fail screening and are diagnosed later in childhood. We reviewed these cases with the aim of analyzing the factors involved in these missed diagnosis.

Methods: Retrospective study of HIV-infected children from mother-to-child transmission born in Portugal that failed prenatal screening.

Results: We identified fourteen patients that failed prenatal screening in 3 different groups. Group A - Untested: 7 patients (4 born before 1998; 2 un surveilled pregnancies).

Group B - First trimester negative serologies: 2 patients. Prenatal surveillance was irregular and no test was performed at delivery.

Group C - 1st and 3rd trimester negative HIV screening: 5 children (4 vaginal deliveries; 4 breastfed). Mean age at diagnosis: 21 months (15 months - 9 years). Clinical presentation: CMV hepatitis (1), hepatosplenomegaly and adenomegalies (2), severe scabies (1) and one asymptomatic (accidental finding on screening for occupational needlestick injury). Two patients had immunodeficiency.

Conclusions: We emphasize the importance of HIV prenatal screening. Testing should be performed at delivery when third trimester serology is missing. We alert to the occurrence of mother-to-child HIV transmission with negative screening on the 3rd trimester.

MOTHER TO CHILD TRANSMISSION OF HIV INFECTION IN PORTUGAL 2007-2010**F.M. Prata**¹, M.G. Rocha², M. Tavares³, GTIVHC*¹Pediatric Department, Infectious Unit, Hospital Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, ²Pediatric Department, Hospital Pediátrico de Coimbra, Coimbra, ³Pediatric Department, Hospital S. João, Porto, Portugal*

Introduction: Preventive interventions for mother-to-child transmission (MTCT) of HIV1 have resulted in transmission rates of less than 2%. Portugal has one of the highest incidences of HIV infection in Western Europe and is a preferred country for immigration from African Portuguese speaking countries with high rates of HIV infection.

Objectives: assess the MTCT rate of HIV infection and its risk factors over a 4-year period - January 2007-December 2010.

Material and method: national, hospital-based, multicentre, prospective, observational study.

Results: Thirty-four public and private hospitals participated. During the 4 year period, 1027 HIV-infected women were included. Country/continent of origin: Portugal 55.5%; Africa 41.5%; South America 1%; Eastern Europe 1.2%. 89.8% was HIV1 and in 66% occurred sexual transmission. 24% of the mothers had at least one co-infection (the most prevalent was hepatitis C in drug-addicted). HIV diagnosis was made before pregnancy in 62%, 35.1 % during and 2.8% at or immediately after delivery. The majority did HAART during pregnancy, completed the ACTG 076 zidovudine prophylaxis regimen and completely avoided breastfeeding - in this group the transmission rate was 0%. The newborn was offered triple-drug prophylaxis when these criteria were not fulfilled. Twenty newborns got infected due to MTCT.

Conclusions: In Portugal the rate of MTCT was 2.3% in 2007, 1.6% in 2008, 2.5% in 2009 and 1.8% in 2010. No prenatal care and no HAART/no adherence during pregnancy, detectable maternal viral load before delivery and prematurity were the main risk factors for HIV infection.

RISK FACTORS TO HIV TRANSMISSION IN HIV POSITIVE UNDER-FIVES WITH DIARRHOEA

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Background: HIV is of major public health importance in developing countries like Nigeria. The dominant mode of transmission in children is vertical, from mother to child. Other routes of infection are from parenteral exposure to blood and blood products, via sexual contact or re-use of unsterilized sharp objects.

Objectives: To determine the risk factors for HIV transmission in HIV positive under-fives.

Methods: Over a 6 month period, 342 under-fives attending the diarrhoea training unit of the University of Port-Harcourt Teaching Hospital were screened for HIV, using the double ELISA test. A self administered questionnaire exploring risk factors for HIV transmission was completed by the investigators. The mothers of the children found to be HIV positive were also tested for HIV with the same test kits.

Results: Thirty three of the 342 children tested positive giving an HIV prevalence rate of 9.6%. Three of the 33 seropositive children had lost their mothers. The mothers of the remaining 30 positive children also tested positive to HIV, giving a vertical transmission risk of 90.9%. Other risk factors were; injections from patent medicine dealers in 14 (42.4%), use of unsterilized instruments in 5 (15.2%) and a history suggestive of sexual abuse in 1 (3.0%).

Conclusion: Vertical transmission is the overwhelming source of HIV infection in children. Efforts aimed at prevention of mother to child transmission of HIV should be intensified.

PREDICTIVE VALUES OF CLINICAL FEATURES IN UNDER-FIVES WITH HIV AND DIARRHOEA

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Background: The Human Immunodeficiency Virus is of major public health concern worldwide. In spite of this, the majority of the population in developing countries like Nigeria are still unaware of their HIV status. Knowing the predictive values of clinical features will increase the index of suspicion when a patient is seen with these features, especially in centres where HIV testing is not routinely done for all patients.

Objectives: To determine the predictive values of clinical symptoms and signs suggestive of HIV infection.

Methods: Over a 6 month period, 342 under-fives presenting with diarrhoea to the University of Port-Harcourt Teaching Hospital were screened for HIV infection, using the double ELISA test. Those who tested HIV positive were interviewed about other symptoms present and were examined for presence of physical signs suggestive of HIV infection.

Results: Thirty three children tested HIV positive, giving a seroprevalence rate of 9.6%. Significantly more HIV seropositive patients had wasting, lymphadenopathy, dermatitis, respiratory distress, hepatomegaly, splenomegaly, oral thrush and weight loss. Oral thrush had the highest sensitivity, specificity, positive and negative predictive values while it was the reverse for fever.

Conclusion: Every child below 5 years with oral thrush should be screened for HIV. If seen at a centre where HIV testing is not routinely done, all under-fives with oral thrush should be referred for HIV testing and counselling.

SEROPREVALENCE OF HEPATITIS B VIRUS IN CHILDREN WITH HIV/AIDS IN CALI, COLOMBIA AND POSSIBLE RISK FACTORS

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Introduction: In children with HIV/AIDS after vaccination for hepatitis B virus (HBV) seroconversion is low compared with healthy children.

Objective: To determine the seroprevalence of HBV in HIV/AIDS infected children in Cali, Colombia and identify possible associations.

Methods: Prevalence study in 85 children under 18 years with HIV/AIDS after 3 doses of vaccination. Were considered clinical, laboratory, environmental and sociodemographic variables. Statistical analysis included estimation of the prevalence of seroconversion in children and its corresponding confidence interval 95%, the estimation of other descriptive measures of interest and association analysis by multiple logistic regression.

Results: In this population of children with an average age of 101 months on HAART with an average of 5 years, found a prevalence of 35.3% seroconversion, female predominance, being natives of Cali, of mixed race, and stage C. Seroconversion was not associated with the time elapsed between the first, second and third doses of vaccination or with the diagnosis and placement of the third dose of vaccination. The associated factor was the temporal relationship between the last dose of vaccination and the onset of treatment for 0-3 years (OR = 4.3 95%CI 0.96 to 19.23 p = 0.056) and > 3 years (OR = 9.69 95%CI 2.37-39.5% p = 0.002).

Conclusion: One third of patients seroconverted, and it was found associated with the temporal relationship between initiation of treatment and last dose of vaccine.

HIV TIRDH GENERATION: PREGNANCY IN YOUNG ADULT AND TEENAGE WOMEN INFECTED VERTICALLY BY THE HIV

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Objective: To identify and describe clinical and epidemiological characteristics of mother-child tandems involving young adult and teenage women infected vertically with HIV.

Method: Descriptive, retrospective, and observational study involving young adult and teenage women infected vertically with HIV who gave birth between 2005 and 2011, and their offspring.

Results: Fourteen patients were analyzed, with a total of 17 pregnancies. The women in the study were predominantly caucasian (71%), had four to 10 years of education (78,57%), live with their partners (64,29%), and had their first pregnancy on average at age 17.5 ($\pm 2,56$), mostly while using barrier contraceptives (condoms) irregularly. Around 59% of the male partners (10) were aware of the patients' HIV status. Almost 70% of the women (12) used antiretroviral therapy during pregnancy. The mean CD4 cell count and viral load from the exams performed closest to delivery were 505.25 cells/mm and 2139.67 copies/mL. C-sections were performed in 76.47% of cases (13). Vertical transmission occurred in two cases (11.76%) whose genotyping profile presented resistance to more than one class of antiretroviral, 41,18% (7) infants were confirmed uninfected (negative antibody test at 18 months), 23,53% (4) were presumed uninfected (repeated negative polymerase chain reaction tests, but not confirmed by antibody testing), and 23,53% (4) still have undetermined infection status.

Conclusion: Acceptance of pregnancy tends to correlate well with adequate and early pre-natal care, as well as regular use of antiretroviral therapy. This was observed primarily in the cases where there was no vertical HIV transmission.

EFFECT OF HIV VIRAL LOAD CONTROL ON CLINICAL AND LABORATORIAL EVALUATION IN VERTICALLY HIV-INFECTED CHILDREN AND ADOLESCENTS ON HAART

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Background and aims: The effects of viral load (VL) control on clinical and laboratory parameters of vertically HIV-infected patients were evaluated.

Methods: 41 HIV-infected patients aged 6-21y and 25 healthy age-matched controls were evaluated. HIV group was divided in VL< 400 or >400 copies/mL (VL< 400 or VL>400). They were on HAART for at least 12 months with at least 1log VL decrease. Lymphocytes were analyzed by flow cytometry; measles and tetanus antibodies, by ELISA; nutritional status, by height-to-age z-score. HIV patients were considered clinically non-stable if they presented in the last 12 months: severe infection, opportunistic infection, hospitalization, cancer, three or more mild infections or change in category.

Results: Patients had lower height-to-age z-score than Controls (VL>400:-1.3, VL< 400:-0.7,Control:+0.2, p=0.012 and 0.002, respectively). There were more clinically non-stable patients among VL>400(50%) than among VL< 400(14%)(p=0.013).

Marker(mean values)	Groups			P		
	1.VL>400	2.VL<400	3.Control	1vs3	1vs2	2vs3
CD4+T cells/mm3	736	889	1120	0.006	NS	NS
CD8+T cells/mm3	1017	1025	642	0.010	NS	0.010
NK cells/mm3	203	204	282	0.030	NS	0.030
CD38 molec/CD8+T cell	3502	1639	1726	0.010	0.010	NS
% CD8+T cell Apoptosis	5.9	2.9	3.6	NS	0.050	NS
Measles Ab(IU/mL)	0.09	0.14	0.88	0.011	NS	0.004
Tetanus Ab (IU/mL)	0.08	0.31	0.78	0.005	NS	0.050

[Table 1]

NS=not significant.

Conclusion: Undetectable HIV VL is associated with low immune activation, low lymphocyte apoptosis and clinical stability, but persistent immune deficiencies (NK, Ab responses) and CD8 elevations compared to controls.

RESEARCH THE CAUSES OF PNEUMONIA IN HIV-INFECTED CHILDREN INPATIENT TREATMENT AT VIETNAM NATIONAL HOSPITAL OF PEDIATRICS

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Background: Pneumonia is one of the leading causes disease and mortality in children under 5 years of age in developing countries. Children with HIV infection at risk died of pneumonia 40 times higher than other children. approximately 2.1 million HIV-infected children, more than 80% will have respiratory disease in the course of life.

Aim of the study: To investigate the cause of pneumonia in HIV-infected children.

Subjects and methods: Cross-sectional prospective study described 77 patients from 1 month - 15 years old was diagnosed with pneumonia in HIV patients at the National Hospital of Pediatrics from april 2010 to april 2011. History, examination, chest radiology and blood tests (including bacterial culture and HIV testing) were performed. Induced bronchoalveolar lavage (BAL) was obtained for culture and P carinii detection. Gastric lavages (GL) were done for M tuberculosis culture.

Results: The cause of virus (63%), bacteria (25.2%), fungi (8.4%) and tuberculosis (3.4%). 36.4% had co-infection from two factors. Isolated 6 kinds of virus: CMV (42.6%), EBV (26.7%), rhinovirus (16%), adenovirus (10.7%), influenza (2.7%) and RSV (1,3%); 14 kinds of bacteria; tuberculosis and 3 kinds of fungi was candida albicans, Penicillium marneffeii, and PCP. Bacterium in order to meet: K.Pneumonia (20%), S. Pneumonia (13.3%), H.influenzae, E. Coli (10%), Acinobacter Baumannii, Moraxella catarrhalis, Burkholderia Cepacia, Mycoplasma (6.7%), Acinobacter Junii, P. Aeruginosa, Streptococcus viridans, S.Aureus, Enterococcus Faccium, Enterobacter cloacae (3.3%).

Conclusions: Isolated 6 kinds of virus, 14 kinds of bacteria, tuberculosis and 3 kinds of fungi

PAEDIATRIC INFECTOLOGY AND INTERNATIONAL COOPERATION. ANTIRETROVIRAL DRUGS ADHERENCE IN HIV-INFECTED CHILDREN IN DEVELOPING COUNTRIES. INVOLVED FACTORS IN ADHERENCE FAILURE

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Background and objectives: Adherence to antiretroviral treatment (ART) in HIV-positive patients is essential to control the development of the disease and to reduce the associated morbid-mortality. Nowadays there are very scarce studies about ART adherence in paediatric population in Latin America.

The objective of our project was the assessment of auto-reported adherence to ART during 2010, in HIV-infected children attended at the Instituto Nacional de Salud del Niño (INSN) in Lima, Peru, and at the Hospital Dr. Rafael Pascacio Gamboa in Tuxtla Gutiérrez, Mexico, as well as to identify the factors involved in adherence failure.

Methods: Multicentric cross-sectional study, using structured and previous validated surveys addressed to each child and its main carer or legal guardian.

Results: As a whole, 42.3% of the patients reported an adherence to ART greater than 95%, while this percentage was higher in the INSN. There were detected as factors involved in adherence failure the oversight to take the medication, the fact of forgetting medication in other place, the fact that the patient felt healthy and thought he wouldn't need the treatment and the fact that the main carer was absent or ill.

Conclusions: This study demonstrate that the degree of auto-reported adherence to ART is suboptimal in more than half of the patients polled, identifying some factors involved in this adherence failure. It reveals that it is necessary to strengthen and reinforce the interventions taking place focused in the optimization of the appropriate treatment compliance, emphasizing the importance of a multidisciplinary approach.

SAFETY OF FOSAMPRENAVIR AND DARUNAVIR IN HIV-1 INFECTED CHILDREN IN THE EUROPEAN UNION: AN ONGOING POST-MARKETING SURVEILLANCE STUDY

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Background: Fosamprenavir (FPV) and darunavir (DRV) are indicated for treatment of HIV-infected children aged ≥ 6 years in Europe. We assessed safety of licensed and off-label use of FPV/rtv and DRV/rtv in children reported to 6 cohorts in the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC).

Methods: Retrospective analysis of individual data for all children aged ≤ 18 years ever receiving FPV and/or DRV up to 31/12/10. Adverse events (clinical events, ALT, TG, TC, AST) were summarised and DAIDS gradings characterised severity.

Results: Among 2,600 children included, 150 had taken FPV, of whom 92 were aged 6-18 years and took the licensed dose and 20 only off-label doses. Similarly 123 children had taken DRV, 55 the licensed dose and 32 only off-label doses. On the licensed dose, median age starting any ART was 6 years [IQR 1-11] for FPV and 3 [1-5] for DRV users, and starting FPV and DRV 15 [12-17] and 15 [13-17] years respectively; fewer of those on FPV than DRV had prior exposure to ≥ 8 ART drugs (24% (22) v 82% (45)). Median FPV and DRV duration at last follow-up was 37 [13-50] and 20 [14-32] months; 46% (42) had stopped FPV, and 9% (5) DRV. Rates of grade ≥ 3 events (/100py) for FPV and DRV were low: neutropenia 5 (95%CI 2-9) and 8 (3-18) per 100py; hypercholesterolemia 4 (2-8) and 3 (0-10); hypertriglyceridemia 3 (1-6) and 7 (2-16); raised ALT 2 (0-6) and 0 (0-11).

Conclusions: Findings suggested no safety concerns regarding current licensed doses. The study provides a potential pharmacovigilance model for other ART drugs in the European paediatric population.

PAEDIATRIC HIV HGM SPANISH BIOBANK CONTRIBUTION TO THE DEVELOPMENT OF RELEVANT MEDICAL THERAPIES SPECIFIC FOR CHILDREN

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Background and aims: The vulnerability of children has long raised ethical concerns resulting in the lack of inclusion of children in research studies. This has impeded the development of relevant medical therapies specific for children. In response to these circumstances, in recent years new national and international policies have been developed in order to promote the inclusion of samples from children in translational research. Paediatric biobanks play an important role in this process.

The HIV HGM Spanish BioBank was created in 2004. Its objective is to promote the progress of scientific knowledge.

Methods: The internal process according to research purposes is made through reception, processing, storage and donation, based on biological samples belonging to numerous patients.

All the processes carried out in the HIV HGM BioBank are done under a severe quality system control, following the policy ISO 9001:2008, which ensures the quality of the samples and the fulfillment of the ethical and legal policies.

Results: Nowadays, the Paediatric HIV HGM Spanish BioBank receives samples from 6 prospective cohorts: the cohort of neonatology, the cohort of vertically HIV-infected children, the cohort of endocrinology, the cohort of diseases of the breathing, the cohort of oncology and the cohort of rare diseases.

Over 5.400 vials of different kind of samples, donated by nearly 700 patients, are stored.

Conclusions: This framework contributes to medical research, represents a strategic commitment that seeks the cooperation among working teams and development of specialized networks along with the investigation and treatment of diverse illnesses.

A NEW TOOL FOR THE PAEDIATRIC HIV RESEARCH: DATA FROM THE SPANISH PAEDIATRIC HIV COHORT(CORISPE) AND THE PAEDIATRIC HIV BIOBANK

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Background and aims: In Spain there are approximately 1000 HIV infected children in follow up. The objective of the Spanish HIV Paediatric Cohort (CoRISpe) is to guarantee the high level of the pediatric HIV/AIDS research quality and to improve the results of the Spanish National Health System through the cooperation among various research groups of hospitals, research centres and universities.

Methods: An open, multicentral, retrospective-prospective cohort (CoRISpe) was created in Spain in 2008. It works in a close coordination with the Spanish Pediatric HIV BioBank.

Results: The CoRISpe is divided into two nodes, CoRISpe-1 and CoRISpe-2, representing geographically almost the whole territory of Spain. The two nodes are responsible for putting the demographic, clinical and laboratory data to the digital database in a central hospital. Since 2008 73 hospitals of Spain have begun to participate in CoRISpe. Up to now the CoRISpe has recruited 838 patients. Out of 838 patients 302 are over 18 years old and they have been translated to the Adult Clinical Units. 536 patients (97%) were vertically HIV infected. Up to now there are 363 samples from 202 pediatric patients in the BioBank.

Conclusions: The CoRISpe and the BioBank represent a novel approach to HIV research that might be of general interest not only for basic and clinical research teams working with HIV, but also for those groups trying to establish large networks focused on researching specific clinical and basic problems. The main objective of this abstract is to show the structure and function of the CoRISpe and the BioBank that allow them to efficiently provide data to different research projects in Spain and in other countries.

THROMBOCYTOPENIA IN CHILDREN INFECTED WITH THE HUMAN IMMUNODEFICIENCY VIRUS/AIDS

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Introduction: The Human Immunodeficiency Virus (HIV) infection causes multi-systemic changes, including hematological system: anemia, neutropenia and thrombocytopenia. Thrombocytopenia is the most frequent finding, with a prevalence range between 5.5 to 23.5% in the HIV infected pediatric population. Diverse pathogenic mechanisms are related: immune-mediated platelet destruction and impaired platelet production. The clinical findings are diverse, but usually are mild or silent. In pediatric population can began like an immune thrombocytopenic purpura (PTI), with only skin or mucose involvement without life-threatening bleeding. HIV infection must be ruled out always against the presence of a PTI.

Objective: Analyze the thrombocytopenia prevalence in the HIV pediatric population attended in the Obstetric and Pediatric AIDS National Center, Montevideo - Uruguay.

Material and methods: Descriptive and retrospective study performed analyzing the medical charts of children infected with HIV between 1990 to 2011. Thrombocytopenia was defined as platelet values of less than 100000/mm³ in blood counts at least 2 within 30 days.

Results: We found a prevalence of 8% of thrombocytopenia, with a female predominance. Chronic thrombocytopenia occurs in two-thirds of patients (67%), and in all of them the clinical presentation was mild or silent. Most of the thrombocytopenia was laboratory findings without clinical manifestations. In 13 patients the viral load was detectable, with values greater than or equal to Log 4. Treatments were varied and with everyone describes successes and failures.

Conclusion: The authors warn about the importance of thinking and rule out HIV infection in all pediatric patients with PTI.

ANALYSIS OF NEW HIV INFECTED CHILDREN DURING THE LAST SEVEN YEARS IN THE SPANISH COHORT OF HIV-INFECTED CHILDREN (CORISPE)

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Background: In the last years, the rate of new HIV-infected children have decreased in developed countries because of a combination of public health interventions such as a widespread routine HIV testing and prophylaxis to avoid vertical transmission. Some of these new pediatric HIV diagnoses correspond to children born in developing countries.

Methods: A cross-sectional study was performed. Data were collected from all children at the Spanish Cohort of HIV-infected children (CoRISpe) who had been diagnosed with HIV infection in the last seven years (January 2005-December 2011). Demographic, clinical, immunologic and virologic data were collected.

Results: Up to now CoRISpe has recruited 838 patients. During the study period 156 patients were new diagnoses. 136 (87,2%) were vertically infected. 73 (53,7%) were female. At the diagnosis the median age was 1,6 years (IQR: 4,9-0,18). 30 (22,1%) were C. Median %CD4 was 23 (IQR: 33-15,25), median CD4/mm³ 930 (IQR: 479-1740), viral load 170000 copias (IQR: 30399- 545750). 9 patients (6,6%) were coinfecting by other viruses or pathogens as HBV (2,9%), CVM (2,9%) or syphilis (0,8%). 80 (58,8%) were born in Spain. 82 (60,3%) were born of an immigrant mother or father. The nationality of the foreign parents were Sub Saharan Africa 53 (64,6%), Central and South America 11 (13,4%), Eastern Europe 6 (7,3%), North Africa 7 (8,5%), Europe 3 (3,7%), Asia 2 (2,4%).

Conclusions: Despite the prophylactic measures taken to avoid vertical transmission of HIV there have been few new cases of infected children born in our country. Furthermore, we had some cases whose infection was vertically-acquired in another country and, therefore, we should consider this possibility in order to avoid a delayed diagnosis in foreign children.

LACTIC ACIDOSIS IN HIV-INFECTED CHILDREN AND ADOLESCENTS WITH ANTIRETROVIRAL TREATMENT

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Background: Highly active antiretroviral therapy (HAART) has increased the survival in HIV-infected children. As treatment expands worldwide HAART-associated toxicity might also be increased. Lactic acidosis is one of the most feared adverse events in adults but less is known in children.

Methods: Retrospective study of HIV-infected children receiving HAART that developed lactic acidosis from 4 Spanish hospitals and 1 hospital in Costa Rica.

Results: Of the 6 patients, 3 were women, and median age was 13,1 years (range 9-17 years). They had a mean CD4 cell count of 194 lymphocytes/mm³. The median CD4 nadir was 38 cells/mm³. The 6 patients had been on therapy for a mean of 73 months (range 9-102). Five children were on 1-2 nucleoside analogue reverse-transcriptase inhibitors (NRTIs) (3 with didanosine+stavudine). Clinical evolution before diagnosis ranged from 4 to 28 days. Nausea, vomiting and abdominal pain were the symptoms at presentation in all of them. 5 patients had accompanying symptoms of infection or fever and 3 had neurological symptoms: paresthesias in the lower limbs, ascending paralysis and seizures; agitation and despondency; and seizures. All had low pH (median 7.25; range 6,92-7.28). 4 had elevated transaminases. 1 was coinfecting with HCV. 4 patients required admission to the intensive care unit and died. The other 2 survived.

Conclusions: Lactic acidosis, although rare, is a potentially fatal complication in children with HIV infection who are treated with antiretrovirals. Children on HAART presenting with nausea, vomiting, abdominal pain or peripheral neuropathy should be monitored for lactate concentration.

FAMILY GROUP PSYCHOTHERAPY FOR HEALTHY MANAGEMENT AND GUIDED DISCLOSURE OF THE DIAGNOSIS IN CHILDREN AND ADOLESCENTS WITH HIV

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Background and aims: Major problems in the management of HIV infected children are related to disclosure of HIV status and other psychosocial issues. We investigated the effects of a family group psychotherapy (FGP) approach in supporting children/adolescents through their families. A FGP was provided to caregivers to promote the disclosure of HIV diagnosis.

Methods: The Psychological General Well-Being Index (PGWB-I) and the Short-Form State-Trait Anxiety Inventory (Sf-STAI), two validated multiple choice questionnaire-based tools, were used to measure the effects of the intervention on families. The intervention consisted in ten monthly group psychotherapy meetings with open discussion led by two psychologists and a welfare worker.

Results: Ten randomly selected carers of children and adolescents (4-18 years) - unaware of their HIV status - received FGP, while 7 carers were the controls. No differences in patients' gender, age, viraemia, CD4+ T lymphocytes, family, orphanity, origin, parental education, income, maternal transmission were observed. Caregivers who received FGP were more likely to disclose the HIV status to their children (60%) than controls (14%; $P=.134$). After the intervention, PGWB-I improved in 70% of FGP vs none of controls, whereas it was further deteriorated in 20% of FGP vs 71% of controls ($P=.017$); Sf STAI improved in 60% of FGP vs none of controls, and worsened in 20% of FGP vs 71% of controls ($P=.037$). Carers' education was correlated to improvements in wellbeing and anxiety ($P=.021$ and $P=.013$, respectively).

Outcome		Psychotherapy group (n = 10)	Control group (n = 7)	<i>P</i>
Carer's PGWB-I n (%)	Improved	7 (70)	0 (0)	.017
	Stable	1 (10)	2 (29)	
	Worsened	2 (20)	5 (71)	
Carer's Sf-STAI n (%)	Improved	6 (60)	0 (0)	.037
	Stable	2 (20)	2 (29)	
	Worsened	2 (20)	5 (71)	
Disclosure of HIV status	Yes	6 (60)	1 (14)	.134
	No	4 (40)	6 (86)	

[Outcomes of the intervention]

Conclusion: FGP fostered diagnosis disclosure and substantially improved the carers' ability to cope with HIV.

CORISPE, THE SPANISH COHORT OF HIV-INFECTED CHILDREN: CURRENT SITUATION

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Background and aims: CoRISpe, a Spanish cohort including HIV-infected pediatric patients, yielding interesting information in our country.

Methods: A cross-sectional study was performed. Data were collected until September 2011. Most recent CD4 (count or percentage depending on patient's age) and plasma viral load were evaluated.

Results: The CoRISpe has recruited 838 patients. 302 are over 18 years old. 536 HIV-1-infected children followed in 53 different hospitals were studied. The median age was 12.6 years (range: 0.04-17.98). Vertical transmission was in (97%). 53.7% were female. Most of the children were born from Spanish parents (67.9%) but in the last years an increasing number of patients were immigrants or were born of immigrants, mainly in Subsaharan Africa (19.6%) and South America (7.5%). 4.6% of patients has Hepatitis C Virus (HCV). 23% of the children had developed AIDS. 95% were receiving HAART, and 5% were without treatment. The most common regimen included two nucleoside reverse transcriptase inhibitors (NRTI) plus a protease inhibitor (PI) (46.6%). The most used antiretroviral were Lopinavir/r (51.1%), 3TC (40%), ABV (39.1%) and FTC (30.2%). Median CD4 was 834/mm³ (IQR: 601-1143) and median CD4% was 33.3% (IQR: 28.2-38), most of the children had a CD4% over 25% (88.8%) and CD4 over 500/mm³ (86.7%). 74.1% of the patients receiving HAART had an undetectable plasma viral load.

Conclusions: The institution of a National Cohort has led to an improve in the knowledge of pediatric HIV infection in Spain. In the last years an increasing number were immigrants. A high proportion of vertical-infected children are becoming adolescents and adults. Most of the children were receiving HAART and they had a good immunological response.

EVOLUTION OVER TIME OF ONCE-DAILY ANTIRETROVIRAL THERAPY IN A COHORT OF HIV-INFECTED CHILDREN AND ADOLESCENTS

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Background and aims: Poor adherence to antiretroviral therapy (ART) is the most common cause of treatment failure in HIV-infected patients. Once-daily therapy (QD) may enhance adherence. The aim of this study was to evaluate the evolution over time of QD therapy in a large cohort of HIV-infected children.

Methods: A retrospective study in the Madrid cohort of HIV-infected children was performed. The proportion of patients on QD and undetectable viral load over the past 8 years was assessed, at four time periods (2003, 2005, 2008, and 2011).

Results: An increase of the prevalence of patients on QD was observed over time: 0,8%(2/226), 5,6%(11/196), 23%(44/191) and 39,4%(65/165), as well as the proportion of undetectable viral load: 21%, 42%, 64% and 76%, in 2003, 2005, 2008 and 2011 respectively.

Among patients on QD in 2011, median age was 16,9 years (IQR:15,3-18,5). Median CD4 count was 657 (IQR: 519-827) and 80% had undetectable viral load. Median duration of QD was 2,4 years (IQR:0,9-3,1). The most common regimen was FTC/TDF/EFV (43%). 70,8% received efavirenz-based HAART and 27,7% atazanavir-based HAART. Median number of daily pills was 2 (IQR 1-3, range 1-8). Fixed-dose combination compounds were given in 77%. Adherence was poor (< 70%) in 10,8%, intermediate (70-90%) in 15,4% and good (>90%) in 73,8%.

Conclusions: QD therapy has increased over time in HIV-infected children. Despite QD adherence continues to be a challenge. Reduction in pill burden and more fixed-dose combination antiretroviral drugs are needed in children and adolescents to improve outcomes.

WHEN TO SUSPECT PERINATAL HIV INFECTION IN POLISH CHILDREN? SINGLE CENTRE EXPERIENCE IN LAST 10 YEARS

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Perinatal HIV infection needs prompt treatment to have a better prognosis. Since infection is rare in Poland and pregnant women are not screened for HIV routinely, it is often diagnosed late.

The aim was to sum up our experience with perinatal HIV infections.

Material: 37 HIV-infected children attending our department in 2002-2011. Our department takes care for paediatric population of about 0.5 million and HIV infection was responsible for 6,4-10,7% of admissions yearly.

Results: HIV infection was diagnosed and confirmed by PCR and culture in 37 children (21 girls) aged 2 weeks-16 years (median 3 years). Most children were diagnosed due to AIDS defining condition (12/37 including the wasting syndrome in 6/12), maternal HIV infection (10/37), opportunistic infection (8/37) or thrombocytopenia (3/37). The most frequent manifestation were: pneumonia (17/37), generalized lymphadenopathy (16/37), hepatomegaly (11/37), anemia (10/37) and failure to thrive (9/37). Children were classified as: B(18/37), C(11/37), A(5/37) and N(3/37). Most patients (35/37) were infected with HIV by their mothers. In 2/37 cases the route of infection remains unknown. Only 5/37 mothers knew about their infection prior to pregnancy and prophylaxis was instituted in 2/5. 10/37 mothers were tested for HIV after their children diagnosis and 8/10 were positive. 3 mothers had died (probably for AIDS) before their children were diagnosed. HAART was started in all children and all survived in analysed period.

Conclusions: Perinatal HIV infection is rare in Polish children, nevertheless should be considered in any child with unexplained generalized lymphadenopathy, hepatomegaly, anemia failure to thrive or recurrent serious infections.

QUALITY OF LIFE FACTORS ASSOCIATED WITH ADHERENCE TO THE TREATMENT IN VERTICALLY HIV-INFECTED CHILDREN

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Background and aims: To study the impact on the quality of life (QL) of HIV-infected children and its effect on adherence to the antiretrovirals.

Methods: Multicenter study, pilot, cross-sectional research on a cohort of 71 HIV-infected children from 3 Hospitals of Madrid and 34 non-HIV children, all between the age of 5 and 14. The non-HIV-group children were selected from state schools of the same neighborhood. To determine the QL, the Spanish version of the profile of child health [CHIP-CE] questionnaire was used. The adherence to treatment, the indirect method of semi-structured family interview was used and compared with markers of effectiveness of the treatment such as CD4 T cells, VL and clinical status.

Results: The HIV-group did not show differences in comparison with the non-HIV-group in the perception of their health status and wellbeing. However, the HIV-group showed a worst psychological wellbeing ($p=0.051$), a lower level in the self-evaluation ($p=0.001$) and in the ability to concentrate ($p=0.002$), worst family relationships ($p=0.032$) and was more prone to perform with threat to achievements ($p=0.008$) and to perform conducts of individual risk ($p=0.047$) than the non-HIV-group. The HIV-group had a poor perception of the overall QL ($p=0.039$) too. The HIV-group children with the worse perception of their physical wellbeing ($p=0.033$) and those who were more prone to individual risk behaviour ($p=0.049$) had the worse compliance to the antiretroviral treatment.

Conclusions: Our study shows that the impact of the HIV infection on children extends to all aspects of QL. Adherence to antiretroviral treatment is directly related to aspects of QL in children.

SUCCESSFUL TREATMENT WITH CHOPP-R PROTOCOL AND HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY (HAART) FOR AIDS-RELATED IMMUNOBLASTIC LARGE B-CELL LYMPHOMA

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Background: B-cell lymphoma is the second most common cancer associated with AIDS. In contrast to Kaposi Sarcoma, lymphoma appears to be a late manifestation of HIV disease. The use of highly active antiretroviral therapy (HAART) concomitantly with chemotherapy seems to improve patient outcomes.

Case: A 16-year-old girl was admitted to our hospital with enlarged and painful axillary and cervical lymph nodes. Subsequent investigation by CT scan and excisional biopsy revealed an immunoblastic large B cell lymphoma at stage III. PET CT of the whole body yielded multiple enlarged lymph nodes in the mediastinum and abdomen simultaneously. She was diagnosed as HIV positive with a RNA copy number of 758,000 copy/mL and was treated with chemotherapy (6 cycles of CHOPP protocol combined with rituximab) and HAART and achieved a complete remission and long-term immunologic recovery. CD4 count was significantly low at the beginning of HAART therapy (80 cells/mL), increased up to a level of 25% (700 cells/mL) with a HIV RNA copy number of < 20 copy/mL at the end of 6 months of antiretroviral therapy. During her hospital stay she experienced CMV retinitis and pulmonary aspergillosis which resolved with gancyclovir and voriconazole therapy. After the completion of chemotherapy a control PET CT scan showed all the lymph nodes totally ametabolic with no FDG reuptake elsewhere in her body.

Conclusion: Our case indicates that intensive chemotherapy with CHOPP-R combined with HAART may be well tolerated and effective in AIDS-related immunoblastic large B-cell lymphoma.

INCREASED SUBCLINICAL ATHEROSCLEROSIS AND IMMUNE ACTIVATION IN HIV-INFECTED CHILDREN AND ADOLESCENTS-THE CAROVIIH STUDY

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Objectives: HIV patients present early cardiovascular disease (CVD). The study of subclinical atherosclerosis in subjects without classic CVD risk factors, such as children and adolescents, may help to clarify the specific influence of HIV infection and immune activation on the atherogenic process.

Methods: Carotid intima-media thickness (IMT) was measured in 122 HIV-infected children and young adults and 53 healthy controls. Markers of immune activation and immune senescence were determined in a subgroup of 34 HIV patients and 11 controls.

Results: The mean age of the HIV-infected and uninfected subjects were 14.9 years (range 2.5 to 23.8) and 13.6 (range 2.9 to 22.6), respectively. Most HIV patients were female (64.8%), had undetectable viral load (76.4%), were vertically HIV-infected (96.7%) and all but 2 patients were on HAART.

IMT was thicker in HIV patients compared to uninfected subjects ($0.434\text{mm} \pm 0.025$ vs 0.424 ± 0.018 , respectively). After adjustment by age, sex, BMI and smoking status, HIV infection was independently associated with thicker IMT (odds ratio, 2.7; 95% confidence interval, 1.4-5.5; $p=0.004$).

Compared with HIV uninfected subjects, frequencies of activated T CD4+ cells were higher among HIV-infected children ($p=0.002$), especially among viremic patients.

Viremic patients with IMT above the median showed a higher frequency of activated T CD4 and CD8 cells that did not reach statistical significance.

Conclusion: In our study, HIV infected children and adolescents had higher IMT than healthy controls. The effect of the immunological status seems to be stronger than the effect of age in the early stages of life.

NEGATIVE FOURTH GENERATION HIV ANTIGEN/ANTIBODY TESTS IN CHILDREN VERTICALLY INFECTED WITH HIV

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Aim: To highlight the phenomena of negative antigen/antibody (Ag/AB) tests in children with vertically acquired HIV infection.

Background: A 12 year old child with HIV was found to have a negative Ag/AB test and 11 years of undetectable viral loads causing diagnostic concern.

Method: Fourth generation antigen/antibody (Ag/AB) tests were performed in 7 HIV infected children in our small paediatric HIV clinic. For comparison, 24 horizontally infected adult patients (22 male and 2 female) over the age of 40 with comparable treatment lengths had the same test performed.

Results: 6/7 children had a positive result and only the index child tested negative (14%). All 24 adults, aged 42-75, had a positive Antigen/antibody detection test. They had been on treatment with viral load suppression for 8-13 years:14 patients and 0-7 years:10 patients. Repeat testing confirmed the results. The index child was well with a good CD4 count and an undetectable viral load. She originally presented to another hospital at 8 weeks with pneumocystis jiroveci pneumonia, and disseminated CMV disease. Initial VL was 1,200,000 c/ml and CD4 count 490. Full VL suppression was obtained by 1 year of age.

Conclusion: Seroreversion may occur in children infected at birth with subsequent early initiation of HAART. Early severe disease may explain the lack of antibody evolution, whilst starting HAART very early in life and remaining well controlled may lead to no detectable antigen. This case highlights this phenomena and the importance of excellent record keeping as patients move between different areas and countries.

CD8-T CELLS SUBSETS INCREASE IMMUNOSENESCENCE IN VERTICALLY HIV-INFECTED CHILDREN WITH DETECTABLE VIRAL LOAD

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Background: CD8 T cells are crucial in the immune responses against HIV-infection. HIV-infected adults suffer a naïve CD8 T-cell depletion and accelerated senescence caused by chronic antigen stimulation. HIV-infected children preserve a better capacity of immune reconstitution but CD8 responses are defective. The objective of this study was to investigate whether HIV vertical transmission and the presence of viral load produced a premature aging of the CD8 population.

Methods: Using multiparameter flow cytometry, we studied within the CD8 population the frequencies of naïve, memory, effector memory and TemRA subsets and we measured markers of senescence, activation and proliferation in these cells.

Results: We found that naïve subset in viremic children was markedly decreased and had a replicative senescence phenotype. Furthermore, viremic children showed increased frequencies of memory, effector memory and TemRA CD8 T cells, with a more activated and replicative senescence phenotype. We found that HIV-infected children with undetectable viral load have an increased senescence in memory and effector CD8 T cells, but the frequencies and phenotype of the CD8 subsets analysed are comparable to healthy children.

Conclusions: Our study shows that CD8 T cells of HIV-infected children have a more senescent phenotype when compared to age-matched healthy children. Moreover, our results support the importance of maintaining undetectable viral load in HIV-infected children to avoid the premature ageing and dysfunction of CD8 T cells.

PERSISTENT SEROREVERSION TILL PREADOLESCENT AGE IN A CHILD VERTICALLY INFECTED BY HUMAN IMMUNODEFICIENCY VIRUS

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Introduction: Although transient absence of active generation of HIV-1 specific antibodies has been described in infants vertically infected, early treated and with permanent suppression of viral replication, no case of persistent seroreversion till preadolescent age is published.

Case report: We present an exceptional case of paediatric HIV early treated with HAART, with maintained undetectable viremia since three months of age, who keeps being seronegative at nine years of age. Infection was confirmed by detection of proviral DNA, and no HAART modification has been done.

DISCUSSION: Children perinatally infected by HIV-1, early treated with HAART may present absent or scarce HIV-1 specific antibody responses after clearance of maternal antibodies, as described in three series of cases with a maximum of 5 years of follow up. The misknowledge of cases with persistent seroreversion may lead to treatment interruptions and consequent loss of the control achieved in these children, as demonstrate two cases published.

Conclusion: Early suppressive HAART initiation in infants vertically infected by HIV may lead to the absence of a specific humoral immune response with negative serologic results which should never be interpreted as HIV eradication. A potentially reactivable intracellular reservoir of proviral DNA is still present and no treatment interruption is recommended nowadays. More is needed to be known in order to improve perinatal interventions and long-term treatment of these patients as they get older, to decrease secondary effects and improve adherence and quality of life, maintaining the excellent control of the infection achieved till nowadays.

IDENTIFICATION AND ROLE OF STRESS PROTEINS INDUCED DURING DENGUE VIRUS INFECTION IN HUMAN MACROPHAGES**Y. Padwad^{1,2}***¹Immunomodulation Division, Defence Institute of Physiology and Allied Sciences, Delhi, ²Biotechnology, Dr. DY Patil Institute of Biotechnology and Bioinformatics, Pune, India*

Heat Shock Proteins (Hsps) or stress proteins are overexpressed in all cell types under different stressful conditions including infections by viruses. In this study effect of dengue virus infection on relative expression of Hsps was evaluated and their role in the progression of the infection was determined. As macrophages are the primary host for dengue, human pro-monocyte U937, monocyte THP1, human blood derived monocytes and mature macrophage cells were infected with dengue type 2 New Guinea strain for the assessment of expression of various Hsps. A significant overexpression of Hsp60 was observed in virally infected U937 cells whereas Hsp70 overexpression was observed in case of monocytes, mature macrophages and THP1 cells as compare to controls. In order to determine the correlation between Hsp60 and 70 overexpression and viral survival in infected cells, levels of Hsp60 and Hsp70 was down regulated by siRNA transfections. Viral titer was determined by quantification of viral RNA using qRT-PCR in cell supernatants. Intracellular viral load was determined by flow cytometry. In Hsp silenced virally infected cells there was a significant decrease in virulent titer as supported by plaque formation assay performed on BHK21 and LLCMK2 cells. Down regulation of Hsp expressions also resulted in increased type-I Interferon which mediate its antiviral effects through double stranded RNA induced protein kinase (PKR). These observations suggests that elevated levels of Hsp60 and 70 in dengue infected cells promote in viral multiplication and could be a possible therapeutic target for the effective management of this prominent pediatric virus infection.

HEPCIDIN LEVELS FALL AND IRON DEFICIENCY INCREASES ACROSS THE MALARIA SEASON IN RURAL GAMBIAN CHILDREN

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Background and aims: Although iron deficiency and anemia are common in children in malaria-endemic settings, iron supplementation strategies are controversial due to concern that iron might increase the risk of malaria and other infection. The antimicrobial peptide hepcidin is the major molecular determinant of systemic iron homeostasis. It is important to understand molecular determinants of iron status in the context of high infectious load and malaria in order to develop safe and efficacious iron supplementation policy

Methods: We measured hepcidin, malaria parasitaemia and other iron/inflammatory markers in 61 rural Gambian children at the start and end of a malaria season.

Results: Hepcidin levels were significantly lower at the end of the malaria season as children became more iron deficient and inflammation waned. Hepcidin levels were higher in children with asymptomatic parasitemia. In multivariable analysis low serum hepcidin levels were associated with low serum ferritin, high soluble transferrin receptor and the end of the malaria season in multivariable analysis.

Conclusions: These data suggest that an infection/inflammation-induced inhibition of iron utilization, acting partly via raised hepcidin, operates during the malaria season and causes iron deficiency. Iron supplementation could be most beneficial at the end of the malaria season when the nutrient is most needed and most likely to be absorbed and utilized.

IN VITRO INFLAMMATORY RESPONSES ELICITED BY ISOLATES OF ALLOIOCOCCUS OTITIDIS OBTAINED FROM CHILDREN WITH OTITIS MEDIA WITH EFFUSION

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Objectives: Recent clinical isolates obtained from children with otitis media with effusion provided an opportunity to determine in a model system, if this species elicited levels of cytokines equivalent to *Streptococcus pneumoniae* and the effects of interferon-g (IFN-g) as a surrogate for virus infection.

Methods: The THP-1 human monocytic cell line was used to assess induction of interleukin (IL)-6, IL-1 β , IL-8 and tumour necrosis factor- α by 39 clinical isolates of *A. otitidis* and two of *S. pneumoniae*, ATCC 49619 and a recent blood culture isolate (SP2). Cytokines were quantified by BioRAD bead assay and the Luminex 200.

Results: All *A. otitidis* and pneumococcal strains induced cytokines tested; higher levels were obtained at higher ratios of bacteria per THP-1 cell. Priming with IFN-g significantly enhanced cytokine responses. ATCC 49619 induced lower responses than SP2: IL-1 β (P < 0.0001); IL-6 (P < 0.0001); TNF- α (P < 0.0001). Although SP2 elicited higher levels than *A. otitidis* SG34 and ATCC 49619, *A. otitidis* LW 27 elicited significantly higher responses than the other isolates except for IL-6 (P > 0.05).

Conclusions: The results reflect the need to use recent clinical isolates in studies of pathogenicity. *A. otitidis* elicited cytokine levels equal to or greater than those of pneumococcal strains. This species needs to be considered in development of preventive measures for otitis media.

A CASE OF STEVENS JOHNSON SYNDROME**O. Marginean¹, C. Marginean²***¹Pediatrics I, ²Medicine, Medicine University Tg. Mures, Targu Mures, Romania*

We present a 9-year-old boy with epilepsy refractory to previous treatment diagnosed with Stevens Johnson syndrome appeared after the introduction of Lamictal in treatment. The boy had fever, polymorphous exanthema, papulopustular erythematous, bullous generalized vesiculobullous elements and skin denudation, conjunctivitis, mouth lesions. We have interpreted the associated pneumonia as a damage of a lower respiratory tract mucous membranes within Stevens Johnson syndrome. The evolution of the disease was favourable after high doses of Ig IV (intravenous immunoglobulin).

In conclusion, even if the Steven Johnson syndrome incidence is low in children, pediatricians should be aware of the possibility of its regression (even after antiepileptics - Lamictal), and even if the use of Ig IV is controversial, it leads to healing when is given in high doses.

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PROBIOTIC LECTINS SUPPORTING HUMAN AGAINST PATHOGENS: NATURAL INTRINSIC POTENTIAL FOR SYSTEM DRUG THERAPY IN FUTURE

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Background and aim: Human probiotic bacterial lectins (hPBL: lactobacillus and bifidobacterial L [LL and BL]) were firstly isolated and described by us. We showed that hPBL are represented and function as systems [1]. The aim was to summarize hPBL activities of usefulness for human organism.

Results:

1. On the one hand, hPBL possess useful activities towards human cells: discrimination of mucins and GalNAc-containing antigens; bifunctional modulation of macrophage migration; inducing lymphocyte cytokine production (acidic[a] PBL); involving in regulating Ig-binding; protection of Ig from proteolysis by fungal pathogen (aPBL); protection of cell layers and intracellular metabolism (aLL>aLB); dissolving agglutinates without cytolysis (basic [b] PBL); specific dissolving PBL-induced cell aggregates (without cytolysis) by polymeric glycoconjugates (aPBL).

2. On the other hand, hPBL reveal activities which are useful within biotope microbiocenosis: microbe static and lytic activities against opportunistic pathogens; pathogen biofilm destruction (aLL>aLB [*Staphylococcus*]; aLB>aLL [*Candida*]); anti-*Candida* species early and late action (aPBL followed by bPBL); multisynergism between PBL and between PBL and azoles; coupled functioning in biotope according to principle: "higher pathogen virulence - higher anti-pathogen activity of hPBL"; biotope disbiose type dependent interaction between biotope pathogen(s) and hPBL (LB or LL).

Conclusion: Taken together, hPBL act as imitators of cellular probiotics and possess additional protective net of reactions which are perspective for human protection against pathogens.

Reference: [1] M. Lakhtin, V. Lakhtin, V. Alyoshkin, S. Afanasyev. Lectins of beneficial microbes: system organization, functioning and functional superfamily. *Beneficial Microbes* (2011) 2: 155-165.

ENTEROVIRUS STIMULATES THE TRANSMIGRATION OF T LYMPHOCYTES ACROSS THE HUMAN BLOOD-CEREBROSPINAL FLUID BARRIER *IN VITRO*

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Background and aims: Despite large progress in prevention and therapy, meningitis is still associated with a high morbidity and mortality. Viral meningitis is almost threefold as frequent as the bacterial meningitis. In newborns and infants, enterovirus is one of the most common viral pathogens. There is large evidence that not the pathogen itself but rather its complex interplay with the host defense system is responsible for CNS-damage. Besides the blood-brain barrier (BBB), the choroid plexus, which forms the blood-cerebrospinal-fluid (CSF) barrier (BCSFB) seems to be involved during enteroviral meningitis.

Material and methods: In an *in vitro* model of the BCSFB based on human choroid plexus papilloma cells (HIBCPP), the chemotaxis rate of T lymphocytes in the absence or presence of CXCL12 before and after enteroviral stimulation with Cox B3 and Echo 30 was analysed. The cytokine response was quantified with a cytometric bead array and rtPCR.

Results: Enteroviral stimulation significantly enhanced the chemotaxis rate of CXCL12-stimulated T lymphocytes across the human BCSFB. Barrier function and vitality of the HIBCPP were not altered by viral infection. The analysis of the cytokine-profile in response to enteroviral stimulation revealed an enhancement of CXCL3, IL8 and CCL5 and was confirmed by rtPCR.

Conclusions: Enteroviral stimulation leads to an increase of T lymphocyte influx across the BCSFB *in vitro*. Chemokine-induction by virus seems to be involved in this process. A profound understanding of the pathogenesis of viral meningitis may lead to more precise diagnostics and treatment.

USE OF RITUXIMAB AND DEXAMETHASONE IN EBV-ASSOCIATED HEMOPHAGOCYtic SYNDROME IN AN IMMUNOSUPPRESSED CHILD

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Introduction: Hemophagocytic syndrome (HS) can be triggered by a broad spectrum of infectious agents, usually in the setting of immune deficiency. It may also occur in conjunction with a rheumatologic disorder. We present a patient with oligoarticular juvenile idiopathic arthritis who developed an EBV induced HS and discuss the therapeutic approach.

Case report: A 5-year-old girl with an oligoarticular juvenile arthritis and uveitis on weekly treatment with methotrexate, presented with acute mononucleosis over two weeks. She developed abdominal pain, pallor and increasing hepatosplenomegaly. Laboratory investigation revealed bicytopenia, hypertriglyceridemia and hypofibrinogenemia, serum elevation of ferritin and soluble interleukin-2 receptor and 3^{10^9} EBV-DNA copies. Since she met the clinical and laboratory criteria for mild EBV-HS on an immunosuppressed child, methotrexate was discontinued and conservative treatment without etoposide was started. She began intravenous immunoglobulin and dexamethasone which was associated with rituximab (375mg/m²; one administration) and acyclovir.

The patient demonstrated a rapid clinical and laboratorial response. There were no EBV-DNA copies after one week.

Discussion: In this case we assumed that the inadequate immunologic response to the virus secondary to the long-term immunosuppressive regimen was the main factor leading to HS.

The single use of IGIV and corticosteroid therapy is well documented in mild disease. Although not considered standard therapy, the use of rituximab was supported by recent data suggesting that anti-CD20 antibodies may reduce morbidity and mortality by depleting B-lymphocytes and reducing the chance of malignant transformation of these B cells, which could be potentiated by methotrexate.

DIFFERENCE IN CYTOKINE PRODUCTION AMONG HEALTHY INFANTS WITH AND WITHOUT COLONIZATION OF COMMON GRAM-POSITIVE BACTERIA IN NASOPHARYNX

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Background and aims: In infants early colonization of pathogenic bacteria has been found to be associated with later development of recurrent respiratory infections. It is known that cytokines play an important role in host defence against bacterial colonization and infections. This study aimed to investigate whether there is a difference in cytokine production among healthy infants with and without nasopharyngeal bacterial colonization.

Methods: Of 412 3-month-old healthy Finnish infants, whose nasopharyngeal and blood samples were tested, 35 were selected. Of them, 8 were culture positive for *Streptococcus pneumoniae*, 9 for *Staphylococcus aureus*, 8 for *Corynebacterium* sp. and 10 were culture negative. Whole blood was stimulated by LPS, polyIC and Pam3Cys. Whole blood without stimulation served as negative control. Supernatants collected at 24h were tested by Luminex multiplexed assay for concentrations of INF- β , INF- γ , IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-17A, IL-23, MCP-1 and TNF- α .

Results: Significant increase in production of all cytokines, except INF- β and MCP-1, were observed after stimulations in studied subjects. For MCP-1, the increase was only observed in colonized subjects when stimulated with Pam3Cys. Colonized subjects had significantly lower cytokine responses than non-colonized (P values < 0.05). *S. aureus* colonization resulted in higher IL-23 production when compared to *S. pneumoniae* and *Corynebacterium* sp colonization (P values < 0.05).

Conclusions: Our results indicate there is a difference in cytokine production between Gram-positive bacteria colonized and non-colonized infants. Further studies are needed to understand its effect on later development of recurrent respiratory infections in children.

DETERMINATION THE PREVALENCE OF GENITAL COLONIZATION WITH MYCOPLASMA HOMINIS AND UREAPLASMA UREALYTICUM OF PREGNANT WOMEN WHO ADMITTED TO RASULAKRAM HOSPITAL**B. Sobooti**¹, M. Abdollahi Nia¹, A. Dehghani Fard²¹Tehran University of Medical Sciences, ²Tarbiat Modares University of Medical Sciences, Tehran, Iran

Background: Mycoplasma hominis and Ureaplasma urealyticum are two important opportunistic pathogens implicated in urogenital infections and preterm delivery. Genital mycoplasmas have been implicated in different neonatal diseases as pneumonia, sepsis and meningitis.

Material and method: To investigate the pathogenicity of Ureaplasma urealyticum and Mycoplasma hominis, this study has been conducted to determine the frequency of colonization from tracheal aspirate specimens in newborns. This study was performed among 165 pregnant women. The mean age of the pregnant women was 25.4 (SD=3.2) (P< .05). The mean gestational age was 38.2 weeks (SD=2.3).

Results: According to definitions, 137 (83%) of infants were terms and 28 (17%) of them were preterm. Our investigations showed that 33 infants (20%) had positive nasopharyngeal cultures and 132 (80%) of them were negative from all cases. Moreover, the percentage of positive cultures in preterm group was 14.3% (4 cases) and in term group was 21.2% (29 cases).

Conclusion: Our study showed the necessity of attending to different genital pathogens, specially Mycoplasma hominis and Ureaplasma urealyticum, in order to prevention of newborns from affliction to diseases such as meningitis and lung infections.

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF ROTAVIRUS NOSOCOMIAL INFECTION OUTBREAKS IN A NEONATAL UNIT DURING A 2 YEAR PERIOD

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Background: Rotavirus (RV) gastroenteritis is a common nosocomial infection and cause of outbreaks in neonatal units (NU).

Objectives: To determine the incidence of RV infections among neonates hospitalized in a NU, the associated clinical manifestations and risk factors.

Methods: A case-control study was conducted in a NU between January 2009 and December 2010. Neonates RV-positive were designated as cases and equal number of neonates RV-negative hospitalized during the same period were considered as controls. RV infection was confirmed by testing fecal samples with rapid immunochromatographic test. Positive samples were further G and P typed through RT-PCR.

Results: A total of 79 RV-cases were identified; 42 females. 95% of cases were hospital-acquired. The annual incidence of RV infection was 7,6/100 and 5/100 admissions in 2009 and 2010 respectively. Three seasonal outbreaks were reported (06/2009, 10/2009, 06/2010). Age of infected neonates varied from 3-71 days old (mean age:21,7±11,7) and the average hospitalization stay was 17,7±17,2 days. Diarrhea was present in the 48% of cases. Other symptoms included vomiting (20%), fever (34%), blood in feces (20%), abdominal distention (8,6%) and septic appearance (7%). RV genotypes detected were:G4P[8] 89,6%, G1P[8] 4,2% and G12P[8] 6,3%. Cases were older than controls ($p < 0,05$). No other significant differences were identified regarding gender, weight at birth, gestational age, type of birth, hospitalization stay, coinfection or antibiotic treatment.

Conclusions: Surveillance and infection control program are essential to reduce rate of hospital-acquired RV infections in NU. Further investigation of risk factors associated with nosocomial transmission of RV is required.

BLOODSTREAM INFECTIONS IN A PEDIATRIC UNIT

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Background and aims: Bloodstream infections are related to high rates of morbidity and mortality in pediatrics. The aim of this study was to evaluate the most frequent agents in bloodstream infections in a pediatric unit.

Methods: During February 2010 to December 2011 we included blood cultures from patients of the Department of Pediatrics from Santa Casa hospital. Data were obtained from medical records and microbiological reports.

Santa Casa hospital is characterized by being philanthropic teaching hospital, tertiary, and the Department of Pediatrics has 150 beds.

Results: During the study period were collected 11,626 blood culture samples. The overall positivity rate was 8.5%, ranging from 3.7% to 33.3%. The contamination rate was 0.8% (n = 88) and we obtained 18 polymicrobial samples.

From the positive samples, 64.5% (n = 572) were Gram positive, 29.1% (n = 258) Gram-negative and 6.4% (n = 57) fungi.

Coagulase-negative *Staphylococcus* was the most frequent agent, isolated in 49.9% (n = 443) of the samples and 58.8% were methicillin resistant. However, in 74.2% of the cases was considered pseudobacteremia or contamination. The other agents most frequently isolated were: *Klebsiella* spp (7.1% / n = 63), and 30.9% of ESBL-producing strains, *S. aureus* (6.7% / n = 59), 32, 6% of MRSA, *Candida* spp (6.4% / n = 57), 65.7% of non-albicans species and *Acinetobacter* spp (5.6% / n = 50), 35,5% of carbapenems resistant strains.

Conclusions: Our results can demonstrate the importance of multi-resistant Gram-negative as a bloodstream infection pathogens.

ATTITUDES REGARDING OCCUPATIONAL VACCINES AND VACCINATION COVERAGE AGAINST VACCINE-PREVENTABLE DISEASES AMONG HEALTH-CARE WORKERS WORKING IN PEDIATRIC DEPARTMENTS IN GREECE

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The aim of the study was to assess the attitudes regarding occupational vaccines and vaccination coverage against vaccine-preventable diseases among health-care workers (HCWs) working in pediatric departments in Greece. A standardized questionnaire was distributed in three tertiary-care hospitals and 306 HCWs answered. Overall, 19.6% of HCWs listed correctly the three vaccines recommended in Greece (against seasonal influenza, hepatitis A, and hepatitis B). Self-reported completed vaccination rates were 33% against measles, 33% against mumps, 41.7% against rubella, 3% against varicella, 5.8% against hepatitis A, 69.2% against hepatitis B, 38.2% against tetanus-diphtheria, and 19% against pertussis. HCWs up to 40 years had higher completed vaccination rates against measles, mumps, rubella, hepatitis B, and pertussis, compared with older HCWs (p-value < 0.001). Susceptibility rates were 14.2% for measles, 15.7% for mumps, 14.6% for rubella, 7.6% for varicella, 87.4% for hepatitis A, 22.6% for hepatitis B, and 61.8% for tetanus-diphtheria. A mandatory vaccination policy was supported by 70.6% of 276 HCWs who answered this question; however, considerable differences were noted by target disease. Physicians and nurses working in general pediatric departments more frequently supported a mandatory vaccination policy compared to those working in non-general pediatric departments (73.5% versus 60.9%; p-value=0.033). In conclusion, completed vaccination rates against vaccine-preventable diseases are suboptimal among HCWs working in pediatric departments in Greece. Campaigns should be organized to increase HCW vaccination coverage and ensure a safe environment for HCWs and patients. The national vaccination policy for HCWs in Greece should be reconsidered to include a broad spectrum of vaccine-preventable diseases.

EXTREMELY LOW RISK FOR ACQUISITION OF RESPIRATORY VIRAL INFECTION IN THE EMERGENCY ROOM OF A LARGE PEDIATRIC HOSPITAL DURING WINTER**H.C. Maltezou¹**, K. Mougkou², H. Asimaki², K. Koniaraki², P. Katerelos¹, M. Giannaki², M. Theodoridou³*¹Hellenic Center for Disease Control and Prevention, ²Aghia Sophia Children's Hospital, ³University of Athens, Athens, Greece*

Waiting areas of health-care facilities represent a particular challenge for infection control, since large numbers of people congregate in close proximity and can be exposed to infectious agents. An important proportion of children who visit Emergency Departments (EDs) are consulting for infectious diseases, especially during winter and early spring, when influenza viruses and respiratory syncytial virus (RSV) circulate in the community. The aim of this study was to investigate the rate of transmission of respiratory viral infections to children visiting the ED of a large pediatric hospital from November 4, 2010 to March 31, 2011 (influenza and RSV season in Greece). A total of 615 children (median age: 5 years (range: 7 days - 15 years) with no respiratory symptoms and/or a discharged diagnosis other than respiratory infection were prospectively studied. During their visit, 92 (15%) of the 615 children had close contact with a coughing and/or sneezing visitor or a visitor with rhinorrhea, including close contact with a symptomatic child (89 patients, 96.7%) or a symptomatic adult (3 patients; 3.3%); none reported close contact with a symptomatic health-care worker. Of the 615 children, 22 (3.6%) children developed at least one symptom compatible with a respiratory viral infection within 1-7 days after the visit, including cough (12 children), fever (8), rhinorrhea (7), and/or respiratory distress (1). Three children (0.49%) developed an influenza-like illness. These findings indicate that transmission of respiratory viral infections to children visiting an ER during the winter season is extremely low.

INVESTIGATION AND CONTROL OF AN OUTBREAK OF IMIPENEM-RESISTANT *ACINETOBACTER BAUMANNII* INFECTION IN A PEDIATRIC INTENSIVE CARE UNIT

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Background: This study investigated clinical details and epidemiology of the imipenem-resistant *Acinetobacter baumannii* (IRAB) outbreak which occurred at a pediatric intensive care unit (PICU), and describes successful outcome of the implemented infection control measures.

Methods: With the recognition of three clustered cases with IRAB bacteremia occurred at the PICU of Seoul National University Children's Hospital, Korea from August to September 2010, the following outbreak control strategies were implemented; reinforcement of hand hygiene and contact precautions, investigation of environmental contamination, disinfection of the contaminated environment and medical equipment, active surveillance culture upon PICU admission, and isolation of IRAB-positive patients. The clinical and microbiological data were reviewed for *A. baumannii* positive cases in the PICU from Apr 2001 to June 2011. Multi locus sequence typing (MLST) was also performed.

Results: Twenty IRAB-positive cases (bacteremia in 10, pneumonia in 3, and colonizers in 7) were detected from January 2010 to February 2011. Thirteen IRAB-infected patients were all placed on a mechanical ventilator, had central venous catheters, received broad-spectrum antimicrobial treatment, and had underlying diseases. Eleven (85%) patients died probably due to IRAB infection. IRAB grew from four samples obtained from sinks and water taps among 38 environmental samples. MLST analysis revealed two sequence types: ST138 (n=16) and its single-locus variant ST92 (n=4). Eleven weeks after the initiation of active surveillance, no further IRAB isolates were identified.

Conclusions: This study identifies the environmental source of an IRAB outbreak in a PICU and describes successful control of the outbreak with a multi-component intervention program.

CONSECUTIVE *SERRATIA MARCESCENS* MULTI-CLONE OUTBREAKS IN A NEONATAL INTENSIVE CARE UNIT

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The aim of this study is to describe three consecutive outbreaks caused by genetically unrelated *S. marcescens* clones that occurred in a neonatal intensive care unit (NICU) over a 35-month period. Carriage testing in neonates and health-care workers (HCWs) and environmental investigation were performed. An unmatched case-control study was conducted to identify risk factors for *S. marcescens* isolation. During the 35-month period, there were 57 neonates with *S. marcescens* isolation, including 37 carriers and 20 infected neonates. The prevalence rate of *S. marcescens* isolation was 12.3%, 47.4%, 42% in outbreaks 1, 2, and 3, respectively. Nine of 20 infected neonates died (45% case fatality rate). There were 10 PFGE types introduced in the NICU in various times. Four PFGE types accounted for the 9 fatal cases. During outbreak 3, a type VIII *S. marcescens* strain, the prevalent clinical clone this period, was detected in the milk kitchen sink drain. Multiple logistic regression revealed that the only statistically significant factor for *S. marcescens* isolation was the administration of total parenteral nutrition (TPN). In conclusion, TPN solution might constitute a possible route for the introduction of the microorganism in the NICU. Gaps in infection control should be identified and strict measures implemented to ensure patient safety.

CATHETER ASSOCIATED CENTRAL LINE INFECTIONS IN PAEDIATRIC ONCOLOGY - IMPACT OF A CENTRAL VENOUS CATHETER MAINTENANCE BUNDLE OF CARE

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Background and aims: Paediatric oncology patients require prolonged intravenous access with central venous lines. This combined with persistent immunosuppression puts these children at high risk for Central Line Associated Blood Stream Infections (CLABSI), yet little data exists in this patient population. **Methods:** We retrospectively assessed the impact of the implementation of a central venous care bundle (including aseptic non-touch technique) on CLABSI rates in a tertiary paediatric oncology unit. Pre-intervention data was collected May 2008-April 2010, Post-intervention data May 2010-October 2011. **Results:** We identified 295 oncology patients with a central access devices totalling 103,404 catheter days. There were 142 CLABSI (153 pathogens) representing an average rate of 1.4 CLABSI per 1000 catheter days (CI 1.19-1.61). One year after the introduction of the care bundle there was a reduction to 0.68 CLABSI per 1000 catheter days; this was not sustained with a CLABSI rate of 1.38 per 1000 catheter days in the last quarter of the study. Fifty % (76/153) of CLABSIs were due to Gram positive organisms; Viridans Group *Streptococcus*(21) and Coagulase negative *Staphylococcus*(21) being most commonly isolated, 39% Gram negative organisms and 11% fungi.

Conclusion: This study describes a stable rate of 1.4 CLABSI per 1000 catheter days in paediatric oncology patients, despite the introduction of a high impact intervention for the care of central venous lines. This may reflect need for long term surveillance, further auditing of the maintenance bundle of care and the possible role of gut translocation in the pathogenesis of CLABSI in immunosuppressed patients.

ANTIBIOTIC-RESISTANT ORGANISMS OF HEALTHCARE-ASSOCIATED INFECTION IN PEDIATRIC INTENSIVE CARE UNIT

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Background and aims: The pathogen results in healthcare-associated infections (HAIs) at various sites, particularly in critically ill patients. However, HAIs not only affects patient safety, also increases morbidity and mortality. Our study was to determine the risk factors and predictors of mortality of antibiotic-resistant HAI in a pediatric intensive care unit (PICU).

Methods: A retrospective cohort study was conducted at a PICU with 14 beds in a 2,900-bed teaching hospital. All patients admitted to the PICU who had developed HAIs from 2005 to 2010 were eligible. The definitions of the US Centers for Disease Control and Prevention were used.

Results: One hundred eighty and one antibiotic-resistant HAIs occurred and the incidence rate was 3.7%. The most frequent antibiotic-resistant HAIs observed were bloodstream infections 6.1%, urinary tract infections 3.3%, surgical-site infections 2.8%, respiratory tract infections 2.2%, and others 5%. The most common antibiotic-resistant organisms were methicillin-resistant coagulase negative Staphylococci 100%, methicillin-resistant *Staphylococcus aureus* 68%, and *Klebsiella pneumoniae* and *Escherichia coli* producing extended spectrum beta-lactamase (ESBL) 22.9%. After controlling for potentially confounding factors, length of stays (LOS) before onset of HAI (Odds Ratio [OR] 1.009, 95% confidence interval [CI] 1.001-1.017) was an independent factor. In addition, after controlling prognostic factors for mortality, LOS more than 31days (OR 2.76, 95% CI 1.02-7.5) and used of mechanical ventilator (OR 2.60, 95% CI 1.20-5.62) were independent factors.

Conclusions: Methicillin resistance is frequent with Staphylococci infection. Invasive devices and LOS were the most important risk factors.

HEALTHCARE ASSOCIATED PNEUMONIA AND EAR, NOSE, THROAT OR MOUTH INFECTIONS IN A NEONATAL UNIT OF A TERTIARY CARE HOSPITAL

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Background and aims: To determine the epidemiological profile of hospital associated pneumonia and eye, ear, nose throat or mouth infections in a tertiary care hospital in India.

Methods: The neonates meeting the criteria of HAIs as defined by CDC were included in the study. Bacteriological & fungal cultures and antimicrobial susceptibility testing was performed using CLSI guidelines. More than 898 neonates were studied in which 20 risk factors were studied and analyzed using EpiInfo software.

Results: The Incidence rate (IR) of hospital associated conjunctivitis was 4.1 infections per 100 admissions. E. coli and S. aureus were the predominant pathogens. All the isolates of E.coli were resistant to ampicillin, ampicillin- sulbactam, amoxicillin-clavulanic acid, ciprofloxacin and ceftazadime.

The risk factors were triple pregnancy ($p=0.00003$), intubation at birth ($p=0.028$) and orogastric feed ($p=0.02$). The IR of hospital associated oral infection was 0.7 infections per 100 admissions. All the cases yielded Candida species. The risk factors were Apgar score < 4 at one minute ($p=0.0047$), blood transfusion ($p=0.001$), total parenteral nutrition ($p=0.035$), orogastric feed ($p=0.049$), antimicrobial administration ($p=0.004$), central vascular catheter insertion ($p=0.008$) and mechanical ventilation ($p=0.012$). The IR of hospital associated pneumonia was 0.3 infection per 100 admissions. The lower incidence could be ascribed to strict CDC guidelines. The risk factors included administration of oxygen through the nasal prongs ($p=0.028$).

Conclusion: To reduce the current incidence of these HAIs, the risk factors have to be appropriately dealt with and the infection control practices have to be strictly implemented.

PAEDIATRIC OSELTAMIVIR PRESCRIPTIONS IN PRIMARY CARE IN UNITED KINGDOM, ITALY AND NETHERLANDS DURING THE 2009 A/H1N1-PANDEMIC: AN ARPEC STUDY

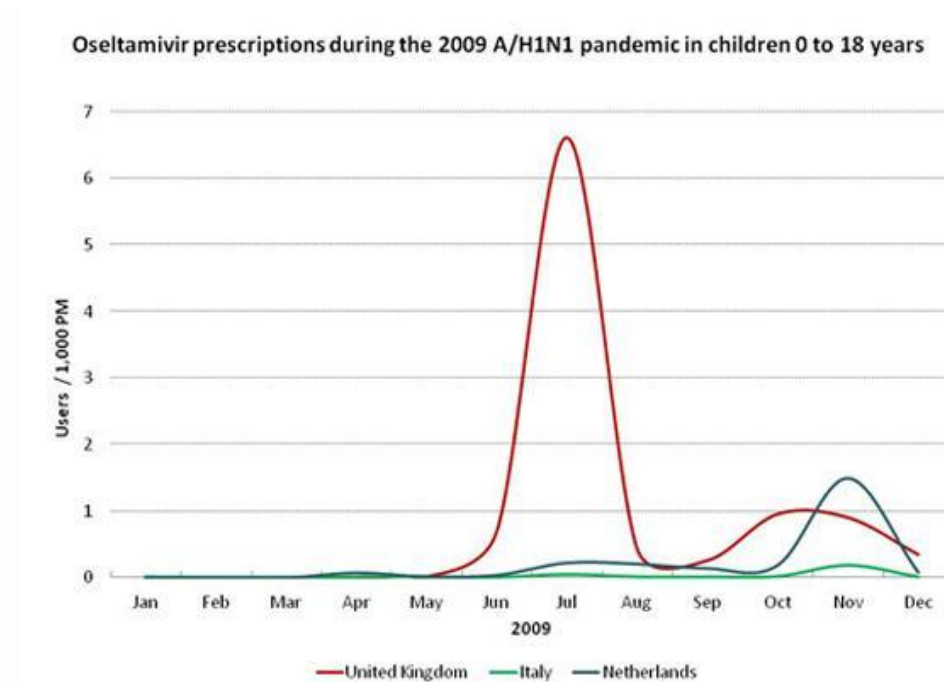
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Background and aims: During the 2009 A/H1N1 pandemic, oseltamivir was widely used in adults, but there has been limited data on its use in children. In this study we aimed to describe the prescription pattern of oseltamivir to children in primary care in the United Kingdom (UK), Italy (IT) and the Netherlands (NL) in 2009.

Methods: We conducted a retrospective cohort-study in three electronic medical records databases; The Health Improvement Network (THIN)(UK), Pédianet (IT), and Integrated Primary Care Information (IPCI)(NL) and included all children (0-18 years) with a total of 27,560,565 person-months(PM) of follow-up in 2009. Monthly prevalence of oseltamivir prescriptions was calculated in 2009; defined as the number of children with at least one prescription/month.

Results: The monthly prevalence of oseltamivir prescriptions showed a large summer-peak followed by an autumn/winter-peak. In line with the number of ILI-cases reported to ECDC, the summer-peak was most prominent in the UK (6.6 users/1,000PM) while the autumn/winter-peak was most prominent in NL (1.5 users/1,000PM). The prevalence in Italy was limited (max. 0.2 users/1,000PM).



[Oseltamivir prescriptions in the UK, NL and IT]

Monthly prevalence was highest for children aged 1 to 5 years (NL: 2.6/1,000PM in November; UK: 10.7/1,000PM in July).

Conclusions: During the 2009 pandemic, oseltamivir prescriptions peaked in July in UK and in November in Netherlands and Italy. The high peak in the UK may reflect changes in prescribing policy at this time. The variation in prescribing rates across Europe suggests inconsistency in the indications for oseltamivir in children.

GERMAN MEASLES OUTBREAK BURSTS IN TWO UNVACCINATED BORDER HILLY DISTRICTS OF NORTHERN HIMACHAL PRADESH, INDIA**S.N. Gupta**¹, N. Gupta²¹*H and FW, RHFWTC, ²Free Lance Researcher, Kangra, India***Background:** We investigated german measles outbreak as a suspected one of measles to confirm diagnosis and recommend for control & prevention.**Methods:** We defined a case of german measles as occurrence of febrile rash in any resident of the eight villages between 20th October to 16th January, 2007. Case patients were line listed and information on age, sex, residence, date of onset, symptoms, signs, traveling, treatment history, vaccination status and pregnancy status were collected. The outbreak was described by time, place and person characteristics. Diagnosis was confirmed clinically, epidemiologically and serologically; first to measles, scrub typhus and later to German measles viruses.**Results:** We identified 116 cases in eight villages (112/116 clinically and 04/116 laboratory confirmed). The overall attack rate (AR) was 11%; highest in the age group of 11-20 years (Range 13% to 44%). Sex specific AR for males was 12%. All case patients were < 20 years of age with median age of 12 years. Complication rate was 05% but no death reported on account of german measles. No pregnant woman was found to be affected. None was immunized against rubella. Four tested positive for IgM antibodies to rubella out of eight samples. 33% (38/116) had opted for the modern medicine.**Conclusions:** A german measles outbreak was confirmed in unvaccinated populations which was possibly due to the frequent traveling of Bengali colony vendors case patients to other areas. We advised the local health authorities to provide MR vaccination to the unexposed in eight affected and neighboring villages.

COLONIZATION OF CHILDREN BY MULTIRESTANT BACTERIA IN THEIR ADMISSION IN A PEDIATRIC UNIT

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Objectives: The community setting-up of the multiresistant bacteria (MRB) is establishing in several regions of the world. The purpose of this work is to estimate the colonization of the children by MRB at their admission in a pediatric unit.

Patients and methods: During a 2-month period, rectal and nasal samples were taken in 80 consecutively hospitalized children, the day of the admission. MRB detected were: meticillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus* (VRE) and multi-resistant Gram-negative bacilli (MRGNB).

Results: Among 164 infants, 37(22. 5%) were colonized by at least one MRB at entrance: The majority came from their domicile (n=32), the average age was of 6 years; the children were essentially hospitalized for bronchiolitis and gastroenteritis. An antibiotic treatment in the last three days was taken in 6 cases: Amoxicillin + clavulanic acid (3cases) and cefotaxim (3cases). A total of 37 MRB were isolated with the predominance of MRGNB (n=21): 10 *Escherichia coli*, 8 *Klebsiella pneumonia*, 1 *Serratia liquifaciens* and 2 *salmonella.spp*. The nasal colonization with SARM was noted in 13 cases and colonization with VRE in 3cases.

Conclusion: The community setting-up of the MRB in children is worrying and interested essentially the BGNMR. The hospitalization and the preliminary antibiotic treatment do not seem the main risk factors.

COMPARISON OF CRP SERUM LEVEL AND WBC IN HOSPITALIZED PEDIATRIC PATIENTS

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Objective: To study the correlation between white blood cell count and CRP level, in pediatric hospitalized population.

Material and method: 130 patients, 55 girls and 75 boys, with median age 3.4 ± 3 years (2 months to 13 years), were hospitalized in Pediatric Clinic during the period of six months (1/1/2011-1/6/2011). Clinical assessment, white blood cell count and CRP were analyzed for all children. From the total of 130 children, 32 (24.6%) were hospitalized with diagnosis gastroenteritis, 26 (20%) with diagnosis of upper respiratory tract infection, 17 (13.0%) with lower respiratory tract infection, 16 (12.3%) with acute asthma, 15 (11.5%) with postinfectious bronchospasm, 14 (0.7%) with bronchiolitis, and 10 (7.6%) patients with others diseases (autoimmune and allergic diseases).

Results: The results of our testings are demonstrated on the table:

DISEASE	CRP>2mg/dl	CRP>20mg/dl	WBC>10000/ μ L	WBC>15000/ μ L
GASTROENTERITIS	6(18,7%)	10(31,2%)		8(25,0%)
UPPER RESP. INFECTION	6(23,0%)	5(19,2%)	2(7,6%)	1(3,8%)
LOWER RESP.INFECTION	7(41,1%)	4(23,5%)		
ACUTE ASTHMA	3(18,7%)	1(6,2%)	1(6,2%)	1(6,2%)
POSTIN.BRONCHOSPASM	6(40%)	1(6,6%)		
BRONCHIOLITIS	7(50%)			1(7,1%)

[DIAGNOSTIC RESULTS]

Conclusions:

- 1) According to the previously reported results, patients with gastroenteritis in a significant proportion, have remarkably elevated CRP value and leucocytosis.
- 2) The majority of patients with respiratory infections, presented elevated CRP value, in contrast with the relatively normal white blood cell count.
- 3) According to our results, CRP test performs better in comparison with WBC, in pediatric infectious and inflammatory diseases.

AN OUTBREAK OF INFLUENZA A (H1N1) 2009 IN A NEONATAL INTENSIVE CARE UNIT

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Background and aims: Outbreaks of influenza A (H1N1) 2009 have rarely been reported in NICUs. Annual immunization of all health care workers (HCW) against seasonal influenza is recommended but compliance rate to vaccination is low and exposure to infected staff as the source of nosocomial outbreaks has been described. We report an outbreak of H1N12009 in a tertiary level NICU that resulted in considerable morbidity.

Methods: A total of 22 neonates were hospitalized at that time in the unit, of which 11 (50%) were born preterm. H1N1 2009 was detected in nasopharyngeal aspirates by indirect immunofluorescence assay (IFA) and PCR. Oseltamivir was administered for prophylaxis and treatment. All infants were closely monitored for the manifestation of symptoms compatible with influenza and for potential clinical and laboratory adverse effects of antiviral treatment.

Results: Two infected infants who were immature by gestational age and birth weight developed pneumonitis requiring respiratory support, while a third full term neonate had a mild uncomplicated illness. No significant adverse effects were noted during antiviral treatment or prophylaxis. The survey conducted identified infected HCWs as the source of the outbreak as well as a very low immunization rate of 15% among nursing staff. Strict infection control measures were applied in the unit successfully.

Conclusion: Nosocomial influenza can cause considerable morbidity especially in the high risk neonatal population and is readily transmissible in the NICU setting by unvaccinated staff members who contract influenza. Therefore, in addition to infection control measures, the implementation of HCW immunization is of utmost importance.

INCIDENCE, RISK FACTORS AND OUTCOME OF VENTILATOR ASSOCIATED PNEUMONIA IN INTENSIVE CARE UNITS AT NATIONAL HOSPITAL OF PEDIATRICS, VIETNAM**N.K. Le¹**, D.T.K. Khu²¹*Infection Control*, ²*Neonatology, National Hospital of Pediatrics, Hanoi, Vietnam***Background and aims:** To identify the incidence, proportion, and outcome of ventilator associated pneumonia (VAP) in 3 intensive care unit - NHP. In addition risk factors for VAP will be identified.**Methods:** Patients under mechanical ventilation (MV) in 3 ICUs. This is an observational, analytic, prospective study. All children undergoing MV we eligible. CDC guidelines were used to diagnose VAP. Demographics, clinical features etc werecollected from study participants. . OR or RR or χ^2 were calculated to identify associated factors of VAP.**Results:** 120 patients under MV fitted the inclusion criteria. There were a total of 1162 ventilator days. The incidence rate of VAP on children under MV developing was 26.7%; The incidence density of VAP was 27.5/1000 ventilator days. The mortality rate of VAP was 46.7%. The only statistically significant risk factor of VAP was length of MV over 4 days ($\chi^2=5.5$; $p=0,018$). Other factors including gender (OR=1,3; $p>0.05$); age (OR=0.65; $p>0.05$); type of ward ($\chi^2=3.05$; $p>0.05$); admission diagnosis: premature newborn (OR=0.91; 95%CI: 0.38-2.17), cardiovascular problems (OR=1.0; 95%CI: 0.25-3.96), respiratory problems (OR=1.83; 95% CI:0.77-4.34), prior sepsis (OR=2.37; 95%CI:2.69-9.13); and endotracheal insertion route (OR=2.71; $p>0.05$) were not risk factors for VAP. The commonest microorganiss isolated were gram negative bacteria (75%), with *P. aeruginosa* being most common.**Conclusion:** The incidence, proportion and mortality rates of VAP were high. There was significant association between VAP and length of MV over 4 days.

INCIDENCE, RISK FACTORS AND OUTCOMES OF NOSOCOMIAL BLOOD STREAM INFECTION IN INTENSIVE CARE UNITS. NATIONAL HOSPITAL OF PEDIATRICS, VIETNAM**D.T.K. Khu¹, N.K. Le²***¹Neonatology, ²Infection Control, National Hospital of Pediatrics, Hanoi, Vietnam***Background and aims:** To identify the incidence rate, time of onset, and outcomes of nosocomial blood stream infection (BSI) from NICU, PICU and SICU, NHP, Hanoi. To identify risk factors of BSI at NHP.**Methods:** Inpatients from three ICU were included. CDC criteria were used to identify a case of BSI. This is an Nested case- control study. OR were calculated to identify risk factors of BSI.**Results:** 417 patients met the inclusion criteria; 34 BSI periods were confirmed on 29 patients; the incidence density was 9.1/1000 patient-days; time of onset was 9.7±1.6 days (mean±SD); the case fatality rate was 38.1%; length of hospitalization was 13.5±1.9 days (mean±SD). These statistically significant risk factors of BSI were identified: mechanical ventilation (OR= 5.7; p=0.01), ; the number of time a new IV catheter was inserted (mean = 5.5; p=0.047); and presence of other infection (OR=5.28; p=0.042); These factors were not found to be statistically significant risk factors for BSI: infection on admission (OR=1.01; p=0.98); prior admission in a health facility (OR=1.16 - 1.84; p=0.82-0.17); antibiotics before admission (OR=1.15; p=0.76); time of antibiotic changed (mean = 2.3; p=0.1).**Conclusion:** The incidence and mortality rate of BSI in this study was middle-high. Risk factors for BSI were the number of time a new new IV catheter was inserted, MV, and presence of another infection. The changing of antibiotic treatment, infection on admission were not a risk factor for BSI.

DEVELOPING A STANDARDIZED EUROPEAN METHOD OF MONITORING HEALTHCARE-ASSOCIATED BLOOD STREAM INFECTION RATES IN NICUS

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Background and aims: Newborns admitted to NICUs are at high risk for developing healthcare-associated bloodstream infections (HABSIs), in particular central line-associated BSIs (CLABSIs). Infection rates reported in literature are often difficult to compare. We aimed to determine whether it may still be possible to use published data for defining standard rates for benchmarking and inter-hospital comparisons.

Methods: A systematic literature review was conducted of studies published after 2000 up to October 2011 carried out in individual NICUs reporting both the rate and cumulative incidence of HABSI or CLABSI and total patient-days in the evaluation period.

Results: 18 studies fulfilled the inclusion criteria. Cohort size ranged from 150 to 5,102 neonates with 2,195 to 64,607 patient-days of observation. Study periods were between 9 and 84 months. Several characteristics differed strongly among NICUs. Although NICUs mostly provided level II or III neonatal care, mean length of stay and proportion of high-risk babies (VLBW ranging from 7.3% to 50.6%) were widely different and therefore difficult to compare. Moreover, few groups provided information about the percentage of surgical neonates. 15 studies reported an overall HABSI rate of 6.6 /1000 pt days (range 2.0-14.9) and 9 studies an overall CLABSI rate of 12/1000 CVC days (range 3.2-21.8), with around a seven fold variation in reported rates.

Conclusion: Reported rates for both HABSI and CLABSI in this group of studies were high. There is a need to develop a standardised method of monitoring HABSI in NICUs taking into account population characteristics such as gestational age and case-mix.

EPIDEMIC SPREAD OF ST1-MRSA-IVA IN A NEONATAL INTENSIVE CARE UNIT, PALERMO, ITALY

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Community-associated (CA) methicillin resistant *Staphylococcus aureus* (CA-MRSA) have recently emerged as important pathogens in neonatal intensive care units (NICUs).

The purposes of this study were to characterize methicillin-resistant (MRSA) isolates from an outbreak in a NICU, to look for the genetic traits of CA-MRSA and clonality, to review the characteristics of the neonatal cases and their outcomes and to investigate the route of entry and transmission of the MRSA outbreak strain in the NICU under study.

Surveillance specimens from the anterior nares were routinely obtained weekly from each neonate. All the first isolates from surveillance cultures and all the clinical isolates were submitted to susceptibility testing and genotyping. Data gathered from each infant's medical record were prospectively included in a database and clinical features and outcomes of the colonized/infected infants were assessed.

In the period April - August 2011, 14 infants were colonized or infected by a strain of ST1-MRSA-IVa. The CA-MRSA strain appeared to be brought into the NICU by an infected infant transferred by another hospital. A multifaceted infection control intervention was able to contain the outbreak.

Our findings confirm that NICU is a healthcare setting with a critical permeability to CA-MRSA. Active surveillance with the support of molecular typing is necessary to implement timely and effective control interventions.

ANTIMICROBIAL COPPER IN ELEMENTARY SCHOOLS - A STRONG TOOL TO PREVENT INFECTIONS

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Aim: Aim of this report is the application of antimicrobial copper alloys in multi-touch surfaces at educational institutions (mass gathering areas) for the reduction of microbial flora in order to protect public health.

Method: We used antimicrobial copper alloys (Cu63%-Zn37%) to cover or replace multi-touch surfaces (door handles, railings, hand-push surfaces etc) in specific elementary school. Estimation of microbial flora and viral load carried out in two phases. Prior and after antimicrobial copper implementation. Samples were taken from surfaces, cultured in appropriate-selective culture media for microbial growth and molecular techniques for isolating viruses.

Results: Results showed clear reduction in the amount of microbial loads in all surfaces and objects replaced by antimicrobial copper. The number of bacteria isolated in the respective surfaces before the copper implementation was a multiple of bacteria isolated after copper implementation. The correlation resulted in the findings of a reduction in the number of bacteria colonies (CFU / ml) after antimicrobial copper implementation.

Conclusions: Researchers have shown great interest in antimicrobial copper since usage of both antimicrobial copper and its alloys for the protection of public health gives encouraging results. Usage of the antimicrobial properties of copper in multi-touch surfaces of mass population concentrations, such as in schools, has already started to apply worldwide. Limiting the spread of germs and viruses in those areas in combination with the implementation of the basic methods of infection preventing (clean hands, etc) is a strong antimicrobial ally to Public Health.

REDUCING RISKS OF CONTAGIOUS DISEASES AS A RESULT OF CONTAMINATED POTABLE WATER**M. Timovska**¹, V. Angelovska²*¹Department for Analysis and Research, Protection and Rescue Directorate, ²PHI Dr Angelovska, Skopje, FYR Macedonia*

Introduction: Contaminated potable water which is a result of natural disaster - flood is a frequent reason of contagious disease with the children. Taking preventive measures reduces the risk of it.

Materials and methods: The study involves 3 regions in Republic of Macedonia (Tetovo, Kumanovo and Strumica) hit by flood in February 2010. It includes 530 children age 1 to 14 years. 270 are female children while 260 are male ones. Analytic and descriptive methods have been used for data processing.

Results: In the 3 regions in Republic of Macedonia (Tetovo, Kumanovo and Strumica) which were hit by the flood in February 2010 the health of 530 had been jeopardized. 37 children got symptoms of vomiting and diarrhea. Later, 8 children got hepatitis of type A. Due to the timely take measures from the competent authorities, outburst of epidemic was prevented. Drinking water from taps in the flooded regions was banned, and the inhabitants were given bottled water. Also, the inhabitants of the regions were trained about some hygienic and epidemiological measures and the flooded houses were disinfected.

Conclusion: Timely taken preventive measures and activities in case of flood reduce the risk of appearance of contagious diseases with children.

EFFECTS OF WIPING AND SPOT DISINFECTION IN REDUCING THE LOAD OF ENTERIC VIRUSES

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Background and aims: Cleaning and disinfection is performed in health care settings to control or reduce transmission of viruses from contaminated surfaces. However efficacy of cleaning and disinfection must be tested and ensured for the pathogens involved. Thus aim of study was to assess effectiveness of cleaning by wiping with liquid-soap and disinfection with chlorine solutions by quantitative carrier test against different human enteric and model viruses.

Methods: Viruses in 1% stool were dried on stainless steel carriers (2.2×2.2 cm) for 1 hour. Procedure consisted of wiping the carrier once with a viscose cloth soaked in water with liquid-soap followed by disinfecting with 1000 ppm chlorine for 0 to 20 min. Single wiping with liquid-soap, 250 and 1000 ppm chlorine were also tested. Virus reduction was quantified by cell culture assays. Human noroviruses (NoVs) were quantified by PCR.

Results: The wiping with liquid-soap alone reduced infectivity of tested viruses with 1-2log₁₀ and is not significantly different with 250 ppm chlorine. The spot disinfection reduced infectivity of poliovirus Sabin1 and adenovirus type5 completely (>4log₁₀) within 10 min and murine norovirus (MNV1) within 5 min. Parechovirus1 was not reduced completely within 20 min. Genomic copies of NoVs GI.4 and GII.4 were reduced completely after 10 and 5 min respectively. MNV1 was reduced with 6.9±0.7log₁₀ PCR units within 20 min.

Conclusions: The spot disinfection by 1000 ppm chlorine for 10 min after pre-cleaning is sufficient to reduce infectivity of poliovirus, adenovirus, MNV1 and genomic copies of the human NoVs (>5.2log₁₀ PCR units) completely.

CHALLENGES FOR TRANSMISSION MODELS IN PEDIATRIC INFECTIOUS DISEASE**M. Prelog**^{1,2}, S. Boese-O'Reilly³, B. Jahn³, U. Siebert^{3,4}

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Most infectious disease transmission models do not appropriately representing the specific issues of pediatric target populations.

Thus, in the following project, advantages and disadvantages of stochastic and deterministic infectious disease transmission models and the challenges of modeling pediatric infectious disease transmission were analyzed by systematic literature research.

Classical models for infectious transmission systems are the SI, SIS, SIR and SIRS, which are defined by the state (Susceptible, Infectious, Recovery) of the individuals and transition probabilities. The most important variable is the basic reproduction ratio R_0 which is defined as the average number of secondary cases caused by an infectious individual in a totally susceptible population. However, several aspects of infectious disease transmission known from adult populations may have a different significance in pediatric populations. In modeling pediatric infectious diseases, researches are faced with complicating issues, such as heterogeneity of transmission, sub-communities, eradication models of childhood disease, latent or chronic infections with variable infectious state and carrier infectiousness, unreported or undiagnosed cases and vertically and horizontally transmitted infections.

Most studies suggest selecting the simplest model that addresses the objectives of the study, the disease structure, the transmission aspects and the management and treatment process. This analysis of specific problems in modeling infectious disease transmission in the pediatric population teaches us, that the nature of the pathogen and of the disease have to be carefully studied before an appropriate model type and structure can be chosen, which considers the peculiarity of infectious diseases in children.

NOSOCOMIAL INFECTIONS IN PEDIATRIC INTENSIVE CARE UNIT: A COMPARATIVE ANALYSIS BETWEEN PRIVATE HOSPITAL AND PHILANTHROPIC HOSPITAL

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Pediatric intensive care units (PICUs) have high rates of nosocomial infection (NI).

Objective: To present an epidemiological profile of NIs diagnosed in PICUs from two Brazilian hospitals.

Methods: Prospective surveillance of NI according to National Healthcare Safety Network (NHSN) protocols for events occurred between oct/2008 and sep/2011.

Results: Device utilization (DU) is a measure of invasive practices and constitutes an extrinsic risk factor for NI. DU is obtained as a ratio of device-days to patient-days. Mean ventilator utilization ratio was 58% for the philanthropic PICU and 31% for the private PICU (p-value < 0.05). Mean central line utilization ratio was 51% for the philanthropic PICU and 41% for the private PICU (p-value < 0.05). Consequently, during the period of analysis (three years), only 31 NIs were diagnosed in the private PICU and 224 NIs in the philanthropic PICU. NI risk was 9% and 20%, respectively for the private and philanthropic PICUs (p-value < 0.01). In both PICUs, primary bloodstream infections (BSI) and cardiovascular system infection (CVS) are the major infections: approximately 55% of all NIs. In both PICUs, the percentage of identification of the etiologic agents of NI was the same (68%), however NIs are caused by different microorganisms. In the private PICU, 44% of all NIs are caused by multiresistant *Staphylococcus epidermidis*, while in the philanthropic PICU NIs are caused by species of *Staphylococcus* (24%) and *Acinetobacter* (16%).

Conclusion: Severity of illness of patients, ie, patients' intrinsic susceptibility to infection is quite different when the PICUs are compared.

PRIMARY BLOODSTREAM INFECTIONS IN NEONATAL INTENSIVE CARE UNIT: THREE YEARS OF SURVEILLANCE

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Central line catheters are important resources in neonatal intensive care units (NICUs). However, they are also risk factors for nosocomial infections in critical ill patients.

Objective: To evaluate the incidence, microbiology and outcomes of bloodstream infections (BSIs) in a NICU from a Brazilian hospital.

Methods: Prospective surveillance of NI according to the device-associated module from National Healthcare Safety Network (NHSN) protocols for events occurred between oct/2008 and sep/2011.

Results: 166 BSIs were diagnosed in three years, 50% of all infections in the NICU. The majority of BSIs (85%) refer to the late-onset sepsis, i.e., diagnosed after 48 hours of birth. Laboratory-confirmed bloodstream infection represents 70% of all BSIs (119 cases). BSIs are the major infections in all weight categories. Incidence of central line-associated primary bloodstream infections (CLABSIs), considering the whole period, all weight categories and all central lines types, was equal 11.9 CLABSIs/1,000 central line-days. The BSI risk associated with umbilical catheter is significantly higher than in other line types (p-value < 0.05): 20.9 CLABSIs/1,000 central line-days (umbilical catheter) versus 8.5 CLABSIs/1,000 central line-days (epicutaneous catheter). The BSI risk decreases with birth weight. CLABSI incidence by birth weight (#CLABSIs/1,000 central line-days): ≤750g = 16.2, 751-1,000g = 12.3, 1,001-1,500g = 11.6, 1,501-2,500g = 10.6, and >2,500g = 6.4. CLABSI was caused mainly by multiresistant *Staphylococcus epidermidis* (29%) and *Klebsiella pneumoniae* (13%).

Conclusion: CLABSI rates in all birth categories are high outliers, i.e., above the 90th NHSN percentile. The BSI risk associated with umbilical catheter is significantly higher than epicutaneous catheter.

SURVEILLANCE OF HOSPITAL INFECTIONS IN PEDIATRIC CLINICS OF AN UNIVERSITY HOSPITAL DURING THE FIRST SIX MONTHS OF 2010

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Background and aims: The aim of this study was to define the hospital infections epidemiology, causative microorganisms, their resistance pattern, underlying risk factors for hospital infections (HI) during the six-month period in the Pediatric clinics of our hospital.

Methods: Patients hospitalized between January and June 2010 in Pediatric clinics included to the study. Data in patient files, nursery observation charts, reports of radiology, microbiology and other diagnostic methods are utilized prospectively to detect HI. Hospital infection rate and incidence density is calculated. Patients with HI are evaluated according to underlying risk factors. Device associated infection rates are determined in intensive care units.

Results: During the study period, 1900 patients evaluated and HI is detected in 176 patients. The HI rate is 9.3 % and incidence density is 10.86/1000 patient days. HI rate was highest in neonatal intensive care unit, pediatric intensive care unit, haematology-oncology ward and bone marrow transplantation unit. The most common seen HI types are blood stream infections, pneumonia and gastrointestinal system infections. HI rate is found to be reversely related with age. Other risk factors were length of stay, invasive processes, co-morbid diseases, transfusion, anti-acid use. Gram-negative bacteria were responsible for 53 % and gram-positive bacteria for 28% of infections.

Conclusions: Hospital infection surveillance is an important step for decreasing the hospital infection rates by recognizing and analyzing the problems, giving feed-back, directing the infection control measures toward the target. Besides the data required from the surveillance can be utilized for benchmarking with other centers.

HAND HYGIENE PRACTICES AMONG HEALTHCARE WORKERS IN THE KENYATTA NATIONAL HOSPITAL NEWBORN UNIT

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Background and aims: The primary objective was to determine the hand hygiene practices among healthcare workers in the Kenyatta National Hospital Newborn Unit. The secondary objective was to assess the knowledge and perception of these healthcare workers regarding healthcare-associated infections (HCAs) and the importance of hand hygiene and to assess barriers to the recommended hand hygiene practices.

Methods: A descriptive cross-sectional study in May 2011 in the Newborn Unit among Healthcare workers using a structured WHO hand hygiene observation form. A questionnaire adapted from the WHO one was used to assess knowledge and perceptions of healthcare workers as well as the barriers to recommended hand hygiene practices.

Results: Opportunities for hand hygiene were observed in 83 healthcare workers as follows: Nurses 39.8%, doctors 22.9% nursing students 18% medical students 12% and clinical officers 7.2%

Hand hygiene compliance was 15%. Barriers to recommended hand hygiene practices were as follows: lack of alcohol based hand rub 64%, lack of hand towels 57%, forgetfulness 46%, use of gloves instead of washing hands 46% and lack of time 37%. The overall level of knowledge regarding HCAs and of hand hygiene was good with 87.7% of the healthcare workers scoring $\geq 50\%$.

Conclusions: The hand hygiene compliance rate in the KNH newborn unit is 15%. Knowledge and perceptions of the healthcare workers regarding HCAs and importance of hand hygiene is good.

The commonly reported barriers to recommended hand hygiene were lack of alcohol-based handrub and hand towels, forgetfulness and use of gloves.

ROTAVIRUS DISEASE BURDEN IN A REGIONAL HOSPITAL IN TURKEY**S.K. Saygili**, Ö. Türel Kurama, G. Aydoğan*Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Turkey*

Objectives: Rotavirus is the leading cause of acute gastroenteritis in children. Data on the burden of rotavirus gastroenteritis are needed to guide recommendations for rotavirus vaccine use in Turkey.

Methods: The retrospective analysis was based on the list of patients from whom our clinical microbiology laboratory received a stool sample for the detection of rotavirus between January 2008 to June 2008 and January 2009 to June 2009. The date of sample submission, the age of the patient, the number of hospital admissions, costs and some hospitalisation characteristics were further analysed. Infections were considered nosocomial if they appeared 48 h or more after hospital admission.

Results: The number of stool specimens collected for rotavirus detection was 723 from January 2008 to June 2008, 758 from January 2009 to June 2009. The proportion of stool samples positive for rotavirus was 18.3% (132 of 723), 23.2% (176 of 758). The proportion of hospitalisation among children with a positive sample during different years was 66.6%, 53.9%, with nosocomial infections in 17.4%, 14.2% cases. The percentage of children younger than two years old was, 68.9%, 72.2%. The total hospitalisation days due to rotavirus-positive gastroenteritis were, 217, 360 with a mean stay of, respectively, 1.65 (1-14), 2.05 (1-13) days. The mean cost for community acquired rotavirus gastroenteritis was 134,8TL (116dollar), 135.7TL (117dollar), exchange calculated by time appropriate dollar price.

Conclusions: Most community-acquired rotavirus gastroenteritis occurs in children aged < 2 years, and a high proportion treated hospitalized. Rotavirus vaccination is expected to reduce the economic burden of rotavirus in Turkey.

CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS IN 6 POLISH NEONATOLOGY INTENSIVE CARE UNITS IN 2009

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Background: Central Line Associated Bloodstream Infections (CLABSI) are the most common form of nosocomial infections among Neonatal Intensive Care Unit (NICU) patients. Understanding the epidemiology of CLABSI in very low birth weight (VLBW) neonates is a key step in development of targeted prevention strategies and reduce antibiotic consumption.

Aims: The aims of study were to analyze epidemiology and microbiology of CLABSI in 6 Polish NICUs.

Materials and methods: Data collection on CLABSI in LBW newborns was made retrospectively from January to December 2009. Study covered 910 neonates of birth weight < 1500 g in 6 Polish NICUs, among which 95 cases of CLABSI (using Gastmeier definition) were detected. Device-associated infection rates are calculated and stratified according to birth weight groups:

(I) ≤499 g;

(II) 500-999 g;

(III) >1000 g.

Results: The CLABSI incidence per 1000 CVC/pds were 0 in group I, 10.6 in group II and 9.2 in group III. The etiological agents were dominated by *Staphylococcus* genus (77%) with a majority of methicillin resistant coagulase-negative staphylococci (64% of all cases) and *Staphylococcus aureus* MRSA (13%). Gram rods were detected in 15% with a majority of *E.coli* (6%); ESBL strains were detected in 25%. Fungemia caused by yeast-like fungi was detected in 4.7% cases.

Conclusions: Between studied units situation with CLABSI epidemiology was statistically different. The key to any successful program to lower the CLABSI rates is an intensive educational program that promotes best practices. Use of a prevention strategy and education of staff is essential. Study financed by N N401 615 340.

A 10-YEAR STUDY OF PATHOGENS ISOLATED FROM BLOOD CULTURES IN A PAEDIATRIC ONCOLOGY UNIT

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Aim: To investigate the long-term trends in prevalence and antimicrobial resistance of pathogens isolated from blood cultures in paediatric oncology patients.

Methods: All positive blood cultures from a single paediatric oncology unit during 2002-2011 were retrospectively included and analyzed.

Results: Overall, 317 bacteraemias and 2 candidaemias occurred in 175 patients (median age 5yrs, 61% boys) suffering from haematologic malignancies (67%) and solid tumors (33%). The leading pathogens were coagulase-negative staphylococci (CNS, 52.7%), *Klebsiella* spp. (9.5%), *Pseudomonas* spp. (8.8%), *Escherichia coli* (7.6%), *Streptococcus* spp. (4.1%), *Enterobacter cloacae* (3.8%), *Staphylococcus aureus* (3.5%) and *Acinetobacter* spp. (2.2%). Since the beginning of the study Gram-negative episodes increased (from 5.2 to 19.9/1000 patients, chi-square for trend $p < 0.01$) and Gram-positive episodes decreased (from 25.2 to 14.9/1000 patients, $p = 0.004$). Among *Klebsiella* spp. and *E. coli* isolates, there were 46% and 50% extended-beta-lactamase-producers (ESBL), respectively. All but one ESBL-producing *E. coli* isolates were susceptible to piperacillin-tazobactam. Resistance to imipenem was noted in 8% of *K. pneumoniae* isolates and in no *E. coli*. 20% of *Pseudomonas aeruginosa* isolates were ceftazidime-resistant. 80% and 9% of CNS and *S. aureus*, respectively, were methicillin-resistant. Vancomycin resistance was noted in 16.7% of *Enterococcus faecium* isolates. An outbreak of ESBL-producing *E. coli* was observed in 2011. The all-cause mortality was 22.8%.

Conclusions: Gram-negative bacteria have recently predominated in our unit bearing considerable resistance to frequently used antibiotics. These results suggest the importance of continuous surveillance for antimicrobial drug susceptibility and of antibiotic stewardship in order to confront the emerging challenge of antibiotic resistance.

INVESTIGATION AND MANAGEMENT OF AN IMIPENEM-RESISTANT ACINETOBACTER BAUMANNII (IRAB) OUTBREAK IN A NEONATAL INTENSIVE CARE UNIT

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Background and aims: IRAB frequently causes nosocomial infection outbreaks difficult to eradicate. We describe investigation and management of IRAB outbreak in a NICU in a general university-affiliated hospital.

Methods: In a 44-bed NICU, a bundle of actions were taken after identification of 7 cases of IRAB infections (including 4 cases of bloodstream infections). The bundle included enhanced infection control measures (patients cohorting, contact precautions, hand hygiene, environmental hygiene), active surveillance screening (ASS), case control study, staff education, daily audits and closure of the unit for 12 days. For ASS, perianal/stool samples were collected weekly from all neonates. IRAB were isolated on McConkey agar supplemented with imipenem (2mg/l) and tested for susceptibility using Vitek2. PCR and PFGE were used for molecular analysis.

Results: A total of 216 samples were obtained from 96 neonates (43% of neonates had at least 2 samples). During the 1st, 5th and 6th week of ASS, 5, 2 and 2 new IRAB acquisitions were detected, respectively. Prevalence of IRAB decreased from 19% (1st ASS week) to 4% (7th week) and finally to 0% (8th and 9th week). One colonised neonate developed IRAB bloodstream infection and died. PCR revealed that all isolates were positive for the OXA-58 gene and the intrinsic chromosomal OXA-51 gene. PFGE revealed that all IRAB isolates belonged to the same clone. No significant risk factors were found between case and controls.

Conclusion: Intense active surveillance and enhanced infection control measures were important to rapidly combat high incidence of IRAB monoclonal colonization/infection in the NICU.

AN ADOLESCENT CASE OF HYPER-IGE SYNDROME WITH RECURRENT HERPETIC INVOLVEMENTS AND SQUAMOUS CELL CARCINOMA

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Background and aims: Hyper IgE- Syndrome (HIES) as a rare primary immune deficiency may present with various recurrent cutaneous manifestations like viral and bacterial abscess formation, eczema and neoplastic lesions. The neoplasms mostly occur in Deducator of Cytokinesis 8 (DOCK 8) deficiency, an autosomal recessive variant of HIES. Here we aimed to demonstrate the progression of a cutaneous malignancy in upper lip and periorbital vesiculopustular lesions in a 15 year old patient.

Methods: measurement of some Immunologic specific tests suggested the underlying defect of HIES (according to Scoring System with Clinical and laboratory Tests for Individuals in Kindreds with HIES). Final diagnosis was confirmed by pathology.

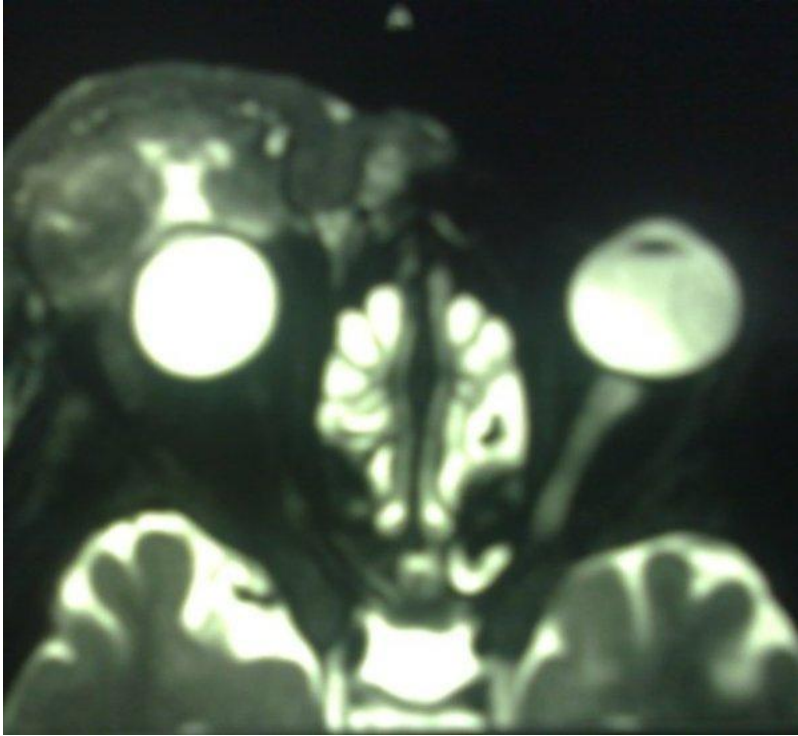
Results: IgE values of 5630 and 6780 mg/dl were detected in two separate blood samples. Pathology reports of upper lip lesion and orbital mass showed severely inflamed and ulcerated squamous cell carcinoma with moderate differentiation.



[Multiple facial pustular lesions]



[Huge periorbital tumoral mass]



[MRI of the patient with tumoral periorbital mass]

Conclusions: Diagnosis of a moderately differentiated Squamous Cell Carcinoma in facial area of a patient with recurrent viral involvement and elevated levels of serum IgE revealed the potential of neoplastic involvement in a HIES case.

RECURRENT MENINGOCOCCAL MENINGITIS CAUSED BY COMPLEMENT C8 BETA DEFICIENCY IN AN 18 YEAR OLD MAN-WHAT IS THE APPROPRIATE MANAGEMENT?

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Complement plays a central role in the defense against meningococcal infections. Here we report on an eighteen year old previously healthy young man, who developed two episodes of meningococcal meningitis with severe sepsis. The first episode was caused by *N. meningitidis*, serotype Y, which accounts for less than 5% of the meningococcal infections in Germany. The second episode 19 months later was caused by a more common serotype B strain. The patient survived both episodes without persistent neurological sequelae. Asplenia was ruled out, leukocyte subpopulations were within normal quantitative limits and immunoglobulin levels including IgG subclasses were unremarkable. However, hemolytic activity of the classical complement activation pathway was completely absent (CH50 assay). Further complement analysis established a deficiency of the complement component 8, with a lack of C8 beta chain, as the cause for enhanced susceptibility to meningococcal infections. Moreover, two of the three healthy siblings of the index patient, but none of the parents, were found to exhibit substantially impaired complement activity with lack of functional active C8. As in the index patient, total hemolytic complement function (CH50) could dose-dependently be resubstituted by the addition of purified human C8.

Controlled studies and guidelines for the management of patients with deficiency in terminal complement proteins are missing. We here propose a management algorithm for those patients consisting of immunization against meningococci, antibiotic prophylaxis and emergency measures, irrespective of prior meningococcal infections.

RECURRENT SUPPURATIVE GRANULOMATOUS LYMPHADENITIS IN A 3-MONTH OLD BOY WITH HYPER-IGE SYNDROME

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Background: Autosomal dominant Hyper IgE syndrome (AD-HIES) is a rare primary immunodeficiency characterized by eczema, recurrent skin and lung infections, elevated serum IgE, and various connective tissue, skeletal, and vascular abnormalities. Because features accrue over time, the clinical diagnosis can be uncertain in young children. Mutations in Signal Transducer and Activator of Transcription 3 (STAT3) have recently been found to account for the majority of the cases.

Case report: A 2-month old boy, with eczematoid skin eruptions on face, scalp and cervical area was referred to our Department because of right cervical lymphadenitis. He was treated with antibiotics, but the patient ultimately required excisional biopsy which revealed a suppurative granulomatous lymphadenitis due to a methicillin-resistant *Staphylococcus aureus* strain. Except from a mild leukocytosis and eosinophilia, the boy had normal laboratory results, including serum IgE and immunologic evaluation for chronic granulomatous disease. The patient was again hospitalized one month later because of a new episode of suppurative granulomatous cervical lymphadenitis. Laboratory evaluation showed marked elevation of IgE levels (3050 IU/mL). With DNA sequencing showing a c.1144C-T (R382W) mutation in STAT3 the diagnosis of AD-HIES was confirmed. Because of his age and the severity of the clinical manifestations, prophylaxis with antibiotics (trimethoprim-sulfamethoxazole) and intravenous immunoglobulin at replacement dose were initiated. The child has not had a recurrent infection for a period of one year.

Conclusions: AD-HIES may present with recurrent suppurative lymphadenitis early during infancy. Early institution of effective prophylactic regimens can prevent many of the infectious complications that would otherwise facilitate diagnosis.

INFECTIOUS AND NONINFECTIOUS DISEASES AS FIRST MANIFESTATIONS OF CGD IN A SPANISH COHORT: THIRTY YEARS FOLLOW-UP

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Background and aims: Chronic granulomatous disease (CGD) is a primary immunodeficiency caused by a functional defect in one of the subunits of the enzyme NADPH oxidase of phagocytes. Recurrent infections are the most common initial presentation. The aim of this study is to characterize the manifestations prior to diagnosis in patients with CGD.

Methods: The clinical charts of patients diagnosed with CGD from January 1982 to December 2011 were reviewed.

Results: Thirteen patients with diagnosis of CGD from a tertiary hospital in Madrid were identified. Their median age at diagnosis was 2.5 years, range [0-9.2]. Mean time between the first infection and diagnosis was 2 years, with a median of 1.4 years, range [0-5.3]. The most frequent infections prior to diagnosis were abscesses (41.8%), followed by pneumonia (16.7%), sepsis/disseminated infection (13.6%), osteomyelitis (5.6%), acute otitis media (4.8%), urinary tract infection (4.8%) and herpes zoster (2.4%). Abscesses could be lymphatic, cutaneous, intra-abdominal, hepatic or peritonsillar. Half of the patients had suffered at least from one abscess. The most frequent pathogens identified were *Salmonella* spp. (35%), *S. aureus* (20%) and *Serratia marcescens* (15%). The causative agent could not be isolated in 52.5% of the cases.

One patient had a brain granuloma and another one has been diagnosed with Crohn disease. Diagnosis was suspected in 14.6% of the patients before any infection because they had a sibling with the diagnosis of CGD.

Conclusions: CGD should be considered in patients with uncommon or atypical infections, mainly abscesses or disseminated infections/sepsis, specially when unusual pathogens, such as *Salmonella* spp. or *Serratia marcescens* are detected.

ACUTE MYELOID LEUKEMIA (AML) PRESENTING WITH ECTHYMA GANGRENOSUM AND FATAL PSEUDOMONAS AERUGINOSA SEPSIS

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Introduction: Almost every reported case of ecthyma gangrenosum (EG) in previously healthy children is associated with some type of immunocompromise.

Case report: A previous healthy 22-month old boy with unremarkable family history was admitted to the ICU with septic shock. Two days prior he had a fever of 40°C, a generalized maculopapular rash and a rapidly evolving ulcer on his left upper arm. On admission, he appeared lethargic, his BP: 60/40 mmHg, HR: 180/min, RR: 70/min, capillary refill time: 5secs. His results reflected pancytopenia (WBC: 1000/ul, Hgb: 9mg/dl, PLT: 155,000/ul), lactic acidosis and DIC. He was immediately intubated and mechanically ventilated and was given fluid resuscitation, inotropic support (intravenous adrenaline, dopamine and dobutamine), FFP, coagulation factors and blood transfusion. Empirical antibiotics were started with gentamycin and ceftazidime. All fluid cultures (blood, bronchial, CSF, skin lesion's) yielded *Pseudomonas Aeruginosa*, sensitive to the administered regimen. Due to the uncommon pathogen and the severe clinical presentation, a bone marrow biopsy was performed that established the diagnosis of AML (>80% atypical promyelocytes, M3 according to FAB classification). Within 2 days the necrotic lesions extended, occupying the face, trunk, upper and lower extremities, he developed MODS and was placed on a peritoneal lavage. Despite massive intensive care efforts the boy expired on the 4th day of hospitalization.

Conclusion: EG can be an early indication of an undetected malignancy. Prompt identification is crucial to initiate appropriate antipseudomonal therapy and to perform a thorough laboratory investigation, to rule out predisposing causes including congenital immunodeficiencies and cystic fibrosis.

EVALUATION OF SEROTYPE SPECIFIC ANTIPNEUMOCOCCAL ANTIBODY CONCENTRATIONS IN 22 PRIMARY HUMORAL IMMUNODEFICIENCY PAEDIATRICS PATIENTS TREATED WITH INTRAVENOUS IMMUNOGLOBULIN (MULTIGAM®)

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Background and aim: The main goal of intravenous immunoglobulin (IVIg) replacement for patients with primary humoral immunodeficiency (PID) is to reduce the frequency and severity of infection, mainly related to *Streptococcus pneumoniae*. For the evaluation of pneumococcal vaccines, an anti-pneumococcal antibody (APAb) level of 0.2 µg/ml is considered a correlate of protection for invasive pneumococcal infection (WHO 14, 22F preabsorption). The protective plasma APAb level in IVIg-treated children with PID has never been established.

Methods: We measured levels of APAbs against 16 serotypes (ST) (1,3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 12F, 14, 18C, 19A, 19F, 23F) in IVIg lots (Multigam®) and in the plasma (trough and peak levels) of 22 PID patients over a period comprising 6 consecutive IVIg infusions in the context of a GCP prospective multicentre open label clinical study. APAbs were determined by an ICH-Q2(R1) validated automated high-throughput quantifying process using the calibrator 89-SF (FDA) and including 22F preabsorption. The trough and peak geometric mean concentrations (GMCs) were determined for all patients and for each serotype.

Results: The trough GMC ranged from 0.13 µg/ml for serotype 12F to 2.76 µg/ml for serotype 14. The median percentage of measurements reaching trough level > 0.2 µg/ml was 100% for all serotypes except serotypes 12F (14%), 4 (71%), and 9V (92%). A good correlation was seen between serum concentrations of APAbs against each serotype in patients and levels in Multigam®, produced from plasma collected in Belgium.

Conclusions: PID patients treated with Multigam® have protective trough levels of APAbs against the most prevalent pneumococcal serotypes.

UNCOVERING THE TRUTH ABOUT HEPATITIS B REACTIVATION: DID YOU KNOW THAT RESOLVED HEPATITIS B CAN REACTIVATE?

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Reactivation of resolved hepatitis B virus (HBV) infection is a complication of allergenic hematopoietic stem cell transplantation and a late-onset complication in immunocompromised hosts. These patients are at risk of developing fulminant hepatitis with high mortality, especially after bone marrow transplant (BMT).

We report a case of a HBsAg negative 17 year-old patient, with detectable pre-transplant anti-hepatitis B antibodies (s, e and c) , who developed a reverse seroconversion (sudden reappearance or rise of HBV DNA) one year after two failed allergenic BMT. At a routine check-up, on exam the patient complained of abdominal pain. Liver function tests were elevated and hepatitis serology showed an active reactivated hepatitis B (AgHBs 2429 index; Ac anti HBc Ig 12,1 index, Ac HBc IgM 31,7 index) with high hepatitis DNA titers (7,5e5 UI/ml).

It is reported that up to 50% of HBsAg-positive patients with lymphoma may reactivate hepatitis B infection during or shortly after chemotherapy.

A less known fact is that up to 50% of patients with anti-HBc positive but HBsAg-negative antibodies may develop a reverse sero-conversion after BMT or immunosuppressive chemotherapy.

It is well established that a 6-12 months lamivudine prophylaxis in Ag HBs-positive patients with BMT or immunosuppressive treatments are recommended, whereas no prophylaxis for Anti-HBc -positive/ AgHbs-negative patients are available. Since the risk for HBV reactivation in these patients may be as high as in the AgHBs-positive, we address the question whether patients with positive Anti-HBc positive/ AgHBs negative should also benefit from a lamivudine prophylaxis.

A PROSPECTIVE STUDY OF NOSOCOMIAL INFECTION IN NEONATAL INTENSIVE CARE UNIT, SHIRAZ-IRAN**N. Pishva***Pediatrics, Neonatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran***Background:** Nosocomial infections are one of the causes of neonatal mortality in neonatal intensive care units.**Material and method:** Nosocomial infection was studied in 9 months period in Shiraz Nemazee hospital neonatal intensive care unit (NICU). Cultures were taken from urine, blood, nose, throat, stool and eye on arrival and repeated after 48 hours of admission or earlier if deterioration of condition has occurred.**Results:** Total cases were 126 neonates 46.8% were full term and 53.2% were premature. Blood culture was positive in 21.4% of patients other positive cultures were eyes discharge 35%, ETT 13%, Umbilicus 2%, stool and urine 2% (each). Prevalence of nosocomial infection was 27.4% with a mortality rate of 32%. There was strong relation between duration of hospitalization and nosocomial infection ($P=0.0000$, $\chi^2=26.39780$). There was no relation between use of urinary catheters and nosocomial infection. ($P=0.7914$ $\chi^2=0.07$), and finally there was no relation between sex and nosocomial infection ($P=0.6137$, $\chi^2=25482$).**Conclusion:** Suggestions for prevention of nosocomial infection are accurate hand washing, revising cleaning procedures, official presence of an infection control nurse, decreasing overcrowding and restrict contact isolation.

SEVERE COMBINED IMMUNE DEFICIENCY SYNDROME: A CASE SERIES OF THIRTEEN INFANTS IN PAKISTAN**A.F. Saleem, S.A. Ali***Paediatrics and Child Health, Aga Khan University Hospital, Karachi, Pakistan*

Severe combined immune deficiency (SCID) is a rare genetic disorder of the immune system. It is universally fatal if left untreated but is curable with hematopoietic stem cell transplantation (HSCT), especially before 3 months of life. Data on the prevalence of SCID in Pakistan is lacking.

Methods: We are reporting 13 infants who were discharged during July 2006 - July 2011 with diagnosis of SCID at our tertiary care center in Karachi, Pakistan.

Results: Median age of diagnosis was five months; five infants presented within 3 months of life. Three fourth (77%) were males. Most of the infants were severely malnourished (85%) at the time of presentation. More than two third (69%) of the patients were products of consanguineous marriages. All subject had severe lymphopenia (absolute lymphocyte count (ALC) ranging between 170 - 2280) and low T and B lymphocyte counts. HIV status was found negative among those who were checked. No patient received HSCT.

Conclusion: SCID is not an uncommon condition in Pakistan. Early diagnosis could save lives. Low ALC ($< 2500 /\text{mm}^3$), which can be easily calculated through routine blood count, is a sensitive and specific screening test for SCID. Physicians should consider the possibility of SCID in infants presenting with severe and recurrent infection. If identified, these infants should be promptly referred to a facility where stem cell transplant can be done.

PREVALENCE OF CLOSTRIDIUM PERFRINGENS INFECTION IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PILOT STUDY

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Introduction: 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). 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 Pediatric Gastroenterology and Nutrition, Warsaw, Poland. All these patients were diagnosed according to Porto criteria. Stool samples were collected at the day of admission. Clostridium difficile and Clostridium perfringens infection diagnosis was based on a positive stool enzyme immunoassay (C. difficile TOX A/B II, TechLab, Blacksburg, VA and C. perfringens enterotoxin test kit TechLab, respectively).

Results: Between March and September 2011, 63 fecal specimens from patients with IBD were collected. The incidence of Clostridium perfringens infection was 11% (7/63), the incidence of Clostridium difficile infection was 27% (17/63). No specimens contained both C. difficile toxins and C. perfringens enterotoxin. Average age of patients was similar in both C. difficile and C. perfringens groups (11.1 vs. 12.3 years). There was more Crohn's patients (5/7) in C. perfringens group than in C. difficile group (7/17).

Conclusion: The prevalence of Clostridium perfringens infection in pediatric IBD patients was 11%. 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.

ISOSPORIA BELLII ASSOCIATED RECURRENT DIARRHEA IN CHILDREN WITH AIDS

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Background and aims: The prevalence of isosporiasis in children is probably underestimated in developing countries because routinely not all HIV-infected patients are examined for this emerging protozoan parasite.

Methods: A 3 year-old girl was admitted 2 times during 1 year, with failure to thrive (FTT), weight loss, fever, productive cough, repeated foul smelling mucoid diarrhea, steatorrhea and emaciation.

Results: Biopsy showed moderate esophagitis and dilated lymphatic channels in lamina propria of duodenum. Esophageal ulceration, exudative otitis, and bilateral consolidation were seen. HIV Ab was positive. HbS, HbC, and HcV Ag/Ab were negative. CD4/CD8 T cell ratio was reduced to 0.09%. The relative count of CD4+ T-cells ranged from 9% to 6.9% and CD19 and CD20 positive cells were reduced to 1.8% and 1.9% of total lymphocyte, respectively. Laboratory findings showed hyper γ -globulinemia and increased liver enzymes. There was a history of sibling death as a result of pulmonary infection and dysentery at 8 month age. The patient's mother was infected with HIV through heterosexual transmission. Modified Ziehl-Neelsen acid fast staining of stool specimens showed many *Isospora belli* oocysts. Small bowel follow-through showed severe hypertrophy of duodenal and jejunal mucosa. She was put under the treatment of Vancomycin, Cefotaxime, Ceftazidim, and Trimethoprim-Sulfamethoxazole, the stool specimens turned negative for *I. belli* oocyst and she was discharged after 9 days, but died after one month.

Conclusions: Isosporiasis should be regarded in HIV-infected children presenting with FTT and recurrent diarrhea. Isosporiasis is a treatable infection in AIDS, if it is detected at proper time.

INFECTION BY MYCOBACTERIA AND FUNGI IN A PATIENT WITH MHC CLASS I DEFICIENCY

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Background: MHC class I deficiency frequently results in recurrent respiratory infections and/or skin granulomas. To date, less than 30 patients with MHC class I deficiency have been reported. Mycobacterial and fungal infections were not previously described.

Case report: An 11-year-old Portuguese girl, born to non-consanguineous parents, was referred to our outpatient clinics. She had chronic necrotizing granulomatous skin lesions on limbs and face, since the age of two. These lesions were recurrently infected by methicillin-sensitive *Staphylococcus aureus* (MSSA) and fungi (*Paecilomyces lilacinus*, *Fusarium spp*, *Candida guilliermondii*). She also had a previous history of cavitary pulmonary tuberculosis (following a close family contact) and MSSA osteomyelitis with necrotizing granulomatous bone lesions without mycobacteria isolation. Initially, the laboratory tests showed normal lymphocytes subsets, hypergammaglobulinemia, normal oxidative burst and IL-12/INF- γ pathway study. Overtime, a CD8 TCR α/β lymphopenia was detected. A low MHC class I expression and a homozygous TAP1 mutation were identified, which confirmed the diagnosis of TAP1 deficiency. Two months ago, she received a bone marrow transplant from an unrelated matched donor.

Discussion: This case illustrates that mycobacterial and fungal infections can also be found in an MHC class I deficient patient. It is also one of the first reported cases of bone marrow transplant in MHC class I deficiency.

SUDDEN SEPTIC SHOCK IN A HEART TRANSPLANT ADOLESCENT

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Background and aims: Heart transplantation in hyper-immune patients requires over-immunosuppression in order to preserve the graft. These treatments result in significant increase of infective risk. Here we describe a case of septic shock in a severely immunocompromised girl.

Case report: A 16 year old female underwent heart transplantation in 2009 because of dilatative and autoimmune cardiomyopathy. Chronic immunosuppressive treatment consisted of Mycophenolate, Cyclosporine and steroids. Shortly after transplantation, she developed persistent humoral rejection which triggered 5 episodes of graft failure, requiring the adjunct of immunoabsorption treatment. A permanent central venous catheter was placed. Her clinical status did not improve and Ig level remained high. Rituximab was added, in 4 doses alternated with immunoabsorption. Cardiac function became eventually stable. One month later she presented to our Emergency Ward with a history of fever and vomit since few hours. Within nine hours, persistent fever, hypotension, oliguria and evidence of DIC propted her transfer to the ICU. Blood cultures grew *Pseudomonas Aeruginosa*, while cultures from the removed venous catheter remained sterile. As soon as control of coagulation derangement was achieved, ECMO and dialysis support were started. ECMO support could be interrupted four days later, but the patient remained unconscious. An MRI study demonstrated ischemic brain damage with hemorrhage and severe oedema.

Conclusion: In heavily immunocompromised transplant patients, each episode of fever should be considered as possible onset of sepsis. Early diagnosis, albeit difficult, plays a crucial role. The balance between rejection and infective risk must be carefully evaluated.

POLYMICROBIAL BLOODSTREAM INFECTIONS IN CHILDREN WITH CANCER**D. Doganis**¹, B. Asmar², M. Yankelevich³, R. Thomas⁴, R. Ravindranath³

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Aim: To identify predictive factors for polymicrobial Blood Stream Infections (BSI) among pediatric cancer patients.

Methods: A retrospective study of blood cultures obtained from oncology patients diagnosed from 1/2005 to 12/2009, was conducted in Hematology-Oncology Division of Children's Hospital of Michigan. We recorded demographic characteristics, clinical and laboratory findings and we correlated all these variables with the type of infection: monomicrobial (M) or polymicrobial (P).

Results: Of the 198 BSI episodes detected in 102 patients, 134 were classified as monomicrobial and 64 as polymicrobial. Patients with polymicrobial BSI were more likely to be younger (median value 2.6 yo) than those with monomicrobial (median value 5.7 yo), $p=0.012$. Factors such as the gender (boys 69% in P-BSI vs 63% in M-BSI), the temperature (median 39°C vs 38.9°C), the presence of chills (16% vs 15%) and/or hypotension (14% vs 17%) were not found to be predictors for a polymicrobial infection. The type of organism isolated (gram positive in P-BSI 60% vs 69% in M-BSI) was not correlated with the type of the infection. Moreover, leucocyte level (median 2.95 vs 1.55 $\times 10^9/L$), absolute neutrophils count (1.7 vs 0.5 $\times 10^9/L$) and absolute monocytes count (0.1 $\times 10^9/L$ vs 0) were not associated with a higher risk of polymicrobial infection. Patients with catheter in place (97% vs 97%) regardless the type of catheter (implanted 29% in P-BSI vs 44.5% in M-BSI) were not found to be in a higher risk for a polymicrobial infection.

Conclusion: Younger children with cancer have a higher risk for a polymicrobial infection. No other factors were found to be risk predictors.

BLOODSTREAM INFECTIONS IN CHILDREN WITH CANCER. A SINGLE-CENTER EXPERIENCE

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Aim: To describe the incidence, the microbiologic and neutropenic profile of bloodstream infections (BSI) in children with cancer.

Methods: The charts of all children diagnosed with cancer from 2006 to 2010 were reviewed. Cases with more than one isolate were excluded from the analysis.

Results: A total of 122 BSI was detected in 94 children (57 boys, 37 girls, median age 5.4 yo) among 425 newly diagnosed children (231 boys, 194 girls) with cancer [(Hematological malignancy (HM):189, Solid Tumor (ST):236]. In 4 patients an episode of polymicrobial infection (HM:2,ST:2) was found. Among 90 patients with monomicrobial BSIs (118 episodes), in 19 more than one episodes were recorded (10 with 2 episodes and 9 with 3 episodes). More than one episode of monomicrobial infection were found in 12/54 patients with HM and BSI and in 7/36 patients with ST and BSI, p=ns. The incidence of monomicrobial BSI was found to be higher among patients with hematological malignancy (54/187, 29%) in comparison with those with solid tumor (36/234, 15%), p=0.0012. Among monomicrobial episodes 64 gram positive organisms (HM:40,ST:24), 53 gram negative (HM:33,ST:20) and one fungus were isolated, p=ns. In 80/118 episodes, the patient was neutropenic and in 38/118 non-neutropenic. In episodes with neutropenia 36 gram positive and 44 gram negative organisms were isolated whereas among non-neutropenic episodes 28 gram positive and 9 gram negative were isolated, p=0.0014. No death was attributed to infection in our group of patients.

Conclusions:

(1) Risk factor for Bloodstream Infections in children with cancer is the type of the disease (Hematological malignancy),

(2) Gram negative organisms are isolated more frequently among neutropenic patients.

SEVERE INFECTIONS DURING THE MAINTENANCE TREATMENT OF CHILDREN WITH ALL TREATED WITH BFM PROTOCOLS

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Aims: To describe the incidence and type of severe infections during the maintenance phase in children with Acute Lymphoblastic Leukemia (ALL) treated with BFM protocols.

Methods: We evaluated the charts of 244 children with ALL diagnosed from 11/92 to 12/08 and we recorded the episodes of serious infections during 244 cycles of maintenance treatment.

Results: Serious infections were seen in 75 patients (42 boys, 33 girls-median age 3^{11/12} years). In these children a total number of 105 episodes of serious infections were recorded. The incidence of serious infections was found to be 33/91(36%), 38/138(27.5%) and 4/15 (27%) among standard risk, intermediate and high risk patients respectively, p=ns. We detected 38 episodes of fever and neutropenia (in 34 patients), 12 episodes of varicella (in 12) and 5 of herpes zoster (in 5). Pneumonia was found in 27 cases (in 20 children), other focal infection in 13 episodes (13 patients), bloodstream infections in 5 cases (5 patients) and other serious infections in 5 episodes (5 children). In children with serious infections data showed 92% overall survival (69/75) whereas the ratio of relapse was 15% (11/75). Among patients without severe infections during maintenance treatment, the corresponding values were 88% (148/169) and 24% (40/169), p=ns. No death was attributed to infection in our group of patients.

Conclusions: Severe infections during the maintenance treatment are not rare and not correlated to the outcome. Among them, cases of fever and neutropenia are the most frequent. Risk group is not a predictor of a severe infection. In our group of patients, no death was attributed to infection.

THE USE OF PEGFILGRASTIM IN CHILDREN AND ADOLESCENTS WITH SOLID TUMORS

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Background: Granulocytes - colony stimulating factor (G-CSF) preparations used in pediatric oncology have the disadvantage of daily use for several days, until recovery from neutropenia. Pegfilgrastim is a preparation of slow release which is used once after each chemotherapy course, but its use in children is still under investigation.

Aims: To study the safety and efficacy of Pegfilgrastim's use in children and adolescents with cancer.

Methods: Pegfilgrastim (a preparation of 6 mgr) was administered to 6 patients with solid tumors, aged 11 to 16 years, with body weight over 40 kg. It was administered once after each chemotherapy course, for a total of 33 courses. To assess safety we recorded all possible side effects, to assess efficacy we evaluated the extent and severity of chemotherapy induced neutropenia after administration.

Results: No serious side effects, except from mild skeletal aches (3%), were noticed. Neutropenia was observed in 60.6%. Recovery from neutropenia occurred 4-10 days after completion of chemotherapy. Febrile neutropenia occurred in 18.2%, but all episodes were minor in severity and duration. Anemia in need for transfusion occurred in 27.3%. Thrombocytopenia occurred in 60.6% and in 24.2% a platelet transfusion was required, nevertheless thrombocytopenia seems to relate more to the chemotherapy regimen rather than the use of pegfilgrastim. No delay in the schedule of chemotherapy due to prolonged neutropenia or thrombocytopenia was noticed in any case (efficacy 100%).

Conclusions: The use of pegfilgrastim is safe and efficient in pediatric oncology patients with body weight over 40 kg.

A RARE FORM OF EXTRAPULMONARY TUBERCULOSIS, OTOMASTOIDİTİS COMPLICATED WITH SIGMOID & JUGULER VEİN THROMBOSİS

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Otomastoiditis is a rare form of extrapulmonary tuberculosis . The diagnosis of tuberculosis in the ear and mastoiditis is difficult because of the necessity of pathological examination. A 11 years old boy was referred to our hospital because of fever, left ear discharge, swelling of the mastoid area. Cranial MRI revealed inflammatory swelling of the left middle ear and the mastoid air cells. The patient was treated with surgery, metronidazol and cefazolin. The pathological specimen showed granulomatous tissue, with necrosis and Langhans giant cells, asidoresistan bacil was positive in tissue. He referred to Pediatric Infectious Clinic for treatment. The diagnosis of tuberculosis confirmed by history, Tuberculin skin test and pathological findings. Cranial MRI revealed efusion in mastoid air cells and Cranial MRI venography revealed thrombosis of left sigmoid and juguler vein and absence of flow. He was treated with three antituberculous drugs consisted of rifampicin, isoniazide, pyrazinamide for six months and low-molecular weight heparin and warfarine. Tuberculosis was considered only after the failure of conventional antibacterial regimens, it must be kept in mind in differential diagnosis of chronic otitis and mastoiditis in developing countries.

PRIMARY TUBERCULOUS MUSCLE ABCESS

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Skeletal muscles are rarely implicated in tuberculosis, even in patients with widespread disease. Tuberculosis can involve skeletal muscle by extension from bone, synovial lining of joint or tendon sheaths; by direct inoculation and by hematogenous dissemination. The authors describe a case of a six-month-old male child with a painless protruding mass on his proximal right thigh, which had developed over three months. There was history of intra-muscular injection at the local site of the mass, one month before the beginning of symptoms. There was no evidence of trauma, previous infection or contact with a tuberculosis patient. Radiographs of the right thigh were normal, showing intact femur. Ultrasonography showed a cystic formation with heterogeneous content, measuring 46 x 16 x 19 cm. Blood counts were normal. The patient was operated with a probable diagnosis of hematoma as complication of vaccination. Drainage of purulent caseous material was observed during the surgical procedure. Gram stain was negative, Ziehl Neelsen showed presence of acid-fast bacilli and *Mycobacterium tuberculosis* was confirmed by polymerase chain reaction. No other sites of tuberculosis infection could be identified by clinical and radiological examinations. Immunodeficiency tests were normal and serology for HIV was negative. The patient was started on a regimen of antitubercular chemotherapy (Isoniazid, Rifampicine and Pirazinamide) and improved clinically with resolution of symptoms within two months.

PATHOGENESIS OF TUBERCULOSIS IN CHILDREN IDENTIFIED BY GENE EXPRESSION PROFILING

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Background: Children have a high risk of developing active tuberculosis (TB) from close contact with an infectious adult. Most children remain undiagnosed since detection is more difficult in children due to unreliable standard laboratory investigations and diagnosis based mainly on clinical symptoms. However, blood transcriptional profiling has improved diagnosis and understanding of disease pathogenesis, leading to the development of serological biomarkers, but this has yet to be applied to children with TB.

Methods: Two cohorts of children (HIV positive and HIV negative) from South Africa and Malawi with active TB, latent TB infection and controls (other inflammatory diseases with similar presentation to TB) were recruited with whole blood collection into PAXgene tubes. After RNA extraction and amplification, biotinylated cRNA was hybridised to Illumina HT-12 BeadChip arrays for 334 samples (TB/HIV-, TB/HIV+, OD/HIV-, OD/HIV+, LTBI/HIV-). We assessed transcriptional biomarker signatures identified from variable selection analysis between the different disease categories for insight into the pathogenesis of the disease.

Results: We identified distinct subsets of genes differentially expressed between the disease categories in the biomarker signatures, with multiple biological pathways activated including those mainly involved with the inflammatory response, dendritic cell maturation and in cell-to-cell signaling and interaction.

Conclusions: RNA expression analysis provides a way of studying the complex inflammatory and metabolic processes in ill children. Our analysis provides an insight into the complexity of the host response to tuberculosis infection in children.

GENETIC ANALYSIS OF *MYCOBACTERIUM TUBERCULOSIS* DRUG-RESISTANCE GENES FROM SAMPLES SHIPPED IN PRIMESTORE MTM AND SEQUENCED USING THE NEXT-GENERATION ION TORRENT

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Background/aims: Mycobacterium tuberculosis (MTB) kills on average 1.7 million people worldwide each year and an increasing number of strains are multidrug-resistant (MDR) or extensively drug-resistant (XDR). Emergence of highly resistant MTB strains has made it critical to detect and track new mutations that may confer novel MTB drug resistance. In previous studies PrimeStore Molecular Transport Medium (MTM) rapidly killed MTB, preserved DNA and facilitated DNA extraction. A novel Ion Torrent drug resistance sequencing chip was evaluated by multiplexing MTB samples collected and preserved in PrimeStore at ambient temperature during prolonged shipment.

Methods: Four sets of PCR primers were designed for amplification of *rpoB*, *katG*, *GyrA*, and *rrs* genes known to confer MDR and XDR resistance in first and second line antibiotics. MTB samples preserved/stabilized in PrimeStore MTM were collected/shipped from Pretoria, South Africa to San Antonio, Texas, USA. Genetic analysis was performed using Ion Torrent sequencing.

Results: Compared to HAIN Line Probe Assay (LPA), this method correctly detected all mutations from 12 of 12 multiplexed MTB strains representing genetically diverse antibiotic resistance patterns. Furthermore, several new amino acid mutations not observed by LPA or by comparison to reference strains were discovered.

Conclusion: Collection and ambient temperature shipment of MTB samples in PrimeStore provides a safe and cost effective approach for global MTB drug resistance surveillance using Ion Torrent sequencing. The developed Ion Torrent method detects MDR and XDR strains with overall performance comparable to LPA testing, and offers potential discovery of novel resistance mutations.

PROTEOMIC PROFILING IDENTIFIES A SERUM SIGNATURE FOR THE DETECTION OF PEDIATRIC AND ADULT TB

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Background: Improved diagnosis of tuberculosis (TB) is essential for reducing the incidence of this disease in sub-Saharan Africa. Currently half of all cases of infectious TB are undiagnosed. This proportion is higher in children, as clinical features overlap those of many chronic infections and microbiological confirmation is complicated by paucibacillary load. The development of a rapid, sensitive and affordable serological diagnostic test for TB in children is urgently needed. Surface-Enhanced Laser Desorption Ionisation (SELDI) technology has been widely employed to identify serum based biomarkers in infectious diseases.

Methods: Serum samples (n=1020) were collected from children and adults (HIV-positive and HIV-negative) with active TB (culture confirmed), latent TB (IGRA+ and TST+) and controls (other infections and inflammatory conditions). Patients were recruited from two regions of sub-Saharan Africa with differing patterns of HIV, TB and malarial infection to ensure that the biomarker candidates would not be population specific. Serum proteomic profiles were obtained by SELDI using cation capture (CM10; pH 4.0 and 6.0), anion capture (Q10; pH 7.5 and 9.5) and immobilized metal affinity (IMAC30; Cu) ProteinChip™ arrays.

Results: SELDI analysis generated 10,200 serum protein profiles. Specific proteins were identified as statistically significant ($P < 0.001$) in distinguishing patients with active TB from those with latent TB and other infections regardless of HIV status or region.

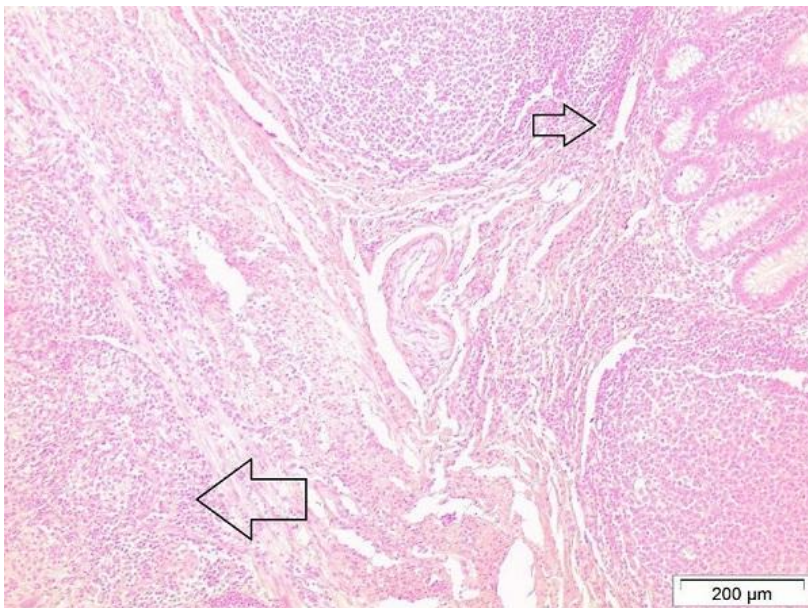
Conclusions: A series of serum proteins have been found that will potentially enhance the diagnosis of TB in children. Variable selection methods are being used to determine which proteins best discriminate TB patients in both populations.

PERSISTING FEVER: UNUSUAL PRESENTATION OF A MYCOBACTERIAL INFECTION

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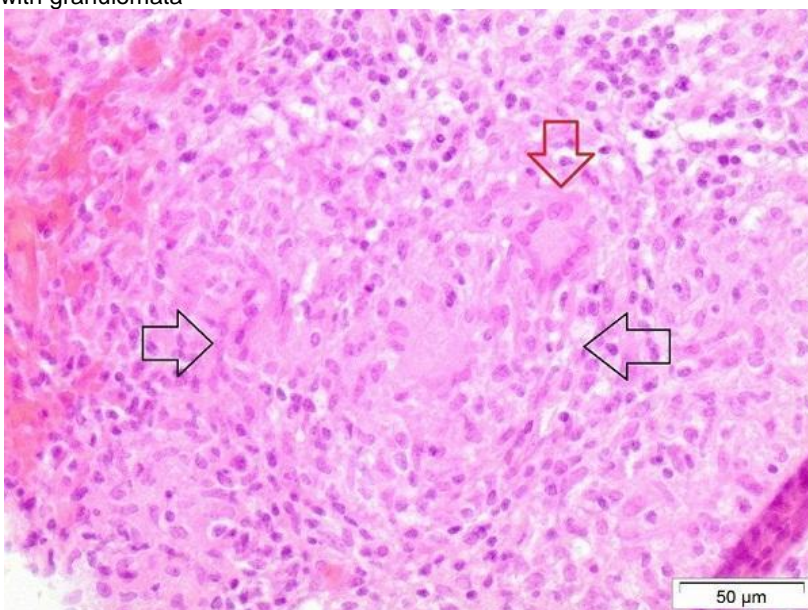
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A 17 month old boy was admitted to hospital because he'd had fever (>39.5 °C) for 4 days. Physical examination was normal. Blood results showed an elevated C-reactive protein (19.6 mg/dl) and a leucocytosis (14470 WBC/ μ l) Urinalysis and chest X-ray were normal. Echocardiography showed no signs of a Kawasaki-disease. Malaria was excluded. Since the fever remained (spikes of fever once a day), for another 5 days, in an apparently healthy child, an ultrasound of the abdomen was performed, which showed intraperitoneal fluid, and enlarged, inflammatory lymphnodes. CT of the abdomen raised suspicion about an appendicitis. A laparotomy was performed, and the appendix appeared to be macroscopically normal. APD of the appendix, however, showed serositis



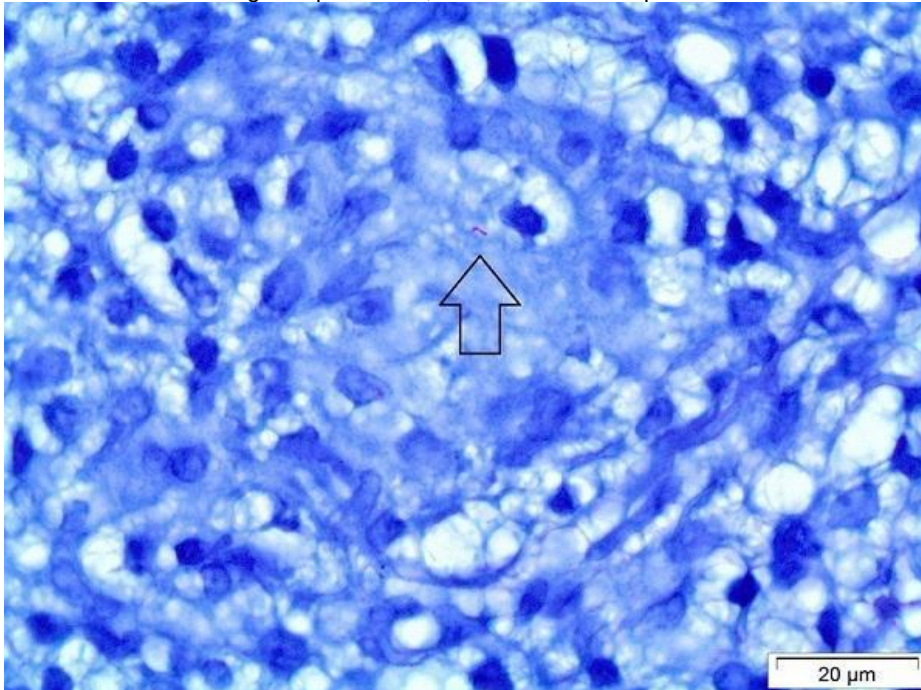
[Appendix 100x: serositis (l) mucosa(r)]

with granulomata



[App.: granuloma (arrows) & Langhans giant cell]

A Ziehl-Neelsen staining was performed, and revealed to be positive.



[Ziehl-Neelsen stain 1000x : acid-fast bacillus]

Mantoux test was positive, and anti-tuberculosis treatment was started, with almost immediate effect on the fever. Although direct PCR on the peritoneal fluid remained negative, 4 weeks later, culture grew the pyrazinamid-resistant *Mycobacterium bovis* ss.*bovis*. *Mycobacterium bovis* was also cultured on gastric aspirate. Since the boy has been staying in Turkey the month before, we suspect that the ingestion of raw dairy products was the cause of this unusual infection. Migration, new habits, social attitude, travel and geo-ecological circumstances can all lead to a new medical landscape.

LONG TERM FOLLOW UP OF A CASE OF CONGENITAL TUBERCULOSIS WITH ENDOBRONCHIAL GRANULOMA

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Background: Congenital tuberculosis (TB) is a rare and severe presentation of *Mycobacterium tuberculosis* infection with high mortality.

Endobronchial TB is quite common in children, although the real incidence is unknown.

To our knowledge, this is the first case of congenital TB with endobronchial granuloma successfully treated with therapeutic bronchoscopy.

Clinical presentation: A 12-week-old girl with congenital TB was transferred to our Hospital. We started treatment with Isoniazid (10 mg/kg/day), Rifampicin (20 mg/kg/day), Pyrazinamide (30 mg/kg/day), Ethambutol (15 mg/kg/day) and Prednisone (1 mg/kg/die). Prednisone was stopped after one month and Pyrazinamide after two months.

She remained well until 6-month-old, when she started to present respiratory distress. The chest X-Ray showed whiteout of right lung with mediastinal shift to the right. The CT scan with enhancement revealed multiple enlarged mediastinal and subpleural lymph nodes with central hypodensity and complete atelectasis of the right lung. She was started back on prednisone.

After two weeks she got worse and bronchoscopy revealed complete luminal obstruction of right main bronchus due to a tuberculous granuloma. Endobronchial treatment with diode laser was applied and her symptoms improved considerably.

At 9-month-old she need another therapeutic bronchoscopy with clearance of a new granuloma in same bronchus.

Prednisone was stopped after three months and antituberculosis treatment at 15 months.

At her 2-year follow-up the patient was well, chest X-Ray and bronchoscopy were normal.

Conclusion: Our case emphasizes the importance of bronchoscopy in every tuberculous patient with sudden onset of respiratory distress.

ANALYSIS OF POLYFUNCTIONAL T CELLS CAN DISTINGUISH BETWEEN LATENT AND ACTIVE TUBERCULOSIS IN CHILDREN

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Background: The diagnosis of tuberculosis (TB) in children remains difficult. Current immunodiagnostic tests, including the tuberculin skin test (TST) and interferon-gamma (IFN- γ) release assays (IGRA), cannot distinguish between latent TB infection (LTBI) and active TB. We investigated whether measurement of mycobacteria-specific, polyfunctional T cells (i.e. T cells producing two or more cytokines simultaneously) allows the distinction between these infection states.

Methods: Participants aged 0-18 years at risk of TB underwent a TST and an IGRA (QuantiFERON-TB Gold-In-Tube). In addition, intracellular cytokine assays were done by incubating whole-blood samples overnight with PPD and the *Mycobacterium tuberculosis* RD1 antigens ESAT-6 and CFP-10. Cells were analysed by multi-colour flow cytometry, using antibody-conjugated fluorochromes for T cell surface markers (CD3, CD4, CD8) and intracellular cytokines (IFN- γ , IL-2, TNF- α , IL-17).

Results: Six participants had active TB, 15 had LTBI (asymptomatic; normal chest x-ray; TST >10mm and positive IGRA) and 61 were uninfected (asymptomatic; TST 0mm and negative IGRA). Proportions of single-cytokine- (TNF- α +) producing, and double-cytokine- (IFN- γ +TNF- α +) producing CD4+ T cells were significantly higher in TB-infected participants (LTBI and active TB) compared to uninfected participants, with all three stimulatory antigens. In addition, proportions of TNF- α and IFN- γ +TNF- α CD4+ T cells were higher in participants with active TB compared to those with LTBI.

Conclusions: Mycobacteria-specific cytokine profiles differ not only between TB-uninfected and TB-infected children, but also between those with LTBI and active TB. Measurement of polyfunctional T cells provides a novel approach for distinguishing between LTBI and active TB in the clinical diagnostic setting.

LARYNGEAL TUBERCULOSIS IN CHILDREN: A CASE REPORT

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Background: In the pre-antibiotic era, involvement of larynx occurred from 35% to 83% of patients suffering from tuberculosis (TB); nowadays, after the introduction of antituberculosis medication, the incidence of laryngeal tuberculosis has decreased to less than 1%.

Methods: A 14 year-old Pakistan girl was admitted to our Department of Paediatrics with a 2 months history of chest pain, night sweats, chills, weight loss and fever.

This girl was born in Italy; her last travel to Pakistan dated back to one year earlier.

Physical examination showed an ill-appearing female, the girl's voice was described as blown, dysphonic; no adenopathy was found; pulmonary examination revealed a reduced murmur on the right side.

A positive Purified Protein Derivative test and Quantiferon test were found; chest radiography and computerized tomography of thorax and abdomen showed an enlargement of different lymphnodes and a pneumothorax of the right lung. Needle aspirate of the bone marrow was negative for tumoral cells. Lesions consistent with a pulmonary and laryngeal location of TB appeared at broncho-laryngoscopy. The histopathologic examination of the pulmonary and laryngeal lesions revealed a granulomatous inflammation. Sputum samples were positive for acid fast bacilli at the microscopic examination. The girl was dismissed with a diagnosis of pulmonary and laryngeal TB.

Conclusions: Laryngeal pathology should be suspected in any patient with dysphonia. As the incidence of TB is nowadays increasing, laryngeal TB should always be considered in the differential diagnosis.

PHLYCTENULAR KERATO-CONJUNCTIVITIS COMPLICATING TUBERCULOSIS**D. Pace**¹, A. Betts²¹*Department of Paediatrics,* ²*Department of Pathology, Mater Dei Hospital, Msida, Malta*

Background and aims: Phlyctenular kerato-conjunctivitis is a rare complication of tuberculosis caused by hypersensitivity to *Mycobacterium tuberculosis* antigens. We describe a child with tuberculous phlyctenular kerato-conjunctivitis in order to promote awareness of this rare presentation.

Methods: A 9 year old Eritrean boy migrated to Malta from Libya during the civil war. A screening Mantoux test resulted in a 15mm induration. A quantiferon-TB gold test was positive. Physical examination was unremarkable and his chest X-ray was normal. He was started on a 3 month course of isoniazid and rifampicin for treatment of latent tuberculosis. Just before starting treatment he developed bilateral conjunctivitis which eventually progressed to kerato-conjunctivitis. Phlyctenules were visible at the corneal limbus and stromal corneal opacities resulted in blurring of his vision. Fluctuations in his eye symptoms and signs were evident with no appreciable response to local antibiotics and steroids. Molecular analyses for herpes simplex and *Chlamydia* infection, performed on conjunctival swabs, were negative. A left conjunctival biopsy, performed 3 months from his initial presentation, showed non-necrotising granulomatous inflammation. No acid fast bacilli were seen and mycobacterial PCR as well as cultures were negative.

Results: Because of his exposure to rifampicin and isoniazid he was treated with rifampicin, isoniazid, ethambutol, pyrazinamide, moxifloxacin and steroids. His kerato-conjunctivitis subsided with fading of the corneal opacities and improvement of his vision.

Conclusion: In tuberculous phlyctenular kerato-conjunctivitis treatment of tuberculosis disease, even if clinically inapparent, in addition to steroids is necessary to prevent permanent scarring of the cornea.

CONGENITAL TUBERCULOSIS: A CASE REPORT

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Background: Congenital tuberculosis (TB) is rare infection transmitted from an infected mother to her foetus, either through an infected placenta or amniotic fluid. A high index of suspicion is required to make a diagnosis.

Case report: We report a case of a 12 month old male admitted at 12 weeks of age with complaints of swelling of the left part of the neck and weight loss of 9 weeks duration, cough of 9 weeks, fever of 10 days, and frequent stooling of 2 days duration. His mother had chronic cough in pregnancy. On examination, he was in respiratory distress, severely pale, had enlarged matted peripheral lymph nodes and massive hepatosplenomegaly. All his anthropometric measurements were below expected for age. He was initially managed for septicaemia with broad spectrum antibiotics but showed poor clinical response. Investigations done, showed features of military TB in both the patient and pulmonary TB in his mother. He showed remarkable response to anti-TB drugs.

Conclusion: A diagnosis of congenital TB should be considered in a newborn presenting with features suggestive of TB, especially in areas like Nigeria with a high adult TB prevalence.

BACILLE CALMETTE-GUÉRIN VACCINATED CHILDREN AND TUBERCULIN SKIN TEST. IS THERE INTERFERENCE REALLY?

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Background and aims: The tuberculin skin test (TST) is the most useful method for classification of tuberculosis (TB). There is no evidence about the effect of BCG vaccine on the interpretation of TST results.

Objective: to evaluate TST results in a population of immigrants and adopted children, analyzing the effect of the vaccine on TST.

Methods: Cross-sectional observational study. Immigrants or adopted children evaluated between January 2003-December 2008 were included. Children diagnosed with TB, or live attenuated virus vaccinated with two months earlier, HIV-infected, chronically ill or under treatment with immunosuppressive agents, were excluded. TST was considered as the dependent variable. Independent variables were: gender, age, national origin, BCG scar, nutritional status, immune status and intestinal parasites infestation.

Results: 1074 children were included, 69.6% girls. Origin: China (34.7%), Latin America (20.8%), India/Nepal (19.4%), Eastern Europe (15.7%) and Africa (9.3%). BCG scar in 79%. Mantoux=0 mm in 84.4%, < 10 in 4.1%, and ≥ 10 in 11.4%. Only two variables influenced TST result: age and BCG scar. Risk of a TST false positive due to BCG disappears after 3 years of vaccine administration.

Conclusions: A history of BCG vaccination at birth does not interfere with TST results in children > 3 years old. Under 3 years of age, BCG interferes and may cause a false positive TST result. In these cases it is recommended to use interferon-gamma release assays (IGRAs). If IGRAs are not available, or when results are indeterminate, it is recommended to ignore the antecedent of the vaccine.

PAEDIATRIC SPINAL TUBERCULOSIS: A CASE STUDY AND REVIEW OF LITERATURE**M. Amirrad***AL Baraha Hospital, Dubai, United Arab Emirates*

Spinal tuberculosis (**TB**) is an uncommon form of paediatric extrapulmonary tuberculosis. Delay in diagnosis leads to delayed treatment and devastating results for the patient.

In this report, a case of spinal tuberculosis is presented with insidious onset of back pain. The father was found to have pulmonary TB and was on treatment. Examination of the back revealed a kyphosis and tenderness at T9 level with thoracolumbar scoliosis to the right, with no paraspinal spasm, swelling or abscess. She had no motor or sensory deficits.

Tuberculin Skin Test (**TST**) was 20 mm with induration and vesicles. X-ray of the spine showed thoracolumbar scoliosis at T 10, T11 levels to the right with paravertebral abscess and destruction of the intervertebral disc space at T10, T11.

Magnetic resonance imaging (**MRI**) of the spine showed multifocal TB spondylitis with large paravertebral and small epidural abscess at T10-T11 level. She completed a course of anti-TB treatment and responded very well with disappearance of all symptoms.

Tuberculosis should be considered in children with insidious musculoskeletal symptoms. A positive culture is regarded as the "gold standard test" to establish a definitive diagnosis of TB in a symptomatic child. In non-endemic areas, the triad of known contact with an adult index case, a positive TST as evidence of latent tuberculosis infection, and suggestive signs on x-ray is used in clinical practice. Our patient had a triad of contact with an adult index case, a positive TST and x-ray and MRI findings suggestive of spinal TB.

EPIDEMIOLOGICAL CURRENT ASPECTS OF TUBERCULOSIS IN CHILD IN GALATI COUNTY OF ROMANIA

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Tuberculosis is still a public health problem in Romania and at European level.

Objective: To study of the main epidemiological aspects of child tuberculosis at national and regional level.

Methods: The epidemiological study effected in period 1990-2004 was based on data from national and district health institutions. Clinical and epidemiological issues was performed in the period 1999-2004 and included 646 children with tuberculosis hospitalized in pneumology hospital of Galati.

Results: There was a recrudescence of tuberculosis from the years 1970-1990, the incidence in 1999 has doubled compared to 1990 and in 2002 they found the maximum incidence of child tuberculosis. In Galati region in this period, the incidence of tuberculosis was higher than the national average values. The most affected age groups were 3-5 years and 10-14 years, with an upward trend and significant increase in period of 2000-2002 years.

Conclusions: The phenomenon of recrudescence of child tuberculosis at nationally and region of Galati peaked in 2002 and in Galati county incidence values being higher than the country averages. The origin of children with tuberculosis, especially from families with poor socioeconomic status, correlated with a disorganized environment, and low education have a negative impact on the management of tuberculosis. Tuberculosis child as major public health problem must remain a great concern to national and regional level to reduce the high incidence.

REGULATION OF MONONUCLEAR PHAGOCYTE PRECURSOR DIFFERENTIATION BY TLR2

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Multinucleated giant cells (MGCs) are the hallmark of granulomas, found in tuberculosis, autoimmune diseases and primary immunodeficiencies such as chronic granulomatous disease (CGD). We have recently established an in vitro system where synthetic lipoproteins binding Toll-like Receptor 2 (TLR2) induce mononuclear phagocyte precursor differentiation into MGCs by a cell-autonomous, TLR2/MyD88-dependent pathway. The current study aimed to test the hypothesis that TLR2 coordinately regulates the cell cycle of mononuclear phagocyte precursors during the process of multinucleation. We show that the cell cycle of mononuclear phagocyte precursors is regulated by TLR2 ligands at multiple levels: a) TLR2 signaling suppresses cell proliferation in response to macrophage colony stimulating factor (M-CSF), as evidenced by decreased cell numbers, decreased percent of cells in G1 phase, downregulation of cyclin D1, D2 proteins and decreased translocation of beta catenin to the nucleus, b) engagement of TLR2 by bacterial lipoproteins negatively interferes with cytokinesis, which temporally follows cyclin D and beta catenin suppression and coincides with multinucleated giant cell formation.

These findings suggest that the M-CSF- directed mononuclear phagocyte precursor differentiation may be altered by TLR2 signaling. Understanding the role and mechanistic induction of multinucleated giant cells by bacterial lipoproteins will significantly advance our understanding of innate immune activation in chronic granulomatous diseases.

MILIARY TUBERCULOSIS IN A YOUNG CHILD - A CASE REPORT

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Tuberculosis represents a public health problem. Young age and HIV infection are the most important risk factors for severe or disseminated disease.

A previously healthy 3-years-old girl presented with a 19-day history of fever associated with abdominal pain and anorexia. She had already received a 10-day treatment with amoxicillin-clavulanate (sub-therapeutic dose) because an *Escherichia coli* was identified in the urine culture performed at the first day of illness. On admission she presented with pallid skin, high fever (40°C) and hepatomegaly on abdominal examination. Laboratory findings included mild anemia, high CRP, increased transaminases, nitrites and bacteria in urinalysis. A diagnosis of urinary tract infection (UTI) was suspected and antibiotic therapy with intravenous cefuroxime was started. Urine culture confirmed UTI by *E. coli*. However, in spite of antibiotic treatment, fever had persisted. On complementary investigation, chest X-ray revealed an infiltrate with a miliary pattern. Tuberculin skin test was negative but *Mycobacterium tuberculosis* was isolated on gastric aspirate, cerebrospinal fluid and urine. Cerebral MRI was normal. Ophthalmological examination revealed tuberculous posterior uveitis. She started therapy with rifampicin, isoniazid and pyrazinamide associated with prednisolone. After two weeks of treatment, she showed significant clinical improvement.

Even in this era of advanced medical technology, tuberculosis is still a diagnostic challenge, especially when the presentation is atypical and extra-pulmonary. Beyond that, in this case, superinfection by other bacteria somewhat delayed recognition of the underlying tuberculosis.

A high index of suspicion by the physician is required because prompt institution of adequate treatment is decisive for final outcome.

INDUCTION SPUTUM VERSUS GASTRIC LAVAGE FOR MICROBIOLOGICAL CONFIRMATION OF PULMONARY TUBERCULOSIS IN INFANTS AND YOUNG CHILDREN

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Background and aims: Diagnosis of pulmonary tuberculosis (PTB) is difficult in infants and young children. For microbiological confirmation of PTB children, sequential gastric lavages (GL) are recommended. Induction sputum (IS) might be an alternative or complementary tool, but the information is limited in children in developed countries.

The aim of this study is to assess the safety and diagnostic yield of IS combined with GL for PTB diagnosis in children.

Methods: The study involved 22 children with suspected PTB admitted at Getafe Hospital, from January 2007-February 2011. IS and GL were done on three consecutive days according to a standardized protocol. In all samples, BK staining, culture and PCR were done, including Genotype MTBDR plus for resistance to INF-RIF since 2008. Preliminary analysis of an ongoing prospective study is presented.

Results: Median age was 74.5 months (1 month-14 years). Seven (35%) were ≤ 5 years. Eighteen were clinically diagnosed of PTB based on positive PPD and radiological criteria. Microbiological confirmation was made in 10 (56%) by either GL or IS. *M. tuberculosis* was identified from GL in 8 (44%) children, and by IS in 7 (39%). One infant (2 IS samples) had transient oxygen desaturation recovered spontaneously.

Conclusions: IS appears to be safe and well tolerated in children for diagnosis of PTB and more convenient. It may be a complementary technique to increase the diagnostic yield of PTB in children with PTB. Further studies are necessary to define the role of IS in pediatric PTB in developed countries.

LATENT TUBERCULOSIS INFECTION IN A TERTIARY HOSPITAL IN SOUTH GREECE, CRETE

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Background and aims: Diagnosis and treatment of latent tuberculosis infection (LTBI) is important for TB control. The epidemiological clinical and laboratory findings of patients that attended our outpatient clinic after a positive tuberculin skin test (TST) were evaluated.

Methods: Data were retrospectively evaluated for a 3-year-period (2009-2011). All patients were also tested with the QuantiFERON-TB-Gold-test, WBC, liver-function-tests, and chest-X-Ray during initial and end-point evaluation.

Results: 26 patients were evaluated. 4/26 (15%) were found to have active pulmonary TB-disease. Median age was 6,5years (range 1,2-13). 8/26 (31%) were younger than 4 years. 50% were boys. 23/ 26 (88%) were Greek, 2 (8%) Albanian and one Dutch (4%). 24/26 (92%) of patients were identified after the performance of standard TST-control in primary school or for acceptance in a nursery and only 2/26 were controlled after the identification of an affected family-member. In only 12/26 (46%) of children, family members with TB-infection were identified. QuantiFERON was found positive in 4/26 (15%) but in only 1 patient with active disease, however 2 of the patients with active disease were infants. LTBI was treated with INH and RIF for 3 months. 20/26 (77%) visited regularly the outpatient clinic. All children with LTBI had normal laboratory findings at all steps of evaluation and none developed TB-disease.

Conclusions: The shorter 3-month-treatment with 2 drugs correlates with good compliance and no adverse effects. None developed TB-disease during follow-up. Only few children had positive QuantiFERON-assay probably due to young age and the small percentage of children with active disease.

EXTENSIVELY DRUG RESISTANT (XDR) TUBERCULOSIS (TB) IN GREECE: REPORT OF TWO PAEDIATRIC CASES

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Background and aim: XDR-TB is a public health emergency in endemic and non-endemic countries. To our knowledge, we present the first microbiologically confirmed XDR-TB paediatric cases in Greece.

Case reports: Patient 1 was a 2.5-year-old girl with XDR pulmonary TB and Patient 2 an 18-month-old boy with pre-XDR central nervous system TB. Both children were previously healthy and born in Greece to mothers from East European countries. The source case for Patient 1 remained unknown. Patient 2 was infected by his father suffering from XDR pulmonary TB and had not received BCG or anti-TB chemoprophylaxis. Patients received individualized treatment with second line anti-TB agents guided by drug-susceptibility-testing results. Patients achieved culture conversion 3 and 1 month after treatment initiation, respectively. Patient 1 had clinical, microbiological and radiological evidence of cure, but requires further medical therapy for at least 18 months. She developed hypothyroidism and mild neutropenia 2 and 7 months, respectively, after initiation of treatment, which included para-aminosalicylic-acid, linezolid, rifabutin and cycloserine. These adverse events were managed without treatment interruption. Patient 2 had extensive brain damages at presentation; gradually he developed hydrocephalus for which he underwent repeated neurosurgical interventions. After 6-month hospitalization complicated by hepatic insufficiency possibly related to anti-TB treatment he had a dismal end.

Conclusions: Treating XDR-TB in children is challenging due to uncertainties regarding efficiency, safety and duration of treatment with second-line anti-TB agents. Prevention of emergence and dissemination of XDR-TB should be a priority for health-care professionals.

EXAMINATION OF CHILD TUBERCULOSIS CONTACTS WITH AN INTERFERON GAMMA ASSAY AND TUBERCULIN SKIN TEST: COMPARISON AND PREDICTORS OF POSITIVE OUTCOME

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Background and aims: Evidence of interferon gamma release assay performance for the detection of TB infection among child contacts with adult cases is limited. We compared the performance of QuantiFERON-TB Gold-In-Tube (QFT-IT) with the tuberculin skin test (TST) in detecting TB infection among children with known exposure.

Methods: A cross-sectional study was conducted among 163 children (mean age \pm SD:7.8 \pm 4.7 years) with known TB exposure evaluated with QFT-IT and TST. Comparison groups were based on patient's history of BCG immunization. Agreement between tests was evaluated with the kappa statistic. Logistic regression was used to examine the predictors of a QFT-IT(+) and TST(+) outcomes.

Results: Approximately one third of participants (n=61; 37.4%) had QFT-IT(+) outcome, while 2.4% had indeterminate results. Among BCG(-) children, concordance between QFT-IT and TST was excellent (κ =0.96) among those with household contact, good (κ =0.78) among those with non-household regular contact, and moderate (κ =0.50) in those with occasional contact. In contrast, among BCG(+) children concordance between tests was moderate among household contacts and poor in the remaining patient groups. QFT-IT(+) outcome was associated (inversely) solely with patient's origin from a low TB prevalence setting (AOR:0.36; 95%CI: 0.18-0.73), but not age, children's place of birth, or BCG immunization. In contrast, TST(+) outcome was associated with patient age (AOR:1.17; 95%CI:1.04-1.32) and prior BCG immunization (AOR:5.47; 95% CI:1.90-15.79).

Conclusions: The high concordance observed between the two tests among BCG(-) close contacts of TB index cases suggests that the QFT-IT is more specific. BCG immunization does not appear to provide protection against TB infection.

A 6 YEAR TREND IN UNIT OCCUPANCY, CVC USE, AND HABSİ IN A PICU

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Background and aims: Central Vein Catheter (CVC) use is intertwined to PICU function. The aim of our study is to present bed occupancy, CVC use, and Hospital Aquired Blood Stream Infection (HABSİ) in a PICU of Northern Greece.

Methods: Retrospective chart reviews of temporary CVCs inserted in a multidisciplinary 8 bed PICU from 2005 to 2011. As HABSİ were defined all positive BSI that occurred during the above period. An approximation for catheters day was done according to bed occupancy and CVCS use.

Results: Our results are shown in Table 1.

	2005	2006	2007	2008	2009	2010	2011
Admissions (N)	125	108	106	115	142	133	127
Bed Occupancy (%)	85.3	72.7	58.9	88.6	86.3	68.3	68.8
CVC use (%)	72.8	65.7	74.5	80.0	71.8	81.9	85.8
Patients with CVC (%)	45.6	46.7	51.8	63.4	52.1	57.1	45.6
Gram+ (N)	12	5	12	24	7	14	19
Gram- (N)	12	12	10	8	8	5	11
Fungi (N)	0	1	4	0	0	3	1
HABSİ	24	18	26	32	15	22	31
HABSİ:1000 catheters day	7.7	12.2	17.1	15.5	8.2	11.6	13.8

[Table 1. CVC use, bed occupancy and HABSİ]

Conclusions: There is an increasing trend in admissions and CVCs use with rest parameters having an irregular pattern. Gram+ pathogens predominated, according to relevant data. HABSİ:1000 catheters day could serve as a crude CLABSİ estimation.

CLABSI IN A PEDIATRIC INTENSIVE CARE UNIT OF NORTHERN GREECE: A PROSPECTIVE ONE YEAR STUDY

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Background and aims: Central Line Associated Blood Stream Infection (CLABSI) is a major concern for a PICU. The purpose of our study is to present our experience with Central Vein Catheter use and the related CLABSI.

Methods: One year prospective study of PICU patients having a CVC catheter in a multidisciplinary PICU. Data collected included demographics, type of CVC catheter (temporary or permanent, number of lumens, site of insertion), location of insertion (inside or outside PICU), length of catheter stay and the associated CLABSI. Insertion and maintenance of CVCs were done according to local standards. CLABSI was diagnosed according to 2008 Criteria.

Results: Among 126 consecutive patients admitted during 2011, 91 patients have had a total of 142 CVCs insertion. There were 118 temporary (109 inserted in PICU) and 24 permanent Hickman catheters inserted in the operating room. 84% were femoral and 14% and 2% were subclavian and jugular respectively, whereas 62% were two lumen, and 29% and 8 % were three and one lumen respectively. Mean CVC length of stay was 12.01 ± 12.51 days with a total of 1622 catheter days. There were 20 cases of CLABSI, given a CLABSI Rate of 12.3:1000.

Conclusions: CLABSI rate of our unit was higher than in relevant studies given an average CLABSI rate for PICU patients of 7.6%. This report of the incidence CLABSI rate represents the first step of our hard work to establish international CVCs standards in our unit, in an effort to lower CLABSI rate at the maximum.

CORYNEBACTERIUM PSEUDOTUBERCULOSIS: A CASE OF FEVER OF UNKNOWN ORIGIN

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Background and aims: *Corynebacterium pseudotuberculosis* is an etiologic agent of caseous lymphadenitis in sheep and goats. Rare cases of human infections by this organism are described in the literature, but none as fever of unknown origin.

Methods: Case report.

Results: A previously healthy 5-year-old boy was presented to the emergency department with an 8-day history of low-grade fever. He lived in a rural area where he had contact with sheep, birds and mice. He had no significant past medical history and had not been bitten by any animal. Physical examination was normal except for small, non-painful, posterior cervical lymph nodes. A complete blood count revealed normocytic normochromic anemia (hemoglobin 9.7g/dL), white blood cell count of $6.27 \times 10^9/L$ and platelet count of $210 \times 10^9/L$. The erythrocyte sedimentation rate was of 15mm/h and C-reactive protein was 7.96mg/dL. Serum electrolytes, renal function and liver enzymes were normal. Chest radiograph and abdominal ultrasound were also normal. Purified protein derivative tuberculin test, immunologic and serologic tests were negative. *Corynebacterium pseudotuberculosis* was isolated from four blood cultures. The child began treatment with azithromycin and then ceftriaxone. Clinical conditions rapidly improved and the patient was discharged after 13 days of hospitalization.

Conclusions: *Corynebacterium pseudotuberculosis* infection was reported once in children. This is the first case described as fever of unknown origin, which challenged us with the choice and duration of treatment. Although it remains a rare situation, it should be considered as new potential zoonosis.

EFFICACY OF OMEGA-3 ON IMPROVEMENT OF VENTRICULAR FUNCTION IN CHILDREN WITH DILATED CARDIOMYOPATHY**S. Abtahi***Department of Pediatrics, Mashhad Branch, Islamic Azad University, Mashhad, Iran*

Background: Dilated cardiomyopathy (DCMP) is one kind of cardiomyopathy that is frequently idiopathic and usually characterized by ventricular dilatation and abnormalities in contractile function. The main problem is residual congestive heart failure symptoms despite maximal medical therapy. Thus, an alternative treatment strategy is needed. Omega 3 fatty acids have several potentially cardioprotective effects. In this study, we investigate the effects of fish oil in children with DCMP.

Methods: 14 patients under 18 years old with DCMP were divided into 2 groups, the **receiving fish oil** group (group1, n= 8) and **non receiving fish oil** group (group2, n=6). fish oil syrup. **0.5 mL/kg/day-once a day** was given to the patients' group1 for 9 months, LV ejection fraction (LVEF), LV fractional shortening (LVFS), LV internal diameter in diastole (LVIDD), LV posterior wall in diastole (LVPWD) Doppler and tissue Doppler indexes were measured . Means values in 2 groups compared by Mann-Whitney Test and Wilcoxon Test.

Results: The mean weight in group1 was increased from 6.33± 2.28 kg to 8.4±2.76 kg and in group2: 17.25± 12.09 kg to 17.55±11.84 kg. (P< 0.05). EF had increased significantly in group1 (31.63 +- 9.30 % was changed to 45.75 +- 14.14 %) (p< 0.05) and for group2: 39.17 +- 13.76 % was changed to 40.50 +-14.03% (p> 0.05).

Conclusion: The results suggest that fish oil could lead to improvement of left ventricular function. We believe that if these results are confirmed in larger studies, fish oil should be added to the standard anticongestive therapy of children with DCMP.

KIDSCREEN-52: AN ASSESSMENT OF HRQOL OF HIV INFECTED CHILDREN ATTENDED IN A TERTIARY CARE HOSPITAL IN LISBON

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Background and aims: Health related quality of life (HRQoL) is a descriptor of perceived health that allows planning, monitoring, and evaluating of health-related interventions in the community. KIDSCREEN-52 is a generic HRQoL instrument that identifies children at risk for low well-being and poor health. HIV infected children are at risk due to the infection's natural history, HAART side-effects, low income and social risk. Some studies have addressed this issue but information regarding the HIV infected Portuguese children scarce or unavailable. This study aims to identify HIV infected children at risk of low HRQoL.

Methods: The self-report HRQoL questionnaire KIDSCREEN-52 (Portuguese version) was administered to all the consenting 11-18yo HIV infected children attending the Immunodeficiencies Pediatric Consult of Hospital de Santa Maria [HSM] during 2011, and to their parents.

Results: 13 patients and their parent/tutor consented to participate in this study (12 female; median age: 13.54yo) 2 are VIH-2, all 13 under HAART. Their reported HRQoL was not inferior to the reference population (except in Physical Well-Being and Financial Resources dimensions) nor their parents' assessments of their HRQoL.

Conclusions: HRQoL of 13 HIV infected children attending the Immunodeficiencies Pediatric Consult of HSM was not inferior to the HRQoL of the Portuguese pediatric reference population. However, they scored low Physical Well-Being and Financial Resources dimensions - this suggest the need for a tailored approach and warrants future follow up with the same instrument. Population oriented health policies and multicentric HRQoL assessment of pediatric HIV patients is currently needed in Portugal

RANITIDINE IS ASSOCIATED WITH INFECTIONS, NECROTIZING ENTEROCOLITIS AND FATAL OUTCOME IN PRETERM NEWBORNS

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Objective: Gastric acidity is a major non-immune defense mechanism against infections. The objective of this study was to investigate whether ranitidine treatment in very-low-birth weight (VLBW) infants is associated with an increased risk of infections, necrotizing enterocolitis (NEC) and fatal outcome.

Methods: Newborns with birth weight between 401 and 1500 g or gestational age between 24 and 32 weeks, consecutively observed in Neonatal Intensive Care Units, were enrolled in a multicenter prospective observational study. The rates of infectious diseases, NEC and death in enrolled subjects exposed or not to ranitidine, were recorded.

Results: We evaluated 274 VLBW infants: 91 had taken ranitidine and 183 had not. The main clinical and demographic characteristics did not differ between the two groups. Thirty-four of the 91 children (37.4%) exposed to ranitidine and 18 of the 183 (9.8%) not exposed to ranitidine had contracted infections (OR 5.5, 95% CI 2.9-10.4, $p < 0.001$). The risk of NEC was 6.6-fold higher in ranitidine-treated VLBW infants (95% CI 1.7-25.0, $p = 0.003$) than in control subjects. Mortality rate was significantly higher in newborns receiving ranitidine (9.9% vs 1.6%, $p < 0.003$).

Conclusions: Ranitidine therapy is associated with an increased risk of infections, NEC and fatal outcome in VLBW infants. Caution is advocated in the use of this drug in neonatal age.

DIAGNOSING AND TRACKING PAEDIATRIC INFECTIOUS DISEASE SYMPTOMS THROUGH PATIENT AND PARENT REPORTS: PAEDIATRIC QUESTIONNAIRE DEVELOPMENT

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Background: Diagnosis and management of paediatric infectious diseases often relies on child or parent reports of symptoms. Systematic evaluation of outcomes is essential for clinical trial research. While guidance for the development and validation of Patient Reported Outcomes (PROs) measures is available from EMA and FDA, little attention has focused on paediatric PRO development methods.

Methods: We summarize considerations for the development, validation and use of paediatric PRO measures. Examples from our research in paediatric infectious diseases (HIV, cold, rotavirus) are used throughout.

Results: When developing paediatric PROs, it is critical to use developmentally appropriate language and techniques to ensure measures have content validity and will be reliable and valid. Concept elicitation using qualitative research requires adequate samples sizes within narrow age bands (0-2, 3-5, 6-8, 9-11, 12-14, 15-17) to take into account rapid growth and development. Special techniques (such as drawings, clay, or props) are used to engage the child. Parent reports of observable behaviors, impact on the parent and what the child tells them also provides important information. PRO items must be worded using simple, age appropriate language. Validation should be performed within narrow age bands and pooling data across ages can only be considered if different age versions are shown to be conceptual equivalent.

Conclusions: Strong paediatric PRO research is needed to ensure that paediatric trials use outcome measures that are "fit for purpose" to ensure we collect robust evidence regarding the safety and efficacy of drugs that will be used in children who have infectious diseases.

THE INFLUENCE OF BIRTHWEIGHT, GESTATIONAL AGE AND FETAL GROWTH ON TOTAL LYMPHOCYTE CONCENTRATIONS FROM BIRTH UNTIL TWO YEARS OF AGE

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Background: Birth weight, gestational age and fetal growth influence lymphocyte counts at birth. However, long term effects need to be studied.

Objective: The aim of this study was to assess the associations of gestational age, birth weight and fetal growth with absolute lymphocyte counts in children from birth until 2 years of age.

Methods: In a population-based prospective cohort study from early fetal life onwards, immunophenotypic analysis was performed on (cord) blood samples in healthy children at birth (n=570), 6 months (n=378), 14 months (n=247) and 24 months (n=196). Total T, B and NK lymphocyte counts were determined by a 6-color flowcytometry. Linear regression models with adjustment for gender, maternal education, smoking, alcohol use and fever were applied.

Results: Gestational age was significantly associated with an increase in total T, B and NK lymphocytes at birth. However, at 6, 14 and 24 months gestational age effects were not significant. Increased birth weight and fetal growth were significantly associated with an increase in B lymphocytes at birth, but not at older ages.

Conclusion: The effect of birth weight, gestational age and fetal growth on total lymphocyte counts at birth disappears in infancy (24 months).

CLINICAL CHARACTERISTICS OF HOSPITALIZED CHILDREN WITH 2009 H1N1 INFLUENZA VIRUS INFECTION IN A SINGLE TERTIARY PEDIATRIC CENTRE

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Background: Human pandemic influenza H1N1 virus as a cause of febrile respiratory infection ranging from self-limited to severe illness has spread globally during 2009.

Aims: To describe the epidemiological and clinical features, complications and outcome in hospitalized children at the single tertiary paediatric hospital in Macedonia.

Methods: All children admitted to the University Children's Hospital (Skopje, Macedonia) from November 2009 to January 2010 with symptoms of influenza-like illness and positive test for H1N1 influenza virus infection, using real-time reverse transcriptase polymerase chain reaction on nasopharyngeal swab were included in the study. Data was analyzed from the medical records for: age, gender, co-morbidity, presenting clinical signs and symptoms, antiviral treatment, complications and outcome.

Results: A total of 188 children (mean age 3.8 years) were studied; of these, 59 (31.4%) had chronic underlying diseases. The most frequent symptoms and signs at admission were fever (96.2%), cough (65.2%), seizures (30.8%), malaise (21.3%) and vomiting (10%).

100 patients (53.2%) had H1N1-related complications: 93 (49.6%) pulmonary diseases including massive pneumonia, and seven patients (3.7%) neurological disorders, such as acute encephalitis, acute disseminated encephalomyelitis, polyradiculoneuritis. Three patients needed ICU care, there were no deaths. All of the children were treated with oseltamivir, adverse events during treatment were noticed in 13 (6.9%); vomiting in 11 and skin rash in 2 patients.

Conclusions: H1N1 influenza virus infection in children was associated with a wide spectrum of clinical manifestations. Disease manifestations were similar between children with or without chronic diseases. Oseltamivir therapy was safely and successfully provided.

DURATION OF POSTINFECTIOUS CYTOPENIA IN CHILDREN ASSOCIATED WITH INFECTIONS BY DIFFERENT INFECTIOUS AGENTS

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Background: Acquired cytopenia in previously healthy children is common in paediatric practice and usually appears during infections.

Aim: To assess the frequency, duration and clinical outcome of postinfectious cytopenia in hospitalized febrile children,

Material and methods: 117 febrile children with cytopenia aged 4.0±3.8 years (range 0-14), admitted to a paediatric department during a 2-year period, were evaluated using inflammatory indices, cultures of body fluids and serological tests.

Results: In 52/117 (44.4%) cases a viral agent was identified. Among them 32/52 had neutropenia/leukopenia, 11/52 had thrombocytopenia and 9 had bilineage cytopenia. In 13/117 (11.1%) cases a bacterial agent was isolated (i.e. Salmonella, Shigella, E.coli, Mycoplasma). Of them 9/13 had neutropenia/leukopenia and 4/13 had thrombocytopenia.

In all 9/117 children (7.7%) with pancytopenia, leishmania was detected and pancytopenia resolved within (mean±SD) 17.6±17.3 days with no significant clinical impact. In cases of viral infections, neutropenia was transient and lasted for 41.3±67.7 days, in 11/52 cases thrombocytopenia lasted for 31.3±65.5 days, while in those with 2 cell lines involvement it lasted for 26.8±38.9 days. In children with bacterial infections, cytopenia resolved within 18.5±21.4 days.

In 85/117 cases (72.6%), cytopenia resolved within 2 months, in 12/117 (10.3%) it lasted for 2-6 months (transient cytopenia), while in 20/117 cases (17.1%) >6 months (chronic cytopenia). Seven of them had positive antineutrophil antibodies, 1 positive antiplatelet antibodies and 3 patients were eventually diagnosed with malignancy.

Conclusion: Postinfectious cytopenia in childhood is usually transient with benign course, it resolves spontaneously and is usually associated with common viral or bacterial infections.

A PIECE OF A WIDESPREAD ARCHETYPAL PUZZLE: PARENTAL FEVER PHOBIA IN THE EMERGENCY DEPARTMENT

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Background and aims: Fever continues to be one of the main reasons why parents bring their children to a Pediatric Emergency Department (PED). The caregivers overconcern about fever, first designated as “fever phobia” in 1980 by Schmitt, revisited in 2000 by Crocetti, seems to be even nowadays a current and widespread phenomenon. This survey aims to establish its influence on Romanian parents and to emphasize particular misconceptions.

Method: During 1th November -31th December 2011 a survey was performed among parents who had brought their children to PED. A 27-item questionnaire was given to them, in order to register their knowledge, attitudes and behavior regarding fever in children.

Results: 313 parents were interviewed, 290 questionnaires were analyzed. 46% considered temperature less than 38°C as fever. 72% stated that rectal measurement registers half a degree more than the real temperature. Moreover, some Romanians have the folk idea of “inner fever” meaning normal body temperature with abnormal physical condition and 29% thought that their child might experience it. 82% considered that moderate fever (less than 39°C) was dangerous, meant infection (50%), and stated that they would wake their child for medication (62%). Most caregivers took information about fever from healthcare professionals.(93%).

Conclusions: Fever phobia is a real fact that the Romanian parents are facing, and it has at least one particular aspect. As the healthcare providers are the main source of information regarding fever, educational programs should be developed in order to alleviate this paradigm instead of maintaining or even boosting it.

THE EFFICACY OF GRANULOCYTE - COLONY STIMULATING FACTOR IN PRETERM NEONATES WITH SEPSIS IN QAEM HOSPITAL NICU

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Background and aims: G-CSF is the physiologic regulator of neutrophil production and function; its biological action consists of stimulating the proliferation of neutrophil precursors and increasing chemotaxis, phagocytosis, superoxide production and bactericidal activity.

G-CSF production by monocytes in new born infants is lesser than adults.

Several studies showed the efficacy of G-CSF in infants. For example Bern Stein and colleagues performed a meta-analysis which clarified the usefulness of G-CSF administration in reduction of neonates' mortality in sepsis.

The aim of this study was to investigate the effect of G-CSF in newborns with sepsis.

Methods: Patients' selection criteria:

From May 2010 To Sep.2011 all preterm neonates hospitalized in Qaem hospital NICU were evaluated for entering this study.

About 50 preterm neonates hospitalized in NICU with sepsis, had been chosen for double-blinded randomized study. Neonates randomly divided into two groups. First group with 25 newborns received 10 μ /kg/d of G-CSF which continued for 3 days and the control group gets the same volume of placebo for the same duration.

Demographic data were compared with t-test and non demographic data were compared by using Mann-Whitney test.

Results: Both groups had similar demographic characteristics. White blood cell count and absolute neutrophil count in G-CSF group was significantly higher than placebo.

Conclusion: Administration of G-CSF to premature neonates who had clinical diagnosis of early onset sepsis resulted in increased WBC and absolute neutrophil count.

THE NON-MALIGNANCY HEMOPHAGOCYtic SYNDROME IN A SINGLE TERTIARY INSTITUTION**F.-L. Huang, P.-Y. Chen, T.-K. Chang***Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan R.O.C.*

Background: Hemophagocytic lymphohistiocytosis (HLH) is a disorder that is characterized by the activation of non-neoplastic mononuclear phagocytic system. Infection is the major cause of the disease.

Methods: We retrospectively collected data on 19 patients who were 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 19 patients (11 children as age under 18 year-old, 8 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 had underlying disease but five adult cases (62.5%) 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. Most of the children cases received IVIG and etoposide but few of adult cases received IVIG (0%) and etoposide (37.5%). Steroid was administrated in most patients of both groups. Overall survival rate was 50% but higher in children (60%) than adults (37.5%). The most common reason of death was septic shock in both groups.

Conclusions: In our study, non-malignancy hemophagocytic syndrome developed in both children and adults. Liver function impairment with jaundice and ascites were found frequently in children group than adults. Otherwise higher survival rate was also noted in children group compared with adults.

KAWASAKI DISEASE IN SLOVENIA - A SINGLE CENTER EXPERIENCE**M. Pokorn**¹, B. Dolenc², D. Baš²¹*Department of Infectious Diseases,* ²*Children's Hospital, University Medical Centre Ljubljana, Ljubljana, Slovenia*

Background and aims: There have been no published data on Kawasaki disease (KD) in Slovenia. The aim of present study was to assess clinical presentation, treatment and outcome of KD at the Department of Infectious Diseases, University Medical Centre Ljubljana.

Methods: A retrospective chart review of all KD cases hospitalized at our Department between 2006 and 2011 was performed.

Results: There were 44 children, 27 boys and 17 girls with a 1.6:1 male-to-female ratio. The mean age of children was 3.5 years, 80% were ≤5 years old and 14% were < 6 months old. There were two incidence peaks in autumn and spring. The mean time from fever onset to admission was 4.6 (1-20) days. Seventy-five percent of children had complete KD. 93% of children were treated with IVIG, 90% responded to treatment. The mean time to IVIG treatment was 7.8 (3-20) days. Three of 4 children responded to a second IVIG dose. Three children recovered without IVIG and had no cardiac sequelae.

In the subacute phase of KD, 55% of children had normal echocardiographic findings. At 6-8 weeks, 11% of children had coronary artery aneurisms (CAA) and 7% had CAA at later follow-up. These children were older, had higher CRP values and received treatment later than those without CAA. One child with IVIG-resistant KD died in the subacute phase in spite of treatment with steroid pulses and infliximab.

Conclusion: Our data are comparable to other European countries. KD should be suspected in older children with prolonged fever.

FACTORS ASSOCIATED WITH HEPATITIS B SURFACE ANTIGEN SEROPREVALENCE IN PREGNANT WOMEN IN SIX REGIONS OF KENYA

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Background and aims: Vertical transmission is an important route of transmission for Hepatitis B Virus (HBV) infection. Other modes of infection include sexual transmission, transfusion of infected blood and percutaneous infection through saliva or traces of blood and tribal scarification among others. The aim was to determine the factors associated with HBsAg seroprevalence in pregnant women from various geographical sites in Kenya.

Methods: A cross-sectional survey of women attending antenatal clinics in Kenyatta National Hospital and 8 other hospitals from 5 provinces in Kenya. All pregnant women in their third trimester of pregnancy attending the respective antenatal clinics from June 2001 to June 2002. For each pregnant woman, age, history of: intravenous drug use, sexually transmitted disease (STD), liver diseases, alcohol ingestion, blood transfusion (BT) and presence of traditional scarification were documented. HBsAg carrier status was determined.

Results: 2241 pregnant women were enrolled of whom 205 (9.3%) tested positive for HBsAg. A significant association was found between HBsAg seroprevalence and traditional scarification ($p=0.029$), history of blood transfusion ($p=0.0024$) and alcohol intake ($p=0.05$). There was no significant association between HBsAg seroprevalence and sexually transmitted disease ($p=0.64$).

Conclusions: In this study significant associations for HBsAg seroprevalence in pregnant mothers in the various geographical sites in Kenya included Traditional scarification, Blood transfusion and Alcohol intake.

RECURRENT KAWASAKI DISEASE (RKD) WITH CORONARY ABNORMALITIES IN A COSTA RICAN (CR) BOY: FIRST REPORT FROM CENTRAL AMERICA (CA)

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Background: RKD is uncommon worldwide, with incidence rates of 0.8% in the US and 3% in Japan. No previous RKD cases have been reported in Latin American children.

Case: A 7-year-old boy was admitted on October 2009 at the only pediatric tertiary referral hospital of CR with 5 days of fever, strawberry tongue, bilateral conjunctivitis, cervical lymphadenopathy, maculopapular rash, swollen hands, diarrhea, abdominal pain, and hyporexia. Days before, oral amoxicillin had been given with no improvement. Investigations showed leukocytosis, hypoalbuminemia, hyponatremia, and elevated CRP. An abdominal ultrasound and echocardiogram were normal. IVIG (2gr/kg) and aspirin (100mg/kg/day) were given for KD. Fever disappeared within 24 hours; he developed finger peeling, and went home. Three follow-up echocardiograms were normal. On July 2011 he presented with a 10-day history of fever, generalized macular rash, mucositis and conjunctivitis, for which amoxicillin had been given days before without improvement. RKD was suspected. He received IVIG (2g/kg) and aspirin; an echocardiogram was normal. He recovered completely and was discharged 48 hours after. On follow-up, Beau lines were seen in all his nails, and following his RKD he developed atopic dermatitis that persists to date despite treatment. Two months after, a repeat echocardiogram evidenced coronary dilation, and he still receives aspirin.

Conclusions: Although rare, the possibility of RKD should be discussed with parents so the disease can be suspected early. In this child, the recurrence of KD, the development of coronary abnormalities, and the atopic dermatitis following the disease, suggests a strong immunologic component of the disease.

EARLY POST-OPERATIVE INFECTIONS IN INFANTS AND CHILDREN FOLLOWING COMPLETE ATRIOVENTRICULAR SEPTAL DEFECT REPAIR - DOES DOWNS SYNDROME MATTER?

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Background: In the paediatric intensive care unit (PICU) setting, reports suggest children with Downs syndrome experience higher postoperative infection rates, prolonged ventilation and stay, attributed to inability to deal with oxidative stress, and airway anatomy.

Aims: Compare early (< 30days after bypass surgery) infection profile after Complete Atrio-ventriculo septal defect(CAVSD) repair in children with Downs syndrome (DSgroup) and those without (NDSgroup).

Method: Retrospective cohort study; single tertiary Paediatric cardiac centre. Data of consecutive children admitted after CAVSD repair, over six years (*January 2004 to December 2009*) and, all clinically relevant positive microbiology cultures post-operatively (for 30days), were analysed.

Results: Of total 107 children, 63% (n=67) had Trisomy21. The median (IQR) 'age at surgery' of DS and NDS groups were 4.2 (3.5-6.9) vs 4.3 (2.6-5.1) months respectively; $p < 0.01$. Infection was identified in 26.8% (n=18) of DS group (26 episodes) and 15% (n=6) of NDS group (10 episodes). They were - (DS; NDS) - Respiratory (13;3), Blood (6;3), Wound/ central lines (6;2) and Urine (1;2) respectively.

Commonest respiratory pathogens in the DS group were Haemophilus Influenza and Streptococcus Pneumonia.

DS group showed a trend for prolonged mechanical ventilation (median, IQR) [41 (20 - 61) vs 27.5 (15 - 62) hours, $p=0.2$]. Duration of PICU stay was similar [DS 2(1.3- 3) vs NDS 2(1-3) days; $p=0.9$].

Conclusion: This study shows a trend for increase in postoperative infections, especially respiratory, in Downs syndrome, with similar pathogens . Larger studies looking at antibiotic resistance profiles are needed, to reduce morbidity of infections in children with Downs syndrome.

EVOLUTIVE ASPECTS IN VIRAL MYOCARDITIS IN CHILDREN

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Background: Infants and young children are much more susceptible to develop myocarditis, due to the increased rate of entero- and adenovirus infection. The evolution of viral myocarditis in children can be unpredictable; there are no valid criteria for predicting evolution.

Aim: To assess the clinical evolution of acute viral myocarditis in children.

Method: A consecutive series of 28 children aged between 6 months and 12 years, diagnosed with acute viral myocarditis, were monitored clinically, electrocardiographically and echocardiographically (left ventricular systolic and diastolic function) over a 3 year period.

Results: The clinical picture at onset was dominated by respiratory (50%), cardiac (25%), gastrointestinal (17.8%), and non-specific (2.2%) symptoms. Viral etiology was demonstrated in 22 subjects by evidencing an increased antiviral antibody titer (Coxsackie B, adenovirus, EBV) and was supposed in 6 patients in clinical context. During the monitoring period, the following were found: death from cardiogenic shock in the first days, 1 case, evolution towards clinical, electrocardiographic and echocardiographic recovery within 6 months in 19 children; evolution towards dilated cardiomyopathy in 8 cases. Of these, at the end of the 3 years of follow-up, 6 were declared healed and 2 with stationary evolution. The cases of dilated cardiomyopathy were young children (0-3 years) and had clinical signs of heart failure since onset.

Conclusions: Viral myocarditis in children evolved towards recovery in the majority of the cases in the first months or towards dilated cardiomyopathy with good or stationary evolution at the end of 3 years of follow-up.

KAWASAKI DISEASE COMPLICATED BY FACIAL NERVE PALSY

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Introduction: Although Kawasaki disease (KD) has a well known clinical and laboratory picture, some cases may manifest interesting clinical findings. Facial nerve palsy is a rare neurological manifestation of KD.

Case: A 10-month-old girl was referred to our university hospital because of fever of unknown origin. She developed bilateral conjunctival injection, maculopapular rash, erythema of the oral mucosa with strawberry tongue and dry cracked lips during first week of his disease. On 8th day of fever there was indurative edema of hands and feet. Left-sided peripheral facial nerve palsy (FNP) was noticed at the end of 14th day of fever. Laboratory investigations revealed a mild normocytic normochromic anemia, leukocytosis, a mild thrombocytosis, a raised C-reactive protein level and elevated erythrocyte sedimentation rate. Urine examination demonstrated leukocytes with sterile urine culture. Cerebrospinal fluid (CSF) examination revealed mild pleocytosis (100 leukocyte/) but the cultures grew no organisms. Cranial MRI was normal. On the admission, she has persistent fever for 25 days. She had left-sided peripheral facial nerve palsy and remarkable desquamation on hand and feet. An echocardiographic examination demonstrated the dilatation of the proximal right coronary artery. The diagnosis of KD was established and the patient was treated with high dose intravenous immunoglobulin (2 g/kg infused over 12 hours) and aspirin (100 mg/kg per day). The fever was disappeared and FNP resolved completely during the follow-up.

PREVALENCE OF PNEUMOCOCCAL SEROTYPE IN CLINICAL ISOLATED IN IRAN BY MOLECULAR METHOD

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Background: Globally, *Streptococcus pneumoniae* is associated with 1 million deaths each year in children less than 5 years of age. Most children are colonized and become carriers of one or more serotypes of *S.pneumoniae* during the first year of life. Most pneumococcal infections in children are caused by a limited number of serotypes. Our aim was to develop a simple, reliable, and economical method for detection of epidemiologically important serotypes in children.

Methods: A total of 500 nasopharyngeal swabs were collected between December 2004 and February 2011. Identification was performed by biochemical and molecular tests. Chromosomal bacterial DNA was isolated by using a DNA extraction kit. Serotyping was done by both conventional immunological techniques and by multiplex PCR. We designed primers based on the sequences available for the capsular types 1, 3, 4, 6AB, 14, 18C, 19F, 19A, and 23F and combined them into seven multiplex PCR.

Results: From 500 nasopharyngeal swabs, 60 isolates of *S.pneumoniae* identified after identification tests. Five serotypes (3, 4, 6A, 14, 6B) of *S. pneumoniae* accounted for 81%. Other serotypes accounted only for 12%, and 7% of isolates could not be typed by multiplex PCR test, respectively. Serotype 3 was the most common serotype, followed by 6A and 14 serotypes.

Conclusion: *S. pneumoniae* is a common cause of respiratory infections requiring hospitalization in young children in Iran with antibiotic resistance increasingly common. Five serotypes account for children in Iran.

ROLE OF IMMUNOTHERAPY(IVIG) IN THE TREATMENT OF NEONATAL SEPSIS

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Background and aims: Despite the advantages in neonatal care, neonatal sepsis remains a major cause of mortality and morbidity in the newborn and 1.6 million neonates die every year from infection. This study sought to evaluate the effect of intravenous immunoglobulin (IVIG) in neonatal sepsis in preterm babies.

Methods: This clinical trial was done at the NICU of Emam Reza hospital in Mashhad (IRAN) from Sep 2006 to Sep 2007. We used a dosage regimen of 1g/kg/d. In this study we had 50 patients with documented sepsis; 25 of them received antibiotics (control group) and 25 of them received antibiotics and IVIG as adjuvant therapy. Finally we compared the outcome of two groups with SPSS.

Results: In this study all septic newborns had positive blood cultures. The most common germ which caused sepsis in these babies was Klebsiella (56% in control group and 36% in case group). About 60% of this sepsis were early onset. There was no significant difference between mortality rate in two groups (52% vs. 48%, $p > 0.05$).

Conclusion: This study did not find any significant decrease in mortality rate with IVIG therapy in neonatal sepsis.

PFAPA SYNDROME IN A CHILD WITH 22 Q 11.2 DELETION: A CASE REPORT**A. Pütsepp**, L.-T. Kõrgvee, E. Tamm*Children's Clinic of Tartu University Hospital, Tartu, Estonia*

The periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome was firstly described in 1987 by Marshall and colleagues and is a relatively common cause of periodic fever of unknown origin with the onset at preschool age (< 5y). The diagnosis is based on clinical criteria and the etiology of the disease is unknown.

Hereby we present the case of a 1y6m old girl born from the 5th pregnancy/3rd delivery at term with specific phenotype (low hairline, epicanthus, dysmorphic ears, narrow upper lip) and normal psychomotor development. From the sixth month of age she has experienced 3-4-days cycles of febrile fever with high inflammatory markers (CRP up to 130 mg/L) within every 4 weeks. Papular rash has been documented twice, vesicular rash on the soft palate three times and febrile convulsions twice during febrile cycles. In between the episodes the child is healthy.

Probable viral and/or bacterial infections and autoimmune/rheumatic diseases as possible etiologies for the condition have been excluded. EEG and MRT of the brain reveal no abnormalities. In FISH analysis deletion in the susceptible region for DiGeorge syndrome (22q11.2) was found.

One year after the beginning of the symptoms PFAPA syndrome was suspected and glycocorticoid-treatment was initiated (prednisolon 1 mg/kg) resulting in the disappearance of fever within 18 hours from the onset of the episode. Prednisolon-treatment has also interrupted consecutive febrile cycles.

Conclusion: PFAPA syndrome was diagnosed based on clinical symptoms and efficacy of glycocorticoid treatment, however, the possible association with the deletion in 22q11.2 needs further elucidation.

CARRIAGE RATE OF HAEMOPHILUS INFLUENZAE AND STREPTOCOCCUS PNEUMONIAE AMONG UNDER 6 YEARS OLD CHILDREN IN TEHRAN, IRAN

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Background: Haemophilus influenzae (Hi) and Streptococcus pneumoniae (pneumococcus) are two important causative agents of respiratory infections. Nasopharyngeal carriage is the paramount importance in the transmission of these bacteria. Because of the lack of Hi and pneumococcal diseases surveillance in Iran, this study was designed to isolation, biotyping, serotyping and determination adhesions factors of these bacteria in healthy children before vaccination program.

Material and methods: In this study 200 nasopharyngeal samples isolated from healthy children between 6 months to 6 years old at attending care centers in Tehran during 2011-2012 and were cultured on chocolate agar and blood agar. Identification was performed by biochemical testing , optochin and xv discs and PCR.

Results: The results showed that 40 cases (20%) of the children were carrier of Hi (58% girls and 42% boys) and 50 cases (25%) were positive for Streptococcus pneumoniae (55% girls and 45% boys). From 40 Hi strains and 50 Streptococcus pneumoniae strains 71%, 60% isolated from 1-3 year old children, 15%, 20% isolated from 4-6 year old children and 14%, 20% isolated from under 1 year old children, respectively.

Conclusion: Changing epidemiology of respiratory infections in recent years underlines the need for periodic surveillance of respiratory infections especially in developing countries. Hi and pneumococcus were prominent infections in this age range and our results suggest that there is strong relationship between the number of the children and Hi and pneumococcus carriers. The most carriers are 1 to 3 year old and this rate is reduced with increasing age.

FULMINANT ABDOMINAL ANGIOSTRONGILIASIS (AA) PRESENTING AS AN ACUTE ABDOMEN IN A 14-MONTH-OLD COSTA RICAN (CR) GIRL

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Background: AA is caused by *Angiostrongylus costarricensis*, a nematode first described in CR. The clinical triad for suspicion is abdominal pain, leukocytosis and moderate to severe eosinophilia. Anthelmintics are contraindicated as erratic disease and mesenteric vascular occlusion can occur once treatment is given.

Case: A 14-month-old girl was admitted to our hospital with 7 days of fever, hyporexia, irritability and abdominal pain. Three weeks before, her mother noticed a slug in her mouth. On admission, she was irritable and had a diffuse abdominal pain predominantly in the right hypochondrium. CBC revealed hemoglobin 10.5 g/dL, leukocytes 22,050/mm³ (23% eosinophils), and stool smears were negative for parasites. A latex agglutination test for *A.costarricensis* was positive. An abdominal CT scan showed thickening of the ileocecal intestinal wall. The child improved slowly and went home asymptomatic 3 weeks after, without eosinophilia. She was readmitted 9 days after because of fever, pallor, irritability, abdominal distention and pain. In addition, decreased bowel sounds, melena, and fecaloid drainage from a nasogastric tube prompted surgery. WBC on admission was 35,480 leukocytes/mm³ (0% eosinophils). She required two laparotomies with resection of distal ileum and ileo-ileal anastomosis due to massive thrombosis of the superior mesenteric artery and massive intestinal necrosis, among other findings. She deteriorated clinically, and died 2 days after admission. Histopathology of different tissues demonstrated the presence of the parasite.

Conclusions: Life threatening complications such as mesenteric artery thrombosis and secondary intestinal necrosis can occur in children with AA even in the absence of eosinophilia.

HYDATID DISEASE OF VARIOUS ORGAN INVOLVEMENT IN GREEK CHILDREN

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Background: Hydatid disease (HD) is a parasitic disease caused by *Echinococcus granulosus* (EG) which is endemic in many regions. Hydatid cysts may be found mainly in the liver and rarely elsewhere in the body causing variable clinical manifestations.

Methods: We report three children from northern Greece with unusual hydatidosis of various location. Indirect Hemagglutination Test (IHA) for determination of specific antibodies to EG was used as diagnostic (IHA >1:80 was accepted as positive).

Results: We report five cysts in three children.

A. Boy (7) with acute haemifacial spasms and dysphasia (10 episodes daily, 5-6 min of duration). The Magnetic Resonance Imaging showed an intracranial mass 20mm, left temporoparietal region. IHA was positive 1:256.

B. Boy (12) with mild dyspnea and daily productive cough for two months. Computed Tomography (CT) of thorax revealed a left-upper-lung lesion of 9 cm in diameter and abdominal CT two hepatic cysts subdiaphragmatically at the dome of the liver 6.7 cm and 4.3 cm respectively. IHA was positive 1:256.

C. Girl (9) with abdominal discomfort and pain, jaundice and palpable epigastric mass. Abdominal ultrasound showed a solitary cyst of 18cm subdiaphragmatically. IHA was positive 1:1024.

All lesions were surgically removed. Oral albendazole has been initiated days to weeks before surgery and continued for several months afterwards (repeated 3-4 cycles).

Conclusion: Hydatid cysts should be considered when evaluating cystic masses especially in the endemic areas and be treated by surgical excision. In addition, pre- and post operative antihelminthic administration seems to minimize recurrence.

PREVALENCE OF UNDERNUTRITION IN COLOMBIAN SCHOOL CHILDREN WITH INTESTINAL PARASITES

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Introduction: Undernutrition [Body mass index (BMI) ≥ 1 standard deviation (SD) according to the WHO tables] in school children with intestinal parasites (IP) is a major cause of morbidity and mortality.

Objective: To determine the prevalence of undernutrition through BMI in Colombian school children with IP and identify possible associations.

Methodology: Prevalence study in 93 rural schools of Cali, Colombia, with IP (*Ascaris lumbricoides*, Hookworm, *Trichuris trichiura* and *Giardia lamblia*). Were considered clinical (weight, height), paraclinical [coprological and hemoglobin (Hb)] and demographic (sex) variables. Statistical analysis included estimation of the prevalence of undernutrition in school children and their corresponding 95% confidence interval (CI), the estimation of other descriptive measures of interest and association analysis by multiple logistic regression.

Results: In this population of students with an average age of 7.3 ± 1.7 years, with Hb 13.4 ± 0.5 g/dl, BMI - 0.48 ± 0.67 SD, we found a 15% prevalence of undernutrition and 69.9% of IP, dominance males and none with anemia (Hb ≤ 11 g/dl). The undernutrition is also associated with IP (OR = 1.1 95% CI 0.27-5.23 $p = 0.02$) and giardiasis (OR = 1.03 95% CI 0.21-4.08 $p = 0.00$). Possible factors associated finally were younger and male.

Conclusion: Almost one-fifth of Colombian school children with IP showed undernutrition and this was found associated with age and sex of the child.

IMPROVED STOOL FOR INTESTINAL PARASITES AFTER ALBENDAZOLE IN COLOMBIAN SCHOOL CHILDREN

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Introduction: Albendazole, benzimidazole, reduces the prevalence of intestinal parasites (IP) in school children.

Objective: To describe the improved stool in Colombian school children with IP (*Ascaris lumbricoides*, *Strongyloides stercoralis*, Hookworm and *Trichuris trichiura*) after management with albendazole.

Methodology: We included 61 schools in rural areas of Cali, Colombia, with IP who were took demographics such as age and gender and anthropometric measures such as weight and height. All received 400 mg oral single dose of Albendazole. Intentionally looked for adverse effects from the use of albendazole. Baseline and day 8, they were taken 3 serial stool for counting eggs for IP. Statistical analysis included measures of central tendency such as mean and standard desviation.

Results: Mean age was 8.5 ± 2.2 years, 36 males, 30 with ascaridiosis, 15 with tricocefalosis, 1 with hookworm, 14 with tricocefalosis more ascaridiosis, and 1 with uncinariosis more tricocefalosis. No significant differences in age, gender, type of IP, weight and height, then on day 8 of treatment with albendazole. There was persistence of IP in 9 children after management with albendazole and adverse effects occurred in 22 (in 12 abdominal pain, in 10 nausea and headache, respectively, in 8 vertigo, in 6 vomiting and in 1 rash).

Conclusion: There was 85.2% improved stool for intestinal parasites at day 8 after treatment with 400 mg oral single dose of Albendazole and presence of adverse effects in 36%.

PREVALENCE OF EOSINOPHILIA IN COLOMBIAN CHILDREN UNDER 12 YEARS OF AGE WITH TISSUE AND MIGRATORY INTESTINAL PARASITES BEHAVIOR

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Introduction: Eosinophilia (eosinophils > 500/mm³) in children with tissue and migratory intestinal parasites (IP) behavior (*Ascaris lumbricoides*, *Strongyloides stercoralis*, Hookworm and *Trichuris trichiura*) has been described.

Objective: To determine the prevalence of eosinophilia in Colombian children and identify possible associations.

Methodology: Prevalence study in 130 schools in rural area of Cali, Colombia, with tissue and migratory IP behavior. Were considered clinical (weight, height), paraclinical (eosinophils) and socio-demographic (origin, sex) variables. Statistical analysis included estimation of the prevalence of eosinophilia in children and their corresponding 95% confidence interval (IC), the estimation of other descriptive measures of interest and association analysis by multiple logistic regression.

Results: In this population of children with a mean age of 41±36 months, found a prevalence of 26.9% [16 mild eosinophilia (500-999 eosinophils/mm³), 7 moderate (1000-1499 eosinophils/mm³) and 12 severe (> 1500 eosinophils/mm³)] and 51% from acute malnutrition, predominantly male and being from Cali, Colombia. Eosinophilia is also associated with IP (OR = 4.7 p = 0.01) but not with a specific IP of the degree of eosinophilia.

Conclusion: Almost one third of Colombian children < 12 years of age with tissue and migratory IP behavior showed eosinophilia, not being associated with a specific IP or the degree of eosinophilia.

SUCCESSFUL TREATMENT OF HYPERSPLENISM DUE TO VISCERAL LEISHMANIASIS BY PARTIAL SPLENIC EMBOLIZATION

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Introduction: Splenectomy had been the treatment of choice for severe hypersplenism. We think that partial splenic embolization (PSE) is another effective alternative modality for splenectomy because it is a safe, less invasive, more simple procedure that is easily performed under local anesthesia and it allows preservation of adequate splenic tissue. PSE usually performed via percutaneous femoral artery approach for embolization of approximate 60-70% of spleen parenchyma

Case report: A two and half year old girl presented with history of prolonged fever, abdominal distension, pallor for 3 weeks with huge splenomegaly and mild hepatomegaly, otherwise she was normal. Her WBC count was 1,700/mm³, platelets count was below 100,000/mm³ and Hgb of 6 gm/dL. Other investigations including Leishmania serology were negative. Normal bone marrow biopsy with No evidence for malignancy or Leishmaniasis

Splenic biopsy sample was heavily loaded by L. Donovanii bodies. The patient received a full course of amphotericin B, there was no improvement of blood cell counts but the fever subsided. Few days after the Amphotericin B and because of high fever splenic biopsy was repeated and the sample turned to be normal. PSE successfully performed to our patient with no complications apart from mild fever and abdominal pains which lasted only for couple of days. Her cell count return to the normal within 2 days after PSE

Conclusion: PSE is an effective and less invasive modality for treatment of hypersplenism in children compared to splenectomy.

PSE allows preservation of splenic tissue to safeguard against overwhelming infections especially in young children.

ACQUIRED OCULAR TOXOPLASMOSIS IN A 13-YEAR OLD BOYG. Spagnut¹, I. Toller¹, G. Cricchiutti¹, F. Menchini², **A. Di Benedetto**¹¹*Department of Paediatrics, ²Department of Ophthalmology, University Hospital of Udine, Udine, Italy*

Introduction: Ocular toxoplasmosis(OT) is the most widespread infection that seriously impairs visual acuity in children.

Case report: A child affected by an acute headache with right unilateral loss of visual acuity with normal neurological status and negative cerebral CT performed an ophthalmologic evaluation: visual acuity was 2/10 in the right eye, the fundus showed a retinochoroidal atrophic area, macular thickening with hard exudates. Fluorescein angiography highlighted the presence of active inflammatory periflebitis along the supero-temporal branch of the central retinal vein, suggestive for OT. Trimethoprim-sulfamethoxazol and oral steroids were administered for 5 weeks when no residual signs of inflammatory reaction were revealed. Nevertheless visual acuity remained abnormal.

Discussion: Acquired OT disease might be more prevalent than previously thought. It tends to be unilateral, and in 80-90 % is an asymptomatic, self-limiting disease that goes unnoticed. The hallmark includes focal necrotizing retinochoroiditis that results in a retinochoroidal atrophic scar .

OT therapy includes antimicrobial drugs with or without corticosteroids for 4-6 weeks, until active lesions were checked. The therapy showed no effect on visual outcomes or future recurrence rates. Recurrence is frequent, probably caused by the release of parasites from tissue cyst in the retina. Chronic iridocyclitis, cataract, secondary glaucoma, cystoids macular edema, choroidal neovascularization, and retinal detachment are other complications of OT. Patients with OT should be strictly followed.

INTESTINAL PARASITE PREVALENCE AND RELATED FACTORS IN SCHOOL CHILDREN OF GANDERBAL DISTRICT, KASHMIR VALLEY, INDIA**S.A. Wani**^{1,2}, D.F. Ahmad², S.A. Zaragr³, D.A. Amin⁴¹*Zoology, Govt. Degree College Beerwah*, ²*Zoology, Kashmir University*, ³*Gastroenterology, SK Institute of Medical Sciences*, ⁴*Zoology, University of Kashmir, Srinagar, India*

Intestinal parasitic infections are amongst the most common infections worldwide. Epidemiological research carried out in different countries has shown that the social and economical situation of the individuals is an important cause in the prevalence of intestinal parasites. Previous studies in Kashmir revealed a high prevalence of intestinal parasitic infection. The objectives of the current study were to determine the prevalence of intestinal parasitic infections in Ganderbal district among 3—15 years old children, to identify associated socio-demographic and environmental factors, behavioral habits and also related complaints. Multistage sampling was used in the selection of the study sample. A questionnaire, cellulose adhesive and a stool specimen examination were done. A total of 309 stool specimens were collected. 221 students (71.5%) were infected with one or more intestinal parasites. The most common infecting parasites were *Ascaris lumbricoides*, *Trichuris trichiura*, *Enterobius vermicularis*, *Taenia saginata*, *Giardia lamblia* and *Entamoeba* spp. Intestinal parasite prevalence was higher in the middle age group than upper and lower age groups, in children with less educated mother, in children who source river or well water, in children who who drank unboiled drinking water, in children who defecated in open latrines and in children with unhygienic conditions. Most of the complaints of the study population were not significantly related with the intestinal parasitic infection. Intestinal parasitic infection is an important public health problem in Ganderbal district. Interventions like mass chemotherapy with anthelmintics and health education on personal hygiene to the students and to the parents, especially to mothers are required.

EFFICACY AND SECURITY OF SINGLE DOSE NITAZOXANIDE VS MEBENDAZOLE IN CHILDREN INFESTED WITH MULTIPLE ENTEROPARASITES

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A randomized double blinded clinical trial of single dose Nitazoxanide (NTZ) vs single dose Mebendazole (MB) was carried out in Corrientes city, northeast Argentina. One hundred children 2 to 18 years old with multiple enteroparasite infection by protozoa and helminths were enrolled. After informed consent was obtained, patients were randomized and assigned to treatment. Stool examinations for ova and parasites were done before and 7 - 10 days after treatment with single oral doses of either NTZ 30mg/kg or MB 500mg.

Results: all children were polyparasited, with a total 220 enteroparasites; *E. vermicularis* 71% of patients, *Giardia* 44%, *Blastocystis hominis* 31%, *A. Coli* 16%, *H. nana* 15%, Hookworm 14%, *T. Trichuria* 12%, *S. Stercoralis* 11%, *Ascaris* 5% and *T.saginata* 1%. Ninety-four children completed the study. Overall cure rates (negative ova and parasite examination) were 71.1% for NTZ and 32.7% for MB ($p < 0.001$). Cure rates for protozoa were for NTZ 76% and 2.8% for MB ($p: < 0.01$) and for helminths 91.5% for NTZ and 79.7% for MB. (p ns). Adverse events: Mild gastrointestinal events were observed in 4% for NTZ and in 2% of MB treated children.

The results of this study suggest that a single dose of NTZ is more effective than mebendazole for the treatment of protozoa and at least as effective for the treatment of helminths in children with multiple enteroparasite infestation. Both drugs showed similar, and excellent, safety profile

IS THERE ANYTHING NEW IN HYDATID DISEASE?B. Yildiz, **S. Sen**, Z.S. Bal, F. Vardar*Department of Pediatric Infectious Diseases, Ege University, Faculty of Medicine, Izmir, Turkey*

Hydatid disease is a parasitic infestation caused by *Echinococcus spp.* It still causes morbidity and mortality in endemic areas. In our country it is often seen in childhood and usually necessary to use medications for long time. The aim of this study is to analyze characteristics and course of disease in a pediatric population. Cases diagnosed with hydatid cysts in Ege University Children's Hospital between 2009-2011 were included. Characteristics and course of disease were evaluated retrospectively. A total of 12 cases aged 6-14 years ($10,5 \pm 1,1$) were admitted to the hospital because of fatigue, neusea, fever and cough, abdominal-back pain or diagnosed incidentally. Eight of these patients had isolated lung, liver or vertebral involvement. Others were diagnosed with concurrent liver-lung, liver-omentum or liver-spleen involvements. Two febrile children had elevated Creactive protein levels and leucocytosis. All were treated with Albendazol, 7 of them were operated, other three treated with percutaneous drainage and others didn't need to investigate invasive procedures. Laboratory tests were performed at the time of diagnosis and at third, sixth and twelfth months of therapy. ELISA-IHA titers remained high for longer time in patients treated with percutaneous drainage. One patient had spontaneous rupture of pulmonary cyst and should be hospitalized in intensive care unit and one patient developed toxic hepatitis during medical treatment. There is still no treatment method to obtain complete cure and it can be difficult to manage the course of the disease. There is still diagnostic dilemma arising from high titers of immunoglobulines despite appropriate treatment. We want to emphasize need for new reliable diagnostic tests for follow up of these patients.

FREQUENCY OF INTESTINAL PARASITE IN CHILDREN REFER TO SELECTED CLINICAL LABORATORIES IN TEHRAN

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Background and aims: Parasites found in the human gastrointestinal tract can be largely categorized into two groups, protozoa and helminths. Performing epidemiological studies about it would help us to treat and reduce the burden of disease. Hence, in this study, the frequency of intestinal parasite in clinical labs in Tehran during 2006-2008 was evaluated.

Methods: This cross-sectional descriptive study was performed in six labs including Mostafa-Khomeini, Mofid, Jafari, Day, Zeynab, and Lashgarak between 2006 and 2008. The frequency of intestinal parasite infection in children (aged < 16 years) was evaluated. A total of 29820 stool samples collected to examine for the presence of adult worm and/or segments of worms. Samples fixed in 10% formal-saline were then examined microscopically after concentration by formal-ether sedimentation technique.

Results: Our results showed that 217 out of 29820 samples (0.73%) were positive for giardiasis. The prevalence of *Entamoeba histolytica* was .1%. *Trichuris trichiura*, *Ascaris lumbricoides* and *Hymenolepis nana* are present with percentages of infection: 0.02, 0.01 and 0.04% respectively. More than 1/3 of patients with giardiasis were aged between 6 and 8 years.

Conclusions: According to our findings, frequency of intestinal parasite in understudy population is lower than worldwide distribution of diseases. *Giardia lamblia* was the most frequently identified species.

CHILDREN WITH INTESTINAL PARASITIC INFECTION. SHOULD WE TRUST THE TUBERCULIN SKIN TEST RESULT?

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Background and aims: The tuberculin skin test (TST) is the most useful method for classification of tuberculosis (TB). Infestation by intestinal parasites could be a cause of a TST false negative result. Published articles in this regard are contradictory. The main objective was to evaluate TST results in a population of immigrants and adopted children; to analyze whether intestinal parasitic infestation may modify or not the TST results.

Methods: Cross-sectional observational study. Adopted children or immigrants evaluated in our hospital between January 2003 and December 2008 were included. Children diagnosed with TB, or live attenuated virus vaccinated with two months earlier, HIV-infected, chronically ill or under treatment with immunosuppressive agents, were excluded. TST was considered as the dependent variable. Independent variables were: gender, age, national origin, BCG scar, nutritional status, immune status and intestinal parasitism.

Results: 1074 children were included, 69.6% female. BCG scar in 79%. Mantoux = 0 mm in 84.4%, < 10 in 4.1%, and ≥ 10 in 11.4%. In 20.3% intestinal parasites were found: *Giardia lamblia* (14.1%), *Hymenolepis nana* (3.3%), *Entamoeba histolytica* (2.5%), *Trichuris trichiura* (2.2%), *Ascaris lumbricoides* (1.4%), *Strongyloides stercoralis* (1.1%). Mixed parasitic infestation in 3.7%. There were no differences in TST results between infested and non-infested children.

Conclusions: Intestinal parasitic infestation did not change TST results in our study. These results based on a large number of children coming from several geographical areas, coincide with most recent articles regarding questionable interference that intestinal parasitic infestations may produce on TST results.

SECONDARY HLH DUE TO LEISHMANIA AND EBV CO-INFECTION

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Hemophagocytic lymphohistiocytosis(HLH) is a rare but lethal disease.

Case report: A 22-month-old girl with 8-day fever (40°C) with mild cough and progressive hepatosplenomegaly.

Personal background: Normal except failure to thrive. On physical exam she was stunted, pale and had painless 5-6cm hepatomegaly and 4cm esplenomegaly confirmed by abdominal ultrasound. CBC revealed leucocytes 5100/mm³ (neutrophils 1200/mm³), Hb 9.1g/dl and platelets 47.000/mm³. She had mild hypertransaminasemia and hypoalbuminemia. Ferritin 1134ng/ml. Soluble IL-2 receptor(sCD25) 22260UI/ml. Blood cultures were negative. Serum immunoglobulins and lymphocyte subsets were normal. Epstein-Barr virus(EBV)serology revealed acute infection. EBV viral load was 637copies/ml. Leishmania serology revealed negative immunocromatography and indirect immunofluorescency with slightly positive ELISA. Urinary leishmanial antigen was negative. Microscopic examination of bone marrow aspirate revealed hemophagocytosis. Bone marrow was cultivated. The patient worsened clinically, presenting malaise, progressive esplenomegaly and petechiae in thorax and legs; CBC showed leucocytes 4800/mm³ (neutrophils 800/mm³), Hb 6.8g/dl and platelets 27.000/mm³; tryglycerydes 686mg/dl, ferritin 3849ng/ml and CD25s 2515UI/ml with normal clotting tests as well as perforin expression by flow cytometry. HLH-2004 protocol for HLH was started. Two days after Leishmania Polymerase Chain Reaction (PCR) performed in bone marrow aspirate revealed a positive result. Standard therapy for immunocompromised hosts with Liposomal anfotericin B was administered. Clinical and laboratory data improved. She completed HLH-2004 protocol without relapse.

Discussion: HLH is a rare but lethal disease. Primary HLH is a genetic disorder which must be treated with chemotherapy, but HLH can be secondary to infections, malignancy, etc. In that case, treatment of underlying disease is the main issue. Leishmania-EBV co-infection is rare; as EBV infection can be the first manifestation of primary HLH, we started specific HLH treatment.

Conclusion: Prompt diagnosis of Visceral Leishmaniasis by PCR in secondary HLH may avoid toxicity derived from drugs contained in HLH-2004 protocol.

IMMUNOGENICITY OF NOVEL PLASMODIUM FALCIPARUM LIVER STAGE ANTIGENS

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Both immunisation with radiation-attenuated sporozoites (RAS) and genetically attenuated parasites (GAP) can induce protection against natural malaria transmission. While several problems preclude licensing GAP and RAS as a whole organism vaccine for wide-scale human use they nevertheless serve as useful tools to study protective immunity. We hypothesise that proteins expressed in the liver by attenuated malaria parasites are able to initiate protective immune responses. We have developed a strategy based on differential expression analysis which has resulted in the description of several antigen candidates in both the human parasite *Plasmodium falciparum* and the rodent pathogen *Plasmodium berghei*. Our studies in the rodent model using wild type and attenuated *Plasmodium berghei* parasites and in malaria-exposed individuals indicate that immune responses against these antigens are developed through experimental vaccination and natural exposure and may therefore form the basis of a novel synthetic vaccine that emulates the live attenuated whole-organism vaccine.

CLINICAL AND SEROLOGICAL DATA FOR THE PREVALENCE OF TOXOCAROSIS AMONG CHILDREN IN BULGARIA**I.G. Rainova***Parasitology and Tropical Medicine, National Center of Infectious and Parasitic Diseases, Sofia, Bulgaria*

Toxocarosis is a parasitic disease, caused by the migration of larvae of ascarids from genus *Toxocara* in the human body. Children between 2 and 12 years old get infected more often due to their contact with little puppies, aptitude for geophagia and bad hygiene habits.

In Bulgaria the prevalence of this helminth infection in children is relatively less studied and the objective of the current work was to determine using serological data the frequency of toxocarosis in child patients attended by the Department of Parasitology and Tropical medicine (DPTM) at NCIPD, Bulgaria. In the study were used 311 sera samples from children suspected for toxocarosis collected during nine years (2000-2009). From all tested sera 151 were of boys and 160 of girls. Depending on the age children were divided into three groups: preschool (0-7 years), primary school (8-13) and high school age (14-18). For toxocarosis patients sera were examined with ELISA and Western blot. Results showed seropositivity for toxocarosis in 49 of all tested children - 26 boys and 23 girls. In the separate age groups the highest number of positive for toxocarosis were found in children of preschool age - 24. Depending on the leading clinical symptoms, visceral form of the disease was the most common in children tested for toxocarosis in the study.

MICROSPORIDIOSIS AMONG CHILDREN WITH MALIGNANT DISEASES IN BASRAH

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Objective: To estimate the rate of microsporidiosis among children with malignant diseases.

Methods: Stool samples were collected from 58 children (37 males and 21 females) with malignant disease and 107 apparently healthy children (55 males and 52 females). Direct smear method was done for all stool samples to detect the intestinal parasites. Fecal smears were prepared and stained by Trichrome stain method for the recovery of *Microsporidium* spores.

Results: The results showed that acute lymphocytic leukemia (ALL) was the most prevalent (55.2%) malignant disease among the studied patients. The highest rate of *Microsporidium* infection among the 12 types of malignant diseases was found in patients with Hodgkin and non-hodgkin lymphoma (83.3%).

Prevalence of various species of intestinal parasites (including *Microsporidium*) was 48.3%. The highest rate of parasitic infections was observed in patients with ALL (34.4%). No *Microsporidium* spores have been observed in stools of the control group.

The clinical symptoms among patients includes weight loss (77.6%), fever (29.3%) and diarrhea (27.6%).

Conclusion: *Microsporidium* and other intestinal parasites should be considered among patients with malignant diseases in order to minimize the symptoms often posed by those patients.

GNATHOSTOMIASIS IN AN INTERNATIONALLY ADOPTED CHILD

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Background: Gnathostomiasis is endemic in many Asian countries but it can be found in other parts of the world. We report a case of gnathostomiasis in a 2-year-old Chinese adopted girl.

Case report: Nine months after her arrival to Spain a Chinese girl, who was adopted at age 22 months, presented with complaints of intermittent migratory swellings and creeping eruptions in her legs, thighs, upper arms, chest, forehead and face. These lesions were reddish, tender and pruritic. The episodes usually lasted for 2 hours. Her leukocyte count was 6.300 /mm³ with 4.1% eosinophils. IgE level was 53.9 KU/L (normal range 0-40). Three fresh stools were negative for ova and parasites. Agar culture method for *Strongyloides stercoralis* larvae in stools and a serologic test for lymphatic filarial were negative.

Gnathostoma serology was performed by using ELISA (enzyme-linked immunosorbent assay) the result was positive for *Gnathostoma* spp.

She was treated with albendazole 400 mg a day, for 21 days, but she had to give the treatment up on the third day because there was no toleration. Then Ivermectin (200 µg/kg/day) was given for 2 consecutive days. Lesions decreased in frequency and intensity.

Discussion: Gnathostomiasis includes a great variety of clinical manifestations caused by cutaneous and/or visceral larva migrans syndrome, due to the migration of the third larva stage of the nematode *Gnathostoma*. Eating uncooked-food is the main risk factor, especially raw fish. Dangerous complications of the central nervous system and ocular gnathostomiasis have also been reported.

PROTOZOAL INFECTIONS IN ZINC DEFICIENT CHILDREN FROM RURAL AREAS AROUND MANSOURA CITY, EGYPT

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Background and aims: Parasitic infections and zinc deficiency in children are important public health problems in developing world. This study was conducted to identify the pattern and intensity of protozoal infections in zinc deficient children compared to children with normal serum zinc.

Methods: Fifty five children (age range from 4-11 years) from rural areas around Mansoura, were subjected to history taking, examinations, serum zinc measurement by colorimetric method, and stool examination by direct smear, formol ether concentration technique, and special stains for diagnosis of intestinal protozoa. Intensity of infection was estimated by Kato-thick smear, and counting the number of cysts/mg stool or oocysts / 10 high power fields.

Results: Serum zinc levels were below normal in 60% of children. Children with low serum zinc had insignificant higher prevalence of *Cryptosporidium parvum* (CP) *Entamoeba histolytica* (EH), and *Giardia lamblia* (GL) compared to children with normal serum zinc (69.7%, 59.1%, p 0.06 for CP, 60.6% , 57.6%, p 0.5 for EH, and 54.5%, 50% , p 0.6 for GL). Zinc deficient children had significant heavier intensity as well as co-infection with 3 protozoa compared to children with normal serum zinc.

Conclusions: There is high prevalence of zinc deficiency and protozoal infections especially CP in our children. No significant differences were detected in the pattern or prevalence of protozoal infections between zinc deficient children and children with normal serum zinc level but significant heavier intensity of protozoal infection and co-infection with 3 protozoa was evident in zinc deficient children.

ELUCIDATING THE PERFECT STORM: MULTIPLE PNEUMOCOCCAL SEROTYPES & BACTERIAL SPECIES, AT HIGH DENSITY & WITH NEAR-UNIVERSAL RHINITIS IN YOUNG CHILDREN

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Background and aims: Nasal ecology changes with age & evolves under vaccine selection pressure. Colonisation in young children is exuberant & complex. Its dynamics underlie disease pathogenesis & epidemiology.

Methods: In February-March 2010 we swabbed the nasopharynges of 586 children, aged 6m-6y, attending 6 nurseries in Coimbra, Portugal. Swabs, stored in STGG broth at -80°C were cultured for pneumococcus (Sp), *M.catarrhalis* (Mc), *H.influenzae* (Hi) & *S.aureus* (Sa). Colonies were counted & scored: 0=none, 1=1-5; 2=>5-20; 3=>20-50; 4=>50-100; 5=>100/50µL broth. Rhinitis symptom scores were recorded (n=566): 0=asymptomatic, 1=mild, 2=moderate, 3=severe nasal discharge. Sp serotyping was by multiplex PCR & microarray.

Results: 56% of children (96% 0-1y, 86% 1-2y) had symptoms. Rates of colonisation were: Sp(45.7%), Mc(68.8%), Hi(51.7%) & Sa(15.5%), colonisation was associated with age (all $p < 0.05$) and highest in youngest for all except Sa. Sp density was associated with symptom score, independently of age ($p < 0.001$). 62.8% had multiple bacterial species & 90% colonised with Sp, also carried another species. ≥ 2 species was commoner in younger children ($p < 0.001$) an association not affected by recent antibiotics or Sp vaccination. Among 267 Sp+ samples, 29 serotypes were detected, including vaccine types 3, 7F, 18C*, 19A & 19F (*previously undetected). 29.1% of Sp carriers had multiple serotypes- 2: 21.4%, 3: 4.5%, >5: 0.8% with higher density than single (OR=1.74; $p < 0.001$)

Conclusions: Traditional culture & serotyping misses serotypes commonly present alongside others. Drivers of pneumococcal transmission (colonisation density & rhinitis symptoms) are mutually associated and, critically, may be important determinants of disease.

INTER-SPECIES BACTERIAL RELATIONSHIPS IN THE NASOPHARYNX IN HEALTHY CHILDREN: PNEUMOCOCCUS AND HAEMOPHILUS MUTUALLY ENHANCE WHEREAS MORAXELLA AND STAPHYLOCOCCUS INHIBIT EACHOTHER

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Background and aims: Previous human and animal studies have suggested inhibitory relationships between pneumococcus(Sp) and both *Haemophilus influenzae*(Hi) and *Staphylococcus aureus*(Sa) in the nasopharynx. Conversely recent research suggests that recurrent otitis media may commonly involve combined populations of Sp and Hi in biofilms.

Methods: Samples from an annual cross-sectional pneumococcal colonisation surveillance study in pre-school nursery children (ages 0-6y) in Coimbra, Portugal in 2010 were used to evaluate relationships between four bacterial species. 586 nasal swabs, taken into STGG broth and stored at -80°C, were cultured using standard techniques. Pneumococcus(Sp), *H. influenzae*(Hi), *M. catarrhalis*(Mc) & *S. aureus*(Sa) were identified and density of colonisation assessed by counting colonies.

Results: 268 (46%) were colonised with Sp of which 184(69%) were at high density (>100 colonies/50µl broth). Corresponding figures for other species were: Hi 303(52%), 214(71%); Mc 403(68%), 266(66%); Sa 91(16%), 30(33%). As colonisation rates for all species varied with age, associations between co-colonisation with species pairs were explored using logistic regression. The odds of finding Sp were doubled in the presence of Hi (OR 2.3, 95%CI 1.6-3.2) a finding unchanged taking age into account. In contrast the odds of finding Mc were greatly reduced in the presence of Sa (0.26;0.16-0.41), again still significant accounting for age (0.32;0.2-0.52). No evidence of other inter-species associations was found.

Conclusions: In this sample, colonisation with Sp and Hi and between Mc and Sa were strongly associated, positively and negatively, respectively and independently of age. In understanding nasopharyngeal carriage, inter-bacterial-species effects need to be taken into account.

ACUTE OTITIS MEDIA WITH SPONTANEOUS OTORRHOEA (AOMSO) IN PORTUGUESE CHILDREN: MULTIPLE BACTERIAL INFECTION IS COMMONER THAN BACTERIAL-VIRAL CO-INFECTION

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Background and aims: Interplay between upper respiratory colonising bacterial species and between respiratory viral infections and bacteria may be important in the aetiopathogenesis of acute otitis media. Ecological changes induced by conjugate pneumococcal vaccines may also affect pathophysiology.

Methods: We studied children with AOMSO presenting to the emergency service at Coimbra Children's Hospital, Portugal prospectively during winter 2010-11. After consent, each child had demographic and clinical data recorded and swabs taken from the nose and aural discharge and stored at minus 80°C in STGG broth until batched analysis by semi-quantitative bacterial culture and PCR for respiratory viruses.

Results: 58 of 120 (48.3%) children (mean age 3.2y range 0.2-13.7y) cultured bacteria from aural discharge(B) of whom 17(29.3%) had two or more otopathogens (pneumococcus(Sp)-28, *H. influenzae*(Hi)-16, *M. catarrhalis*-16, *S. pyogenes*-18 isolates). Few (17/120;14.2%) were on antibiotics at the time of study and current antibiotic use or in previous month did not predict culture negative results. 96/118(81.4%) had received PCV(\geq 1dose). In 12/15 children with aural Hi, Sp was also present either in ear, nose or both. 53 viruses(V) were identified in 48 children (14FLU, 23ADV, 11RSV, 1HMPV, 4PIF3). Among 120 children there were 23 with V only, 37 B only, 25 V+B, 35 neither.

Conclusions: This study reports a higher frequency (29%) of mixed bacterial middle ear infection in children with AOMSO than previously reported. It also suggests Hi AOMSO is usually associated with Sp colonisation or infection. However bacterial-viral co-infection was detected in only 22% of these children.

TRANSMIGRATION OF POLYMORPHONUCLEAR NEUTROPHILS AND MONOCYTES THROUGH THE HUMAN BLOOD-CEREBROSPINAL-FLUID BARRIER AFTER BACTERIAL INFECTION *IN VITRO*

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Background: Bacterial meningitis causes severe morbidity and mortality in humans. After bacterial invasion leukocytes are recruited into the CNS secreting mediators such as IL-8, causing massive inflammation. The aim of this project is to identify the cellular and molecular mechanisms of the leukocyte transmigration of PMN and monocytes during the transepithelial transmigration (TEM) process in a human blood-CSF barrier model.

Materials and methods: Using inverted and standard transwell filter systems of human choroid plexus papilloma cells (HIBCPP), we studied PMN and monocyte recruitment over infected HIBCPP cells mimicking the blood-cerebrospinal fluid (CSF) barrier (BCSFB). Within this model we determined TEM rates of the immune cells, their migration route by immunofluorescence, electron microscopy and secretion of cytokine by cytokine bead array.

Results: PMN show a significantly increased level of TEM after infection with wild-type *Neisseria meningitidis* (MC58), but not with its unencapsulated mutant. Paracellular permeability and transepithelial electrical resistance remained stable during TEM. With help of electron microscopical-images and immunofluorescence we observed para- as well as transcellular migrating PMN. Further analysis of secreted cytokines/chemokines showed increased levels of GRO/IL6/IL8/IL1 α /IL1 β /IL1ra/MIP1b/MCP-1/TNF α . In contrast to PMN transmigration we found a significantly decreased monocyte transmigration after infection of HIBCPP.

Conclusions: These findings provide evidence that PMN can migrate para- and transcellular over the BCSFB after *N. meningitidis* infection. Chemokines such as GRO may be involved in this process. However, a possible downregulation of cytokines, chemokines or cell adhesion molecules after bacterial infection may be responsible for the decreased transmigration rate of monocytes.

NO IS A MACROPHAGE AUTONOMOUS MODIFIER OF THE CYTOKINE RESPONSE TO STREPTOCOCCAL SSRNA**S. Deshmukh, P. Henneke***CCI, University Medical Centre Freiburg, Freiburg, Germany*

The cell autonomous intercalation of bacterial processing with inflammatory activation in tissue macrophages is important for the control of mucocutaneous colonizers such as group B streptococci (GBS). This study introduces a novel signaling pathway, which comprises induction of nitric oxide (NO) via the interaction of bacterial ssRNA with MyD88/ Unc93B1 in a phagocytosis-dependent fashion. NO propagates acidification of the bacteria-containing phagolysosome, which in turn enhances modification of bacterial nucleic acids. NO-dependent bacterial processing amplifies transcriptional activation of cytokine genes. This NO-dependent amplification loop is specific for Gram-positive bacteria and in part conserved between kingdoms. It has important mechanistic implications for the anti-streptococcal macrophage response and sepsis pathogenesis.

INTERPRETATION OF TUBERCULIN SKIN TEST IN CHILDREN WITH ALTERATION OF T CD4 LYMPHOCYTE CELL-MEDIATED IMMUNITY

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Background and aims: The tuberculin skin test (TST) is the most useful method for classification of tuberculosis (TB). An immunosuppression status, regardless of the reason, could be a cause of a TST false negative result. The main objective was to evaluate TST results in a population of immigrants and adopted children; to analyze whether the alteration of CD4 lymphocytes mediated cellular immunity may modify or not the TST results.

Methods: Cross-sectional observational study. Adopted children or immigrants evaluated in our hospital between January 2003 and December 2008 were included. Children diagnosed with TB, or live attenuated virus vaccinated with two months earlier, HIV-infected, chronically ill or under treatment with immunosuppressive agents, were excluded. TST was considered as dependent variable. Independent variables were: gender, age, national origin, BCG scar, nutritional status, immune status and intestinal parasitic infections.

Results: 1074 children were included, 69.6% girls. BCG scar in 79%. Mantoux = 0 mm in 84.4%, < 10 in 4.1%, and ≥ 10 in 11.4%. The study of lymphocyte subpopulations was performed in 884 children. CD4 values were < 25% in 5.3%. There were no differences in TST results between children with normal and abnormal CD4 lymphocytes percentage values.

Conclusions: Several studies, including this one, have shown no direct correlation between CD4 percentage values and TST results. These results should be confirmed with larger series and with a higher percentage of children with CD4 lymphocyte percentage values < 25%.

KAWASAKI DISEASE (KD) AND MYCOPLASMA PNEUMONIAE INFECTION: REPORT OF THE FIRST CASE IN GREECE

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Background and aims: The clinical and epidemiologic features of KD support an infectious cause and there is evidence suggesting a pathogenetic role for superantigens in the disease. The superantigenic pathogenesis of *Mycoplasma pneumoniae* in KD has also been proposed. The authors present a case of KD preceded by confirmed *Mycoplasma pneumoniae* infection in a 6-y-old boy.

Methods: The patient presented with fever of 6 days duration, headache and cough, for which he had received amoxicillin/clavulanic acid for 5 days and clarithromycin for 1 day prior to admission. Breath sounds were coarse with crackles. His chest X-Ray showed bilateral interstitial infiltrates. Several cervical lymph nodes were palpable bilaterally.

Results: The cold agglutinin test was positive and *Mycoplasma pneumoniae* IgM antibody titers were high. The patient was put on cefotaxime and azithromycin. On the third day of hospitalization he developed bilateral conjunctival injection, lip fissures, strawberry- coloured tongue, a generalized maculopapular rash, enlargement of the cervical lymph nodes (maximum diameter 2cm), and induration of his limbs, while the spiking fever persisted. His blood test results were also indicative of acute KD. Echocardiography revealed slightly decreased LV systolic function without signs of coronary dilatation. He received intravenous immunoglobulin and oral high dose aspirin. His fever subsided two days later. Periungual desquamation was observed on day 17.

Conclusions: It is postulated that *Mycoplasma pneumoniae* infection in our patient may have triggered the development of KD. To the author's knowledge, this is the first report of KD following *Mycoplasma pneumoniae* infection in our country.

PHARMACOKINETICS OF PHENOBARBITAL IN CRITCALLY ILL NEONATES TREATED FOR PERINATAL ASPHYXIA WITH MODERATE WHOLE BODY HYPOTHERMIA

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Background and aims: Induction of moderate hypothermia (MH) in neonates with hypoxic-ischemic encephalopathy (HIE) results in improved outcome. Phenobarbital (PHE) is believed to have its neuroprotective effect. Pharmacokinetics (PK) of PHE in neonates under MH was described at two clinical studies. The aim of this open-label, prospective study was to evaluate individual PK of PHE and determinate impact of covariates (eg, perinatal asphyxia (PA), MH/rewarming and sepsis) on PK of PHE in term neonates during first week.

Methods: Neonates (40,2±2,7 weeks of gestational age) undergoing MH (33°C-34°C) were admitted from June 2007 to December 2011. Treatment schedule of PHE, consisted of a loading dose 2,5-30 mg/kg, followed by a maintenance dose of 3-5 mg/kg, administered intravenously, every 12 h. Plasma profile of PHE was determined using a validated HPLC method. PK parameters: clearance (Cl), volume of distribution (Vd), and elimination half-life ($t_{1/2}$) were estimated using a non-compartment analysis, PC Programme MWPharm Version 4.0 (Mediware Prague, Czech Republic). Results were reported as mean (SD) and Student's *t* test.

Results: Twelve of thirty six neonates were included in to PK study. The dosage regimen of PHE was individualized in 9/36 neonates, in 6/9 with sepsis, respectively. Two subjects were identified as outliers with computed half-life values exceeding 500 h. In 10 neonates, the mean (±SD) predicted total clearance was 0.0046 (±0.0026) L/kg/h, volume of distribution 0.52 (±0.18) L/kg and half-life was 87.9 (±32.6) h.

Conclusions: Dosing regimen of PHE should be based on individual PK parameters because of present covariates.

HOW MUCH DO YOU NEED FOR INITIAL VANCOMYCIN DOSAGE IN CHILDREN UNDERGOING ECMO AND CHDF?

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Background and aims: Critically ill patients with extracorporeal membrane oxygenation (ECMO) and continuous hemodiafiltration (CHDF) demonstrate different pharmacokinetics of vancomycin in adult study. Little is known regarding to infant and young children. Critically ill children need to achieve therapeutic level immediately. We evaluated vancomycin dosage and initial trough level to determine an optimal regimen.

Methods: We prospectively registered pediatric patients undergoing ECMO and CHDF who received vancomycin therapy from March 2010 to December 2011 at Tokyo Metropolitan Children's Medical Center in Japan. We evaluated vancomycin trough level before 4th dose and vancomycin dosage per body weight and draw the approximate line. We analyzed serum vancomycin level by enzyme immunoassay (SRL, Japan). Polymethyl methacrylate dialysis membrane (HEMOFEEL CH-0.3N®, Toray Medical Co., Japan) was used for CHDF in these patients. We measured vancomycin level at pre- and post-membrane.

Results: Eight patients were enrolled for this study. Mean age and mean body weight were 9 month-old (range, 1-33 month-old) and 4.9 kg (range, 2.5-7.8 kg), respectively. There was significant correlation between vancomycin dosage and trough level. Estimated vancomycin dosage per day to achieve 15 and 20 mcg/dl was 58.6 and 71.4 mg/kg/day, respectively. Polymethyl methacrylate dialysis membrane eliminated vancomycin by 13.9% (mean, n=5).

Conclusion: In our study, pediatric patients with ECMO and CHDF required higher dosage than conventional dosage of 40 mg/kg/day to achieve trough level between 15 and 20 mcg/dl. Although these patients need frequent therapeutic drug monitoring, initial vancomycin dosage may be loaded with 60 mg/kg/day.

METHODS FOR OPTIMISING NEONATAL ANTIMICROBIAL USE: TIME- AND CONCENTRATION-DEPENDENT AGENTS

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Objectives: Pharmacokinetic studies in neonates are increasingly common; it is important their results are used rationally. This study arose from two questions on treating sepsis in neonates. Firstly (time-dependent): what infusion length maximises time above MIC (T>MIC) for meropenem? Secondly (concentration-dependent): what is the optimum dose of gentamicin? We aimed to answer the above questions and in doing so develop methods for finding optimal treatments.

Methods: A meropenem pharmacokinetic model was derived from premature neonates receiving infusions of 0.5 or 4h [1], and a gentamicin model from a freely available dataset [2]. For meropenem utility the aim was 100% T>MIC, and penalties for increasing infusion length were explored. For gentamicin utility, a model for clinical response was fitted to literature data [3] and target set to 100%; the penalty function was a model for uptake kinetics into renal cortical cells [4] and set to 0%. Uncertainty on benefit and risk functions was incorporated. For meropenem a fixed dose was used, and infusion length optimised; for gentamicin dose was optimised. EUCAST MIC distributions [5] for *E. coli* were used to assign values to simulated subjects. Optimal infusion length/dose was derived for a range of fixed MIC values.

Results: For meropenem pharmacokinetics a 1-compartment model provided best fit and optimal infusion length for a 20mg/kg dose with randomly assigned MIC was 0.99h, although this was sensitive to individuals with outlying MIC values. At fixed MIC values below 0.08mg/L optimal infusion time was 5min, rising steeply to 6.07 and 6.98h for the sensitivity and resistance breakpoints of 2 and 8mg/L. For gentamicin a 2-compartment model was chosen, and the optimal dose for randomly assigned MIC was 2.25mg/kg. Optimal doses for sensitivity and resistance breakpoints of 2 and 4mg/L were 4.54 and 6.74mg/kg respectively.

Conclusions: Optimising utility functions provides a more efficient method than exploring dose recommendations by simulation. Details of the approach used will be discussed to show how these methods can be applied.

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RITONAVIR-FLUTICASONE: AN INTERACTION TO BE AVOIDED IN PATIENTS INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS. A STUDY OF FOUR CLINICAL CASES

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Treatment with inhaled fluticasone improved quality of life of children with asthma and allergies. Ritonavir can inhibit P450 3A4 cytochrome metabolism by interfering with the metabolism of the corticoid.

The aim of the presentation was to show 4 cases of exogenous Cushing syndrome, two probable and two confirmed, between 2006 and 2010.

The first two cases, aged 5 and 13 were receiving lopinavir-ritonavir since they were 4 and 9. Then, they began fluticasone. After a month the result was weight gain, moon facies and central obesity. One of them also developed a dorsal hump. A paraclinical confirmation was not achieved. When Fluticasone was discontinued the signs disappeared. The dosage of cortisol and ACTH at 3 months was normal.

The third case, a 13 year-old patient treated with fluticasone since she was 10. At the age of 12, she started lopinavir-ritonavir. After 2 months weight gain and moon facies were observed. Adrenocorticotropin and cortisol levels were below the normal range. The drug was replaced by Efavirenz. The outcome was good at the fourth month.

The fourth case, a 9 year-old patient with lopinavir / ritonavir since he was 5. At the age of 7 he developed an allergic rhinitis and started fluticasone. After a month, weight gain, moon face, central obesity, hirsutism, streaks on the thighs were observed. The cortisol levels was undetectable. Fluticasone was discontinued and after a month ACTH returned to normal.

Ritonavir with fluticasone should not be prescribed and parents should be alerted about the danger of this interaction.

COST-EFFECTIVENESS OF PALIVIZUMAB FOR RESPIRATORY SYNCYTIAL VIRUS INFECTION IN HIGH-RISK CHILDREN BASED ON LONG-TERM EPIDEMIOLOGICAL DATA FROM AUSTRIA

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Background: To assess the cost-effectiveness of palivizumab, a monoclonal antibody against respiratory syncytial virus (RSV), in infants at high risk for severe RSV lower respiratory tract infection (LRTI) such as premature infants, infants with bronchopulmonary dysplasia (BPD), and those with congenital heart disease (CHD), including long-term epidemiological data from Austria.

Methods: A decision tree model was used, and the analysis was based on a life-time follow-up investigating cost-effectiveness of palivizumab versus no RSV infection prevention. The primary perspective of the study was that of the health care system, the second that of society. Cost and effects were discounted by 5%. The base case analysis included only direct medical costs, a scenario analysis included various indirect costs.

Results: Analyses were based on epidemiological data on a total of 1579 children hospitalized due to RSV lower respiratory tract infection over 16 seasons. The incremental cost-effectiveness ratio for the first outcome measure (life years gained) amounted to discounted costs of €34,956 for all preterm infants, €35,056 (< 33 wGA), €35,233 (33-35 wGA), €35,611 (BPD) and €8,956 (CHD). Use of palivizumab compared with no prophylaxis had an incremental cost-utility ratio of €26,212, €26,292, €24,392, €24,654, and €8,484, respectively, per quality-adjusted life years. Results from the society perspective were more cost-effective in all study populations. An additional scenario analysis with seven injections for the 33-35 wGA group revealed cost-effectiveness as well.

Conclusion: Our results based on nationwide long-term epidemiological data suggest palivizumab being cost-effective in prevention of RSV disease in high-risk infants.

COMPLIANCE AND SAFETY OF OSELTAMIVIR TREATMENT IN CHILDREN AND INFANTS LESS THAN ONE YEAR. A PROSPECTIVE ANALYSIS

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Background: Data regarding the compliance and safety of oseltamivir in infants < 1 year are limited.

Aim: To compare the rates of adverse effects and compliance with oseltamivir treatment among hospitalized children aged < 1 yr with suspected influenza and older children.

Methods: A telephone follow up was carried out with parents of children admitted to hospital during the 2009-influenza pandemic within a week after their discharge, and their medical records were reviewed.

Results: 91 children were included (median age -1.2 yr). 39.5% were < 1 year old. Only 8.8% were diagnosed with pH1N1 influenza. The mean duration of therapy was 2.9 days. Difficulty in the administration of oseltamivir was reported in 52% of the children. Adverse effects were reported in 53% of the children. The most common were vomiting and/or diarrhea (32%) followed by restlessness (31%), and rash (6.6%). Treatment of only one child was discontinued due to possible adverse event. The rates of adverse effects and of difficulties in oseltamivir administration were similar among infants < 1 yr and older children. Laboratory tests which include CBC, electrolytes and renal function tests, taken 2 days in average after starting treatment were within normal limits.

Conclusions: The compliance and safety of oseltamivir therapy were similar among infants < 1 yr and older children. Laboratory abnormalities were not identified during oseltamivir treatment. Difficulties in oseltamivir administering and/or possible adverse effects have rarely influenced compliance. Liberal treatment with oseltamivir has led to prominent overuse of the medication.

TEICOPLANIN THERAPEUTIC DRUG MONITORING (TDM) IN PAEDIATRIC PATIENTS

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Background and aims: Teicoplanin is a glycopeptide antibiotic active against Gram-positive bacteria including methicillin-resistant Staphylococci. Trough levels (TL) between 10-30mg/L are recommended. Due to toxicity, peak levels (PL) >60 mg/L should be avoided.

Methods: At the Department of Paediatrics and Adolescent Medicine, Medical University Graz, the initial dose of Teicoplanin (10-15mg/kg every 12h three times, every 24h thereafter) is adapted according to TLs analysed by a fluorescence-polarisation-immuno-assay on treatment day 2 or 3. PLs are analysed in selected cases 30 minutes after end of infusion. We retrospectively analysed Teioplanin levels measured at our institution in the years 2005 through 2011.

Results: 1493 TLs (0.3 - 82.2; mean 21.6mg/L) and 333 PLs (5.0 - 399.7; mean 65.7mg/L) from 484 treatment episodes (45.2% female; patient age: 2 days - 36.6 years) were analysed.

123/1493 TLs (8.2%) were < 10mg/L, 177/333 PLs (53.2%) were >60mg/L.

Patients < 10a had significant higher TLs (mean 22.8 vs. 19.2; $p < 0.001$) and significant lower PLs (mean 59.5 vs. 68.7; $p = 0.024$) than patients >10a.

Female patients >10a had significant ($p < 0.001$) higher TLs (mean 20.9 vs. 17.5) and PLs (mean 80.1 vs. 57.0) than males. In patients < 10a no gender-specific difference was observed.

A significant ($p < 0.001$) though moderate ($r = 0.487$) correlation between TLs and PLs were only found in patients >10a.

Conclusions: TLs and PLs vary widely. Too low TLs, too high PLs and significant age- and gender-specific differences were observed. As long as further pharmacokinetic studies in paediatric patients are pending TDM is strongly recommended.

LOW LEVELS OF CASPOFUNGIN IN CEREBROSPINAL FLUID (CSF)

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Background and aims: Caspofungin is an echinocandin active against most *Aspergillus* spp. as well as most *Candida* spp. Data on levels in cerebrospinal fluid (CSF) is extremely scarce.

Methods: In a 14-year-old patient an Omayo reservoir was implanted for intraventricular treatment of a relapsed germ cell tumor of the pinealis gland. After autologous stem cell transplantation pre-emptive caspofungin treatment was initiated due to repeatedly elevated galactomannan-tests (up to 2.60). Due to liver failure (Child-Pugh-Score 8) reduced dosage of caspofungin (35 mg, i.e. 0.7 mg/kg) was administered once daily. CSF was obtained from the Omayo reservoir (after omitting 10ml of CSF) on caspofungin treatment day 22 (3h level) and 28 (24h level).

Caspofungin levels were measured by liquid chromatography-tandem mass spectrometry using serum standards. For CSF samples a standard addition method was applied taking possible matrix effects into account.

Results: Three h post dose Caspofungin CSF level was 9 ng/mL, 24h post dose Caspofungin CSF level was 70 ng/mL while the corresponding 24h post dose serum level was 8524 ng/mL.

Conclusions: Despite scarce reports of successful treatment of fungal infections of the central nervous system (CNS) with caspofungin, CSF levels of Caspofungin were far below the concentration required for the treatment of *Aspergillus* and *Candida* infections, respectively. This is in line with the only case study (in an adult patient with meningeal coccidioidomycosis) reporting CSF levels of caspofungin which were undetectable. Thus, caspofungin seems to be of limited value for the treatment of fungal CNS infections.

INCIDENCE OF CHILDHOOD PNEUMOCOCCAL PNEUMONIA IN HELLENIC POPULATION IN THE POST VACCINATION ERA

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Background and aims: Streptococcus pneumoniae is the most important aetiological agent of childhood pneumonia. The current study is aiming to analyze the incidence and clinical manifestation of pneumococcal disease in the era of 7-valent and 13-valent pneumococcal conjugate vaccination.

Methods: We conducted a two-phase, retrospective, mono-centered researched that involved all children admitted to a pediatric clinic of a 3rd level general hospital because of pneumonia through the years 2008 and 2011. We studied medical records, laboratory and imaging testing results and registered all cases where pneumococcal pneumonia was diagnosed. We also registered vaccination status of the study group patients. A comparison of the results between the study period years was made in an attempt to clarify the incidence and natural course of the disease in the Hellenic child population after the recommendation of 13-valent pneumococcal vaccination.

Results: During 2008, 44 children were hospitalized because of pneumonia. A 50% of them were vaccinated with 7-valent vaccine. In 9 children -20%-streptococcus pneumoniae was confirmed as the bacterial cause by laboratory techniques. During 2011, 56 children were hospitalized because of pneumonia of which only 28,5% were vaccinated. However, 26 children were older than 7 years old. Pneumococcal pneumonia was diagnosed in 13 patients-23%.

Conclusion: As concluded to our study, the introduction of 13-valent vaccine of streptococcus pneumoniae did not cause any reduction to the number of children hospitalised for pneumonia in our department, as a possible cause of bad compliance to vaccination program for streptococcus pneumoniae.

SEROTYPE DISTRIBUTION AND ANTIMICROBIAL SUSCEPTIBILITY OF STREPTOCOCCUS PNEUMONIAE FOLLOWING INTRODUCTION OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN GREECE

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Background: The aim was to continue reporting the serotypes and antimicrobial susceptibility of Streptococcus pneumoniae isolates causing invasive pneumococcal disease (IPD) or acute otitis media (AOM) in children ≤14 y.o. following the introduction of PCV13 to the Greek National Immunization Programme.

Methods: Data from the 3rd 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 and interpreted by the CLSI criteria.

Results: Among 94 isolates collected (51 boys; 73.4% ≤5 y.o.; IPD: 44, AOM: 50) between November 2010-October 2011, the commonest serotypes for IPD were 19A (27.3%), 7F (25.0%) and 1 (13.6%) while for AOM 19A (22.0%), 3 (10.0%) and 11A (8.0%). In children 0-5 y.o. with IPD, the anticipated coverage for PCV7, PCV10 and PCV13 is 6.7%, 40.0% and 73.3% respectively whereas for AOM is 15.4%, 15.4% and 56.4%. Resistance to penicillin (MIC≥2µg/mL) exhibited 4.6% of IPD and 10.0% of AOM isolates, while percentages for erythromycin rose to 18.6% and 36% respectively. The most prevalent serotypes with resistance to penicillin and erythromycin were 19A and 19F.

Conclusions: One and a half year after the introduction of PCV13 residual pneumococcal disease by PCV7 serotypes is very low. In children ≤5 y.o. with pneumococcal infections, although there is substantial increase of non-vaccine serotypes especially in AOM, the 6 additional serotypes in PCV13 still cause the majority of cases and 19A remains the most prevalent one.

INVASIVE PNEUMOCOCCAL DISEASE DUE TO S.PNEUMONIAE TYPE 3

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18-month child - previously healthy, has been transferred to PICU, with a recent history of right upper lobe pneumonia under triple antibiotic regimen.

Computed tomography scan in the pediatric ward before admission confirmed the X-rays' findings of multiple confluent cavities within the right upper and lower pulmonary lobe, with air-fluid level.

On admission the patient had respiratory distress, tachypnea and hypoxemia.

A chest tube along with fibrinolytic therapy with Urokinase resulted in a total drainage of 190 ml of empyema. PCR isolated *Streptococcus pneumoniae* type 3. Afterwards the patient was clinically stable. Following chest x-rays, did not show any significant changes .

On day 10, chest x ray showed a large air-filled cavity, occupying the right hemithorax.

Chest MRI revealed large tension pneumatocele of the right hemithorax, with left sided displacement of the mediastinum and complete atelectasis of the lower part of the lower lobe.

A pigtail catheter was placed and decompressed the giant pneumatocele. It was removed after 48 hours of no air drainage. Patient remained in a good clinical condition with no needs for oxygen. On day 21, MRI showed complete expansion of the pulmonary parenchyma, and the presence of some small confluent cavities. Patient was discharged home after 21 days.

This is a case of life-saving percutaneous decompression of an acquired giant pneumatocele using minimal invasive procedures. Decompression should always be decided in collaboration with thoracosurgeons. More clinical cases are needed to establish a generally applicable method of how we treat this medical condition.

HUS: RARE COMPLICATION OF SEROTYPE 19A S.PNEUMONIAE

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Background: A 2,5 year old boy , was referred to PICU with the diagnosis of pneumonia with pleural effusion, anuria, severe respiratory distress, anemia and thrombocytopenia with the possible diagnosis of disseminated intravascular coagulation and multiple organ failure.

Methods: At admission he was on oxygen mask, lethargic, with tachycardia, capillary refill time< 2 sec and anuric.

His laboratory tests revealed: HGB 6,9gr/dl, PLT 11000C/ μ l, urea 199mg/dl, creatinine 1,5mg/dl ,normal hepatic enzymes, LDH 2880 U/L, mild prolongation of coagulation tests and direct coombs negative with stochocytosis and acanthocytosis.

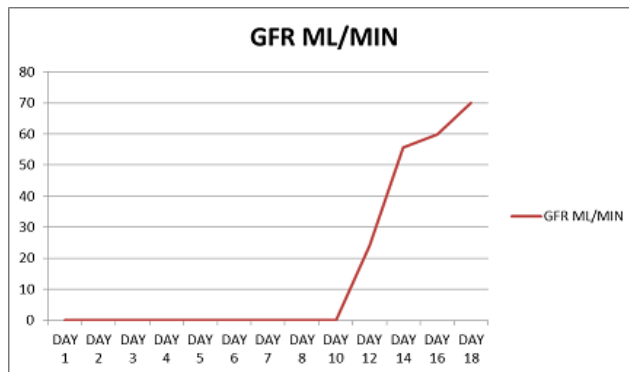
The diagnosis of streptococcus pneumonia associated hemolytic uremic syndrome was considered regarding pneumonia combined with hemolytic anemia, thrombocytopenia and acute kidney injury.

Results: Our patient was successfully managed with continuous renal replacement therapy (CRRT) for 7 days, (Figure 1) and plasma exchange therapy (TPE), which probably reduced the level of circulating anti-T, and neuraminidase. Although he developed mild transient hypertension.

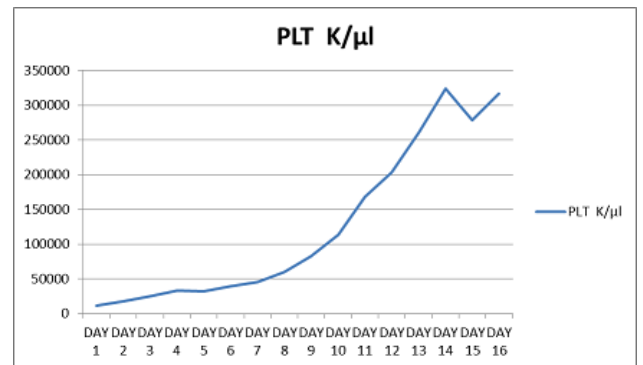
PCR in the pleuric fluid isolated Streptococcus Pneumoniae serotype 19A.

The patient was transfused repeatedly during his stay with target of hemoglobin up to 8 gr/dl. There was a gradual increase of platelets.(Figure 2)

The boy was discharged after 19 days, in a good condition and having established normal diuresis.



[Figure 1]



[Figure 2]

Conclusions: Incidence of HUS after pneumococcal infections is as low as 0.4%, most commonly related with loculated empyema. Plasmatherapy remains first line treatment of SP-HUS . Clinicians should have high suspicion of the entity in cases of hemolytic anemia, acute renal failure, and bacteriological evidence of pneumococcal infection.

IMPACT OF IMMUNIZATION WITH PNEUMOCOCCAL CONJUGATE VACCINES IN MADEIRA**H. Cavaco**¹, A. Barros¹, H. Leitão¹, T. Afonso², G. Rocha²¹*Pediatric*, ²*Clinical Pathology, Hospital Dr. Nélio Mendonça, Funchal, Portugal*

Background: Invasive Pneumococcal Disease (IPD) in children is the major vaccine preventable infectious disease. The heptavalent pneumococcal conjugate vaccine (PCV7) was licenced in Portugal in 2001 and the 13-valent pneumococcal conjugate vaccine (PCV13) in 2010, with an estimated vaccination rate in Madeira Island of 77,9% and 76,1%, respectively.

Method: Descriptive observational prospective study, conducted in Hospital Central do Funchal between July 2006 and June 2011, in children younger than 15 years old with positive culture for *Streptococcus pneumoniae* in normally sterile body fluids.

Results: 35 cases of IPD were analyzed, with a male preponderance (65,7%) and 62,9% of children attended a daycare center/school. Clinical presentation: pneumonia (n=22), occult bacteremia (n=6), meningitis (n=5) and pneumonia with effusion (n=2). Age range: 1-169m, median 63m, with 31,4% under 24m (n=11). Complications occurred in 22,9% (n=8). None of the serotypes included in PCV7 were isolated in the vaccinated subset (n=21). The majority of serotypes are included in PCV13 (n=31). Serotype 1 (n=13): associated with pneumonia (54% of cases) and children >60m (54%); serotype 19A (n=9): associated with occult bacteremia (50% of cases) and children < 24m (45%). Only 1 child had a booster dose of PCV13. There were no fatalities.

Conclusions: Only 3 serotypes included in PCV7 were isolated (6B, 14, 19F), belonging to the non-vaccinated subset. PCV13 covers the majority of isolated serotypes (88,6%). Only 1 child had a booster dose of PCV13. Herd immunity might have been accomplished due to the high rate of vaccination. Continuous epidemiological surveillance is extremely important.

PCR IMPROVES DETECTION AND QUANTIFICATION OF NASAL PNEUMOCOCCUS IN CHILDREN WITH RADIOGRAPHIC ALVEOLAR PNEUMONIA, BUT PNEUMOLYSIN-PCR PICKS UP FALSE POSITIVES

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Background and aims: High density nasal colonisation with pneumococcus, detected by PCR, has recently been reported in children with radiographic pneumonia. However the performance of PCR has not been compared to semi-quantitative culture.

Methods: We studied 131 children with radiographic pneumonia presenting to the emergency service at Coimbra Children's Hospital, Portugal prospectively during winter 2010-11. After consent, each child had demographic and clinical data recorded and a swab taken from the nose and stored at minus 80°C in STGG broth until batched analysis by semi-quantitative bacterial culture and realtime (quantitative) PCR for pneumococcal genes for Pneumolysin(Ply) and LytA using previously published primers.

Results: The children (median age 44 months, range 2-178), 64 boys, 67 girls, included 46 already on antibiotics at the time of sampling. Percentages culture positive were 47% *S.pneumoniae*(Sp), 28% *H.influenzae*, 51% *M.catarrhalis*, 16% *S.aureus* and 1.5% Group A strep. Percentages positive for Sp by PCR were 60% using LytA primers and 84% using Ply primers. However the large majority of Ply+LytA- samples were found to have cultured alpha-Streps not identified as pneumococci by optochin testing. Most of the LytA+Ply+ culture neg samples were from children on antibiotics. There was a highly significant correlation between culture density score and PCR detection cycle number for culture+ PCR+ samples.

Conclusions: PCR can be used to detect and quantitate nasal colonisation with pneumococcus as well as recent colonisation in children taking antibiotics. Ply may return false positives from Ply-expressing non-Sp alpha-Streps, although optochin resistant Sp have been described in children in Portugal

EARLY IMPACT OF A UNIVERSAL IMMUNIZATION PROGRAM WITH THE 13-VALENT CONJUGATE PNEUMOCOCCAL VACCINE IN SANTIAGO DE COMPOSTELA AREA (SPAIN)

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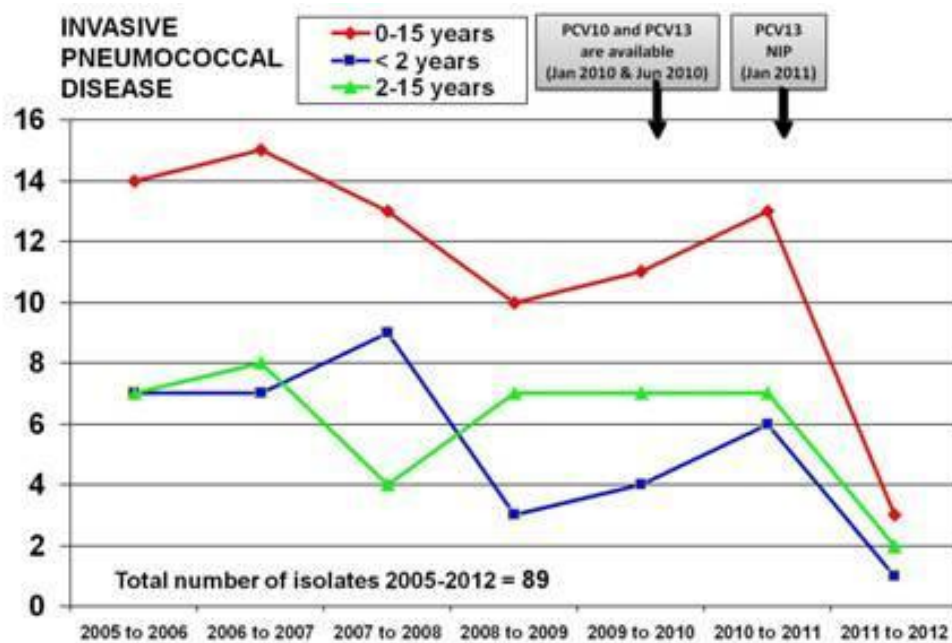
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Background and aims: The 10 and 13-valent pneumococcal conjugate vaccines were introduced in Spain during 2010 (average coverage = 70%). In January 2011 the PCV13 was included in the immunization program of Galicia (north-west Spain). We aim to assess the initial impact of PCV13 in our area on: 1) hospitalization cases of invasive pneumococcal disease (IPD); and 2) serotype distribution in children with pneumococcal suppurative acute otitis media cases (PSAOM).

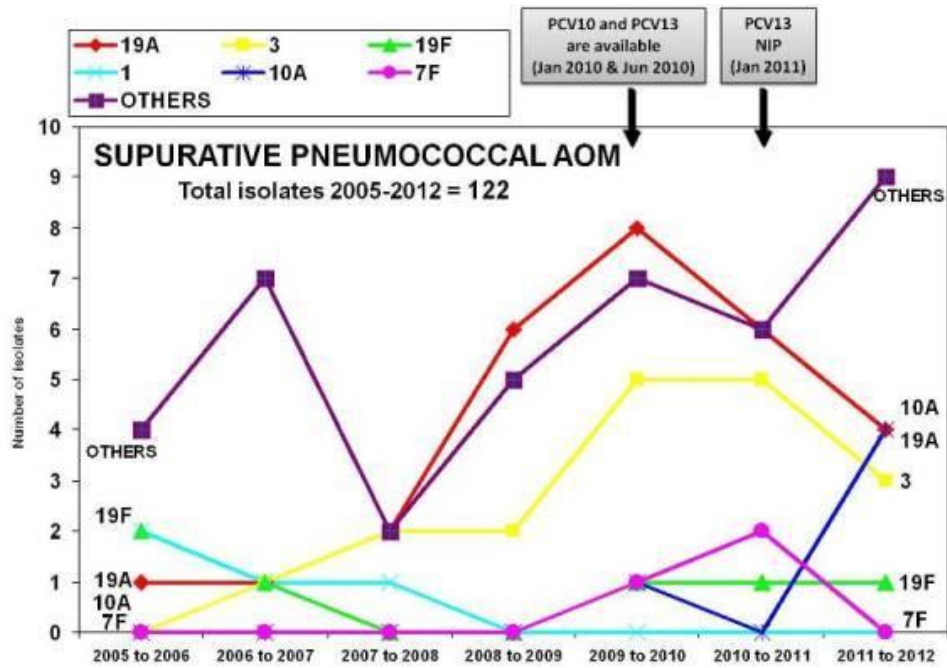
Methods: All IPD cases (isolation of pneumococcus from sterile sites) and PSAOM isolates of children < 15yo admitted/collected from jan 2005 to dec-2011 in our hospital were included and serotyped.

Results: For IPD 89cases of 2.9 (2) yo were included: 19A(25%), 1(15%), 7F (10%) and 3 (10%) were the more prevalent serotypes, and 72% were penicillin-susceptible. A significant decrease in IPD hospitalizations was observed since PCV introduction (figure).



[IPD CASES]

For PSAOM 122 cases of 3.5 (3) yo were included: 19A (25%) and 3 (16%) were the more prevalent -being 50% of all isolates from 2009 to 2011- and 79% were penicillin-susceptible. A decrease in PCV13 included-serotypes has been also observed, with an increase in 10A isolates in PASOM during 2011 (figure)



[SPAOM serotypes distribution]

Conclusions: Despite the very recent introduction of PCV13 in the national immunization program there has been a dramatic decrease in IPD admissions, and SPAOM isolates covered by the vaccine. Our data are preliminary and limited, but consistent with other early impact data reported. Active surveillance remains essential.

CHANGES IN THE MOLECULAR EPIDEMIOLOGY OF PNEUMOCOCCAL MENINGITIS FOLLOWING THE INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINATION IN ENGLAND AND WALES

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Background and aims: The introduction of 7-valent pneumococcal conjugate vaccine (PCV7) in September 2006 markedly reduced the burden of invasive pneumococcal disease (including meningitis). This study aimed to assess changes in the molecular epidemiology of pneumococcal isolates causing meningitis in England and Wales 2 years before and 3 years after the introduction PCV7 vaccination.

Methods: Pneumococcal isolates from blood or cerebrospinal fluid causing meningitis between July 2004 and June 2009 and sent to the Health Protection Agency Reference Laboratory for serotyping were genotyped by multi-locus sequence typing (MLST).

Results: 1,030 pneumococci from meningitis cases were serotyped and genotyped. Fifty two serotypes, 238 sequence types (ST) and 87 clonal complexes were identified. STs associated with PCV7 serotypes all declined after PCV7 introduction, with a proportionally greater decline in ST 124 (usually associated with serotype 14) which caused meningitis predominantly in children < 5y. There was no evidence of capsular switching. Replacement disease after PCV7 introduction was mainly due to serotypes 1, 3,7F, 19A, 22F and 33F through clonal expansion, suggesting a limited number of genotypes are replacing PCV7 genotypes. There was no association between case fatality and any serotype or ST.

Conclusion: Following PCV7 introduction in England and Wales, serotype replacement has changed the genetic composition of the pneumococcal population causing meningitis. The replacement of PCV7 with the 13-valent pneumococcal conjugate vaccine (PCV13) will lead to a further decline in IPD, including meningitis. Continued epidemiological and molecular surveillance is therefore essential to monitor the impact of the higher valency vaccines.

INVASIVE PNEUMOCOCCAL DISEASE AND INDIGENOUS STATUS POST INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN SOUTH AUSTRALIAN CHILDREN

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Background and aims: Streptococcus pneumonia causes invasive pneumococcal disease (IPD) worldwide. A 7-valent pneumococcal conjugate vaccine (7vPCV) was introduced into the Australian National Immunisation Program for Aboriginal and Torres Strait Islander (ATSI) children in 2002, followed by universal vaccination for all Australian children from 2005.

Methods: This cross-sectional study compared causative pneumococcal serotypes and disease severity in children admitted to the Women's & Children's Hospital, South Australia with IPD between 2000-2010, and examined associations with ATSI status. Pneumococcal serotypes were identified from culture confirmed cases. Disease severity was measured using a modified Paediatric Logistic Organ Dysfunction (PELOD) score.

Results: 145 cases of IPD were identified, with ethnicity stated in 140 cases and serotyping available for 116 cases. 129/145 (89.0%) IPD cases occurred in non-ATSI children and 11/145 (7.6%) in children identified as ATSI. ATSI children with IPD were no more likely to score moderate or severe on the PELOD severity scale than non-ATSI children ($p=0.166$). A higher proportion of serotyped IPD cases were caused by non-7vPCV serotypes for ATSI children (6/7, 85.7%) than non-ATSI children (40/104, 38.5%) ($p=0.02$). Following widespread introduction of 7vPCV, the proportion of IPD cases occurring in ATSI children was significantly higher (9/58, 15.5%) than prior to universal introduction of the vaccine (2/82, 3.8%) ($p=0.005$).

Conclusions: 7vPCV appears to have had a greater impact on IPD in non-ATSI children than in ATSI children. Understanding the differences in the epidemiology of IPD between Indigenous and non-Indigenous populations is essential for immunisation program and policy decision making.

INFLAMMATORY MARKERS COMBINED WITH PNEUMOCOCCAL URINARY ANTIGEN PREDICT PNEUMOCOCCAL ETIOLOGY IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA

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Background and aims: Lower respiratory tract infections are still a common cause of antibiotic overuse in children. At the emergency room, our objective was to evaluate parameters that could predict a pneumococcal etiology of community-acquired pneumonia in children (P-CAP).

Methods: Children hospitalized for pneumonia following the WHO definition were enrolled in a prospective study. The following parameters were determined: antibodies against pneumococcal surface proteins (anti-Ply, PhtD, PhtE, LytB and PcpA), viral serology, naso-pharyngeal culture and PCR for 13 respiratory viruses, blood pneumococcal PCR, urinary pneumococcal antigen, procalcitonin and C-reactive protein. Presumed P-CAP was defined as a positive blood culture or PCR, or as a pneumococcal surface protein seroresponse (≥ 2 -fold increase).

Results: 75 patients were included and 37 (49%) met the criteria of P-CAP. PCT and CRP were strongly associated with P-CAP with OR of 23 for PCT and 19 for CRP in multivariate analysis. The sensitivity was 94.4 % for PCT (cut off: 1.5 ng/mL) and 91.9% for CRP (cut off: 100 mg/L). The combination of elevated inflammatory markers with a positive pneumococcal urinary antigen or with the absence of a viral etiology greatly improved the post test probability: 79/83% for high PCT/CRP combined with a positive urinary test and 88% for high PCT/CRP combined with virus negativity.

Conclusion: Elevated PCT and CRP in combination with a positive pneumococcal urinary antigen are reliable predictors of pneumococcal pneumonia. The use of these tests could improve the management of pneumonia in children at the emergency room.

INCIDENCE SURVEILLANCE OF INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN UNDER FIVE YEARS OF AGE IN LOMBARDY (NORTHERN ITALY)

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Background and aims: The incidence rate of invasive pneumococcal disease (IPD) varies across geographical areas; in Italy only local studies have been conducted. The aim of this study is to estimate the IPD incidence in the Lombardy region, Northern Italy, and to identify the circulating *S. pneumoniae* serotypes.

Methods: An observational, prospective, multicentric, population-based active surveillance system of IPD and pneumococcal serotyping ranging from 01 September 2008 to 31 December 2010 recruited children < 5 years with suspected IPD at emergency room visit in 10 hospitals, and involved one central laboratory for antimicrobial sensitivity and serotyping of isolates (culture and PCR analyses).

Results: A total of 251 children (55.8% males) with suspected IPD was recruited (47.4% aged < 24 months). Data on IPD status were available in 236 (94.0%) children. 20 children (8.5 %) had *S. pneumoniae* isolated (9 cases aged < 24 months). The pooled annual incidence rate of IPD was estimated around 28.9/100.000 (95% CI). Pneumonia was found in 11 cases (55.0%), sepsis in 2 (10.0%), meningitis in 1 (5.0%), bacteremia in 6 (30.0%). Strains included in the 13-valent vaccine accounted for 14 of 17 cases available for serotype determination; not included serotypes accounted for 3 cases (12B; 15C; 23B).

Conclusions: PCV 13 showed serotype coverage rate in children aged < 5 years higher than PVC 7 coverage (82.3% vs 29.4%). Vaccination by the 13-valent vaccine option might notably decrease the incidence of IPD.

SEROTYPE 19A *STREPTOCOCCUS PNEUMONIAE* NASOPHARYNGEAL CARRIAGE AMONG CHILDREN ATTENDING DAY-CARE CENTERS IN GREECE DURING 2011

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Background and aims: In Greece, the 7-valent pneumococcal conjugate vaccine (PCV7) became available in Oct. '04, the 10-valent (PCV10) in May '09, and the 13-valent (PCV13) in Jun. '10. The present study investigated the nasopharyngeal (NP) colonization with serotype 19A *Streptococcus pneumoniae* (Sp).

Methods: Between Dec. '10 and Jun. '11, NP specimens were obtained from children attending day-care centers (DCCs) located in an urban (Athens, 4 DCCs, 113 children) and a rural/semi-urban area (prefecture of Viotia, 6 DCCs, 120 children). Each child had to be sampled four times (every 8±2 weeks). When an Sp isolate with a certain serotype and phenotype was repeatedly isolated from a specific child, only the initial isolate was included in the present analysis.

Results: A total of 874 NP cultures were obtained. Of the 233 children, 87.6% had been vaccinated with PCV7, 7.7% with PCV7 and PCV13, and 1.7% with PCV7 and PCV10±PCV13. During the 4 visits, 358 isolates were recovered; 341 were typeable. Of the 273 isolates included in this analysis, 42 (15.4%) belonged to serotype 19A, 16 (5.9%) to another PCV13 serotype, and 215 (78.8%) to a non-PCV13 serotype. Among the 42 serotype 19A isolates, 1 (2.4%) was penicillin-resistant (oral penicillin V breakpoints), 34 (81%) were penicillin-intermediate (MIC₉₀=0.5 µg/ml), 27 (64.3%) erythromycin-resistant, and 14 (33.3%) clindamycin-resistant. The most common non-PCV13 serotypes were 23B (16.7%), 15B/C (14.4%), 11A (9.3%), 15A (9.3%), 6C (8.8%), 16F (8.4%), and 21 (7.9%).

Conclusion: In Greece during '11, a significant circulation of penicillin-nonsusceptible serotype 19A was noted.

NASOPHARYNGEAL CARRIAGE OF INDIVIDUAL STREPTOCOCCUS PNEUMONIAE SEROTYPES DURING PEDIATRIC RADIOLOGICALLY CONFIRMED COMMUNITY ACQUIRED PNEUMONIA FOLLOWING PCV7 INTRODUCTION IN SWITZERLAND

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Background: Community-acquired pneumonia (CAP) is a serious cause of morbidity among children in developed countries. The real impact of 7-valent pneumococcal conjugate vaccine (PCV7) on pneumococcal pneumonia is difficult to assess accurately.

Methods: Children aged ≤16 years with clinical and radiological pneumonia were enrolled in a multicenter prospective study. Children aged ≤ 16 years admitted for a minor elective surgery were recruited as controls. Nasopharyngeal samples for PCR serotyping of *S. pneumoniae* were obtained in both groups. Informations on age, gender, PCV7 vaccination status, day care/school attendance, siblings, tobacco exposure were collected.

Results: In children with CAP (n=236), 54% of the nasopharyngeal swabs were PCR-positive for *S. pneumoniae* compared to 32% in controls (n=105) (p< 0.0001). Serotype 19A was the most common pneumococcal serotype carried in children with CAP (13%) and in controls (15%). Most common serotypes were non-vaccine types (39.4% for CAP and 47.1% for controls) and serotypes included only in PCV13 (32.3% for CAP and 23.5% for controls). There was no significant difference in vaccine serotype distribution between the two groups. In fully vaccinated children with CAP, the proportion of serotypes carried only in PCV13 was higher (51.4%) than in partially vaccinated or non vaccinated children (27.6% and 28.6% respectively, p=0.037).

Conclusions: Two to 4 years following introduction of PCV7, predominant *S. pneumoniae* serotypes carried in children with CAP were non PCV7 serotypes, and the 6 new serotypes included in PCV13 accounted for 51.4% of carried serotypes in fully vaccinated children.

VIRAL COINFECTION IS HIGHLY PREVALENT IN CHILDREN < 5 YEAR-OLD WITH INVASIVE PNEUMOCOCCAL DISEASE

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Background and aims: The burden of respiratory viral coinfection with invasive *Streptococcus pneumoniae* disease (IPD) caused by different serotypes is unknown. The objectives of this study were to know the proportion of invasive IPD episodes which were coinfecting concomitantly with respiratory viruses, and to investigate the association between coinfections and pneumococcal serotypes.

Methods: Children < 5 y-old with proved IPD (by culture and/or PCR in any sterile fluid) and in whom Multiplex-PCR to detect viral coinfection (adenovirus, coronavirus 229E, coronavirus OC43, human metapneumovirus, influenza A, influenza B, Parainfluenza 1-4, Respiratory syncytial virus A and B and rhinovirus) was performed in nasal swap were prospectively included from 8/2008 to 12/2009. Serotypes were classified in high-invasive disease potential serotypes (1, 4, 5, 7F, 9V, 14, 18C and 19A) and lower-invasive disease potential serotypes (all others) according to the classification of Brueggemann and Sleeman.

Results: Seventy-one patients with IPD were included. Pneumococcal serotype 1 was detected in 12 (17%) patients followed in frequency by serotype 19A (n=7; 10%) and serotype 3 (n=6; 8%). In 31 (44%) a serotype with a high-invasive disease potential was identified. Of 71 children with IPD, coinfection with respiratory viruses was highly prevalent (62%). Rhinovirus was the main detected virus (23/44; 52%). The rate of IPD episodes caused by serotypes with a lower-invasive disease potential was higher in the coinfecting patients (29/44; 66% vs 11/27; 41%, $P=0.03$).

Conclusions: Coinfection with respiratory viruses is highly prevalent in children with IPD. Viruses may facilitate the invasiveness of less invasive pneumococcal serotypes.

SEROTYPE DISTRIBUTION AND ANTIMICROBIAL RESISTANCE OF INVASIVE PNEUMOCOCCAL ISOLATES IN CHILDREN < 14 YEARS OF AGE IN CROATIA, 2005 TO 2009

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Background and aims: *Streptococcus pneumoniae* is a leading cause of bacterial pneumonia, meningitis, and sepsis in children worldwide. The aim of this study was to assess serotype distribution and antibiotic resistance in pneumococci causing invasive infections in children < 14 years of age in Croatia from 2005 to 2009.

Methods: Invasive pneumococcal strains were collected through the microbiological laboratory network organised by the Croatian Committee for Antimicrobial Resistance Surveillance. Capsular typing was performed by the Quellung reaction (Statens Serum Institut, Copenhagen). In vitro susceptibility testing was performed by disc diffusion method according to CLSI guidelines. In strains with reduced susceptibility to penicillin (as detected by oxacillin screen disk), MIC for penicillin was determined (E-test, Biomerieux, France).

Results: A total of 192 invasive pneumococcal isolates (186 from blood and 10 from CSF) were isolated in children < 14 years of age between 2005 and 2009. The most prevalent serotypes were 14 (45 isolates), 18C (26 isolates), 6B and 23F (24 isolates each) comprising 62% of all invasive pneumococcal isolates. Dominance of these serotypes was best seen in children 12- < 60 months of age. Non-susceptibility to penicillin was 22% and isolates mostly belonged to serotypes 14 and 19A. Resistance to macrolides was 35% and isolates mostly belonged to serotypes 14, 19A and 6B.

Conclusions: Incidence of invasive pneumococci varies with child's age and is the highest in children 12- < 60 months. Non-susceptibility to penicillin and resistance to macrolides was mostly associated with serotypes 14 and 19A. Serotype 14 is covered by all the available vaccines whereas serotype 19A is covered by 13-valent vaccine only.

ANTIMICROBIAL SUSCEPTIBILITY AND SEROTYPE DISTRIBUTION OF STREPTOCOCCUS PNEUMONIAE ISOLATES IN CHILDREN IN ALGERIA, 2005 TO 2011

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Antibacterial resistance in *S.pneumoniae* is increasing worldwide. The aim of the study was to determine the antimicrobial susceptibility and the serotypes distribution in children.

Methods: Non repetitive 202 *S.pneumoniae* strains were collected from 2005 to 2011. Antimicrobial susceptibility was tested by a disk diffusion method according to CLSI guidelines. The MICs of β -lactamins were determined using the E.Test (ABBiobisk). One hundred and eleven strains were serotyped by rapid latex agglutination (Pneumotest latex) and the Quellung reaction using antisera (Statens Serum Institute). Some serotypes were further determined at the French National Reference Center for Pneumococci (HEGP, Paris).

Results: Out of 202 strains, 151 were from children below 5 years and 115 of it were from infant. Seventy nine isolates were invasive with 46 from infant. Meningitis (43) was the most common diagnosis followed by pneumonia (35), acute otitis media (16) and sepsis (10). About 57% of the isolates were penicillin non susceptible pneumococci (PNSP) with 26% high-level resistance. Among the invasive isolates 55.6% were PNSP. Penicillin MICs ranged between < 0.012 -8 μ g/ml. The susceptibility was decreased to cefotaxime in 12%. The PNSP were more frequently resistant to erythromycin 68%, co-trimoxazole 56,5% and tetracycline 45%. The predominant serogroups were 19(29%), 14(26%), 6(11%), 1(6%), 23(6%), 3(4.5%), 5(3%) and 7(2%). Serotypes 14(27%), 1(10%), 19F(8.5%), 19A(7%), 6B(7%), 6A(4%), 3(4%), 5(4%), 7F(3%) and 23F(3%) occurred most frequently among the invasive isolates. The majority of PNSP belonged to serotypes 14, 19F, 19A and 6B.

Conclusion: Ongoing multicenter surveillance is necessary to monitor the change in epidemiology of *S.pneumoniae*

EPIDEMIOLOGICAL REPORT OF INVASIVE PNEUMOCOCCAL DISEASE IN A PRIVATE HOSPITAL IN ARGENTINA

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Background and aims: Invasive infection by *S. pneumoniae* is a frequent cause of mortality in children. The aim of this study was to analyze *S. pneumoniae* serotypes in invasive disease at a private hospital and compare them with those obtained at public hospitals.

Methods: Patients admitted to Sanatorio Mater Dei (2007-2011) with pneumococcal infection in usually sterile fluids were studied. The isolates were identified according to standard methods. All *S. pneumoniae* isolates were sent to INEI-ANLIS "Dr. Carlos G. Malbrán" for serotyping by Neufeld-Quellung reaction. Each case was compared 1:1 with children from public hospitals of similar age, pathology and geographic region (control group not vaccinated).

Results: 34 patients were admitted in 5 years with the following rates of hospitalization: 36.7‰, 37.5‰, 35.4‰, 15.0 ‰ and 15.5‰ respectively. The median age was 44.5 m in 2010-2011 with the possibility of being vaccinated with new conjugate pneumococcal vaccines (PHiD-CV/PCV-13) vs. 36.5 m in 2007-2009. 18/34 patients were vaccinated with 7-valent pneumococcal conjugated vaccine (PCV-7), 7/8 of them in 2010-2011. The serotypes more frequent found in cases were: 1(n:10), 5(n:8), 19A(n:5), and 1(n:9), 5 (n:7), 14(n:6) 22F(n:2) in controls.

Conclusions:

1. The risk of hospitalization due to invasive Pneumococcal infections was strongly reduced after the introduction of new conjugate vaccines in the private practice.
2. The most frequent isolated serotypes in these cases are not included in PCV-7.
3. Proportion of pneumonia/pleural effusion due to serotypes 1 and 5 was high in group of cases and controls.

MICROBIOLOGICAL ANALYSIS OF MIDDLE EAR FLUID (MEF) AND NASOPHARYNGEAL CARRIAGE (NC) OF INFANTS WITH AOM IN GERMANY, THIRD STUDY-YEAR

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Background and aims: In December 2009, the pneumococcal conjugate vaccine PCV13 was introduced in Germany, where a general recommendation for pneumococcal conjugate vaccination was issued in 2006. 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.2010-Oct.2011.

Methods: MEF- and NC-swabs were taken from children with spontaneous 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: From Oct.2010 to Oct.2011, 213 children with AOM with efflux were documented, considerably less patients than in the two previous periods (Oct.2008-Oct.2009: 459, Oct.2009-Oct.2010: 310), although the study base remained unchanged. Nasopharyngeal swabs were obtained from 193 patients (90.6%).

Following pathogens were identified from 65 of these patients: *S.pneumoniae* (12/18.5%), *S.pyogenes* (25/38.5%), *S.aureus* (17/26.2%), *H.influenzae* (14/21.5%) and *M.catarrhalis* (0/0.0%). NC-rates were: *S.pneumoniae* 57.5%, *M.catarrhalis* 42.0%, *H.influenzae* 34.2%, *S.pyogenes* 9.3% and *S.aureus* 1.6%.

Unchanged to the previous study periods, pneumococcal serotypes 3 and 19A were most prevalent both in MEF and NC. Thus, coverage of the 13-valent vaccine was the highest. The vaccination rate increased from 71.9% (year1) to 84.5% (year3).

Conclusions: While the spectrum of pathogens recovered was almost unchanged, considerably less children with AOM with efflux were documented in the third study year. This could be explained as a positive result of the high vaccination rate against *S.pneumoniae* and has to be carefully studied in the coming years.

NASOPHARYNGEAL CARRIAGE OF STREPTOCOCCUS PNEUMONIAE IN HEALTHY TURKISH CHILDREN AFTER THE INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE

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Background and aims: The 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in Turkey in September 2005 and it was added to Turkish national vaccine schedule in November 2008 for children born in May 2008. The aims of this study were investigating nasopharyngeal carriage of *Streptococcus pneumoniae* in healthy Turkish children and assessing related risk factors in the era of community-wide PCV7 use.

Methods: The study was conducted on 1101 healthy children less than 18 years of age, visiting a well child outpatient clinic and a general pediatric outpatient clinic in Ankara University Medical School, Ankara, Turkey. Specimens were collected with nasopharyngeal swabs between April 2011 and June 2011.

Results: The average age of the children was 45.7±49.6 months. Of the children included in the study, 679 (61.7%) received PCV7. The pneumococcal carriage rate was 21.9%. The carrier frequency was significantly increased by decreasing the children's age and especially in children under 2 years of age and under 5 years of age carrier rates were found to be significantly higher (0-24 months: 25.5%, 25-60 months: 20.2% and >60 months: 13%). According to multivariate analysis, having sibling attending at day-care centers (OR: 1.93), recovering from respiratory infection within 1 month (OR: 1.43), being a member of a family with low income level (OR: 3.96) and being a member of family with more children (OR: 1.38) were found to be the risk factors for the nasopharyngeal pneumococcal carriage.

Conclusions: Community-wide PCV7 vaccination did not influence the nasopharyngeal pneumococcal carriage in healthy children in Turkey.

INCREASING ANTIBIOTIC RESISTANCE IN STREPTOCOCCUS PNEUMONIAE COLONIZING HEALTHY TURKISH CHILDREN AFTER THE INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE

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Background and aims: The 7-valent pneumococcal conjugate vaccine (PCV7) was added to Turkish national vaccine schedule in November 2008 for children born in May 2008. The aim of this study was determining antimicrobial resistance patterns and related risk factors of *Streptococcus pneumoniae* in healthy Turkish children in the era of community-wide PCV7 use.

Methods: The study was conducted on 1101 healthy children less than 18 years of age. Specimens were collected with nasopharyngeal swabs between April 2011 and June 2011. Penicillin and ceftriaxone susceptibilities were determined with E-test according to the 2008 Clinical Laboratory Standards Institute.

Results: Using the meningitis criteria of MIC values, 73% of the isolates were resistant to the penicillin and 47.7% of them was non-susceptible to the ceftriaxone. According to multivariate analysis, being a member of crowded family, living with a family health care provider and increasing in the average number of antibiotics used within 3 months were found to be related with the increase in the rates of penicillin resistance. In addition, penicillin resistance was significantly more in non-vaccinated or vaccinated partially children with PCV7 than the vaccinated fully children with PCV7 aged under 5 years. Being a member of family with more children, being age of over 2 years and increasing in the average number of antibiotics used within 3 months and 1 year were found to be related with the increase in the rates of ceftriaxone resistance.

Conclusions: Despite the community-wide PCV7 vaccination the antimicrobial resistance of pneumococci significantly increased in healthy Turkish children.

SEROTYPE DISTRIBUTION OF STREPTOCOCCUS PNEUMONIAE IN HEALTHY TURKISH CHILDREN AFTER THE INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE

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Background and aims: The 7-valent pneumococcal conjugate vaccine (PCV7) was added to Turkish national vaccine schedule in November 2008 for children born in May 2008. The aim of this study was determining serotype distribution and related risk factors of *Streptococcus pneumoniae* in healthy Turkish children in the era of community-wide PCV7 use.

Methods: The study was conducted on 1101 healthy children less than 18 years of age. Specimens were collected with nasopharyngeal swabs between April 2011 and June 2011. Serotypes of the isolates were determined by Quellung reaction.

Results: The pneumococcal carriage rate was 21.9% (241/1101). Of the pneumococci isolated from children, 184 (76.3%) could be serotyped. Half of all pneumococcal isolates were serotyped as 19F (15.2%), 6A (15.2%), 23F (10.3%) and 6B (9.3%). Serotype coverage rates of the PCV7 and non-PCV7 were 46.2% and 53.8%, respectively. However, a recently introduced 13-valent pneumococcal conjugate vaccine (PCV13) covered 62% of isolates. The most common penicillin and ceftriaxone resistant serotypes were 6A, 6B, 14, 19F and 23F. Also, resistant isolates to the penicillin and ceftriaxone were more in serotypes covered by PCV7 and PCV13 than the non-PCV7 and non-PCV13 serotypes.

Conclusions: After the community-wide PCV7 vaccination an increasing trend of the rates in non-PCV7 serotypes was seen especially in serotype 6A in healthy children in Turkey.

CHARACTERIZATION OF *STREPTOCOCCUS PNEUMONIAE* FROM INVASIVE INFECTIONS, OTITIS MEDIA AND NASOPHARYNGEAL CARRIAGE IN BULGARIA BEFORE INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINE

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Background and aims: In 2010, universal immunization with PCV was introduced in the Bulgarian immunization programme. The aim of the present study was to identify the most prevalent pneumococcal serotypes before the introduction of PCV.

Methods: Thirty six invasive *S. pneumoniae* isolates, 50 from acute otitis media and 31 nasopharyngeal carriage isolates were included in the study. Sixteen IPD isolates were obtained from children ≤ 5 years and 20 - from children > 5 years and adults. The AOM and nasopharyngeal isolates were collected from children ≤ 8 years. Serotyping was performed using quellung reaction and susceptibility to antibacterial agents was determined according to CLSI 2010.

Results: The most frequently encountered serotype among invasive isolates was 19F (13,9%), followed by 1 (11,1%), 4 (8,3%), 6B, 23F, 9V and 3 (5,6% each). Serotypes 6A, 19A, 18C and 7F were represented by one isolate each. Among the 16 IPD isolates from children ≤ 5 years the most frequent serotypes were 19F (n=4) and 1 and 4 (n=3 each), followed by 6B, 23F, 9V and 18C (n=1 each). The most commonly encountered serotype among AOM isolates were 19F (24%), followed by 6B (14%), 14 (8%), 9V and 3 (6% each) and 23F and 18C (4% each). Among nasopharyngeal strains 19F was the most frequent (26%), followed by 6B and 3 (13% each), 9V and 23F (6% each).

Conclusions: Most of the detected serotypes are included in the available PCVs. A significant reduction in the incidence of the pneumococcal infections could be expected after the introduction of universal immunization.

EVALUATION OF A COMMERCIAL RAPID URINARY TEST (BINAX NOW, STREPTOCOCCUS PNEUMONIAE URINARY ANTIGEN TEST) IN CHILDREN WITH NASOPHARYNGEAL PNEUMOCOCCAL CARRIAGE

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Aim: A commercial rapid urinary pneumococcal antigen test (Binax NOW, Portland, USA) have been used in diagnosis of pneumococcal infection. In the study, we aimed to evaluate the influence of nasopharyngeal pneumococcal carriage on the results of the antigen detection test.

Method: The study was performed in Ege University Medicine Faculty Health Child Polyclinic between September 2009 and March 2010. Urine samples for the antigen detection test and nasopharyngeal swab specimens for culture were obtained from enrolled children.

Results: 223 children, aged 2-60 months, 89 (40%) females were included in the study. All the children have been vaccinated with 7 valent-pneumococcal conjugate vaccine. Pneumococcal nasopharyngeal carriage was present in 24 (10.8%) of 223 children. Pneumococcal antigen in the urine samples with the Binax NOW test was determined in 16 (66.7%) of 24 nasopharyngeal carriage children. Whereas, in 17 (8.5%) of 199 non-nasopharyngeal pneumococcal carriage children, pneumococcal antigen was determined positive in urine samples.

Conclusion: Binax NOW test can be positive in the children who are nasopharyngeal pneumococcal carriage. Therefore, the rapid urinary pneumococcal antigen test can't be useful to diagnose pneumococcal infection in children.

CHARACTERISTICS OF INVASIVE PNEUMOCOCCAL DISEASE (IPD) CAUSED BY SEROTYPE 1 (SP1) COMPARED WITH OTHER SELECTED COMMON PEDIATRIC SEROTYPES (OSIPD)

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Background: We questioned whether IPD caused by SP1 differed from that caused by serotypes 5, 14, 6A, 6B, 19A, 19F, and 23F.

Methods: All IPD cases in children < 18y old treated at our medical center during 2000-2009 were included. Data were retrieved retrospectively, and were compared between SP1 and OSIPD (the latter as all serotypes grouped and as individual serotypes). The analyses were adjusted for age and ethnicity.

Results: 96 SP1 and 251 OSIPD episodes were documented. SP1 was more prevalent in older children ($68.3 \pm 52.6m$ vs. $30.4 \pm 39.2m$; $P < 0.001$) and in Bedouin children (87.5% vs. 58.6%; $P < 0.001$) than OSIPD. SP1 was less frequently isolated from patients with underlying disease than OSIPD (24% vs. 39.4%; $P < 0.001$; RR 0.25 [95% CI: 0.13-0.47]). SP1 was more often associated with bacteremic pneumonia and primary peritonitis than OSIPD (70.8% vs. 38.6% and 7.3% vs. 0.8%, respectively; $P < 0.001$ for both), while bacteremia without focus was more prevalent in OSIPD (32.3% vs. 12.5%; $P < 0.001$). There were no differences in rates of hospitalization and mortality (70.8% vs. 68.1% [$P=0.22$] and 4.2% vs. 5.6% [$P=0.26$], respectively). SP1 had higher mean temperature ($39.4 \pm 0.9^\circ\text{C}$ vs. $38.9 \pm 1.3^\circ\text{C}$; $P=0.001$) and peak absolute neutrophil counts (PNAC; $17.7 \pm 9.0 \times 10^3/\text{mm}^3$; $13.0 \pm 8.2 \times 10^3/\text{mm}^3$; $P < 0.001$) than OSIPD.

Conclusions: SP1 was found less frequently than OSIPD in children with underlying diseases, and more frequently in older children, children with bacteremic pneumonia or primary peritonitis and Bedouin children. SP1 was characterized by higher temperature and PNAC.

SLOWER REDUCTION OF MENINGITIS VS. NON-MENINGITIS INVASIVE PNEUMOCOCCAL DISEASE (IPD) RATES, POST PCV7 INTRODUCTION - HOW TO EXPLAIN THE PARADOX?

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Background: PCV7 was introduced to the Israel National Immunization Program in July 2009 (2, 4, 12 months schedule; catch-up 2 doses, 2nd year). Nationwide active IPD surveillance has been conducted since 1989.

Methods: All 27 centers performing blood/CSF cultures reported monthly all IPD (positive blood/CSF cultures). Capture-recapture was used for completeness.

Results: During 1989-2010, 6,022 IPD cases were reported; 572 (9%) were meningitis. Children < 6 months constituted 31% of the meningitis vs. 12% of the non-meningitis group. PCV7 serotypes+6A (VST) were only 30% of meningitis < 6 months (incidence rates of ~2.6/100,000 for VST and ~4.6/100,000 for serotypes 1, 3, 5, 7F and 19A).

In contrast, in children 6-59 months, non-VST meningitis rates were low (~1/100,000) and stable throughout the study period.

Compared to 2003-7, by 2010, overall and VST meningitis incidences < 5 years decreased by 21% and 50%, respectively, vs. 44% and 83% in non-meningitis IPD, with no replacement so far. (**Table 1**)

Conclusions: We speculate that the main reasons for the slower reduction in pneumococcal meningitis compared with non-meningitis rates were: 1) Most children < 6 months (age group with highest meningitis rates) were too young to be fully vaccinated; 2) The short period (18 months) post PCV7 did not allow sufficient herd immunity needed to protect infants < 6 months; 3) VST were found only in a minority of meningitis cases < 6 months.

Table 1. Incidences of pneumococcal meningitis, non-meningitis and overall IPD in children <5 years in Israel, 2003-2007 vs. 2010

	Mean ± SD incidence/100,000 population				% reduction overall	% reduction VST	P-value*
	2003-2007		2010				
	Overall	VST	Overall	VST			
Meningitis (N=572)	3.85±0.43	2.02±0.31	3.06	1.02	21% ^a	50% ^c	<0.01
Non-meningitis (N=5,450)	46.82±3.16	29.28±1.84	26.18	4.98	44% ^b	83% ^d	
Overall IPD (N=6,022)	50.68±3.40	31.30±1.87	29.24	6.0	42% ^e	81% ^f	

*P-value <0.01 for a vs. b, a vs. c, b vs. d, c vs. d, e vs. f

[Table]

SEROTYPE DISTRIBUTION AND ANTIBIOTIC RESISTANCE OF STREPTOCOCCUS PNEUMONIAE ISOLATED FROM CHILDREN WITH ACUTE OTITIS MEDIA IN RUSSIA

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Background and aims: There are scarce data on actual role of *S. pneumoniae* in etiology of acute otitis media (AOM) and its serotype and antibiotic resistance profile in Russia.

Methods: Tympanocentesis material or ear discharge in case of spontaneous draining was taken from children (age < 5 years) with AOM by eSwab kit (Copan). Swabs were inoculated in plates for microbiological analysis. *S. pneumoniae* serotyping was performed by Neufeld reaction. Antibiotic resistance was checked by the disk diffusion method.

Results: We analyzed 105 patients with AOM. Relevant bacteria were detected in 55 patients (52%): *S. pneumoniae*, n=24 (44%); *S. pyogenes*, n=11 (20%); *P. aeruginosa*, n=7 (13%); *H. influenzae*, n=5 (9%); *M. catarrhalis* and *S. aureus*, n=4 each (7%). No growth was observed in 28 patients (27%), and in 22 patients (21%) irrelevant/physiological flora was detected. Twenty eight *S. pneumoniae* strains from 23 patients were serotyped, but since in 5 patients both ears were infected with the same serotype, we considered only 23 strains for further analysis. We found the following *S. pneumoniae* serotypes: 19F, n=6 (26%); 6B, n=5 (22%); 3, n=4 (17%); 6A, n=2 (9%); serotypes 8, 9V, 14, 15B, 19A, 23F – n=1 each. Isolated *S. pneumoniae* strains demonstrated resistance to oxacillin (25%), erythromycin (33%), azithromycin (30%), clindamycin (30%), cotrimoxazole (54%). No penicillin resistant strains were detected.

Conclusions: Our data indicate that *S. pneumoniae* is a leading bacterial pathogen responsible for AOM in children under 5 years in Russia. Moreover, 25-30% of circulating strains display resistance to a number of antibiotics. PCV-13 vaccine coverage of AOM-associated *S. pneumoniae* serotypes is above 90%.

NASOPHARYNGEAL CARRIAGE OF STREPTOCOCCUS PNEUMONIAE IN CHILDREN WITH ACUTE BACTERIAL INFECTION IN RUSSIA

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Background and aims: Nasopharyngeal colonization is an essential step for the pathogenesis of S.pneumoniae-associated infections. Hereby, we study current S.pneumoniae carriage rate and serotype distribution in children with acute bacterial infection in Russia.

Methods: Nasopharyngeal swabs from children (age < 5 years) with acute bacterial infections were taken by an eSwab kit (Copan). After swab inoculation for culture, DNA was extracted from the eSwab medium and used for RT-PCR targeting specific S.pneumoniae gene *lytA*. Serotyping of isolated S.pneumoniae was performed by Neufeld reaction.

Results: In total, we examined 130 patients (acute otitis media, n=101; sinusitis, n=15; community acquired pneumonia, n=10; fever without source, n=4). The following pathogens were isolated: S.pneumoniae, n=35 (27%); S.aureus, n=14 (11%), M.catarrhalis, n=8 (6%), H.influenzae, n=7 (5%), P.aeruginosa, n=5 (4%), S.pyogenes, n=4 (3%), S.agalactiae, n=2 (2%). Nonsignificant/normal flora was found in 42 patients (32%), in 13 samples (10%) no growth was observed. Serotype distribution for 24 available S.pneumoniae isolates was as follows: 19F, n=5; 6A, n=4; 6B and 23F, n=3 each; 3 and 14, n=2 each; 9V, 11A, 15B, 19A, 38, n=1 each. In 50 samples we perform culturing and RT-PCR analysis in parallel. Ten samples (20%) were culture/RT-PCR-positive, and additional 24 samples (48%) were positive only by RT-PCR. Thus, 34 samples (68%) tested by RT-PCR were positive for S.pneumoniae-specific *lytA* gene. No culture-positive/RT-PCR-negative samples were found, 16 samples (32%) were culture/RT-PCR-negative.

Conclusion: These data indicate that in children with acute bacterial infection nasopharyngeal carriage of S.pneumoniae is frequent, with serotypes 19F and 6A/B being predominant. Perhaps, the real carriage rate is even higher when RT-PCR results are considered.

IDENTIFICATION OF IMMUNODOMINANT B-CELL EPITOPES WITHIN SURFACE PNEUMOCOCCAL PROTEINS (PNPS)

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Background: Previous screening of a whole-genome- λ -display *Streptococcus pneumoniae* library with patients' sera revealed epitope-containing fragments within 6 virulent surface PnPs (CbpB, PhtD, PhtE, ZmpB, PspA and spr0075), consisting of about 2000 amino-acids. This study aimed to unveil the fine specificity of host antibody response against these antigenic fragments and identify the immunodominant epitopes in amino-acid resolution level.

Methods: To map the immunodominant epitopes, 150 synthetic 20-mer overlapping peptides (OLPs #1-#150), covering the sequence of antigenic fragments, covalently attached in polystyrene rods, were screened using 12 sera from children aged 2-16 years convalescing from invasive pneumococcal disease (IPD). Healthy children with no history of IPD, aged 1-4 years, were used as controls.

Results: Controls' sera exhibited no specific immunoreactivity with any of the 150 OLPs. However, 10 peptides were consistently recognized by patients' sera: OLP#4 (p 0.06) within CbpB, OLP#11 (p 0.002), OLP#18 (p 0.01) within PhtD, OLP#40 (p 0.002) within PhtE, OLP#125 (p 0.01), OLP#138 (p 0.06) within ZmpB OLP#76 (p 0.002), OLP#79 (p 0.002), OLP#90 (p 0.002), OLP#100 (p 0.08) within spr0075. Uniprot searches revealed that these epitopes are conserved in most pneumococcal strains, whereas they show a 80-90% amino-acid sequence similarity to other streptococcal species (e. g. oralis, mitis). Interestingly, 4/10 epitopes exist in up to 6 repeats within their parent protein, a finding suggesting stronger antibody binding.

Conclusions: Antigenic fragments of known virulent surface PnPs include specific immunodominant B-cell epitopes, consistently recognized by sera from patients with IPD, encouraging further investigation of their role in host-pathogen interaction.

MACROLIDE RESISTANCE DETERMINANTS AMONG *STREPTOCOCCUS PNEUMONIAE* ISOLATED FROM CARRIERS IN CENTRAL GREECE

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Background: We sought to characterize the temporal trends in nasopharyngeal carriage of macrolide-resistant pneumococci during a period with increased heptavalent pneumococcal conjugate vaccine (PCV7) coverage in Central Greece.

Methods: *Streptococcus pneumoniae* nasopharyngeal isolates were recovered from 2649 day-care center attendees in Central Greece during 2005-2009. A phenotypic and genotypic analysis of the isolates was performed, including the identification of macrolide resistance genes *mef(A)*, subclasses *mef(A)* and *mef(E)*, as well as *erm(B)*.

Results: Of the 1105 typeable *S. pneumoniae* isolates, 265 (24%) were macrolide-resistant; 22.2% in 2005, 33.3% in 2006, 23.7% in 2007, and 20.5% in 2009 ($P=0.398$). Among these macrolide-resistant isolates, 28.5% possessed the *erm(B)* gene, 24.3% the *erm(B)+mef(E)* genes, 41.8% the *mef(E)*, and 5.3% the *mef(A)*. A *mef* gene as the sole resistance determinant was carried by 30.8% of macrolide-resistant PCV7 isolates and 70.2% of the non-PCV7 ones. Across the 4 annual surveillances, pneumococci carrying the *mef(A)* gene were gradually disappeared, whereas serotype 19F isolates carrying both *erm(B)* and *mef(E)* genes persisted without significant yearly fluctuations. Non-PCV7 serotypes exhibiting macrolide resistance were 6A, 19A, 10A, 15A, 15B/C, 35F, 35A, and 24F. In 2009, 59% of the macrolide-resistant pneumococci belonged to non-PCV7 serotypes.

Conclusions: Across the study period, the annual frequency of macrolide-resistant isolates did not change significantly, but in 2009 a marked shift to non-PCV7 serotypes occurred. Overall, more than half of the macrolide-resistant isolates possessed the *erm(B)* gene either alone or in combination with *mef(E)* gene. *erm(B)* gene dominated among PCV7 isolates, but not among the non-PCV7 ones.

PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASES IN 2009-2011 IN MINSK, BELARUS**O. Simachenko**, I. Germanenka*Belarussian State Medical University, Minsk, Belarus*

Background and aims: *Streptococcus pneumoniae* takes one of the leading place among invasive pathogens of children and older adults in the whole world. In Belarus the diagnostic of invasive disease for *Streptococcus pneumoniae* is very poor. This study analyses invasive pneumococcal disease (IPD) in hospitalized patients in Children's Hospital of the Infectious Diseases in Minsk in 2009-2011 years.

Methods: The retrospective study of children with a diagnosis of invasive disease for *Streptococcus pneumoniae* was conducted at the Children's Hospital of the Infectious Diseases in Minsk . Criteria for inclusion was isolation of pneumococcus from a normally sterile fluids.

Results: The study included 19 children. Of these, 54% of meningitis, 31% of sepsis, 15% cases of pneumonia. The youngest patient was 8 month, the oldest 17 years old, but 86% were children under 5 years old. In all cases children wear hospitalized in poor condition and long-term therapy was necessary. The mean length of hospital stay was 20 and in intensive care unit 8 days. All patients were successfully treated with antibiotics. The mean duration of antibiotic therapy was 14,5 days and included from 1 to 6 drugs.

Conclusions: Improvement of the diagnostic of invasive disease for *Streptococcus pneumoniae* is necessary. The group of risk among children -patients younger than 5 years old.

PNEUMOCOCCAL MENINGITIS IN CHILDREN - LAST TEN YEARS EXPERIENCE

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27 cases of pneumococcal meningitis in children (0-18 years) from East Bohemian region were identified on our clinic in 2002-2011. 17 (63%) patients were less than 24 months old. In 21 (77.8%) cases *Streptococcus pneumoniae* was confirmed by cerebrospinal fluid (CSF) cultivation, in 6 (22.2%) cases PCR detection of CSF was positive. Intracranial complications (subdural hygroma, hydrocephalus, intracranial vein sinus thrombosis and nasal encephalocelacele) were observed in 10 (37%) children, surgical treatment was necessary in 7 (25.9%) patients. None of our patients died, 8 (29,6%) children have survived with long term sequelae (mostly hearing disorders). The pneumococcal vaccination in the Czech Republic is optional and reimbursed in the framework of public health insurance from 2009. Only one child had been immunized before the disease occurred. 15 pneumococcal strains (1 non-typable) were identified in our patients, 6 (40%) of them being not contained in any conjugate vaccine.

PNEUMOCOCCAL MENINGITIS BEFORE AND AFTER PNEUMOCOCCAL CONJUGATE VACCINE, 7 AND 13 VALENT UNIVERSAL VACCINATION. 2001-2011 MONTEVIDEO, URUGUAY

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Background and aims: Prior 2008 *S. pneumoniae* was suppurative meningitis leading cause in children in Uruguay; pneumococcal meningitis (PM) case fatality rate was 35%. March 2008 PCV7 was incorporated into vaccination program for < 2 years old. April 2010 PCV13 replaced PCV7 (both 2+1 schedule), catch-up for older children was offered. National data demonstrate high compliance with PCV7/13, >93% 2008-2009, > 95% 2010.

Assess the impact of this strategy in PM hospitalization in Hospital Pediátrico-Centro Hospitalario Pereira Rossell.

Methods: Cases and annual rates per 10,000 discharges (95%CI) for PM are described: before PCV7 (2005 - 2007), year of vaccine implementation (2008), after (2009-2011). Age, PCV7/PCV13 doses, and serotypes were obtained from hospital databases.

Results: 38 PM cases were identified in ≤14 years old; 30 (2005-2007), 1 (2008), 7 (2009-2011). PM rates decreased yearly pre-PCV7: 11.2 (5.87-16.53), 5.5 (1.7-9.3), 3.3 (0.4-6.2) in 2005, 2006, 2007. In 2008, 2009, 2010, 2011 rates were 0.8 (-0.7-2.3), 3.5 (0.07-7.05), 0.9 (-0.8-2.7), 1.9 (-0.7-4.5).

Significant rates reduction (75%) was observed in < 5 years old; median rates pre-vaccination decreased from 11.1 (6.9-15.2) to 2.8 (0.3-5.2) post-vaccination. Serotypes were, prior PCV: 14 (7); 5 (8); 1 (3); 7F (3); 6B (3); 12F (2); 6A/C (1); 23B (1); pool D (1). 2008: serotype 3. 2009-2011: 6A/C, 10A, 7F, 24A, 18C, 8 and 3. Children with VST (3, 6A/C, 18C, 7F) were not vaccinated. Eight children died in 2005-2007 and 1 in 2009-2011.

Conclusion: Data following introduction of PCV7/13 demonstrate that PCV7/13 are highly effective preventing PM.

INVASIVE PNEUMOCOCCAL DISEASES IN NEONATES BEFORE AND AFTER UNIVERSAL VACCINATION WITH PNEUMOCOCCAL CONJUGATED VACCINE 7 AND 13 VALENT, URUGUAY

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Background: *S. pneumoniae* is cause of neonatal serious infections. Pneumococcal (PCV7/13) vaccination in children aged ≥ 2 months would protect neonates by changing pneumococcal carriage in those too young to receive the vaccine. In Uruguay, March 2008: PCV7 was incorporated into vaccination program for < 2 years old. April 2010: PCV13 replaced PCV7 (both 2+1 schedule), catch-up for older children was offered. National data demonstrate high compliance with PCV7/13, $>93\%$ 2008-2009, $>95\%$ 2010.

Aim: To describe isolates from neonates (0-30 days) with invasive pneumococcal disease (IPD) hospitalized in: Centro Hospitalario Pereira Rossell (CHPR) and Hospital Escuela Litoral Paysandu (HELP) before introduction of PCV (2001-2007) and after universal vaccination (2009-2011)

Material and methods: *S.pneumoniae* isolated from sterile body sites and diagnosis in newborns with IPD at CHPR and HELP are described before PCV7 (2001 -2007), implementation year (2008) and after vaccination (2009-2011). Data were obtained from hospital databases.

Results: 25 cases of IPD were identified (20 CHPR, 5 HELP). *S.pneumoniae* was isolated from blood (10), CSF (9), blood and CSF (5) and blood and pleural fluid (1). Most frequent diagnoses were: meningitis, sepsis, pneumonia and bacteremia. Nineteen cases occurred in 2001-2007, 4 in 2008, 2 in 2009-2011. Serotypes in 2001-2007 were: 5 (8), 1 (4), 18C (2), one isolate: 7F, 11A, 19A, 19F, Pool D (89 % coverage with PCV13). 2008 serotype 5 (1), 2009-2011 serotype 1 (1).

Conclusions: These preliminary data may be due to PCV13 herd effect. Surveillance is mandatory to confirm the sustained reduction in IPD in neonates.

MOLECULAR EPIDEMIOLOGY OF PNEUMOCOCCI RECOVERED FROM THE NASOPHARYNX OF YOUNG CHILDREN IN NEPAL

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Background and aims: Although rates of pneumococcal carriage and disease are highest in developing countries, the pneumococcal molecular epidemiology within these regions is poorly understood. Nasopharyngeal isolates from urban (Kathmandu) and rural (Okhaldhunga) sites were genotyped by multilocus sequence typing (MLST). The main aims were to characterise the overall population structure and identify major genotypic differences between locations.

Methods: 599 pneumococcal isolates, 299 from Kathmandu and 300 from Okhaldhunga, were recovered from healthy children < 2 yrs of age and genotyped. Alleles and sequence types (STs) were assigned; 576 isolates with complete STs were analysed. goeBURST was used to define clonal complexes (CCs).

Results: 302 unique STs were detected; 187 STs were found in Kathmandu and 160 in Okhaldhunga. 229 STs were newly recognised and described 330 isolates (57% of the collection). There were 11 major CCs with ≥ 10 isolates (n; predominant serogroup/type(s)): CC63 (28; 14, 15BC); CC4209 (27; 15BC); CC193 (22; 21, 17F); CC6025 (22; 11A); CC5613 (20; 6, 15A); CC7695 (17; 35B, 18); CC4217 (12; 6); CC5080 (12; 23A); CC1439 (12; 34); CC4881 (10, 9V); and CC176 (10; 23F, 19F). Some CCs predominated in Kathmandu (CC193, 5080, 1439) and others in Okhaldhunga (CC6025, 7695, 4881); the rest were roughly equally distributed between locations.

Conclusions: The majority of genotypes in this study were novel and thus provide important information about the molecular epidemiology of carriage pneumococci in Nepal. These data also provide a baseline from which to measure genetic changes after a pneumococcal conjugate vaccine is implemented.

TRENDS OF COMMUNITY-ACQUIRED PNEUMONIA (CAP) AND ASSOCIATED COMPLICATIONS IN CHILDREN DURING THE PERIOD 2004-2011 IN ATHENS, GREECE

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Background: The epidemiology of CAP and associated complications has changed following 7-valent pneumococcal conjugate vaccine (PCV7) extensive uptake. In Greece, PCV7 was introduced in June 2005 and 2 years later vaccination coverage in children < 5 years reached 90%. We aimed to determine pediatric CAP hospitalizations trends during the period 2004-2011.

Methods: An 8-year retrospective cohort study was performed at "Aghia Sofia" Children's Hospital, which serves approximately 50% of the Greek population. Children hospitalized with pneumonia, bronchopneumonia and lower respiratory tract infection were defined as CAP cases. Patients with pleural effusion, empyema, lung abscess, SIRS/sepsis, hemolytic uremic syndrome or acute respiratory failure were defined as complicated CAP cases. Children with co-morbid conditions were excluded. Annual CAP and complicated CAP rates were calculated and compared using test for trends.

Results: During the study period a total of 2504 CAP hospitalizations were identified. Annual CAP rates remained relatively stable ranging from 1.7 to 2.5% and total CAP rates for children aged 0-9 years did not change significantly between 2004-2011; however, there was a statistically significant increase in CAP in children > 9 years ($p=0.027$). Over the study period, a total of 138 (5.5%) complicated CAP cases were identified, 40% in children aged 1-4 years, while there was a continuous and significant increase in complicated CAP hospitalizations ($p=0.023$).

Conclusion: Admission rates for CAP in older children and CAP-associated complications have increased over time despite PCV7 implementation. Potential explanations for our findings include serotype replacement, increased viral outbreaks and increasing antimicrobial resistance.

CHILDREN WITH COMPLICATED PNEUMONIA

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Pneumatocoeles that required surgery: Report of 2 cases.

Pneumatocoeles are thin-walled filled with air cystic lesions that have been recognized as a potential complication of pneumonia. Although, they are usually asymptomatic, they may enlarge and compress the adjacent lung and mediastinum.

The aim of this report is to describe 2 cases of severe pneumonia complicated by pneumatocoeles that required surgical intervention.

Case 1: A one year old girl presented with a 2 day history of pyrexia. Radiological investigation revealed a right sided consolidation with pleural effusion. Pleural fluid culture revealed staphylococcus aureus. Antibiotic treatment and drainage failed and a CT scan on day 21 revealed an enlarging pneumatocoele on the right causing mediastinal shift. The child developed acute respiratory failure; Successful decompression of the pneumatocoele was achieved after initial urgent needle aspiration. Radiologic resolution was complete 2 months post initial presentation.

Case 2: A previously healthy 8 month old boy was admitted to our institution with a tension pneumatocoele following a severe necrotic pneumonia. Blood culture was positive for Pneumococcus type 3F. On auscultation there was dramatically decreased air entry on the left side. CXR and CT revealed hyperinflation, large air cyst causing mediastinal shift to the right. Conservative management was initially attempted, but when oxygen saturation decreased dramatically surgical excision (pneumonectomy) was decided. The patient is now asymptomatic 2 months post discharge

Conclusion: Tension pneumatocoeles, although rare, are a serious complication of pneumonia that may need surgical intervention when the patient is in critical condition.

RISK FACTORS FOR HOSPITALIZATION OF PRETERM INFANTS WITH NON-RSV BRONCHIOLITIS

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Background: Bronchiolitis is the most common cause of rehospitalization in late preterms. Risk factors for non-RSV bronchiolitis have not been identified.

Aim: This study primarily aims to analyze risk factors to hospitalizations caused by non-RSV bronchiolitis in the first year of healthy late preterm infants in the Netherlands.

Methods: A prospective healthy birth cohort study of late preterm infants born at 33-35 weeks of gestational age was conducted. Excluded were infants with congenital abnormalities and/or palivizumab prophylaxis. The presence of 17 risk factors was determined. At age 1, parents were contacted to determine hospitalizations due to an episode of bronchiolitis. Hospitals charts were analysed to determine proven RSV infections and non-RSV bronchiolitis.

Results: 172/2257 (7.6%) parents reported a hospitalization for respiratory complaints. 27/2257 (1.20%) infants were hospitalized for non-RSV bronchiolitis. Univariate analysis indicated male sex, presence of siblings, breastfeeding < 2 months, household crowding, birth in weeks 35-46 and intended day care attendance as risk factors for non-RSV related bronchiolitis. After multivariate logistic regression, male sex [OR: 2.850, 95%CI 1.110-7.091], presence of siblings [OR: 6.861, 95%CI 2.553-18.443], birth in week 35-46 [OR: 2.809, 95%CI 1.261-6.256] and intended day care attendance [OR: 2.553, 95%CI 1.006-6.483] were independently associated with non-RSV bronchiolitis.

Conclusions: This is the first birth cohort study of preterm infants analyzing risk factors of non-RSV bronchiolitis. Although the number of cases was small, remarkable similarities were found between risk factors of RSV and non-RSV bronchiolitis.

DETECTION RATES AND GENOTYPING OF HUMAN METAPNEUMOVIRUS AND HUMAN BOCAVIRUS IN CHILDREN WITH RESPIRATORY TRACT INFECTIONS IN SOUTHERN GREECE

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Background and aims: Our aim was to examine the presence as well as the genetic diversity of the recently identified human metapneumovirus (hMPV) and human bocavirus (hBoV) in children diagnosed with respiratory tract infections (RTI).

Methods: Rhinopharyngeal or throat swabs from 3307 patients aged 0-18 yo, collected over the winter period of the years 2005-2008, were analyzed. Molecular assays, including a conventional PCR specific for the F gene of hMPV and a real-time PCR specific for the NP gene of hBoV, were employed for their detection. Viral strains selected throughout the study period were further amplified using non-conserved regions, including G gene of hMPV and VP1/VP2 gene of hBoV, for genotypic characterization.

Results: HMPV presence was confirmed in 188 (5.7%) samples and hBoV presence in 193 (5.8%) samples. Simultaneous presence of these two viruses was established in 8 (2.1%) of the above positive samples. The majority of positive cases concerned preschool children.

Phylogenetic analysis of a total of 50 viral strains for the two viruses, revealed circulation of hMPV genetic subtype B2, presenting with a nucleotide identity of 92-100% with each other, while hBoV isolates clustered within species 1 with the majority of them belonging to genotype ST2.

Conclusion: In total, hMPV and hBoV contributed to a proportion of up to 11.5% of the total samples examined. HMPV B2 and hBoV ST2 were the predominant viral genotypes circulating within the Greek population, an observation also made by other European countries during the same period including France, Italy and Germany.

HMPV UPPER RESPIRATORY TRACT INFECTION WITH SECONDARY STAPHYLOCOCCUS AUREUS LARYNGOTRACHEITIS AND SEPTIC SHOCK IN A 10 YEAR OLD BOY

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Background and aims: Human metapneumovirus (hMPV) is a newly discovered ubiquitous pathogen causing respiratory tract infection in children and adults. As seroconversion approaches 95% by the age of 5 years, infection at an older age is presumed to be a re-infection, typically presenting with upper respiratory tract symptoms. In this case report we describe a 10 year old boy with hMPV upper respiratory tract infection with subsequent bacterial laryngotracheitis and septic shock.

Methods: A week before admission the boy was seen at the outpatient clinic because of fever cough and sore throat. RT-PCR for respiratory viruses was positive only for hMPV. After a week he was admitted because of acute deterioration with severe upper airway obstruction, hoarseness and high fever (40.2 C). A chest radiograph showed swelling of the subglottic mucosa. Because of progressive respiratory failure he had to be intubated.

Results: At intubation a purulent laryngotracheitis was observed. Subsequently he progressed to fulminant septic shock and was treated with volume resuscitation, high doses of inotropes and antibiotics (clindamycin and flucloxacillin). Cultures of his purulent secretions showed enterotoxin A and B producing *staphylococcus aureus*. He was ventilated for 5 days and extubation was uneventful. He fully recovered over time.

Conclusion: HMPV infection may facilitate secondary *S. aureus* laryngotracheitis and septic shock.

SURVEILLANCE OF INFLUENZA AND OTHER ACUTE RESPIRATORY INFECTIONS IN PAEDIATRIC INTENSIVE CARE UNITS IN BAVARIA, GERMANY

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Background: In Germany, epidemiological data on severe influenza in children are limited (Streng et al. 2011). In a prospective, active surveillance study in paediatric intensive care units (PICUs) we determined the frequency of severe, laboratory-confirmed influenza and other viral acute respiratory infections (ARI) in Bavaria (Germany).

Methods: From October 2010 until July 2011, children >1 month and < 17 years of age admitted to PICUs with ARI were included; naso-pharyngeal secretions were tested by multiplex PCR for ARI-associated viruses.

Results: Out of 184 patients from 22 (73%) PICUs, 124 (67%) were PCR-positive (21 with multiple infections): RSV 46%; rhinovirus 23%; influenza virus 14%; parainfluenzavirus 13%; coronavirus 10%; bocavirus 7%; enterovirus 2%, metapneumovirus 2%, parechovirus 2%, adenovirus 1%. From 16 influenza patients (15xA, 1xB; 44% male, median age 6.1 years, IQR 2.0-11.9), 63% belonged to risk groups with chronic medical conditions; none had been vaccinated. The most frequent complication was viral pneumonia (50%); 4 (25%) were admitted in a life-threatening condition. From 103 patients with other viral ARI (53% male, median age 0.5 years, IQR 0.2-2.7), 58% belonged to risk groups. The most frequent complication was bronchitis (53%); 17 (17%) were admitted in a life-threatening condition; 4 risk-group patients died.

Discussion: In the season 2010/2011, influenza was among the three most frequent viral pathogens leading to paediatric intensive care treatment, with life-threatening conditions in 25% of the patients. Two-third of influenza patients belonged to risk groups with chronic medical conditions, similarly to patients with other viral ARI.

CONSERVATIVE MANAGEMENT OF COMMUNITY ACQUIRED NECROTIZING PNEUMONIA

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Introduction: A significant increase of community acquired necrotizing pneumonia (CA-NP) has been observed during the last two decades. However, large series regarding etiology and management of CA-NP in children are scarce.

Methods: Retrospective observational study of paediatric patients (< 18y) hospitalised with CA-NP from 2001 to 2011. We define NP as lung segment consolidation with tissue necrosis. Exclusion criteria were: nosocomial, aspiration or foreign body pneumonia, immunosuppression, and chronic airway infection.

Results: A total of 62 CA-NP cases (mean age 40 months, 47% males) were included. Diagnose was reached by CTscan (47%), chest X-ray (36%) or chest sonography (17%). Etiology was found in 25/62 (40%) of cases by pleural fluid (56%), blood culture (28%) or both (16%). The most common bacteria identified was *S.pneumoniae* (84%), followed by *S.aureus* (8%) and *S.pyogenes* (8%). Serotyping was performed in 12/21 *S.pneumoniae* isolates, being the most common serotypes 1 (5/12) and 5 (3/12). Mean duration of parenteral therapy was 19 days, being the main antibiotics used meropenem (42%) and cefotaxime/clindamycin (35%). Mean duration of fever after admission was 7 days (0-15 days). Mean total duration of therapy was 37 days. Pleural effusion was present in 85%, requiring drainage 73% of them: 28% by thoracoscopy, 60% by chest tube thoracostomy and 14% by thoracocentesis. None required surgical lung resection.

Conclusions: CA-NP is mainly caused by *S.pneumoniae*. It is frequently accompanied by parapneumonic pleural effusion. Treatment should be conservative with prolonged antibiotic therapy, and drainage of significant associated pleural effusions. Surgical resection should be considered only in refractory cases.

INFANT EXPOSURE TO FUR-BEARING ANIMALS PROTECTS AGAINST HOSPITALIZATION FOR RSV BRONCHIOLITIS IN LATE PRETERM INFANTS WITH ATOPIC PARENTS

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Background: Preterm infants have an increased risk of hospitalization for RSV bronchiolitis. Fur-bearing pets have been reported to protect against childhood asthma, allergic rhinitis and eczema in atopic children. The role of fur-bearing pet exposure during childhood on RSV hospitalization is unclear.

Aim: This study aims to discover risk factors for RSV bronchiolitis. This analysis focuses on whether fur-bearing pets decrease incidence of hospitalization for RSV bronchiolitis in healthy late preterm atopic infants.

Methods: An ongoing prospective healthy birth cohort study was performed in late preterm infants with gestational age of 33-35 weeks. Infants with congenital abnormalities were excluded. At birth, multiple risk factors were determined by a questionnaire including presence of fur-bearing pets at home. After one year, parents were contacted to determine whether their child had been hospitalized for RSV bronchiolitis.

Results: 2257 patients were studied of which 1171(51.8%) had at least one atopic parent. 556 children(47.5%) with atopic parents had fur-bearing animals compared to 497 children(45.8%) without atopic parents. The risk of hospitalization for RSV bronchiolitis in patients with atopic parents with and without fur-bearing animals was respectively 4.5 versus 7.6% (OR:0.57.; 95% CI:0.35 - 0.94; p=0.02). After multiple regression analysis the effect was no longer statistically significant (OR:0.64;95%CI:0.39-1.01;p=0.08). This protective effect of fur-bearing pets was not seen in patients without atopic parents (OR: 1.06;95%CI:0.57-1.99;p=0.85).

Conclusions: This ongoing study shows that exposure to fur-bearing animals has a modest protective effect on the risk of hospitalization for RSV bronchiolitis in healthy late preterm infants with atopic parents.

PNEUMONIA IN CHILDREN: RETROSPECTIVE STUDY

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Background: Pneumonia is an inflammation of the lungs caused mainly by bacteria or viruses. This study evaluates the epidemiological, clinical, radiological findings and laboratory results.

Method: We retrospectively examined the records of children hospitalized at the paediatric department with pneumonia as diagnosis, divided into two 2-years groups (2004-2005, group A and 2009-2010, group B) based on the introduction of PCV7 (2006).

Results: Our sample consisted of 336 children (boys 51,8% and girls 48,2%) with an average age of 4 years (50% of the children ranged from 21 months to 6,5 years). Group A consists of 140 children while B of 196. The majority of cases were recorded in spring time in both groups (35,7%). Symptoms were the following: fever (88%), abdominal or thoracic pain (19,3%) and tachypnea (17,3%). Blood cultures, collected from 155 children, were all negative. ESR and C-reactive protein had median values of 51,50 mm and 3,88 mg/dl respectively. X-ray findings showed pneumonia located on the right lung in 184 cases (54,8%), left lung 112 (33,4%) while 40 (11,9%) were bilateral. The most frequent inflammation concerned the lower lobe in both right (66/184) and left lung (82/112). Pleural effusion was found in 29 children, 19 of which belonged to group B (9,6%) and 10 to group A (7,1%). 42 cases (12,5%) were caused by *Mycoplasma pneumoniae*.

Conclusion: There is no significant change in the incidence of pneumonia in children during our recorded periods. A slight increase in cases with pleural effusion was observed in the post PCV7 years.

SEROPREVALENCE OF ATYPICAL PATHOGENS CAUSING COMMUNITY-ACQUIRED LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN

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Ethiology of atypical pneumonia often remains undetermined with conventional microbiology. The object of this study was to determine the presence of IgG and IgM antibodies against respiratory pathogens in children with atypical CAPs.

This study enrolls 490 sera from patients with CAP (52% male and 48% female, median age 11) in two year period (2009 - 2011). The following assays were performed in all patients: full blood count; conventional bacteriology analyses of respiratory samples; and indirect immunofluorescent assay on sera (IFA), (Pneumslide,E) for simultaneous detection of IgG and IgM antibodies against 9 pathogens: *L.pneumophila* (LP), *Chl.pneumoniae*, *C.burnetii*, *M.pneumoniae* (MP), Respiratory syncytial- (RSV), Adenovirus, Influenza A(IAV), Influenza B(IBV) and Parainfluenza virus.

IFA revealed IgM or IgG positivity against atypical pathogens in 318 sera (65%). The majority of IgM positive sera to a single pathogen LP, IAV, MP and IBV were detected in 40, 29, 23 and 5 cases, respectively, all being IgG negative. Only IgG positive were 38 patients (RSV, IAV and LP). Concomitant IgG and IgM positive were 170 patients (53%). The most frequent combination (28%) was IgG positive to paramyxoviruses and IgM positive to MP or LP. Isolation of *Str. pneumoniae*, *H influenzae* and *M. catarrhalis*, was detected in 32% of IFA positive patients in 42, 29 and 13 cases, respectively.

The selected population revealed relatively high IgM positivity rate to LP and MP, suggesting that regular screening for presence of atypical pathogens, when other microbiology findings are negative, is necessary and highly recommended for appropriate antimicrobial therapy.

EFFECT OF CAESAREAN SECTION ON WHEEZING DISORDERS

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Background: Caesarean-section delivery has been showed associated with the subsequent development of wheezing disorders in childhood.

Objective: To examine the association between caesarean section and development of wheezing disorders in hospitalization children in changchun.

Methods: A retrospective study was explored, all children hospitalized in chuangchun 1 January 2008 to 1 October 2010 were included in this study. Children born mode of delivery was categorized as vaginal (including forceps and ventouse extractions) or caesarean section (elective and emergency). All patients grouped according to disease categories.

Results: Total 8285 patients were included in this study. Of these patients, 1748 were wheezing disorders, 3025 were unwheezing respiratory system diseases, 1065 were cardiovascular system diseases, 1129 were urinary system diseases, 1318 were nervous system disease. Of all the children, 3877 (46.8%) were delivered vaginally and 4408 (53.2%) by caesarean section. The percentage of caesarean section in different diseases were available for 1182 (67.6%) subjects for wheezing disorders; 1525 (50.4%) subjects for unwheezing respiratory system diseases; 503 (47.2%), 579 (51.3%), 668 (50.7%) for cardiovascular system diseases, urinary system diseases, and nervous system disease, respectively. Significantly increased risk of wheezing disorders was seen among children delivered by cesarean section. Findings were similar among children delivered by acute and elective cesarean section. However, cesarean section could not increase the risk of unwheezing respiratory system diseases, cardiovascular system diseases, urinary system diseases, and nervous system disease.

Conclusion: Delivery by caesarean section was associated with the subsequent development of asthma, obliterative bronchiolitis, and bronchiolitis.in later childhood in this population.

VIRAL AND BACTERIAL INTERACTIONS IN THE UPPER RESPIRATORY TRACT OF HEALTHY CHILDREN

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Background and aims: Several virus-induced mechanisms following viral infection in the upper respiratory tract predispose to bacterial overgrowth and invasion. Consequences of viral asymptomatic presence on the bacterial community are, however, scarcely documented. To obtain insight in these interactions, we studied the co-occurrence of respiratory viruses and bacterial carriage by conventional and metagenomic approach.

Methods: Nasopharyngeal microbiota profiles of 200 healthy children at 12 and 24 months were analyzed by conventional culture and GS-FLX-Titanium-Sequencing of the V5-V7 regions of the 16S-rDNA gene. Twenty common respiratory viruses were detected by Real-Time PCR. We performed multivariate regression analyses to determine independent associations between viruses and bacteria.

Results: Respiratory viruses were detected in 77% and 68% of the nasopharyngeal samples in children at 12 and at 24 months, respectively. Rhinoviruses were detected most frequently followed by Enterovirus, WU and Bocavirus. We found that increased abundance of Rhinoviruses coincided with higher carriage rates of *H.influenzae* and *S. pneumoniae* (OR 1.9 and 2.0 respectively). In contrast, increased abundance of *M.catarrhalis* coincided with lower viral abundance (OR 0.381). Network analyses clearly showed associations between several viruses, specific clusters of bacterial OTUs and phenotypic characteristics.

Conclusions: Respiratory viruses are frequently present in the upper respiratory tract of healthy children and are associated with potential pathogenic bacterial carriage and specific bacterial community profiles. These interactions may play a role in pathogenesis of respiratory disease.

CLINICAL FEATURES OF INFLUENZA 2009 - 2011 IN DEPARTMENT OF INFECTIOUS DISEASE IN PRAGUE

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Objective: To describe clinical and epidemiological features of influenza diagnosed patients in the department of infectious diseases in Prague.

Material and methods: 3yrs retrospective study (2009-2011) of children (< 19 years) with confirmed influenza (RT-PCR, Ag, serology). It was collected and evaluated data on demographics, epidemiology, clinics, laboratory variables and outcomes.

Results: A total of 40 cases were included with a median age of 11,5 years old (M=F=20). Most frequent features were fever and cough, rhinitis, cefalea and gastrointestinal features. The most frequent complication was pneumonia in 7, neurological symptoms in 6 cases. There were risk factors of complications in 3 children. Chest X-ray was performed on 20 cases, in 1 case was interstitial infiltrations. Oseltamivir was used in 13 cases. One child of 15 was required ICU. Extrapulmonary complications were found in 18 patients (encephalopathy, gastroenterological complication and myositis). In 2009 majority of influenza was influenza A H1N1 pandemic, in 2010 were found adenoviruses and RSV as a cause of the RTI in children. In the year 2011 we registered pandemic AH1N1 and an increase of influenza B. All cases with complications recovered without sequelae. None of patients died

Conclusion: The profile of patients with pandemic influenza A H1N1 in 2009 was adolescents presenting with respiratory symptoms and fever of a short time with average time of hospitalization. The most frequent complication was the pneumonia and neurological symptoms

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RESPIRATORY SYNCYTIAL VIRUS IN YOUNG CHILDREN HOSPITALIZED WITH PNEUMONIA

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Background: Respiratory syncytial virus (RSV) is the main cause of bronchiolitis in infants and young children. Aim of the present study was to evaluate its importance in children >2 years old hospitalized with pneumonia.

Methods: During May 2003 to May 2004, 101 Greek children >2 years old (2.5-14 years, median 8.25) hospitalized with pneumonia were tested for a probable RSV infection. A serum and a throat swab samples were taken from each child upon admission, while for 75 patients a second serum sample was also available. IgG and IgM antibodies against RSV were determined by ELISA, while throat swab samples were examined by nested RT-PCR. All PCR products were sequenced in order to identify the type of the virus.

Results: RSV IgM antibodies were detected in 21 (20.7%) cases, either in the first or/and in the second serum sample, while RSV genome was detected in 14 throat swab samples. PCR-positive results were obtained up to the 7th day of illness. Among the 14 cases, one was of type B, and all the rest were type A. The median age of the RSV-positive children was 4 years (range 3-13). Although RSV was detected in all seasons, the majority (31%) was detected in winter. Co-infection was detected in 3 cases (two with *Mycoplasma pneumoniae*, one with adenovirus).

Conclusions: RSV is an important respiratory pathogen in young children hospitalized because of pneumonia. Although a co-infection with other viruses or bacteria cannot be excluded, its role remains to be further estimated.

EVALUATION OF RESPIRATORY VIRAL INFECTIONS IN CHILDREN WITH CANCER WHO DEVELOPED FEVER AND NEUTROPENIA

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Background: Respiratory viral infections may cause significant morbidity and mortality in children with cancer. We present a cohort of children with cancer with fever and neutropenia (FN) evaluated for respiratory viral infection.

Methods: All children with cancer with FN admitted to the hospital from October 2010 to December 2011 were prospectively enrolled. Children were evaluated for respiratory infections by performing viral PCR in nasal/nasopharyngeal wash on admission. We also determined cytokine levels in blood. Children with a viral respiratory isolate (group 1) were compared with children without viral isolate (group 2) by analyzing demographics, symptoms, laboratory parameters and outcome.

Results: Twenty four children were enrolled in this study with 10 (41.7%) having a respiratory viral isolate; 80% of them diagnosed by PCR. Two children had a severe infection, both in group 2. There was a significant difference in the percentage of children with any positive cytokine level (14% for group 1 vs 90% for group 2; $p=0.004$) and a trend in the time since cancer diagnosis (144 vs 77 days; $p=0.09$) at presentation. Group 1 had lower CRP at 48 hours (5 vs 10; $p=0.05$) with fewer children with CRP > 10 mg/dl (0% vs 50%; $p=0.019$). There were several significant correlations between cytokines and CRP/procalcitonin, especially with interleukin (IL)-12 and TNF.

Conclusions: In our cohort a high proportion of children with FN had a respiratory viral isolate. This group of children may have less risk for developing a severe infection, especially if IL-12 and TNF are not detected.

ASSOCIATION OF RSV BRONCHIOLITIS WITH THROMBOCYTOSIS

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Introduction and aim: Thrombocytosis has been reported in infants with bronchiolitis and is occasionally of high grade. Aim of the study is to clarify the association of thrombocytosis with RSV bronchiolitis, to correlate thrombocytosis with the severity of health status and its value as a potential marker for RSV infection.

Methods: medical records of 148 infants diagnosed with bronchiolitis were retrieved. Patients were divided in RSV positive or negative. Thrombocytosis was defined as $PLT > 450000 \times 10^9 / L$. The severity of clinical condition was also recorded (Sat $O_2 \leq 95\%$, BR $> 55/min$, limited food intake, use of adjuvant respiratory muscles etc) as well as the need for admission in Intensive care unit, the use of drugs and O_2 and the results of laboratory tests. **Results:** Infants aged between 1-12 months with RSV (+) and (-) infection was 68 and 80 respectively. The distribution of thrombocytosis rate is shown in the table.

RSV +		
PLT		
Age (months)	< 450000	> 450000
1-3	20 (29,4%)	26 (38,2%)
3-12	14 (20,5%)	8 (11,7%)
RSV -		
1-3	16 (20%)	22 (27,5%)
3-12	20 (25%)	22 (27,5%)

[Table 1]

Were recorded two cases of severe thrombocytosis (900000 & $1000000 \times 10^9/L$) in RSV positive infants of 1 and 2 months old respectively. **Conclusions:** no correlation was defined between RSV and thrombocytosis. In the RSV+ group aged 1-3 months, thrombocytosis is more frequently by 8.8% over normal counts but of no statistical significance. Thrombocytosis was not correlated with the severity of clinical condition.

CONTRIBUTION OF RSV BRONCHIOLITIS TO THE RISK OF RECURRENT WHEEZING DURING THE FIRST YEAR OF LIFE IN LATE PRETERM INFANTS

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Background: Although late preterm infants often appear healthy at birth, they more often experience wheezing than healthy term children. The contribution of RSV bronchiolitis to the risk of wheezing in late preterm infants is not known.

Aim: This study aims to determine risk factors for wheezing in the first year in healthy late preterm infants.

Methods: A prospective healthy birth cohort study of late preterm infants born at 33-35 weeks gestational age was conducted. Excluded were infants with congenital abnormalities or palivizumab prophylaxis. At birth a general questionnaire quantifying risk factors was completed by parents. At age 1, parents were contacted to determine the incidence and frequency of wheezing. Recurrent wheezing was arbitrarily defined as 3 or more episodes of wheezing.

Results: 648 of 2257 included children (28.7%) experienced a median of 3 episodes of wheezing during the first year of life. 351 children (15.1%) experienced recurrent wheezing. Univariate analysis pointed out 7 possible predictors for wheezing. After multiple logistic regression, RSV hospitalization (OR 3.8, 95%CI 2.6-5.7) presence of siblings (OR 1.6, 95%CI 1.3-2.1), presence of an atopic family member (OR 1.6, 95%CI 1.2-2.0), male sex (OR 1.7, 95%CI 1.3-2.2), smoking of the mother (OR 1.6, 95%CI 1.2-2.1) and day-care attendance (OR 2.2, 95%CI 1.7-2.9) were shown to be independently associated with recurrent wheeze.

Conclusions: Late preterm infants have increased risk of recurrent wheeze. This study shows that hospitalization for RSV bronchiolitis is the most important determinant of wheezing in the first year of life in late preterm infants.

HIGH BACTERIAL COLONISATION AND DENSITY IN CHILDREN WITH FEVER, RESPIRATORY SYMPTOMS AND RESPIRATORY VIRAL INFECTION

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Background and aims: We have previously shown significant age-independent association between rhinovirus infection and pneumococcal (Sp) colonisation and density in healthy children attending daycare. Respiratory syncytial virus (RSV) and influenza virus (flu) infections may also interact with Sp to promote transmission. We studied a series of children under 6 years of age presenting with fever ($\geq 38^{\circ}\text{C}$ axillary) and respiratory symptoms (cough and/or rhinorrhea).

Methods: We performed PCR for flu and RSV on nasal secretions from 336 children (median age 19 months, range 1-71 months) presenting to the Emergency Service at Coimbra Children's Hospital, Portugal during winter 2010-11. We selected nasal swab samples from 40 who were flu positive, 40 RSV positive, 9 with both (DP) and 20 with neither (although likely to be infected with other viruses) (DN) and performed analysis by semi-quantitative bacterial culture.

Results: Carriage rates and mean density scores among carriers for Sp, *M.catarrhalis* (Mcat) and *H. influenzae* (Hflu) are shown in the table and were higher in all groups than previously seen in healthy children. *S. aureus* and *S. pyogenes* were present in < 10% of cases.

	Double negatives	Influenza A+B	RSV A+B	Double positives
<i>S.pneumoniae</i>	70.0%/3.79	50.0%/4.25	75.0%/4.32	66.6%/5.0
<i>M.catarrhalis</i>	75.0%/4.53	75.0%/4.61	72.5%/4.27	77.8%/4.43
<i>H.influenzae</i>	40.0%/4.1	25.0%/3.62	27.5%/4.2	22.2%/5.0

[Bacterial Carriage/Average Density Score]

Conclusions: These results are consistent with our hypothesis that nasal bacteria, especially Sp, exploit viral respiratory infections to proliferate and transmit.

COMPARISON SAFETY AND EFFICACY OF PHNYLEPHRINE WITH PLACEBO IN TREATMENT OF HOSPITALIZED CHILDREN WITH BRONCHIOLITIS

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Bronchiolitis is the common lower respiratory infection in the first year of life. In this diseases upper respiratory tract was involved that ultimate to nasal congestion, respiratory distress and hypoxia. In this study the efficacy of drop phenylephrine (as a decongestant) in treatment of acute bronchiolitis was assessed.

Material and methods: This is a double blind randomized involving 100 children bronchiolitis that divided into two groups, the first group received 0.1 ml of drop phenylephrin 0.5% in both nostril and the second group received 0.1 ml of drop Nacl 0.9% (placebo) in both nostril. Respiratory rate, heart rate, O2 saturation, dyspenea, retraction and wheezing were assessed before and 30 minutes after intervention.

Results: After intervention, O2 saturation and retraction in the first group were significantly different from the second group. In the first group, O2 saturation and retraction and wheezing were significantly different before and after intervention. In the placebo group there were no significantly different before and after intervention.

Discussion: Use of Phenyiephrin as a tropical decongestant is a inexpensive, available and suitable way in the treatment of mild to moderate bronchiolitis.

RECURRENT WHEEZING ATTACKS (RWA) ARE MORE PREVALENT IN CHILDREN HOSPITALIZED AS INFANTS WITH ACUTE BRONCHIOLITIS(AB)

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Background: The study aimed to assess the prevalence and clinical manifestations of RWA during the first 3 years of life in children hospitalized as infants with AB.

Patients and methods: Included two groups of children aged 3-4 years:

1. Research group - 150 children hospitalized at < 6 months of age with AB, with sputum tested by antigen detection tests and/or PCR for 11 possible pathogens.

2. Control group - 66 age and sex matched children who had not been hospitalized. Data collected by telephone from parents, from ambulatory visit charts, and from **research group** charts included:

1. Pathogen/s detected at hospitalization.
2. RWA prior to 3 years of age: age at onset, number, treatment.

Results: At least one possible pathogen was detected in 95% of children in **the research group**. Overall 89 (58%), and 18 (27%) children in the **research** and the **control** groups respectively had RWA (P= 0.001). Parameters of RWA that significantly different in the **research** and the **control** groups respectively were: age of onset: 9.8 (± 6) and 10.8 (± 3) months (P=0.016), number of attacks: 9.3 (± 8.5), and 4.5 (± 1.8) (P=0.005), number of bronchodilator treatments: 8.9 (± 8.2), and 4.4 (± 1.8) (P=0.006), and number of systemic steroids treatments: 5 (± 7.6), and 1.3 (± 1.6).

By multivariate analysis only hospitalization with AB was a risk factor for RWA (OR 2.73, 95% CI - 1.48-5.14, P= 0.001).

Conclusions: Hospitalization at < 6 months with AB is, by it self, a significant risk factor for early, frequent and more severe RWA.

HYPERTONIC SALINE NEBULIZATION IN ACUTE BRONCHIOLITIS: HIGHER CONCENTRATION OR HIGHER FREQUENCY?**B.S. Sharma**¹, M.K. Gupta², S.P. Rafik³¹*Pediatrics, SPMCHI, SMS Medical College,* ²*Pediatrics, Mahatma Gandhi Medical College,* ³*Pediatrics, SMS Medical College, Jaipur, India***Objective:** To compare the improvement in clinical severity scores and length of hospital stay among children with bronchiolitis nebulized with 3% hypertonic saline (HS) and 0.9% saline (NS).**Design, material and methods:** Randomized, double-blind, controlled trial. 250 hospitalized infants & children aged 1 to 24 months with acute bronchiolitis were assigned to receive either 4 ml of nebulized HS or NS every 4 hourly, six treatments daily along with nebulized salbutamol 2.5 mg in each group till the patient was ready for discharge.**Results:** Two study groups were similar in baseline characteristics. Mean age was 4.93 ± 4.31 months in HS group and 4.18 ± 4.24 months in NS group, male (76.2%) outnumbered females and majority (79%) of patients were below 6 months of age. Mean duration of symptoms at enrollment was 3.6 ± 1.87 days in HS group and 3.8 ± 1.34 days in NS group. Baseline O₂ saturation % was 93.43 ± 2.77 in HS group and 94.23 ± 2.45 in NS group. Base line median clinical severity score was 6 in both groups. Clinical severity scores monitored 12 hourly till discharge (132 hours) did not show statistically significant differences in NS group and HS group. Mean length of hospital stay was 63.93 ± 22.43 hours in HS group and 63.51 ± 21.27 hours in NS group ($P=0.879$). No adverse events were reported by the parents, caregivers or treating medical attendants in both groups.**Conclusion:** Nebulized 3 % hypertonic saline is not superior to 0.9% saline in children with acute bronchiolitis.

ACUTE RHINOSINUSITIS COMPLICATED: 10 YEARS STUDY IN AN INFECTIOUS DISEASE UNIT OF A PEDIATRIC DEPARTMENT

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Objectives: To evaluate the clinical presentations, management and the outcome of the children admitted to a tertiary hospital for complicated rhinosinusitis.

Methods: A retrospective study of all children hospitalized between 2001 and 2010 with complicated rhinosinusitis was performed.

The age, symptoms, imaging studies, diagnosis, treatment and outcome were evaluated.

Results: Thirty-two children, 2-15 years old, mean age 7,5 years, were identified. The most common complication has been preseptal cellulitis (62%), followed by postseptal cellulitis (13%), subperiosteal abscess (13%) and orbital abscess (3%). Only 3 intracranial complications were observed (9%) (two epidural abscess and one meningitis).

At the time of admission, these children had an average 5 days history of symptoms, being orbital swelling (86,7%) and fever (66,7%) the most frequently observed, followed by rhinorrhea (53,3%) and cough (40,6%). Half of them received oral treatment (amoxicillin-clavulanic acid) prior to admission. Imaging studies (TC or MRI) were performed in all the children admitted, the most frequent choice being TC. Maxillary and etmoid sinuses were the most involved (79,3% and 61,9% respectively). Intracranial complications were linked to frontal sinusitis. All the children received only medical treatment (cefotaxime or cefotaxime+vancomycin) and had a favorable evolution with no sequels.

Conclusions: Rhinosinusitis in children is a common problem with potentially severe complications. Imaging studies are essential for diagnosis but must be guided by clinical findings. The pediatric sinus anatomy and development should be taken under consideration for an early diagnosis of the complications.

STREPTOCOCCUS PNEUMONIAE AND NON-TYPABLE HAEMOPHILUS INFLUENZAE CAUSING BACTERIAL BRONCHITIS IN CHILDREN AND THE IMPACT OF VACCINATION ON ORGANISM SEROTYPES

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Background: Longstanding infection of the conducting airways is an important cause of chronic cough in childhood. The most common organisms responsible for this disease are Streptococcus pneumoniae (SP) and non-typable Haemophilus influenzae (NTHi) yet no studies have addressed their typing. The UK and Greece introduced vaccination with the pneumococcal conjugate vaccine, PCV-7, in 2006 with the UK adopting the universal immunization of those under 2 whilst in Greece the uptake is lower.

Methods: A retrospective review was independently undertaken in Sheffield, UK, and Athens, Greece, looking at organism serotypes isolated from the bronchoalveolar lavage samples from children being investigated for chronic cough.

Results: In the Greek data, SP was positively correlated with recurrent pneumonia (OR 4.11, 95% CI 1.05-16.10, p=0.042) and of those in whom SP was isolated, only 2 (11.1%) had been vaccinated with PCV-7 whilst in those who were negative, 34% (n=47, p< 0.01) had been vaccinated. In the UK only 1 of the 18 SP samples were covered by PCV-7 compared to 9 of 18 in Greece. All were from unimmunised children.

Conclusion: The data suggests that both vaccine and non-vaccine SP serotypes play a role in persistent bacterial bronchitis and that while vaccination may protect against colonisation with more virulent strains capable of causing invasive disease, serotype replacement appears to occur with less virulent strains being identified in the majority of children. Different NTHi strains were identified suggesting that there is no specific strain or related strains responsible for this condition.

COLONIZATION OF ORAL CAVITY AND TRACHEAL TUBE IN VENTILATED CHILDREN WITH AND WITHOUT VENTILATOR ASSOCIATED PNEUMONIA IN ALI-ASGHAR CHILDREN HOSPITAL, TEHRAN, IRAN

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Background: Microaspiration of tracheal tube colonized organisms may cause VAP . Concerning lack of information about common strains in our referral center we tried to evaluate PICU patients with and without VAP.

Methods and materials: All children 1 mo to 15 years old who were ventilated in PICU of Aliasghar children hospital, were evaluated in this cohort study. Patients were divided in two groups , with VAP and without it. Patients with initial radiography with diagnosis of pneumonia and reintubation were excluded. Tracheal tube aspiration samples were examined for cultures, smear and antibiogram . For each case,samples were taken in first 48 hours of hospitalization ; the second and third ones were taken between 48 hours to 7 days and after 7 days of ventilation and when VAP was diagnosed.

Results: From the total of 63 patients,26 had VAP. 57.1% were male. Mean age was 22.32 ± 37.844 months. There was no statistical difference between two groups in terms of previous hospitalization, position change, chest physiotherapy, nasogastric tube, reintubation, head elevation , antacid usage, immunosuppressive drugs and length of admission before intubation,but there was significant difference in terms of duration of intubation ($p=0.001$) between patients with and without VAP in first and second cultures' result but not for third culture ($p=0.007$, $p=0.009$, $p=0.541$) .The most common microorganism in all of the cultures was *Pseudomonas* spp.

Conclusion: Common colonizing organism for all ventilated kids was *Pseudomonas* spp,just duration of assisted ventilation was a risk factor for VAP in our study.

PERTUSSIS AS A CHILDHOOD ILLNESS IN IRAN

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Background and aims: Whooping cough (pertussis) caused by *Bordetella pertussis* is a hazardous respiratory illness mostly among infants. Despite decreasing the incidence of this disease by extensive vaccination around the world, pertussis has been re-emerged especially in those under 5 months old and also over 10 years over the last decade. The aim of this research was phenotypic and molecular detection of *B. pertussis* strains in clinical samples isolated from patients in Iran.

Methods: Totally 779 respiratory tract specimens were used for both culture and real-time PCR assay based on IS481 and BP283 targets to rapid detection of *B. pertussis* in the samples.

Results: Among all specimens collected, 11 specimens (1.4%) were culture positive and 122 (15.6%) and 100 (12.8%) specimens were diagnosed as infected by *B. pertussis* using IS481 and BP283 primers, respectively. Nine, two and one isolates of culture positive specimens were from patients ≤ 2 years of age, $2 < \text{age} \leq 10$ years and > 10 years of age, respectively. From PCR positive specimens, 79 cases (89%) were isolated from patients 2 years of age or younger.

Conclusions: Although *B. pertussis* causes pertussis in adults and adolescent in some of the countries, this illness has still been seen significantly among children younger than 2 years of age in Iran. Vaccination has a significant effect on the rate of pertussis obtained from real-time PCR assay according to our results. Our data showed that only 10 cases of PCR positive specimens were from vaccinated adults.

SEVERE ARDS IN TWO CHILDREN WITH RESPIRATORY-SYNCYTIAL-VIRUS (RSV) AND INFLUENZA A-H1N1-COINFECTION

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Introduction: Acute viral respiratory tract infections (RTI) are a leading cause of illness and mortality among young children. Respiratory syncytial virus (RSV) is the most common cause of RTI. In 2009 a pandemic due to a novel swine-origin influenza A-H1N1 strain has been characterized by widespread illness in young children.

Case presentation: We report two cases of RSV and Influenza A-H1N1 induced severe acute respiratory distress syndrom (ARDS). The first child was a 2-year-old boy with suspected congenital disorder of glycosylation (CDG) Typ IIb, who was hospitalized for pneumonia. The second case refers to a 3 ½ - year-old girl with a previous medical history of pneumonia, who was admitted to our hospital after an episode of generalized convulsion and consequent aspiration. Both cases needed prolonged mechanical ventilation due the development of severe ARDS. In both cases RSV and Influenza A-H1N1 were detected by RT-PCR in tracheal aspirate. Interestingly, in the second case human Bocavirus (hBoV) has been additionally detected. The boy died after 7 weeks because of a cardiovascular failure and the girl was dismissed from the Hospital after 6 weeks.

Discussion: Several studies have directly compared the clinical course of children with RSV and Influenza infection, but RSV and Influenza A-H1N1 co-infection have not been reported before. Co-infection with these two viruses seems to be associated with a severe clinical course and outcome.

ACUTE RESPIRATORY FAILURE AFTER PNEUMONIA WITH BOCAVIRUS**A. Beyersdorff**¹, S. Armbrust¹, K. Schulz², R. Bruns¹¹*Department of Paediatrics University Hospital, ²Institute of Medical Microbiology University Hospital, Greifswald, Germany***Introduction:** Bocavirus is a Parvovirus and has been detected 2005 in association with respiratory symptoms in children mostly in milder forms. Serious cases have been reported.**Case report:** 18 month old boy, father German, mother Chinese, living in Germany, but have been to China. Nothing special in history or family.

Since 3 days cough with worsening wheezing, tachydyspnoea, temperature 38.5°C. Treatment at peripheral hospital with cefuroxime i.v., nasal oxygen application, prednisolone, bronchospasmin (reproterol) and chloral hydrate. Increasing airway obstruction, tachycardia, coetaneous emphysema, admission at our PICU.

X-ray/ CT: Pneumothorax left, atelectasis left side, partial collapse right, pneumomediastinum, emphysema, serious air trapping right side with shift of the mediastinum to the left.

At the following drainage of pneumothorax, but increase of air trapping and atelectasis. Pneumonian infiltrates medial both sides. Intubation and mechanical ventilation at respiratory failure. Antibiotic treatment with ampicillin/sulbactam and gentamicin. Inhalation with sultanol, atrovent, epinephrine, initially prednisolone i.v.. Fluid balance i.v., at fluid retention furosemide.

Extubation after 3 days, oxygen dependence for further 3 days.

Microbiology findings: Bocavirus PCR positive. Exclusion of other causative organisms including TB.

Laboratory findings: Mild leucocytosis, CrP at maximum 22 mg/l.

Conclusion: Bilateral pneumonia with pneumothorax left side, serious airway obstruction with air trapping and following respiratory failure with need for mechanical ventilation. Short previous course of illness, low inflammation signs in serum. Detection of Bocavirus as causing pathogen agent. Serious illnesses are described after infection with Bocavirus, especially in children as well as Bocavirus is endemic in China.

CARRIAGE OF THE ALLELE-G AT POSITION -1082 OF THE IL-10 PROMOTER PROTECTS CHILDREN FROM POST-BRONCHIOLITIS ASTHMA

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Acute bronchiolitis is a common cause for hospitalization among infants and even up to 40% of hospitalized post-bronchiolitis patients have symptoms of asthma later in childhood. The individual variation between genetic factors and immune responses to viral infections have been suggested as potential asthma driven factors. IL-10 is an anti-inflammatory cytokine, and the IL-10 promoter polymorphism has been connected to asthma and atopic dermatitis. Previously, from this same cohort, we showed that those who were non-carriers of allele-G of IL-10 were in greater risk for rhinovirus infection, and possibly asthma, in early life. In this study we evaluated the associations between preschool asthma and polymorphism of IL-10-1082 G/A, IL-18-137 G/ C, TLR4-896 A/G and IFNG-874 T/A after bronchiolitis in early infancy.

In all, 205 infants were hospitalized for bronchiolitis at < 6 months of age. Asthma and allergy were studied from a total of 166 children at 6.4 years (mean). 135(81.3%) frozen whole blood samples were available for cytokine genotyping.

Asthma was present in 17 (12.6%), atopic eczema in 47(34.8%) and allergic rhinitis in 36(26.7%) patients. Those who were homozygous for allele-G at position-1082 of IL-10 were rarely asthmatics, only 1/32(3.1%) had asthma at 5-7 years of age ($p=0.04$). 10% of those with allele-G vs. 21% of non-G allele carriers of IL-10 had asthma at preschool age.

The results of this study suggest that carriage of the allele-G at position -1082 of the IL-10 promoter protects children from post-bronchiolitis asthma.

NEONATAL VENTILATOR-ASSOCIATED PNEUMONIA (NVAP): A SURVEY OF CLINICAL PRACTICES**G. Suresh¹, M. Klompas²***¹Pediatrics, Dartmouth-Hitchcock Medical Center, Lebanon, NH, ²Infectious Diseases, Brigham and Women's Hospital, Boston, MA, USA*

Although the evidence on NVAP is scant, influenced by campaigns to prevent VAP in adults, many neonatal units are treating, and trying to prevent NVAP. To identify practice patterns related to NVAP, we surveyed attendees of a large international neonatology meeting (Hot Topics in Neonatology). Of the 1344 meeting registrants, 330(24%) responded. Of these, 66% were from teaching hospitals; and 86% were neonatologists. Numbers in parentheses are percentages of respondents. Criteria most frequently considered as very or critically important for NVAP diagnosis were: new opacity on chest radiograph(76%), worsening gas exchange(72%), purulent or changed endotracheal secretions(71%), fever or temperature instability(56%), and increased endotracheal secretions(55%). Tracheal aspirates(TA) were used by 74% of the respondents to diagnose NVAP, and by 16% for surveillance in asymptomatic babies. One or more features on the TA considered indicative of VAP were: high quantitative culture(66%), high cell count(54%), high neutrophil percentage(49%), neutrophils with intracellular bacteria(54%), positive Gram stain(23%), any culture positivity(15%). Antibiotics were used against all organisms identified on TA by 15%, and only those judged to be pathogens by 85%. Organisms absent in the TA were also targeted by 27%. Antibiotics were given for a fixed duration by 43%(range 3-14 days). Measures for prevention of adult VAP were used for NVAP as well: daily assessment for extubation(94%), oral care(62%), elevation of the head of the bed(60%), avoidance of gastric acid inhibitors(36%). Current imprecise methods to diagnose NVAP may lead to antibiotic overuse. Unproven preventive measures extrapolated from adult practices were commonly used in neonatal units.

IMPACT OF RHINOVIRUSES IN CHILDREN HOSPITALIZED FOR LOWER RESPIRATORY TRACT INFECTION IN BURUNDI, CENTRAL AFRICA

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Background and aims: Circulation of rhinovirus (RV) subtypes in the different countries during the year and their importance in causing lower respiratory tract infections (LRTIs) is not completely defined. This study was planned to evaluate these problems in Burundi, a country sited in central Africa, a continent for which no data are available.

Methods: A nasopharyngeal swab was performed in all the children aged < 5 years hospitalized in Kiremba hospital during a whole year (from 01/09/2010 to 31/08/2011) for LRTI. Real time polymerase chain reaction for the identification of RV and on positive cases sequencing for detection of subtypes were performed. Results were stratified according to month of sample collection, RV subtype, age and type of LRTI.

Results: RV was detected year-round in 165 of 388 enrolled children (42.5%) with a peak period in November and December (prevalence of positivity, >60%). Pneumonia was the commonest diagnosed disease (53.9%), followed by bronchitis (36.9%) and wheezing (9.1%). Subtype A was identified in 44.2%, B in 9.7% and C in 27.9% of the cases. Distribution of subtypes was not age-related. Subtype C was the one most frequently identified in children with pneumonia.

Conclusions: This study confirms that RV is commonly associated with LRTIs of young children including pneumonia and all the known subtypes seem to play a role, although subtype C seems to be associated with the most severe disease. Contrarily to what has been described in countries with temperate climate, in Burundi peak period of RV infection is late fall.

INCREASED RISK OF PHYSICIAN-DIAGNOSED WHEEZE AT AGE THREE AFTER RHINOVIRUS-ASSOCIATED WHEEZING DURING INFANCY: A LOW-RISK BIRTH COHORT STUDY

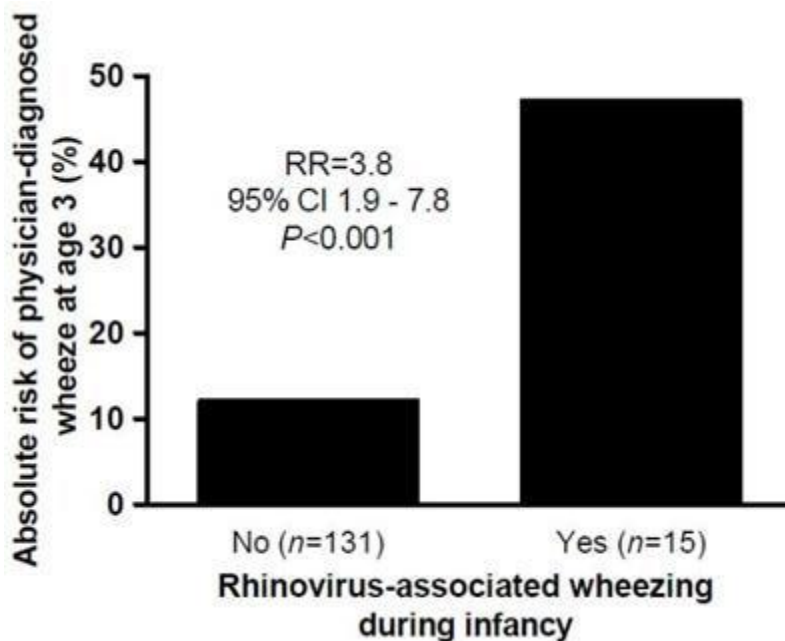
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Introduction: The prevalence of asthma and recurrent wheezing after rhinovirus respiratory tract infection in low-risk children is unknown. In high-risk children, rhinovirus respiratory tract infection during infancy is associated with an increased risk of recurrent wheeze at age three. We aimed to determine the effect of rhinovirus wheezing illness during infancy on third year physician-diagnosed wheezing in children without a background of parental asthma.

Methods: In a prospective birth cohort study, 178 healthy term children, born in two large hospitals in The Netherlands, were followed throughout the first three years of life. Children were considered to be *low risk*, if neither parent had a doctor's diagnosis of asthma. Rhinovirus-associated wheezing illness was defined as the simultaneous presence of parent-reported wheeze (based on daily logs) and molecular detection of rhinovirus in nose-throat samples collected during respiratory episodes in the first year of life. Physician-diagnosed wheeze was defined as a doctor's diagnosis of wheeze or the use of inhaled asthma medications in the third year of life.

Results: Of 146 low-risk children, 10% (n=15) developed rhinovirus wheezing illness in the first year of life. Third-year physician-diagnosed wheeze was detected in 47% of children with rhinovirus wheezing illness (7 of 15) as compared to 12% of children without rhinovirus wheezing illness (16 of 131) (risk ratio 3.8, 95% CI 1.9-7.8, $P < .001$). Adjustment for potential confounders yielded similar results.



[Absolute risk of physician-diagnosed wheeze at age]

Conclusions: Rhinovirus wheezing illness during infancy is associated with an increased risk of physician-diagnosed wheeze at age three in low-risk children without parental asthma.

SORE THROAT IN CHILDREN AT THE EMERGENCY DEPARTMENT: BEST MEDICAL PRACTICE?**I. Roggen**¹, G. van Berlaer¹, F. Gordts², I. Hubloue¹¹*Emergency and Disaster Medicine, ²ENT, UZ Brussel, Vrije Universiteit Brussel, Jette, Belgium*

Background: Even though Belgian antibiotic (AB) policy guidelines clearly state the uselessness of AB in sore throat, in otherwise healthy individuals, 35% of all children in our Pediatric Emergency Department (ED) receive a prescription for AB.

Objective: We wanted to discover if there were specific factors influencing our physician's AB prescription rate.

Methods: Using a retrospective cohort study design, we analyzed all medical records of children below the age of 16, who were diagnosed in 2009 and 2010 with sore throat. Children with underlying chronic diseases and those already on AB treatment were excluded. Out of a total 33,152 PED visits, 1345 met our criteria.

Results: Children below the age of 5 received more easily an AB prescription (38 vs. 28%; $p=0.0006$), while the incidence of β Hemolytic Group A Streptococcus (GAS) is lower in this group (23 vs. 41%; $p=0.0002$). Children of Caucasian origin received less frequent AB compared to children from other origins (32 vs. 37%; $p=0.03$). More AB were prescribed during nightshifts (39 vs. 32%; $p=0.008$). Physicians with a Belgian degree prescribed less frequent AB compared to doctors who studied in The Netherlands (23% vs. 46%; $p < 0.0001$).

Conclusion: Assessing at adherence to AB guidelines in children with sore throat, we find several "practical" factors, rather than clinical arguments, to have an influence on the AB prescription rate.

CENTOR CRITERIA IN CHILDREN: FOR WHAT IT'S WORTH

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Background: Centor criteria (fever > 38.5°C, swollen tender anterior cervical lymph nodes, tonsillar exudate and absence of cough) are often used to assess the probability of β Hemolytic Group A Streptococcus (GAS) as the origin of sore throat, for both adults and children. Yet Centor et al. developed these criteria only to be used in adults¹.

Objective: To evaluate the correlation between Centor criteria and presence of GAS in children with sore throat admitted to our Pediatric Emergency Department (PED).

Methods: Using a retrospective cohort study design, we analyzed all medical records of children below the age of 16, who were diagnosed in 2009 and 2010 with the diagnosis of sore throat; who received a throat swab and had all four Centor criteria scored. Out of a total 33,152 PED visits, 423 met our criteria.

Results:

Number of criteria present	none	1	2	3	4
Number of patients	8	49	139	161	66
Probability according to Centor	2.5%	6.5%	15%	32%	56%
Our results	50%	31%	26%	27%	23%

[Results]

Conclusion: Our results confirm the uselessness of Centor criteria as a predicting factor for finding GAS in a throat swab culture in children below the age of 16 years old.

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ASSOCIATION OF RESPIRATORY SYNCYTIAL VIRUS WITH LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN

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Background and aims: Molecular methods are more sensitive for diagnosis of the main pathogens that cause respiratory tract infections (RTIs) compared with conventional methods. Viral RTIs are the predominant respiratory infections in children, and the leading cause of hospitalization of children, particularly infants younger than one year.

Methods: This study used a multiplex PCR assay to detect 12 different respiratory pathogens including influenza A, influenza B, parainfluenza (PIV) types 1, 2 and 3, respiratory syncytial virus (RSV) groups A and B, adenovirus, human rhinovirus, human metapneumovirus (MPV) and human coronavirus OC43/HKU1 and 229E/NL63 from respiratory specimens of 62 children treated for possible acute viral RTI.

Results: Viruses were identified in 54 (87.1%) of the children. RSV was detected in 29 (46.8%), PIV in 25 (40.3%), rhinovirus in 17 (27.4%), MPV in nine (14.5%), adenovirus in six (9.7%) and coronaviruses in three (4.8%) of the patients. Coinfections with two or more viruses were observed in 27 (50%) patients. Eighteen patients (60%) infected with RSV had a coinfection, while six out of nine patients tested positive for MPV had a coinfection. RSV was significantly associated with lower respiratory tract infections ($p < 0.01$). Presence of a multiple infection was not significantly associated with severity or localization of the infection ($p > 0.05$).

Conclusions: Multiplex PCR assay is a new and sensitive method for rapid microbiological diagnosis. Further investigations are needed to broaden our understanding of the significance of multiple viral infections and RSV coinfection in pathogenesis of lower RTI in children.

ETIOLOGY AND EPIDEMIOLOGY OF VIRAL RESPIRATORY TRACT INFECTIONS IN HOSPITALIZED CHILDREN USING A MICROARRAY PLATFORM

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Background and aims: To study the etiology of respiratory viral infections (RVI) in hospitalized children using a microarray platform.

Methods: Rhinopharyngeal washes were taken from children (1 month-14 years) who hospitalized for upper (URTI) or lower respiratory tract infections (LRTI), from 6/2010 - 6/2011. A microarrays assay (CLART[®] Pneumovir kit - GENOMICA, Spain), that detects 17 different viruses or subtypes simultaneously, was performed to diagnose the etiology of RVI.

Results: Samples were taken from 312 children and 203(65%) were positive for viral infections. Single viral infection was detected more often in children with pneumonia ($P=0.042$) and viral coinfections (VC) in children with bronchiolitis ($P=0.038$). The most prevalent viruses among children with positive samples (203) were Respiratory Syncytial Virus (RSV) in 130(64%) children, Parainfluenza viruses (PIV) in 52(25.6%), Rhinoviruses (RV) in 37(18.2%), Influenza viruses (INFL) in 31 (15.2%), Adenoviruses (AD) in 17(8.3%), Human Bocavirus (HBoV) in 16(7.8%) and Human Metapneumovirus (HMPV) in 7(3.4%). VC were found in 97 children (31%). Most common coinfections were RSV- RSVB in 29 (29.8%), RSV- RV in 13 (13.4%), PIV-INFL-RSV in 9 (9.2%), PIV- RV in 6(6%) and RSV- INFL in 6 (6%). There was a statistically significant association of VC with severity index of asthma ($P=0.036$) but not with severity of pneumonia or bronchiolitis.

Conclusions: Viral coinfections and recently discovered viruses are involved in a significant percentage of acute RVI. Microarray assays could be useful for simultaneous detection of common viral respiratory pathogens.

ACUTE BRONCHIOLITIS (AB) AND RESPIRATORY FAILURE (RF) AT PEDIATRIC INTENSIVE CARE UNIT (PICU): EPIDEMIOLOGICAL, CLINICAL, MICROBIOLOGICAL AND THERAPEUTIC CHARACTERISTICS

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Background: 1-3% of patients with AB may require hospitalization and 10-15% of them need treatment in PICU.

Study objectives: To characterize the epidemiological, clinical, laboratory and therapeutic spectrum of AB in infants with AB and RF.

Patients and methods: All patients admitted during 2006-2010 to NICU with AB and RF were enrolled. Virological diagnosis was done by RT-PCR.

Results: 3,194 AB patients were hospitalized and 129 (4.0%) were admitted to PICU (100, 77.5%, < 5 months of age and 51, 39.5%, pretermatures). Lowest numbers of AB and of RSV(+) cases were recorded during the 2009-H1N1 outbreak. The percentage of RSV(+)-AB cases decreased during study years ($P=0.035$). Fifty-eight (45%), 59 (45%) and 60 (46.5%) patients were hypoxemic on admission, had apneas and received ventilatory support, respectively. RSV was identified in 88 (68.2%) patients (83, 64%, as single pathogen and in 5 additional cases as mixed infection with *Bordetella pertussis*-3 cases, adenovirus-1 and H1N1-1). Human metapneumovirus, bocavirus, rhinoviruses or coronaviruses were not isolated. Complications were recorded in 28/129 (21.7%) cases; the most common were acute otitis media (11 cases, 8.5%), septicemia and UTI (6 each, 4.7% each). Pulmonary infiltrates were found in 62 (48.1%) patients (55 alveolar, 88.7%). No differences were recorded between RSV(+) and RSV(-) patients clinical and laboratory characteristics. Mortality was 3/129 (2.3%).

Conclusions:

- 1) RSV was the dominant causative organism of AB;
- 2) Co-infection between RSV and other viruses was rare;
- 3) High rates of alveolar pneumonia were recorded, suggesting frequent bacterial coinfection.

THE EFFECT OF NEBULIZED XYLOMETAZOLINE 0.1% IN CHILDREN WITH CROUP: A RETROSPECTIVE COHORT STUDY

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Background: Croup is a frequent respiratory tract infection in children. Treatment of first choice is a corticosteroid, which needs time to have its effect. For fast relieve of symptoms we present nebulized xylometazoline 0.1% as an alternative for epinephrine. Xylometazoline has a similar alpha-adrenergic effect, but at lower costs and a longer duration. We use xylometazoline as a standard first therapy, additional to an oral, intramuscular or nebulized steroid. To our knowledge there are no studies concerning the use of xylometazoline in croup. In this study is we describe the results of xylometazoline treatment in croup in our hospital.

Methods: We performed a retrospective cohort study of all children (< 18 years) diagnosed with croup in a general teaching hospital in a 10 year period (2000-2010). We collected clinical data such as symptoms, modified Westley croup score, secondary diagnoses, treatment and hospital admission.

Results: We included 228 cases (208 children) of croup, with a mean age of 2.7 years. Xylometazoline was nebulized in 210 cases (92%). Of 92 cases with a known croup score, the mean score before treatment was 4.64 and after treatment 2.35 ($p < 0.01$). Seventy cases had another diagnosis besides croup. In 78.5 % (124 / 158) of the presentations only with croup, the child was admitted to the hospital less than 24 hours. These data are comparable with the literature. Side-effects were not reported.

Conclusion: Our results suggest the additional use of nebulized xylometazoline in croup has advantages above systemic or local steroid as only therapy.

INVASIVE GROUP A STREPTOCOCCAL PNEUMONIA WITH EMPYEMA IN CHILDREN

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Invasive Group A streptococcal (iGAS) disease encompasses syndromes where Group A *streptococci* (GAS) are isolated from a normally sterile site. Mortality is approximately 20% - higher in patients presenting in shock(1). Surveillance data confirms increased incidence in the UK (2). Pneumonia accounts for 10-20% of paediatric iGAS and is associated with significant morbidity (3-5).

We present 4 cases (aged 1, 3, 5 and 7 years) of severe GAS pneumonia with empyema, who universally required PICU admission for circulatory and respiratory compromise.. All were treated with high dose cephalosporins, and remained febrile for 48 hours following initiation of antibiotics and insertion of chest drains. Blood and pleural fluid grew GAS within 48 hours.

All children required inotropic support and ventilation. In all, effusions re-accumulated after drainage and required multiple drains, readmission to PICU and re-ventilation despite continued appropriate high-dose antibiotic therapy and successful drainage following urokinase infusion. However, none required thoracotomy or decortication.

Three made a full recovery after 7-14 days of intravenous therapy, followed by 2-4 weeks oral treatment. One developed endocarditis and cerebral septic emboli with neurological sequelae.

All isolates were fully susceptible, and identified as M/emm1 type with expression of exotoxins SPE A and B. This phenotype is associated with more severe disease (6) and accounts for the majority of iGAS in the UK. SPE toxin expression is associated with toxic shock (7).

These cases highlight that GAS pneumonia with empyema typically has a protracted course and re-accumulation of effusion is common. Toxic-shock is a frequent feature at presentation (8).

THE INTER-OBSERVER VARIATION OF CHEST RADIOGRAPH READING IN OUTPATIENT CHILDREN WITH ACUTE LOWER RESPIRATORY TRACT INFECTION

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Background and aims: This study assessed the inter-observer agreement in interpretation of several radiographic features in the chest radiographs (CXR) of 803 outpatient children aged 2-59 months with non-severe acute lower respiratory tract infection.

Methods: Inclusion criteria comprised: report of respiratory complaints, detection of lower respiratory findings and presence of infiltrate on the CXR taken on admission and read by the pediatrician on duty. Data on demographic and clinical findings on admission were collected. CXR was later read by 2 independent pediatric radiologists blinded to clinical information and pneumonia was finally diagnosed if there was agreement on the presence of pulmonary infiltrate or pleural effusion. The kappa index (k) of agreement was calculated.

Results: The radiologists agreed that 774(96.4%) and 3(0.4%) CXR were appropriate or inappropriate for reading ($k=0.173$; 95%CI:-0.011-0.356) and that 222(28.7%) and 459(59.3%) CXR presented or not pneumonia ($k=0.735$; 95%CI:0.685-0.785). The overall agreement was 78.7% (normal CXR [n=385,60.9%], pneumonia [n=222,35.1%], other radiological diagnosis [n=22,3.5%], inappropriate for reading [n=3,0.5%]). For the whole study group, the concordance was assessed for consolidation ($k=0.689$, 95%CI:0.619-0.759), alveolar infiltrate ($k=0.578$, 95%CI:0.512-0.644), pleural effusion ($k=0.441$, 95%CI:0.371-0.511), atelectasis ($k=0.369$, 95%CI:0.225-0.514), peribronchial thickening ($k=0.212$, 95%CI:0.117-0.307), hyperinflation ($k=0.207$, 95%CI:0.025-0.388) and interstitial infiltrate ($k=0.173$, 95%CI:0.111-0.235). For the patients without concordant CXR with pneumonia or normal the concordance of other radiological diagnosis was evaluated for atelectasis ($k=0.419$; 95%CI:0.228-0.609), hyperinflation ($k=0.181$; 95%CI:-0.050-0.412) and peribronchial thickening ($k=0.102$; 95%CI:-0.001-0.204).

Conclusions: The kappa index ranged widely in regard to the different radiological findings; it was better for consolidation and worse for interstitial infiltrate.

PANDEMIC INFLUENZA IN MAZOVIAN REGION IN POLAND IN 2009/2010 SEASON - THE SURVEILLANCE OF LABORATORY CONFIRMED CASES

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Objective: Description of epidemiology of laboratory-confirmed pandemic influenza cases in Poland, country where pandemic vaccine was unavailable during 2009/2010 season.

Methods: We prospectively studied influenza cases, reported to sanitary authorities. Each case was examined with questionnaire. The samples were tested for influenza A and B by RT-PCR.

Results: 561 cases of influenza (including 185 children < 14 years) were detected. 484 people were hospitalized, including 73 children < 4 year of age and 69 children 5-14 years old. The most common serious complications were: pneumonia (130 incl. 19 children < 4 y and 17 children 5-14 y), cardiac arrest (12 incl. 1 child < 4 y and 2 in 5-14 y), septic shock (5 adults), circulatory insufficiency (4 incl. 1 child < 4 y), multiorgan failure (3 adults), myocarditis in 2 and arrhythmia (tachycardia in 1 child). 388/484 patients were treated with oseltamivir, 53 patients (incl. 2 children < 4 y and 7, 5-14 y) were mechanically ventilated, 52 patients were given oxygen only. 32 patients died, all with preexisting chronic conditions as diabetes, obesity, hypertonia, asthma, cerebral palsy, nephritic syndrome, cancer, heart disease, solid organ transplantation, arthritis, insult or mental retardation. Influenza was primary reason in 15/32 cases. Only 11/ 561 patients were immunized against seasonal influenza and no influenza complication was observed in this group.

Conclusions: Pandemic influenza is an emerging problem in Poland. Flu vaccinations are neglected even in high risk population. Seasonal vaccination may offer some protection against pandemic influenza.

MYCOPLASMA PNEUMONIAE ACUTE INFECTION AMONG CHILDREN WITH NON-SEVERE PNEUMONIA TREATED WITH AXOMICILLIN

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Background and aims: Childhood pneumonia is frequently attributable to *Mycoplasma pneumoniae* but it is not evident that empirical treatment is necessary. We aimed to assess association between clinical failure and acute *M. pneumoniae* infection in children with non-severe pneumonia receiving amoxicillin.

Methods: Patients aged 2-59 months were prospectively followed-up. The finally diagnosed pneumonia was based on agreed detection of pulmonary infiltrate/pleural effusion by 2 independent radiologists. Amoxicillin (50mg/kg/day) was given. Demographic data and clinical findings on admission, daily evolution and 2-4 weeks after enrollment were collected. Acute and convalescent blood samples were collected. Clinical failure included persistence of fever, difficulty breathing or tachypnea >first 48h of treatment or of cough >first 96h of treatment or sign of severe/very severe disease up to the fifth day of treatment. IgM antibodies to *M. pneumoniae* were searched for to detect acute *M. pneumoniae* infection.

Results: Out of 382 patients studied, 372(97.4%) had concordant radiographic diagnosis which was pneumonia(n=192;52%), normal chest radiograph(n=152;41%) and others(n=28;7%). Overall, IgM against *M. pneumoniae* was detected in 53(14%) and clinical failure occurred in 10(2.6%) cases. No difference was found between children with or without IgM against *M. pneumoniae* when clinical failure rates were compared (3.8%vs.2.6%, $p=0.6$) Acute *M. pneumoniae* infection was significantly more frequent among pneumonia cases in comparison with the others (21%vs.7%, $p< 0.001$). For the 192 radiographically diagnosed pneumonia cases, no difference was identified when children with or without acute *M. pneumoniae* infection were compared (5.3%vs.2.1%, $p=0.3$).

Conclusions: Clinical failures were rare and not associated with acute *M. pneumoniae* infection.

APPLICATION OF NESTED POLYMERASE CHAIN REACTION AND SEROLOGY TO DETECT *CHLAMYDOPHILA PNEUMONIAE* IN PEDIATRIC COMMUNITY-ACQUIRED LOWER RESPIRATORY TRACT INFECTIONS

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Background and aims: Diagnosis of *Chlamyphilas. pneumoniae* in lower respiratory tract infections (LRTIs) is challenging. The detection of antibodies in paired serum samples has been considered the standard laboratory diagnostic method but polymerase chain reaction (PCR) has recently been found to be useful for rapidly detecting this pathogen in respiratory secretions. This study aimed to investigate the role of *C. pneumoniae* in LRTIs in children by serological tests and PCR.

Methods: One hundred children (2 months-12 years) with community acquired LRTIs were investigated for IgM and IgG antibodies to *C. pneumoniae* by enzyme linked immunosorbent assay (ELISA) and PCR to amplify an outer 333 bps and internal 207 regions on the major outer membrane protein(ompA)gene of *C. pneumoniae* applied to nasopharyngeal aspirate(NPA).

Results: Forty two (42%) children were of age group 2-6 months: 31((31%) 7-12 months; 04 (4 %) 13 months to 2 years; 12(12%) 25-60 months and 11(11 %) 5 to than 12 years of age. The radiological features in infected children were: consolidation 29(29%); bronchopneumonia 6(6%); hyperinflation 26(26%); infiltration 7(07%); collapse 02(2%); X-ray 30(30%) within normal limits. Serological evidence of *C pneumoniae* infection was observed in 12(12%) and nested PCR was positive in 2(2%) children. Together PCR and/or ELISA detected *C pneumoniae* in 13(13%) cases.

Conclusion: *C. pneumoniae* has a role in community-acquired LRTIs, even in children aged < 1years. The data suggest that PCR supported by ELISA is effective in the detection of *C pneumoniae* in pediatric LRTIs in better management of *C. pneumoniae* infections.

VITAMIN D DEFICIENCY IS ASSOCIATED WITH AN INCREASED RISK OF RECURRENT ACUTE OTITIS MEDIA WITH REPEATED TYMPANIC MEMBRANE PERFORATION

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Background: Several studies have demonstrated that VD has relevant immunomodulatory effects and that its deficiency can lead to an increased risk of respiratory infections. This study was planned to evaluate whether VD deficiency can be considered an additional risk factor for RAOM.

Methods: Children with a documented history of RAOM were enrolled. 25OHVD3 level was determined on blood sample drawn 28-30 days following the last episode of RAOM. Multiple linear regression analysis was applied to assess the association between VD level and RAOM events during all time of life. Models with event as dependent variable included terms for VD level, number of older siblings, pacifier use, day-care attendance and exposure to passive smoking.

Results: A total of 128 children (mean age, 35.7 ± 19.8 months) were enrolled. VD level was < 20 ng/mL in 39 (30.5%), 20-30 ng/mL in 34 (26.6%) and >30 ng/mL in 55 (42.9%). RAOM was non-significantly inversely associated with VD level both in the unadjusted and in the multivariate model. However, when children with RTMP were analyzed separately, it appeared that RTMP was significantly inversely associated with level of vitamin D in the multivariate model ($\beta = -0.002$, $p=0.03$). Risk of RTMP was associated with a VD level of < 30 ng/mL.

Conclusion: VD deficiency seems to be an independent and additive risk factor for the development of RAOM with RTMP. These data suggest that in children with RAOM and RTMP determination of VD level has to be performed and VD supplementation could be considered.

WHOOPING COUGH IN CHILDREN-5 YEARS CLINICAL AND LABORATORY EXPERIENCE USING REAL TIME (RT) PCR DIAGNOSTICS

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Background and aims: Pertussis is an endemic respiratory tract infection causing significant morbidity and mortality. At this tertiary referral paediatric hospital RT PCR for *Bordetella pertussis*/*Bordetella parapertussis* was introduced 5 years ago. We have analysed clinical and laboratory data from specimens submitted from this period with the aim to recognise trends from data and to communicate learning outcomes.

Methods: Validated RT PCR (IS481) has now replaced culture for diagnosing pertussis. Turnaround times, sensitivity and specificity of diagnosis have significantly improved, with most results being available same working day. We analysed 5 years of laboratory and clinical data, and generated user initiatives as a result of this analysis.

Results: From Jan 2006 - Dec 2011, 692 clinical specimens were tested with an overall positivity rate of 15.6% (108/692). Yearly variance ranged from 11-20%. 94 % of the specimens received were pernasal swabs of which 15% (99/648) were positive. Of the 104 positive patients, 39% were inpatients. Overall 59% (61/104) of the positive patients were under 4 months old and of these 13% (8/61) were admitted to PICU for a mean duration of 11 days with 38% (3/8) mortality, all having required extracorporeal membrane oxygenation (ECMO).

Conclusions: The majority of presenting cases were infants aged ≤ 4 months old, with incomplete vaccination schedules, and 13% required intensive care support. Our in-house diagnostics has extended to other hospitals, laboratories, and GPs. We provide visual aids to enhance specimen collection and public health awareness has heightened via newsletters detailing service availability and optimal specimen collection.

NASOPHARYNGEAL (NP) COLONIZATION WITH PATHOGENIC BACTERIA (PB) IS ASSOCIATED WITH INCREASED DISEASE SEVERITY IN CHILDREN WITH RSV BRONCHIOLITIS

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Background: The impact of NP bacterial colonization on RSV disease has not been characterized. We evaluated the frequency of pathogenic bacteria (PB) colonization in children with RSV bronchiolitis, and determined its association with disease severity.

Methods: Previously healthy children < 2yrs hospitalized with a first episode of RSV bronchiolitis and healthy controls were enrolled. NP bacterial swabs collected within 24h of admission were cultured for: *S. aureus*, *S. pneumoniae*, *M. catarrhalis*, *H. influenzae*, and β -hemolytic *Streptococcus*. Demographic, clinical, laboratory and disease severity parameters were compared between patients who tested positive or negative for PB.

Results: From 12/2010 to 9/2011, 136 children with RSV bronchiolitis (62% males; 2.53 [1.5-4.4] months) and 23 matched controls were enrolled. NP cultures were negative for PB in 43% (59/136) of RSV children and among those 76% had received antibiotics. Patients not treated with antibiotics (69/136; 51%) were colonized more frequently with Gram-negative bacteria (GNB, 43%; 15/35) whereas healthy controls were mostly colonized with Gram-positive bacteria (GPB, 93%; 13/14)($p=0.01$). RSV patients colonized with PB had higher WBCs in NP samples ($p=0.03$), higher blood neutrophil% ($p=0.02$) and lower basal O₂ sats ($p < 0.05$) than those not colonized with PB. Moreover, colonization with GNB, but not GPB, was associated with longer needs for O₂ ($p=0.04$).

Conclusions: Infants with RSV colonized with PB showed a clear trend for increased disease severity, especially those colonized by GNB that required O₂ for longer periods of time. Further studies are needed to elucidate the clinical significance and mechanisms of RSV-bacterial interactions.

A RANDOMIZED CONTROLLED TRIAL OF ZINC AS ADJUVANT THERAPY FOR SEVERE PNEUMONIA IN YOUNG CHILDREN

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Background: Diarrhea and pneumonia are the leading causes of illness and death in children under five years of age. Zinc supplementation is effective for treatment of acute diarrhea and can prevent pneumonia. In this trial, we measured the efficacy of zinc when given to children hospitalized and treated with antibiotics for severe pneumonia.

Methods: We enrolled 610 children 2 to 35 months of age and presenting with severe pneumonia defined by the World Health Organization as cough and/or difficult breathing combined with lower chest indrawing (LCI). All children received standard antibiotic treatment and were randomized to receive zinc (10 mg in 2-11 month-olds and 20 mg in older children) or placebo daily for up to 14 days. The primary outcome was time to cessation of severe pneumonia.

Findings: Zinc recipients recovered marginally faster but this difference was not statistically significant (hazard ratio = 1.10, 95% CI 0.94 to 1.30). Similarly, the risk of treatment failure was slightly but not significantly lower in those who received zinc (risk ratio = 0.88 95% CI 0.71 to 1.10). The proportion of children who vomited after the first dose of zinc was 14%, while 9% of the placebo recipients vomited.

Conclusion: Adjunct treatment with zinc reduced the time to cessation of severe pneumonia and the risk of treatment failure only marginally, if at all, in hospitalized children.

CHLAMYDIA, CHLAMYDOPHILA AND MYCOPLASMA: "ATYPICAL" ORGANISMS EXTENDING BEYOND THEIR "TYPICAL" PERIODS IN CHILDHOOD LOWER RESPIRATORY INFECTIONS

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Background: The major atypical bacterial pathogens causing lower respiratory infections in children (*Chlamydophila pneumoniae*, *Chlamydia trachomatis* and *Mycoplasma pneumoniae*) have long been regarded as relatively confined to certain periods of childhood.

Methods: Nasopharyngeal aspirate specimens of children with lower respiratory infections in 295 university hospital visits were evaluated for the antigens of above mentioned organisms by immunofluorescence.

Results: *Chlamydophila pneumoniae*, *Chlamydia trachomatis* and *Mycoplasma pneumoniae* antigens were detected in 18 (6.5%), 11 (4.4%) and 9 (3.2%) patients, respectively among 295 nasopharyngeal aspirate samples. Atypical bacterial pathogens were most common in 0-6 months of age and lowest in 60 months and over. No statistically significant difference existed between the children with atypical bacterial pathogens and those without, in terms of respiratory rate, chest retractions, white blood cell count, C-reactive protein concentration, erythrocyte sedimentation rate and duration of recovery. The children with atypical bacterial pathogens were more likely to have prolonged expiration and relatively low body temperature.

Conclusions: According to our results, atypical bacterial agents tend to extend beyond their typical periods in childhood lower respiratory tract infections. This should be kept in mind when starting empirical antimicrobials to a child with such an infection.

IGG SUBCLASS AND ANTIPOLYSACCHARIDE ANTIBODY DEFICIENCY ARE OFTEN NOT RECOGNIZED

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Especially in young children, the incidence of recurrent respiratory infections is high. In most cases, these subside with age. However, an underlying cause like IgG-subclass (IGsD) and/or antipolysaccharide antibody deficiency (SPAD) may be present.

From Jan 1, 2009, until Jan 1, 2012, a monthly questionnaire was sent to all Dutch paediatricians asking about patients diagnosed with IGsD and/or SPAD, using a nation-wide signalling system (<http://www.nvk.nl/Onderzoek/NSCK.aspx>). All patients ≥ 2 yrs with a serum IgG > 4.0 g/l, and ≥ 1 IgG-subclasses under the age-related normal values and/or inadequate response to 23-valent unconjugated pneumococcal vaccination at ≥ 3 yrs were included.

About 3.9 million children live in the Netherlands. In total, 124 patients were reported by 38 (out of 101) hospitals; in most, only IgG subclasses were determined. 13 did not meet the inclusion criteria (*reported* prevalence 3/100,000). The prevalence of reported patients was 0-8 (median 0, mean 1.4) in university hospitals (n=8), 0-22 (median 8, mean 10) in general hospitals with a paediatric immunologist (n=5), and 0-5 (median 0, mean 0.6) in general hospitals without a paediatric immunologist (n=88).

Most patients with IGsD and/or SPAD show a milder phenotype, and patients will not be referred to a university hospital. In general paediatric practices, most patients were reported when immunological expertise was available. They were probably missed elsewhere. Since these 'milder' antibody deficiencies can develop into full-blown hypogammaglobulinemia with time, and by themselves can also lead to pulmonary damage, it is important to increase awareness of these diagnoses in non-immunologists.

NATURAL IMMUNITY TO HEMOPHILUS INFLUENZA TYPE B IN CHILDREN, SOUTH OF IRAN**A. Sotoodeh Jahromi, K. Rahmanian***Jahrom University of Medical Sciences, Jahrom, Iran*

Background and aims: Hemophilus influenza type b (Hib) infection has a high morbidity and mortality rate especially in children less than 5 years of age. The incidence of Hib disease in Iran is not known, and Hib vaccine is not included in the National Immunization Program. The aim of the present study was to investigate the level of antibody to Hib of children five years or younger living in Jahrom, Iran.

Methods: Three hundred eighty six children 5 years or younger were selected by random sampling method. A blood samples were taken from those children. Anti-Hib IgG antibody (anti-PRP) level was determined in the serum by using anti-Hemophilus influenza IgG EIA kit (IBL, Germany). An anti-PRP antibody levels equal 0.15 µg/ml and over were accepted as the natural immunity to Hib.

Results: The mean concentration of Hib antibody was 0.94 ± 0.480 µg/ml. Natural immunity was determined in three hundred and twenty six (84.5%) of the children. The proportion of natural immunity was increase from 64.9% among children ≤ 12 month old to 95.2% in children aged 49-60 month ($p < 0.001$).

Conclusions: The exposure rate of children with Hib was higher than expected, even in children who were just a few months old. Our data revealed need to be introducing Hib conjugate vaccine in the National Immunization Programs.

ALLERGY TREATMENT IN CHILDREN WITH RECURRENT OR CHRONIC SINUSITIS**M. Sadeghi-Shabestari**¹, S. Abdolahi-Fakhim²*¹Pediatric, TB and Lung Research Center of Tabriz, Tabriz University of Medical Sciences, ²ENT, Tabriz University of Medical Sciences, Tabriz, Iran*

Introduction: Diagnosis and treatment of Chronic and recurrent sinusitis in children is of the potential importance and many factors have an influence on it. The aim of this study is to assess children with Chronic and recurrent sinusitis, its affecting factors and the Role of allergy in the process and treatment of this disease.

Materials and methods: In this survey, 106 children with the diagnosis of chronic and recurrent sinusitis who were referred to specialty clinics of otolaryngology and allergy during 12 months were studied. History and physical examination of patients were recorded and allergy skin Prick test was done for all of them. Then the Response to treatment was evaluated.

Results: From 106 children, 54 of them (50.9%) were male and 52 of patients (49.1%) were female. The mean age of patients was 6.5 ± 2.9 . Skin Prick test was positive in 69.8% of them. Allergic rhinitis (67%) and then Asthma (34%), allergic conjunctivitis (19%) were the most common allergic diseases in our patients. Family history of allergy was positive in 59 (55.7%) of patients. Response to allergy treatment was seen in 92 patients (86.8%) of patients. Patients with positive skin Prick test had a better response to treatment than the patients with negative skin prick test.

Conclusion: The prevalence of allergic disease in children with chronic and recurrent sinusitis is considerable and allergy treatments can lead to favorable outcomes in children with sinusitis.

MICROBIOLOGIC CHARACTERISTICS AND PNEUMOCOCCAL CONJUGATE VACCINE (PCV) COVERAGE OF ACUTE OTITIS MEDIA (AOM) IN CHILDREN IN BRASOV, CENTRAL ROMANIA (2009-2011)

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Aims: A prospective study was initiated in Brasov, Romania in 2009 to assess the epidemiological and microbiological characteristics of AOM in children before PCV introduction to the routine national immunization program.

Patients and methods: AOM patients < 5 years of age who underwent tympanocentesis or presented with purulent otorrhea of < 24 hours duration were enrolled. Antibiotic susceptibility and *S. pneumoniae* (SP) serotyping were performed in Beer-Sheva, Israel.

Results: Middle ear fluid (MEF) cultures (Cxs) were obtained in 206 episodes. Average age (\pm SD) was 18.0 \pm 14.2 months; 132 (64%) episodes occurred in children < 2 years old; 105 (51%) of episodes were culture-positive. Compared with children with Cx(-) episodes, children with Cx(+) episodes were older (20.6 \pm 15.2 vs. 15.4 \pm 12.6 months, respectively (p=0.008), and had more spontaneous perforations (38 [51%] vs. 34 [32%]; p=0.002). Overall, 108 isolates were recovered: SP-75 (67%), *H. influenzae* (HI)-26 (24%) and others-7 (9%). Nonsusceptibility to penicillin was found in 25/27 (93%) evaluable SP (30% MIC>2.0 μ g/mL). SP resistance to TMP/SMX, erythromycin and clindamycin and multidrug resistance were 22/27 (82%), 16/27 (59%), 13/27 (48%) and 15/27 (56%), respectively. Thirty-nine (54%) evaluable SP were serotyped. The most common serotypes were 19F (26%), 6B (18%), 14 (15%), 23F (15%) and 19A (8%). 35/39 (90%) of all SP isolates are included in PCV-13 and 77% in PCV-10.

Conclusions: In MEF culture-proven AOM episodes, SP was the most common pathogen, with frequent and diverse antibiotic resistance and multi-resistance patterns. Most SP episodes can be prevented by PCVs.

BORDETELLA PERTUSSIS IN INFANTS ADMITTED FOR BRONCHIOLITIS DURING WINTER 2005-2006 IN NORTHERN ISRAEL: EPIDEMIOLOGY, CLINICAL COURSE AND PROGNOSIS

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Background: While acute bronchiolitis (AB) is caused primarily by *Respiratory Syncytial Virus* (RSV), co-infection with *Bordetella pertussis* (Bp) is known to occur. Miron's recent study found that infection with Bp occurred in 6.2% of cases of children < 2 years hospitalized with AB.

Aim: To assess how Bp may affect the clinical course of bronchiolitis.

Methods: 474 infants < 2 years admitted with AB between 11/2005 and 3/ 2006 to three Medical Centers in Northern Israel were included. Demographic and clinical data were recorded. Subjects were divided into Bp-positive and Bp-negative groups.

Results: RSV was detected in 346 (72.8%) cases, Bp was identified in 29 (6.1%) cases, and co-infection of RSV and Bp in 18 (3.8%) cases. In two children, Bp was the sole detected pathogen. There were no significant differences between the Bp positive- and Bp negative- AB groups with respect to their clinical course. Infants who received 2 doses of dTaP were more likely to contract Bp than infants who received 3 doses of vaccine (OR: 36.84; 95% CI 2.83-480.0; p< 0.006).

Conclusion: Among children with AB, no evidence was found to suggest that Bp is associated with unique epidemiological characteristics or clinical course. While our findings undermine the testing of Bp in all children with AB, its identification is useful for purposes of infection control. Moreover, given the small sample in the current study, future research should be designed to identify particular subgroups for whom such testing is likely to be positive.

S. PNEUMONIA AND H. INFLUENZAE IN OTITIS MEDIA WITH EFFUSION

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Background and aims: Acute otitis media (AOM), otitis media with effusion (OME) and recurrent acute otitis media (rAOM) are common in children in Iceland. The aim was to identify bacteria in middle ear effusions of children with OME or rAOM.

Methods: Children < 12 years old undergoing myringotomy or tympanostomy tube placements (usually for OME or rAOM) were invited to participate. Middle ear effusions were cultured and the parents completed a questionnaire on antibiotic usage.

Results: 181 children (55% boys, median age 21 months) participated, 56% had used antibiotics the preceding month, most commonly amoxicillin with clavulanic acid. Altogether, 337 ears from these 181 children were examined, 245 (72.7%) had effusion and 241 samples were cultured. Potentially pathogenic bacteria were cultured from 123 (51.1%). Eighty-five samples (35.3%) yielded nontypable *Haemophilus influenzae*, 35 (14.5%) *Streptococcus pneumoniae* and 20 (8.3%) *Moraxella catarrhalis*. Pathogenic bacteria were cultured from 18 (38,3%) ears with effusions from children currently taking antibiotics, 4 multiresistant strains of *S. pneumoniae*, (serogroups/types 19 and 6B) and 14 strains of *H. influenzae* resistant to amoxicillin and/or trimethoprim/sulphamethoxazole.

Conclusion: Potentially pathogenic bacteria were cultured from as many as 51% of the samples, most frequently *H. influenzae* and *S. pneumoniae*. A concerning proportion of the children were taking antibiotics in the preceding months or on the day of sampling. This increased the risk of multiresistant pathogenic bacteria in the middle ear fluid.

EPIDEMIOLOGY OF RESPIRATORY SYNCYTIAL VIRUS (RSV) BRONCHIOLITIS IN HOSPITALIZED CHILDREN IN GREECE, 2009-2011

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Background: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infections in children. The aim was to describe the epidemiology and clinical characteristics of RSV bronchiolitis cases hospitalized in a major tertiary hospital in Athens.

Methods: Records of confirmed acute RSV bronchiolitis cases were reviewed retrospectively in children admitted to Aghia Sophia Children's Hospital for two consecutive epidemiological periods (October 2009-September 2011). Nasal washings obtained within 48 hours of admission were tested for RSV antigen by a rapid immunochromatographic assay (Coris, Belgium).

Results: Totally, 368 cases (136 and 232 in each period respectively) were reviewed of which 53.5% were boys. Prematurely born were 10.6%. The mean age was 3.7 ± 5.3 months with 96.2% < 12 m.o.. Cough was present in all patients while among other clinical manifestations most prevalent were: rhinitis (98.1%), crackles (97%), wheezing (78.6%), respiratory distress (74.8%), retractions (67.1%), tachypnea (65.1%) and fever (54.8%). Hypoxemia ($SpO_2 < 95\%$) was detected in 31.5%. X-ray findings were abnormal in 70.4%. Acute otitis media was diagnosed in 9.3%. In 8 cases H1N1 co-infection was established. A considerable 56.2% had received antibiotics and 38% corticosteroids as part of their treatment. Admission in ICU was required for 4.1% (mean duration 3.8 ± 2.2 days) and 1.1% were mechanically ventilated. Among Palivizumab eligible children 4/20 had received it.

Conclusions: RSV bronchiolitis is responsible for a large number of annual hospitalizations and frequent misuse of antibiotics in treatment. Steps towards reducing the burden of disease with proper prophylaxis must be taken.

TEMPORAL EVOLUTION OF ADMISSIONS DUE TO COMPLICATED PNEUMONIA WITH PLEURAL EFFUSION OR EMPYEMA

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Introduction and objectives: Pleural effusion is a pneumonia complication in hospitalized children. The main etiological agent is *Pneumococcus*. Since 2001, a Heptavalent pneumococcal conjugate vaccine was introduced in our region (Navarra, Spain). Our objectives are to describe the temporal evolution of these pathologies and to evaluate the possible vaccine effects.

Methods: We retrospectively analyzed from 1995 to 2010 all the admissions for pneumonia with pleural effusion (PE) or empyema (E). Statistical analyses were performed using Student's t test and Pearson's r. We considered *Pneumococcal pneumonia* (NN) those with: positive culture, or positive Ag / PCR in pleural fluid.

Results: 270 cases were recorded, mean age:52.66 months(DS:40, 94).

A significant increase of this pathologies was found ($p < 0.001$):PE(Rp:0.906), E(81,Rp:0.860) and NN (110,Rp:0.834). Comparing the annual average of cases in the pre-vaccination years (1995-2001) with post-vaccination years (2002-2010), there was a significant increase ($p < 0.01$) in PE (6.1vs25,2), E(1vs8,2) and NN(1.7vd10, 8).

This increase in the incidence of PE was significant ($p < 0.01$) in all age groups.

The vaccination rate rose steadily from 5.26% in 2002 to 68% in 2010.

Comparing the initial post-vaccine period (2002-2005: vaccination rate: 20.99%) with the late post-vaccination period (2006-2010 vaccination rate:53.18%) a significant increase was found ($p < 0,05$) of PE(19vs30,2) and E (5vs10,8)

Conclusions: During the last 15 years in our country, an increase number of admissions for pneumonia with PE and E has been found. This increase is directly proportional with the increase of vaccination rates.

IS THERE ANY RELATIONSHIP BETWEEN DENTAL CARIES AND RECURRENT UPPER RESPIRATORY TRACT INFECTION?

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Background: Dental caries is one of the most prevalent infectious disease affecting individuals from childhood. Dental caries results from overgrowth of specific organisms that are part of normally occurring dental flora and might be related to diseases such as tonsillitis. This study aims to show the possible association between poor oral hygiene and upper respiratory tract infection (URTI) rates. For this purpose, a questionnaire was developed and medical records were studied.

Methods: Children without any systemic disease were enrolled in the study and divided into two groups; 100 children (53 boys, 47 girls) with dental caries as patient group, 100 children (48 boys, 52 girls) without caries as control group. URTI rates and antibiotic usage in both groups since birth were identified according to the medical records. Dental caries was scored according to decayed, missing and filled teeth index.

Results: The mean age of patients group was significantly higher than control group ($8,1 \pm 3,1$ years vs. $5,4 \pm 3,4$ years, respectively). The mean initial age to brush teeth was significantly lower in control group ($p < 0,01$). URTI and antibiotic usage rates were significantly higher in patient group with respect to control group ($p < 0,01$). In patient group, they had greater rate of URTI after they had caries ($p < 0,01$).

Conclusions: In our study, the URTI rates were significantly higher among children with poor oral hygiene and dental caries. Oral hygiene care and education should start at infancy.

ASYMPTOMATIC CARRIAGE OF *MYCOPLASMA PNEUMONIAE* IN THE UPPER RESPIRATORY TRACT OF CHILDREN

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Background and aims: Although *Mycoplasma pneumoniae* is regarded as a common cause of respiratory tract infections (RTIs) in children, little is known about the prevalence of asymptomatic *M. pneumoniae* carriage. Our objective was therefore to determine the prevalence of *M. pneumoniae* in children in the absence of RTI symptoms.

Methods: 412 asymptomatic children and 321 children with RTI symptoms were enrolled between July 2008 and November 2011. Extensive sampling was performed on all children, which included pharyngeal and nasopharyngeal samples and capillary blood samples. This allowed us to detect serum-antibodies against *M. pneumoniae* by ELISA, to detect and quantify genomic copies of *M. pneumoniae* by real-time PCR, and to detect other bacterial and viral respiratory pathogens.

Results: *M. pneumoniae* DNA was detected in 20.7 % of the asymptomatic children and in 16.7 % of the children with an RTI. There was no significant difference between the two groups in distribution of genomic copy number or in prevalence of anti-*M. pneumoniae* serum-antibodies. Interestingly, the presence of serum-antibodies did not correspond to real-time PCR results. Longitudinal follow-up showed the persistence of *M. pneumoniae* in the absence of symptoms for up to 4 months. Other pathogens were also found to be commonly present in the respiratory tract of asymptomatic children

Conclusion: The presence of *M. pneumoniae* DNA in the upper respiratory tract is not indicative for symptomatic RTI in children. In addition, the detection of pathogens in the upper respiratory tract is generally not sufficient to determine the aetiology of an RTI.

IMPACT OF VIRAL INFECTIONS IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA: RESULTS FROM THE CAP-PRI STUDY GROUP

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Background and aims: Little is known about the prevalence of viral infections in children with community-acquired pneumonia (CAP). The aim of this study was to describe the clinical and virological data collected from children with radiographically confirmed CAP hospitalized in 7 different European countries in whom 17 respiratory viruses were sought in respiratory secretion samples during the acute phase of the disease.

Methods: The study involved 359 children with radiographically confirmed CAP whose respiratory secretion samples were tested using the Luminex xTAG Respiratory Virus Panel Fast assay, which simultaneously detects influenza A virus, influenza B virus, respiratory syncytial virus (RSV)-A and -B, parainfluenzavirus-1, -2, -3 and -4, adenovirus, human metapneumovirus, coronaviruses 229E, NL63, OC43 and HKU1, enterovirus/rhinovirus, and bocavirus. A real-time PCR assay was used to identify the rhinovirus in the enterovirus/rhinovirus-positive samples.

Results: A total of 259 children (72.1%) were positive for at least one virus: the most frequently detected was rhinovirus, which was found in 116 (32.3%), followed by RSV (n=89, 24.8%), bocavirus (n=32, 8.9%), influenza viruses (n=20, 5.6%), and hMPV (n=16, 4.4%). Viral co-infections were found in 59 children (16.4% of the enrolled children; 22.7% of those with viral infections). Marginal differences were found between the infections due to a single virus and between single viral infections and co-infections.

Conclusions: The findings of this study highlight the importance of respiratory viruses (mainly rhinovirus and RSV) in children with CAP across Europe, and show the characteristics of both the single infections and co-infections associated with the disease.

MOLECULAR EPIDEMIOLOGY OF ADENOVIRUSES IN CHILDREN WITH LOWER RESPIRATORY TRACT INFECTION

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Background: Adenoviruses (Ad) are common causative agents of lower respiratory tract infections, especially in infants and young children. They have been associated with both sporadic and epidemic cases. Aim of the present study was to detect adenoviruses and identify their types in Greek pediatric patients with acute respiratory infection. Co-infections were also investigated.

Materials and methods: Throat swab samples were collected during a 13-month period (1.3.2007-31.3.2008) from 305 pediatric patients (163 males-142 females), hospitalized for respiratory infection. Their age ranged from 0.02 to 13 years (median 1.5). After DNA extraction, the hexon gene was amplified by a nested PCR, while sequencing and phylogenetic analysis followed.

Results: Adenoviral DNA was detected in 15/305 (4.9%) patients: 12 (80%) were Ad3, 2 (13.3%) Ad1, and 1 (6.6%) was Ad5. The median age of these patients was 2.25 years (range 0.16-7). All patients had pneumonia or bronchopneumonia, except 3, who had acute bronchiolitis. Most cases were observed in May 2007 and in March 2008; in these months only Ad3 was detected. A second, or a third pathogen (co-infection) was detected in 4 cases (26.6%): RSVA, RSVB, and *Mycoplasma pneumoniae* in one each, while bocavirus and metapneumovirus were detected in the fourth case.

Conclusions: Adenoviruses constitute a major respiratory pathogen in childhood, and molecular typing is a helpful tool for the epidemiological investigation. This study was the first to report the prevalent and circulating Ad types in Greece. It was shown that Ad3 was the predominant genomic type during the study period, while co-infections were often observed.

COMMUNITY-ACQUIRED PNEUMONIA AND ASTHMA: TWO SIDES OF ONE CLINICAL COURSE**Z. Nesterenko**¹, O. Ivanina²*¹Department of Pediatrics, State Institution 'Lugansk State Medical University', ²Lugansk Municipal Children's Hospital #2, Lugansk, Ukraine***Background:** Changes in clinical symptoms of community-acquired pneumonia (CAP) in asthmatic patients cause diagnostic and therapeutic errors.**Objective:** To study clinical features of CAP in children with asthma (A).**Material and methods:** 80 children aged 3-18 with partly-controlled allergic A (according to GINA Guidelines 2009) were studied. 33(41.6%) patients had mild persistent A, 37(49.5%) - moderate persistent A, 10(8.9%) - severe persistent A. 55(68.8%) patients with A had clinically and radiographically diagnosed CAP. All patients had signs of connective tissue disorders (CTD).**Results:** CAP caused by *Mycoplasma pneumoniae* was in 44(80.0%) patients, by Cytomegalovirus - in 20(36.3%), by *Chlamydia pneumoniae* - in 16(29.1%) children. Recurrent course of CAP was in 47.3% of asthmatic patients with CAP, causing A exacerbation in them. Pulmonary hypertension (PH) was found in 23 (28.8%) patients, with pulmonary fibrosis (PF) in 37.2% of asthmatic children with CAP, 33% of which had severe A with CT evidence of pneumatocele (PC). Patients with A exacerbation provoked by CAP received antibiotic treatment (ABT) (macrolides) besides controller therapy for better asthma control.**Conclusions:**

1. CAP causes A exacerbation in 2/3 of asthmatic patients, *Mycoplasma*-associated CAP - in 4/5 of asthmatic patients with CAP.
2. Recurrent course of CAP was in 47.3% of patients with A and CTD.
3. PH and PF was diagnosed in 37.2% of asthmatic patients with CTD and CAP, one third of them had severe A with CT evidence of PC.
4. Basic therapy of asthmatic patients with CAP included ABT to achieve asthma control.

ACUTE CARE UTILIZATION DUE TO HOSPITALIZATIONS FOR PEDIATRIC LOWER RESPIRATORY TRACT INFECTIONS (LRTI) IN BRITISH COLUMBIA, CANADA

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Introduction: Pediatric LRTI hospitalizations are a significant burden on patients, families and healthcare systems. This study describes the burden of pediatric LRTIs and LRTIs due to respiratory syncytial virus (RSV) on hospitals in British Columbia (BC).

Methods: LRTI admissions for patients < 19 years during 2008-2010 were extracted from the BC Discharge Abstract Database. Annual hospitalizations and required acute care beds were estimated. Sub-analyses determined the burden of infants < 1 year and infants at high risk for RSV infection (e.g. premature infant). Population statistics were attained to calculate hospitalization rates.

Results: LRTI accounted for 32% hospitalizations for diseases of the respiratory system in patients < 19 years, that increased to 75.9% in infants < 1 year. 73.1% pediatric LRTI hospitalizations occurred between November and April. Most (63.9%) LRTI hospitalizations were for an unspecified infectious cause. In infants < 1 year, acute bronchitis due to RSV was the most frequent LRTI diagnosis (44%). The next four most prevalent diagnoses were unspecified infectious origin (42.9%). Average hospitalization was 3.1 days which increased to 9.1 days for high-risk infants ($P < 0.0001$). On average, 19.6 acute care beds were required for pediatric LRTIs which peaked to 64.0 beds in winter 2010. Hospitalization rates per 100,000 children were 235 and 2410 for 1-19 year and < 1 year, respectively.

Conclusion: Pediatric LRTI hospitalizations require significant hospital resources particularly between November and April. Public health prevention strategies may be important to reducing this demand and contribute to future sustainability of pediatric healthcare resources.

RESPIRATORY DISTRESS SYNDROME (RDS) AT BIRTH IS A RISK FACTOR FOR LOWER RESPIRATORY TRACT INFECTION (LRTI) HOSPITALIZATION IN INFANCY

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Objective: Preterm infants are at risk of RDS at birth, and of hospitalization for LRTI (specifically, respiratory syncytial virus) in infancy. Whether RDS at birth is an independent risk factor for LRTI is unknown. We therefore estimated the risk of LRTI-related hospitalization among preterm infants with RDS at birth.

Methods: The population-based cohort was identified from Québec administrative data, and included all late preterm babies (32 to 36 weeks gestational age) from 1996-1997. RDS at birth was identified by ICD code 769, and a comparison cohort generated from all late preterms without RDS. A multivariable model estimated the risk of LRTI-related hospitalization before age 1 among late preterms with RDS at birth, adjusted for other significant risk factors.

Results: Of the 7,488 late preterms, 459 (6.2%) had RDS at birth and 525 (7.0%) were hospitalized for LRTI before age 1. The adjusted odds ratio (OR) for LRTI-related hospitalization after RDS at birth was 1.6 (95% confidence interval (CI), 1.2-2.2). Other significant risk factors included male sex (1.4 (1.1-1.7)), or diagnosis with other respiratory conditions (1.5 (1.2-1.9)), diaphragm anomalies (6.7 (1.2-37.4)), bacteremia (3.6 (1.2-10.7)), intraventricular hemorrhage (4.5 (1.5-13.4)), congenital heart disease (2.3 (1.6-3.2)), or congenital respiratory system anomalies (3.2 (1.6-6.3)) within the first year of life.

Conclusion: Late preterm infants with RDS at birth are at a 60% increased risk of LRTI-related hospitalization before age 1, compared to late preterm infants without RDS. Such infants may benefit from interventions that decrease the risk of contracting respiratory viruses causing acute LRTI.

THE IMPACT OF VIRAL INFECTIONS ON NASOPHARYNGEAL BACTERIAL COLONIZATION AMONG CHILDREN

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Background and aims: There is accumulating evidence indicating a close association between viral respiratory infections and bacterial superinfections. Our study examines nasopharyngeal bacterial colonization among children with and without a viral respiratory tract infection.

Methods: Nasopharyngeal colonization with *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and nasal colonization with *Staphylococcus aureus* was assessed in children < 5 years of age with symptoms of viral respiratory tract infection, and in controls without respiratory symptoms. The presence of respiratory syncytial virus, influenza virus, parainfluenza virus, rhinovirus and adenovirus was examined via PCR. A questionnaire including demographic and clinical data was completed.

Results: A total of 391 children were recruited and the average age of the 355 children finally included was 26.6 months, among which, 128 were asymptomatic controls and 227 had symptoms. A higher percentage of asymptomatic subjects was found negative for all bacteria examined ($p < 0.01$). *S. pneumoniae* and *M. catarrhalis* were more frequently isolated ($p < 0.01$) from children with symptoms of respiratory tract infection as compared to asymptomatic children. *S. pneumoniae* plus *H. influenzae* plus *M. catarrhalis* and the concurrent presence of any 4 bacteria were more frequently observed among symptomatic children ($p < 0.05$). Colonization of virus positive children with any bacterium or *S. pneumoniae* was higher than in virus negative children ($p < 0.05$). Colonization with *H. influenzae* was significantly different among children in which different viruses have been isolated ($p < 0.05$).

Conclusions: Viral infections influence nasopharyngeal bacterial colonization among children possibly leading to accentuation of disease severity or invasive disease.

COMMUNITY ACQUIRED PNEUMONIA ETIOLOGY IN THE ERA OF *H.INFLUENZAE* AND *S.PNEUMONIAE* CONJUGATED VACCINES. CENTRO HOSPITALARIO PEREIRA ROSSELL, URUGUAY 2003-2011

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Background: Prior 2008 *S.pneumoniae* serotypes 14, 1 and 5 were leading cause of Community-Acquired Pneumonia (CAP) in children. *H.influenzae* type b (Hib) was not CAP cause in vaccinated children. Other *H.influenzae* (Hi) serotypes, non typable Hi or *S.aureus* were infrequent as CAP cause. 2003 Community-Acquired Methicillin Resistant *S.aureus* emerged as severe cause of CAP. 1994 Hib conjugated vaccine was incorporated to routine childhood vaccination. March 2008 Pneumococcal Conjugate Vaccine 7 valent (PCV7) was incorporated for < 2 years old. April 2010 PCV13 replaced PCV7 (both 2+1 schedule), catch-up for older children was offered. National data demonstrate high compliance with PCV7/13, >93% 2008-2009, >95% 2010.

Aims: To describe CAP's etiology in children ≤14 years old hospitalized at Hospital Pediátrico-Centro Hospitalario Pereira Rossell in 2003-2011.

Methods: Cases and annual rates per 10,000 discharges (CI 95%) were described before PCV7/13 vaccination (2003-2007), year 2008 and three years after (2009-2011). Doses of PCV7/PCV13 and serotypes were described for pneumococcal-CAP (P-CAP). Data were obtained from hospital databases.

Results: Significant decrease (69,6%) was observed between P-CAP rates in (2003-2007): 71,8 (65,8-77,9) and 2011, first year after PCV13: 21,8 (12,9-30,8). Significant reduction (68,8%) was observed for PCV13 vaccine serotypes P-CAP from 61,2 (55,5-66,8) in 2003-2007 to 13,3 (6,3-20,3) in 2011. Median rates for staphylococcal CAP were 4,3 (0,9-7,6) in 2003-2007 and 0,6 (-0,8-2) in 2009-2011. Median rates for Hi CAP were 3,3 (0,4-6,3) in 2003-2007 and 3,6 (0,07-7,2) in 2009-2011.

Conclusion: The surveillance is mandatory to evaluate natural changes and the changes induced for health care strategies.

THE CLINICAL CHARACTERISTICS AND TREATMENT OF PERTUSSIS PATIENTS A TERTIARY CENTER OVER A FOUR-YEAR PERIOD

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Background and aims: To study the characteristics of patients diagnosed with pertussis (whooping cough) at a tertiary center in Ankara, Turkey.

Methods: We performed a retrospective study of pertussis cases occurring a period of July 2007-December 2011. All patients were microbiologically confirmed through a polymerase chain reaction (PCR) or culture.

Results: Thirty-one patients (18 boys, 13 girls) with positive *Bordetella* spp. culture or PCR were identified with a median age of two months (range:13 days-10,5 years); 54.8% and 35.4 % were aged 2 and 6 months or less respectively. 80% of cases occurred between May and Augst. Bordetella spp. was associated with a virus in one patient. Seventeen patients had no pertussis vaccination for being under the age of 2 months and additional four patients for other reasons. Most frequent symptom paroxysmal cough (100%) and cyanosis (87.1%).Mean duration of the symptoms prior to admission was 12.8±8.0 days. Leucocytosis with lymphocytosis occurred in 58%. Fifteen patients (48.4%) had clinical and radiological findings of pneumonia. Cough-related cyanosis recovered in 4.6±3.8 (range) days. The mean hospital stay was 9.5±5.5 days (range 3 to 28 days). No patients died.

Conclusions: Pertussis is a severe disease with cough related cyanosis especially in young infants. We think that patients who have characteristic paroxysmal cough with cyanosis and haven't have fever should alert clinicians about pertussis and should be without delay. New preventive strategies are required to protect infants who have not yet developed full immunity to this infection.

RISK FACTORS IN CHILDREN LESS 12 MONTHS WITH RESPIRATORY SYNCYTIAL INFECTION**K. Serhiyenka***Belarussian State Medical University, Minsk, Belarus*

The purpose of our work was studying of risk factors in children who have transferred respiratory syncytial infection during first year of age.

For achievement of an object in view we carry out the analysis of 61 case records of children who have transferred respiratory syncytial infection (RSI) during first year of age. For control group we took patients less 12 months with influenza (n=34).

The analysis of the anamnesis of life of children who have transferred RSI has shown presence of risk factors at 32 patients (52 %) from them congenital heart diseases - 7, bronchopulmonary dysplasia + a congenital heart disease + a congenital pneumonia - 1, a perinatal encephalopathy (PEP)/ PEP+ a delay of psychomotor development - 6, a congenital pneumonia + PEP - 1, congenital cardiopathy + PEP - 1, a chronic pneumonia + not rheumatic carditis - 1, prematurely born - 4, small-for-date (less than 3 kg.) - 11.

In control group in 29 % of cases the following accompanying pathology is revealed: congenital heart diseases - 1, PEP - 2, congenital heart diseases + a children's cerebral paralysis + plural congenital developmental anomalies-1, bronchopulmonary + congenital pneumonia + an epilepsy-1, prematurely born - 3, small-for-date - 2.

Thus in group of the patients who have transferred respiratory syncytial infection during first year of age authentically is more often presence of risk factors than in group with a influenza ($\chi^2=0,05$).

SEVERE PNEUMONIA CAUSED BY 2009 INFLUENZA A VIRUS (H1N1) IN CHILDREN AND CORTICOSTEROID TREATMENT**S.H. Ma¹**, E.Y. Choi², K.I. Lee³, J.H. Kang²¹*Pediatrics, Fatima Hospital, Changwon*, ²*Pediatrics, College of Medicine, The Catholic University, Seoul*,³*Pediatrics, College of Medicine, The Catholic University, Taejeon, Republic of Korea*

Purpose: The effect of corticosteroid on severe pneumonia caused by pandemic 2009 H1N1 influenza A virus is controversial. This study was aimed to present the effects of early, short-term corticosteroid treatment for severe pneumonia with this virus infection.

Methods: A retrospective analysis was performed on severe pneumonia patients (37 patients) who had severe respiratory distress at presentation requiring oxygen therapy and received intravenous methylprednisolone (MP, 8-10 mg/kg, divided in 4 doses/day for 2-3 days) with oseltamivir. The clinical and laboratory characteristics of the patients were evaluated through the medical records and chest radiographic findings.

Results: The mean age and male-to-female ratio of the patients were 6.5±2.9 years of age, and 3.4:1 (male 29 patients), respectively. The 5-9 aged group was predominant among the age groups (25 patients, 67.6%). Duration of fever prior to admission was 1.4±0.6 days and dyspnea developed within 24 h after beginning of respiratory symptoms in the all patients. All patients were previously healthy and received oseltamivir within 48 h. Thirteen patients (35.1%) developed dyspnea during oseltamivir treatment. Following MP infusion, all 37 patients including 13 progressive pneumonia patients during oseltamivir treatment showed an immediate halt in the progression of pneumonic infiltration with rapid clinical improvement. There were no side-effects following steroid use.

Conclusions: For severe pneumonia patients, early corticosteroid treatment halted clinical exacerbation, and possibly prevent progression to acute respiratory distress syndrome. Further controlled clinical studies are needed for the role of corticosteroids and antivirals on severely affected patients with influenza virus infections.

INFLUENZA A (H1N1) VIRUS IN A PICU

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Background and aims: H1N1 influenza A virus infection involved the public Health System worldwide so much that on June 2009 WHO announced the disease from epidemic as pandemic. Our purpose was to investigate the incidence, clinical characteristics, treatment and outcome of H1N1 in children with respiratory tract infection required hospitalization in PICU.

Material and methods: Influenza A in children hospitalized in our unit with respiratory infection during the period April 2009-March 2011 was confirmed by special pharyngeal sample

Results: During this period, 36 out of 194 children were admitted in our Unit with respiratory infection. Four patients (11.1%) (2 girls and 2 boys, age 2.5, 4.5, 9 and 10 years respectively), all unvaccinated for H1N1, were influenza A infected. Their initial symptoms were:

- Fever > 38° C (3 cases)
- Respiratory infection (2 cases of pneumonitis)
- Bronchial asthma and pneumomediastinum
- Febrile + status epilepticus
- Cardiac arrest, multiorgan failure

Three children needed intubation and mechanical ventilation. Two had underlying disease - one had bronchopulmonary dysplasia and heart disease, and the other had cerebral palsy.

Oseltamivir (Tamiflu) was administered immediately and for 5 days in all cases and in one case, with persistent infection, for 15 days.

The outcome was good in 3 cases and only the child with bronchopulmonary dysplasia and heart disease developed multiorgan failure and eventually died.

Conclusion: 11,1% of patients with respiratory infection in our PICU was H1N1 positive. One patient with severe underlying disease died. 75% need mechanical ventilation and half of them had co-morbidities.

INCREASED RISK OF PERTUSSIS IN PATIENTS WITH MANNOSE-BINDING LECTIN DEFICIENCY**K. Gröndahl-Yli-Hannuksela**¹, M. Viander², J. Mertsola³, Q. He¹¹*Department of Infectious Disease Surveillance and Control, National Institute for Health and Welfare,*²*Department of Medical Microbiology and Immunology, University of Turku,* ³*Department of Paediatrics, Turku University Hospital, Turku, Finland*

Background and aims: Despite the extensive childhood vaccinations, pertussis has resurged in many countries. The protection against pertussis is thought to be mediated by both innate and adaptive immunity. However, studies concerning innate immunity in pertussis are limited. Mannose-binding lectin (MBL) is an important molecule of the innate immunity and its low concentration is associated with increased susceptibility to respiratory infections. The aim of this study was to evaluate the role of MBL in pertussis infection by determining the prevalence of MBL deficiency in patients with pertussis and to elucidate MBL levels in different phases of pertussis.

Methods: In this retrospective study, paired sera of 125 laboratory-confirmed pertussis patients (age range 1-71 years; median 15 years) and single sera of 430 control subjects (age range 0.5-97 years; median 15 years) were included. The median interval between the paired sera of pertussis patients was 20 days (range 5-72 days). The serum MBL concentration was measured using double-antibody sandwich ELISA.

Results: Severe MBL deficiency (< 50 ng/ml) was found more often in the patients than in the controls (11.2% vs 5.8%, $p=0.038$). Moreover, the deficiency was detected more frequently in the adult patients than the controls (19.6% vs 8.3%, $p=0.037$). Thirty-four (27.2%) patients had significant changes in MBL concentration between the paired sera.

Conclusions: Our results suggest that MBL deficiency might be associated with pertussis infection especially in adults. However, during pertussis infection MBL does not seem to work uniformly as an acute phase reactant.

CHARACTERISTICS OF RESPIRATORY ISOLATES AMONG MIDDLE EASTERN PATIENTS WITH CYSTIC FIBROSIS - EXPERIENCE AT TAWAM HOSPITAL, UNITED ARAB EMIRATES

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Background and aims: Respiratory infection is very frequent in patients suffering from cystic fibrosis (CF); a disease common among Caucasians. Data on CF from Middle East is scanty. We report on the prevalence and antimicrobial resistance pattern of pathogens isolated from lower respiratory tract secretions among Middle Eastern patients with CF.

Methods: In this retrospective case review study, microbiological data of respiratory isolates (616 samples) was collected from 28 patients with CF managed in the CF clinic at Tawam hospital, UAE, during the years of 2000-2010. MDR *Pseudomonas aeruginosa* was defined as isolate being resistant to ceftazidime, piperacillin, aztreonam, ciprofloxacin and gentamicin.

Results: Patients' ages ranged from 2 months to 26.7 years. *Pseudomonas aeruginosa* was the most commonly isolated pathogen (47%), followed by *Staphylococcus aureus* (13%). Other pathogens included *Haemophilus influenzae* (5.8%), *Streptococcus pneumoniae* (1%) and *Stenotrophomonas maltophilia* (1%). Fungal isolates represented 5.2% of all isolates; *Candida albicans* (6) and *Aspergillus fumigatus* (3). Early colonization/infection with *Pseudomonas aeruginosa* was already evident in infants (< 1 year); representing 19.6% of all isolates in this age group. MDR *Pseudomonas aeruginosa* accounted for 22% of all *Pseudomonas aeruginosa* isolates. Only one *Staphylococcus aureus* isolate (3.8%) was resistant to oxacillin (MRSA).

Conclusions: The detection of MDR *Pseudomonas aeruginosa* and MRSA in CF patients highlights the need for ongoing surveillance of antimicrobial resistance patterns. Infection control measures should help minimizing the spread of those resistant bacteria.

DELAYED VERSUS IMMEDIATE ANTIMICROBIAL TREATMENT FOR ACUTE OTITIS MEDIA

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Background and aims: Watchful waiting with the option of delayed antimicrobial treatment for acute otitis media (AOM) is recommended in several guidelines. Our aim was to study if delayed, as compared to immediate, initiation of antimicrobial treatment worsens the recovery from AOM.

Methods: This was a subanalysis of a randomized, double-blind, placebo-controlled trial. Children (6-35 months) with AOM received either delayed or immediate antimicrobial treatment (amoxicillin-clavulanate for 7 days). The delayed antimicrobial treatment group consisted of children in the placebo group, to whom antimicrobial treatment was initiated before day 9 (n=53). The immediate antimicrobial treatment group consisted of children allocated to receive antimicrobial treatment immediately (n=161).

Results: Improvement during antimicrobial treatment was observed in 91% and 96% of children in the delayed and immediate antimicrobial treatment groups, respectively (P=0.10). The median wait-and-see period was 48 hours, during which two children in the delayed antimicrobial treatment group developed severe infections. Delayed initiation of antimicrobial treatment was associated with prolonged resolution of fever, ear pain, poor appetite, and decreased activity, but not ear rubbing, irritability, restless sleep, or excessive crying. Parents of the children in the delayed antimicrobial treatment group missed more workdays (mean 2.1 vs. 1.2 days, P=0.03). Diarrhea, vomiting, and rash were equally common in both groups.

Conclusions: Our results indicate that delayed initiation of antimicrobial treatment does not worsen the recovery from AOM. However, observation period before the initiation of delayed antimicrobial treatment might be associated with worsening of child's condition, prolongation of symptoms, and economic losses.

PREVALENCE OF OTITIS MEDIA IN HOSPITALIZED CHILDREN IN BURUNDI, CENTRAL AFRICA**E. Baggi**¹, P. Marchisio^{1,2}, M. Semino¹, N. Principi^{1,2}, S. Esposito^{1,2}¹*Department of Maternal and Pediatric Sciences, University of Milan, ²Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy*

Background and aims: Otitis media (OM) is deemed to be a serious health problem in several developing countries but data regarding Africa are scanty. We evaluated the prevalence of otological diseases in children in Burundi, a country for which no data are available.

Methods: In winter (Jan-March) 2011 in Kiremba all the children aged < 5 years hospitalized for respiratory infections underwent, at admission, an otological examination with a pneumatic otoscopy and a tympanometry. Acute OM (AOM) was defined as an acute onset of signs and symptoms with evidence of middle ear effusion or otorrhea. OM with effusion (OME) was defined as the presence of middle ear effusion without signs and symptoms of inflammation.

Results: A total of 108 children (median age 17 months, 44 males) were enrolled (pneumonia, 57.4%; bronchitis, 42.6%; co-existing malaria, 25.0%). One third of the children (33, 30.6%) had normal middle ear. No AOM was diagnosed. OME was detected in 74 children (68.5%) and most of them (68.9%) had bilateral effusion. One child had chronic tympanic perforation. The prevalence of OME depended on age (< 12 m. 86.5%; 12-24 m. 73.7%, > 24 m. 43.8% $p < 0.001$) but not on sex (males 72.7%, females 66.7%, $p = 0.13$) nor type of respiratory infection (pneumonia 67.8%, bronchitis 69.6%, $p = 0.16$) or coexisting malaria (present 74.1%; absent 66.7%, $p = 0.15$).

Conclusions: OME is highly prevalent in children in Burundi. As it can lead to long-term sequelae and complications, efforts to prevent adequately and treat it are desirable even in this unprivileged setting.

EPIDEMIOLOGY OF RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN IN GREECE (2004-2011)

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Background and aims: Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis and pneumonia among infants and young children. The aim of the study is to determine the epidemiology of RSV infection in pediatric patients over seven years (July 2004 to June 2011).

Methods: During this period, 4802 nasal washings or nasopharyngeal aspirates were tested from children [2666 male (55.5%)] hospitalized for acute respiratory infection in a paediatric hospital in Greece. The age distribution of children was: < 1 month 830; 1-2 month 862; 2-3 month 1044; 3-6 month 750; 6-12 month 528; 12-24 month 430; >24 month 358. The samples were evaluated for RSV detection using a direct immunofluorescence assay (MONOFLUO™ Screen R.S.V.).

Results: Positive to RSV were found 37.42% of samples (1797/4802) without statistically significant difference ($p > 0.05$) between boys (36.23%) and girls (38.90%). The proportion of positive samples according to age was: < 1 month 41.6% (345/830); 1-2 month 44.5% (384/862); 2-3 month 43.4% (453/1044); 3-6 month 40.7% (305/750); 6-12 month 32.2% (170/528); 12-24 month 24% (103/430); >24 month 10.3% (37/358). The seasonal distribution was characterized by epidemic peaks from January to March. The main clinical manifestations were in children < 2 years bronchiolitis and >2 years bronchitis or pneumonia).

Conclusions: RSV is a major cause of lower respiratory tract infections in children < 2 years of age, mainly in winter months and it may be rapidly transmitted to the environment in a number of ways. It suggests that a vigorous with delay epidemiological strategy should be pursued.

CONFORMITY OF ANTIBIOTICS PRESCRIPTIONS WITH THE CURRENT RECOMMENDATIONS IN CHILDREN PNEUMONIA IN FRANCE

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Pneumonia is a frequent cause of antibiotic treatment in children. Non adhesion to recommendations could be responsible for a misuse of antibiotics, leading to bacterial resistance and additional cost. The objective of this study was to determine the frequency of the “out of recommendation” antibiotic prescriptions and then to identify their characteristics, determiners and consequences.

Cases of pneumonia were prospectively collected by a network of 10 paediatric emergency departments between May 2009 and 2011 and classified according to the 2005 AFSSAPS French recommendations.

Among 3034 antibiotic treatments, 1472 (48 %) were considered “out of recommendation”. The deviations concerned the nature of the molecule (69,8 %), the route of administration (37,2 %) and the use of a first line antibiotics association (13,2 %). Logistic regression analysis showed that the main factors associated with “out of recommendation” antibiotherapy were: age of less than 1 year (OR=0,32 [0,22-0,50]), severity signs (OR=0,48 [0,40-0,58]), pneumococcal infection risk factors (OR=0,41 [0,28-0,60]), emergency department centre (OR=0,22 [0,13-0,36]), winter and spring seasons (OR=0,76 [0,61-0,95]). Moreover, the incidence of adequate prescription increased in 2011 (OR= 1,46 [1,05-2,04]). The clinical outcome was not influenced by the conformity of the prescriptions antibiotics (99 % of favourable outcome, 6 deaths).

This snapshot of antibiotic use to treat pneumonia in french children shows that half of the prescriptions are not in compliance with the current recommendations. An urgent improvement is needed to generalize amoxicillin by oral route as the first line treatment, even in young children with signs of severity.

MORTALITY AFTER HOSPITALIZATION FOR SEVERE RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN INFANCY: A SYSTEMATIC REVIEW AND EVIDENCE SYNTHESIS

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Background and aims: RSV is the most common cause of severe bronchitis and pneumonia among infants. Data on case fatality are variable. This study aimed to characterize the fatality risk for infants hospitalized for RSV, considering the presence of underlying RSV risk factors.

Methods: A systematic literature search was conducted to identify studies reporting case fatality estimates after RSV hospitalizations, between 1975 and 2011. Descriptive and outcome data were extracted from all eligible studies according to severe RSV risk categories: prematurity; congenital heart disease (CHD); or bronchopulmonary dysplasia (BPD). Infants were mixed high-risk if insufficient data were presented for classification in one specific risk group, and not at high risk if no risk factors were reported. Case fatality rate (CFR) data were aggregated using ranges, medians, and unadjusted weighted means.

Results: 1,219 articles were identified; 32 articles provided 53 estimates of CFR by risk group. CFR estimates were: prematurity (n=22) range 0-20% (weighted mean CFR, 2.4%; median, 0%); CHD infants (n=16) range 0-40% (weighted mean, 8.2%; median, 3.0%); BPD infants (n=9) range 0%-10.5% (weighted mean, 1.6%; median, 0.0%); infants of mixed high-risk status (n=6) range 0-12.5% (weighted mean, 5.0%; median, 4.0%). CFR among infants without known risk factors range 0-1.5% (weighted mean and median, 0%).

Conclusions: Mortality during hospitalization for severe RSV is rare among infants without underlying risk factors for RSV, but occurs more commonly among high-risk infants. Infants with CHD who are hospitalized for RSV may be at particularly high risk of mortality during the RSV hospitalization.

VIRAL CO-INFECTIONS IN ACUTE BRONCHIOLITIS - IMPACT ON DISEASE SEVERITY IN HOSPITALIZED CHILDREN

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Background and aims: In last decade new respiratory viruses (RV) were discovered, but their influence, especially as co-infections on bronchiolitis severity is still poorly understood. This study evaluated the impact of RV co-infections in hospitalized children with bronchiolitis.

Methods: Rhinopharyngeal swabs were taken from children with acute bronchiolitis who were admitted to Department of Infectious Diseases, University medical Centre Ljubljana in two year period. RV were detected by a real-time RT-PCR assay performed on Step One Real-Time PCR system (Applied Biosystems, USA). Samples were simultaneously tested for influenza virus (A, B), RSV, PIV (1-3), rhinovirus (hRVs), adenovirus (AdV), human metapneumovirus (hMPV), coronaviruses (hCoV) and human bocavirus (HBoV). Median bronchiolitis severity score (BS) at admission was calculated (comprised of: wheezing, retractions, O₂ saturation, respiratory rate, heart rate, general condition); maximum total score 18 indicated severely ill patient.

Results: 332 children with acute bronchiolitis were included. Viral infection was confirmed in 283 (85,2%) patients; single virus was detected in 201 (71%) and co-infections in 131 (29%) cases. HCoVs, AdV, HBoV and PIV appeared mostly as co-infections (95, 84,4, 73,3 and 52,4% respectively). Co-infections with RSV and AdV had higher BS (6) compared to mono-infections with these viruses (BS 5). There were no differences in BS for mono- and co-infections caused by hRV and HBoV (6 and 5,5).

Conclusions: Viral co-infections in acute bronchiolitis are commonly diagnosed. The presence of RSV and AdV and not hRV and HBoV co-infections adds to the severity of bronchiolitis. Further research is needed to evaluate the real impact of different viruses in co-infections.

INCREASING INCIDENCE OF PARAPNEUMONIC PLEURAL EFFUSIONS (PPES) REQUIRING DRAINAGE IN CHILDREN: AN EXPERIENCE FROM A UNIVERSITY PEDIATRIC DEPARTMENT

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Background: Various reports have demonstrated an increased incidence of PPEs in children despite introduction of heptavalent pneumococcal vaccine (PCV). In our country PCV7 was introduced in 2006, PCV10 in 2009 and PCV13 in 2010.

Aims: To study the incidence of PPEs in our area and examine the possible influence of pneumococcal vaccination.

Methods: We reviewed records of children \leq 14yrs hospitalized for PPE requiring drainage from 1-1994 to 12-2011. The annual rate and its change trend was evaluated. Culture, PCR results and PCV history were collected. Serotyping of *Streptococcus pneumoniae* isolates for 1, 3, 4, 6, 14, 18C, 19A, 19F, 23F was conducted routinely after 2006.

Results: Among 111 PPEs treated during 18 years, a continuously increasing annual rate was recorded (mean 2.68%, $p=0.017$). *Streptococcus pneumoniae* was indentified in 24 pts (6 by culture and 18 by PCR), *Streptococcus pyogenes* in 3, MRSA in 1, *Haemophilus* spp. in 1 and H1N1 in 3 pts. No patient had received newer PCVs. Among *S. pneumoniae* serotyped, 3 belonged to serotype 1, 4 to serotype 3, 2 to serotype 19A and 1 to serotype 19F while, 10 were non-typable). All but one positive samples serotyped including the non-typable ones were non-PCV7 serotypes. All identified serotypes are included in the PCV13.

Conclusions: PPE incidence in children has been continuously increasing despite adequate PCV7 coverage. Recently, pneumococcal PPEs have been almost exclusively caused by non-PCV7 serotypes. Future studies should investigate the benefit of the use of new PCVs on the incidence and etiology of PPEs.

PREDICTING DISEASE SEVERITY WITH ACUTE PHASE PROTEINS IN PEDIATRIC PATIENTS WITH VIRAL LOWER RESPIRATORY TRACT INFECTIONS

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Background: Viral lower respiratory tract infections (vLRTI) are common in pediatric patients and can deteriorate fast into respiratory failure. Prediction models to guide admission could reduce hospitalizations. In infectious diseases C-reactive protein (CRP), an acute phase protein, is commonly used to assess the extent of inflammation. In this study the role of CRP, other pentraxins and properdin is evaluated for their ability to predict disease severity in pediatric patients with acute vLRTI.

Methods: Children < 3 years of age presenting in a hospital with acute vLRTI were included in this study. Blood samples were collected at presentation (acute) and after 4-6 weeks (recovery). Levels of serum amyloid A (SAA), serum amyloid P component (SAP), pentraxin-3 (PTX3), properdin and CRP in plasma were determined by ELISA. Patients were retrospectively allocated into mild (no oxygen needed) or severe disease (supplemental oxygen needed).

Results: All proteins were significantly increased in the acute (n=63) compared to the recovery (n=37) samples. Only CRP, SAA, PTX3 and properdin could differentiate between mild and severe disease. Combinations of the individual markers and age (< 2 months) increased the test performance reflected by sensitivity and specificity, with an optimal performance by CRP, properdin and age (sensitivity 92% and specificity 92%, PPV 92% and NPV 76%).

	Total N=100	Mild N=52	Severe N=48	P-value
Properdin (SEM)	275,3 (44,5)	744,1 (31,9)	492,8 (74,6)	< 0.05
PTX3 (SEM)	169,4 (26,7)	771,6 (27,3)	271,9 (42,8)	<0.01
SAP (SEM)	950,2 (157,0)	196,5 (124,9)	1766,8 (250,1)	NS
SAA (SEM)	456,7 (96,3)	1,45 (0,6)	949,8 (1752,3)	0.01
CRP (SEM)	1703,4 (350,8)	4,6 (1,3)	3543,8 (633,7)	0.001

[Table 1. Disease severity and mean protein levels]

	Cut off	Sensitivity	Specificity	PPV (positive predictive value)	NPV (Negative predictive value)	AUC (Area under the curve)
Properdin	15,5 ug/l	84,6%	68,8%	74,6%	80,5%	0,763
PTX3	85,8 ng/l	82,7%	75,0%	78,2%	80,0%	0,843
SAP	31,3 mg/l	80,8%	79,2%	80,8%	79,2%	0,828
SAA	2,1 ug/l	86,5%	75,0%	78,9%	83,7%	0,856
CRP	10,8 mg/l	86,5%	75,0%	78,9%	83,7%	0,849
≥ 1 CRP, Properdin and age < 2 months		92,3%	91,7%	92,3%	75,9%	

[Table 2. Test characteristics of different markers]

Conclusion: Our preliminary results indicate that a combination of age, properdin and CRP might be useful in clinical decision making. Currently a new validation cohort of vLRTI patients is used to confirm our findings.

EARLY CONGENITAL SYPHILIS - PUBLIC HEALTH PROBLEM IN AN EASTERN EUROPEAN COUNTRY

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Congenital infections represent by themselves a public health problem, mostly in a developing country. Syphilis, as a sexually transmitted disease, may generate serious sequelae for a newborn contaminated by transplacental transmission.

Aim: The present study is designed to evaluate the actual incidence, diagnostic and consequences of congenital syphilis in a level III maternity hospital from an eastern European country, between 2007-2010.

Methods: A prospective retrospective epidemiological study was performed on a group of 61 cases, diagnosed with congenital syphilis from a total of 28226 births. The study focused on incidence, maternal risk factors, maternal and neonatal serology, gestational age, Apgar score, neonatal clinical signs and complications.

Results: The incidence of 2,16 ‰ still represents a public health problem. The main risk factors were poor social-economic status: 68,85% mothers from rural, 85,3% mothers without work or income, 65,57% poor educational level, lack of perinatal care during pregnancy (78,69%). The average maternal age was 25,6 years. Symptomatic syphilis was present in only 14,75% of cases confirmed through serum tests. There was a significant statistical correlation between congenital syphilis and restricted intrauterine growth.

Conclusion: More efforts should be done for a better implementation of maternal programs of syphilis screening in pregnancy, as a part of infection program screening. Also, better prevention methods for mothers with high risk are needed.

MISSED OPPORTUNITIES TO TREAT - SYPHILIS MANAGEMENT IN A LONDON HOSPITAL

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Background: Adequate treatment of syphilis in pregnancy reduces risk of congenital transmission to < 10% but requires effective communication between Genitourinary Medicine (GUM), Neonatology and Obstetrics.

Methods: Retrospective review 1/1/2009 and 31/12/2010 of maternal positive syphilis serology in pregnancy and their infants. To establish: maternal treatment in GU clinic, pregnancy outcomes, investigation and treatment of the newborn.

Results: 22 women had positive syphilis serology in pregnancy representing 20 livebirths and 2 miscarriages. 11 women had late latent syphilis, 1 early latent, 1 reinfected since last pregnancy, 9 unknown syphilis status. 16 infants had syphilis serology checked. Two had lumbar puncture, fundoscopy and long bone radiographs as mothers were not treated in pregnancy (one refused, one delayed notification from microbiology of positive result). Both infants received penicillin until syphilis serology results available. No confirmed cases of congenital syphilis. 14 mothers were asylum seekers in temporary accommodation. Four children were not screened at birth and lost to follow up: one moved away, three mother/baby casenotes had inaccurate/missing documentation of maternal syphilis status at postnatal check. 40% complete documentation from all departments for mother and infant, 80% of infants received correct investigations and follow up.

Conclusions: Opportunities to treat women, and reduce the risk of vertical transmission of syphilis, were missed due to interdepartmental communication weaknesses and exacerbated by population mobility. Recommendations include the use of a modified multidisciplinary proforma for GUM/neonatal and obstetric departments, clear accountability, improved communication networks, education and documentation combined with close microbiology liaison to expedite and disseminate results.

EPIDEMIOLOGY OF HPV INFECTION IN A SAMPLE OF GIRLS AGED 13-19 YEARS

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Background and aims: Few data are available on the epidemiology of HPV infection in adolescent age. This information is important considering that HPV vaccination is recommended in girls aged 11-12 years and in some countries also in those aged 13-19 years.

Methods: A sample of 804 girls (mean age \pm SD, 16 ± 1.3 years) attending two pediatric units in Milan, Italy, was enrolled. A questionnaire on subjects' demographic and medical history was completed and a urine sample for HPV DNA detection was obtained. Genotyping of HPV-DNA positive samples was obtained by RFLP.

Results: Of the 771 (95.9%) girls who already had a result of the HPV test, 9 (1.2%; 95% confidence interval: 0.5-2.2) were positive. Among the 240 sexually active girls (age range, 14-19 years), 3.8% had HPV positive tests (median age, 16.4 years). In the 239 girls aged 13-15 years, 54 (22%) were effectively vaccinated, whereas the proportion of vaccinated girls among those aged 16-19 years was 9% (n=49). Among the 9 HPV positive tests, 8 were associated to high-risk genotypes (HPV 16, HPV 31, HPV 35, HPV39, HPV 51, HPV 56, HPV 58, HPV 82) and one with a low-risk genotype (HPV6).

Conclusions: In this sample, no HPV infection was found in girls aged 13-15 years and the overall HPV prevalence observed was low, although the small sample size limits any generalization. The proportion of vaccination remains low in girls in the age group 13-15 years (supposed to be potentially involved in the HPV vaccination program).

FIVE YEARS OF PEDIATRIC APPENDICITIS: ANTIBIOTIC PROPHYLAXIS AND TREATMENT, GERMS AND COMPLICATIONS

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Background: Controversy persists in the management of appendicitis with regards to antibiotic choice and duration. Perhaps the fear of complications may lead to an overtreatment of the simple forms.

Methods: We reviewed our case records focusing on intraoperative diagnosis, treatment, germs and complications. All children undergoing appendicectomy from August 2006 to August 2011 in our Surgery Clinic and being hospitalized in our Pediatric Clinic were admitted in the study.

Results: We analyzed 192 cases (114 M, 78 F; mean age 9,9 years). We had 6 negative appendicectomies, 147 simple forms, 39 (20,3%) complicated appendicitis (gangrenous/perforated) and 24 (12,5%) post-operative complications (half in the simple forms and half in the complicated ones). Peritoneal swabs were obtained in 78% of the cases and 27% were positive. We found E coli in 83% of swabs (alone or with other germs), most of them sensible to all antibiotics. 13 multiresistant E.coli were isolated, 10 of which in the same 14 months (Dec 2007-Jan 2009) and 5 in simple appendicitis. Other germs found were streptococci, pseudomonas (half antibiotic-resistant) and bacteroides. All the patients received antibiotic prophylaxis with ceftazidime (30mg/kg) ev 30' before surgery. 85 patients (44%) received an antibiotic therapy; 39% of them with ceftazidime alone for 3-6 days (simple forms), and 60% with multiple antibiotics for a longer period (complicated forms).

Conclusions: Because of the presence of complications and antibiotic resistance also in simple appendicitis, our data suggest that a careful behaviour with a wide spread antibiotic therapy may be reasonable also in simple forms.

ANTIREFLUX SURGERY AND PREVENTION OF RECURRENT URINARY TRACTION INFECTIONS IN CHILDREN (WITH VESICoureTERAL REFLUX)

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Introduction: Reflux is one of the common causes of recurrent urinary tract (UTIs) infection in children, which may lead to pyelonephrosis, renal failure and finally need for renal transplantation. This study is evaluated the relation of antireflux surgery and prevention of recurrent UTIs.

Material and methods: A total of 40 child with vesicoureteral reflux which was accompanied with recurrent febrile and non febrile UTIs and documented grade II-IV reflux underwent antireflux surgery. All the patients had a history of UTI 2 - 4 time per year.

Results: From the 40 patients, 22 were operated using bilateral Gil-vernet antireflux surgery, 9 treated with Urocol injection, 6 treated with Vantris injection and 3 patients operated with Leadbetter-Politano type surgery. 3 months after antireflux surgery, the treatment was successful in 26 patients and in 4 patients it was failed. In 3 month up to 2 years follow up of 26 successful treated patients urinary tract infection was eradicated in 70% and relapse was seen in 30% of cases. In the 4 failed treated patients also relapse of UTI was seen.

Recommendation: Antireflux surgery in children with vesicoureteral reflux is highly successful treatment option which greatly decreases the relapse of urinary tract infection. If medical treatment is failed in treatment of reflux, surgery specially in grade III, IV or V is recommended.

RISK FACTORS FOR SURGICAL SITE INFECTION IN PEDIATRIC SURGERY IN DEVELOPING COUNTRY: A FIVE YEARS PROSPECTIVE ANALYSIS

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Surgical site infections (SSIs) continue to represent a real risk associated with any surgical procedure. SSIs have a multitude of risk factors and awareness of these can help to promote preventive strategies.

Objective: To identify SSI risk factors in pediatric surgery patients.

Methods: Prospective surveillance of SSI according to National Healthcare Safety Network (NHSN) protocols for events occurred between nov/2006 and oct/2011.

Results: The SSI rate during the period under study was 1% (36 cases in 3,836 patients). American Society of Anesthesiology (ASA) score, duration of operation (hours), wound class and patient age (years) were the main risk factors for SSI. Besides, pre-operative length of stay (days) was identified as an important SSI risk factor: patients with more than four days of length of preoperative hospital stay have 10 times more risk than patients operated before this period of time. SSI incidence was, according to pre-operative length of stay ≤ 4 days: 0.6% = 20/3568; pre-operative length of stay > 4 : 5.4% = 14/259 (p-value < 0.001). The incidence of infection was, according to Risk index category of NHSN - IRIS 0: 0.3% = 2/791; IRIS 1 or 2: 3.9% = 6/154 (Relative Risk = 15; p < 0.001). Type of surgery (urgency versus elective), general anesthesia and prosthesis surgery were not associate with SSI.

Conclusions: We identified risk factors for infection in patients undergoing pediatric surgery in a Brazilian philanthropic hospital. The preoperative length of stay was the most important extrinsic risk factor identified.

COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS SECRETING PANTON-VALENTINE LEUKOCIDIN (PVL) PNEUMONIA IN CHILDREN

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Background and aims: Few studies have focused on community-acquired *Staphylococcus aureus* (SA) pneumonia in children. We aimed to describe their clinical and microbiological characteristics in a French tertiary care center.

Methods: Data were retrospectively collected from children aged < 18 years, who were hospitalized for community-acquired SA pneumonia between 2005 and 2010 in Robert Debré University Hospital, Paris, France. Panton-Valentine Leukocidin (PVL) gene detection was performed by polymerase chain reaction.

Results: A total of 18 patients were included. The incidence of SA pneumoniae increased from 0.72 per 1000 patients admitted during 2005-2008 to 2.84 during 2009-2010. The median age was 11 months (range 46 days to 16,5 years) and 83 % of the patients were < 2 years. Methicillin-susceptible SA (MSSA) caused 72,2 % of the infections. PVL gene was detected in 17 out of 18 cases (94,4%) and 72 % of the PVL positive strains were methicillin-susceptible. Clinical presentation was pneumonia with pleural effusion or empyema in 14 patients (78 %), acute respiratory distress syndrome with diffuse bilateral infiltrates in 2 patients, and lung abscess in 2 patients. Eight patients were admitted in intensive care unit, 7 required mechanical ventilation and 2 patients needed surgical drainage for empyema. Median duration of antibiotic therapy and length of stay in hospital were 46 days (range 34-66) and 16 days (range 10-43) respectively. .

Conclusion: The incidence of community SA pneumoniae increased during the study. Most of them were caused by MSSA secreting PVL and concerned children of less than 2 years.

MICROBIOLOGICAL CHARACTERIC PATTERN OF STAPHYLOCOCCUS AUREUS WITH STAPHYLOCOCCAL SCALDED SKIN SYNDROME IN TOKYO

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Background: Staphylococcal Scalded Skin Syndrome (SSSS) is a common toxin mediated disease in young children. Community Acquired Methicillin Resistant Staphylococcus aureus (CA-MRSA) is a common cause of SSSS in Japan.

Objective: To identify the characteristic pattern of Staphylococcus aureus with pediatric SSSS patients in Japan.

Method: We retrospectively reviewed medical charts and microbiological results with diagnosis of SSSS between January 2008 and December 2011 at Fuchu hospital and Tokyo Metropolitan Children's Medical Center in Tokyo, Japan. We performed susceptibility tests, coagulase typing and toxin tests on these Staphylococcus aureus isolates.

Result: We identified 19 cases of SSSS in children. Seventeen cases(89.4%) were caused by MRSA. All of MRSA isolates were susceptible to Vancomycin and Sulfamethoxazole-Trimethoprim. Fourteen cases(73.6%) of Staphylococcus aureus had Coagulase I. Exfoliative A toxin and B toxin were found in 1 and 17 isolates, respectively. TSST-1 was found in 2 isolates. Staphylococcal enterotoxin and Pantone-Valentine leucocidin (PVL) were negative from all the tested isolates.

Conclusion: MRSA with Coagulase I was a major organism that causes SSSS in Tokyo area. Exfoliative B was a dominant etiologic toxin. PVL strain was not found in our study. If patient is severe enough to treat with antimicrobial agents, Vancomycin and Sulfamethoxazole-Trimethoprim would be the choice of empiric treatment for SSSS.

OUTBREAK OF HAEMOLYTIC UREMIC SYNDROME IN A SINGLE ITALIAN INSTITUTION: EMERGING OF NEW STRAINS OF NON-O157 ENTEROHEMORRAGIC ESCHERICHIA COLI

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Background and aims: Diarrhea associated Hemolytic uremic syndrome (HUS) is a leading cause of acute renal failure in children and it is mainly caused by enterohemorrhagic *Escherichia coli* producing Shiga-toxins (STEC). The most common organism is STEC O157, but recently other serotypes especially O26 have emerged as significant causes of HUS. During a 18 month-period from March 2010 to September 2011, five children aged between 9 months and 4 years were hospitalized in our Pediatric Infective Unit for vomiting and bloody diarrhea. Hospitalization was required in order to perform rapid intravenous rehydration. Emergency laboratory tests revealed a HUS complicated by severe renal failure in all children.

Methods: Stool cultures and serology were performed for every patient by the Public Health Laboratory Service in order to find Shiga toxin-producing organisms (*Escherichia coli* O157 and non-O157).

Results: Microbiological investigations revealed an underlying infection sustained by STEC non-O157 in all patients. Three children had *Escherichia coli* O26 toxin isolated; the two other episodes of HUS were sustained by *Escherichia coli* O11 in both children. Four out of five patients required dialysis and survived to severe renal failure. One patient unfortunately died despite prompt blood exchange.

Conclusions: We report on the largest cluster of STEC O26 occurred in a single pediatric Italian institution and responsible of severe and complicated HUS. Recent evidences suggest that new strains of STEC non-O157 are emerging causes of HUS in pediatric population. Laboratory studies for diagnosis have not been standardized yet and only few cases are reported in literature.

INFANT BOTULISM: A DIAGNOSTIC AND THERAPEUTIC CHALLENGE

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Background and methods: Botulism, a potentially fatal acute paralytic illness, is caused by *Clostridium botulinum* neurotoxin; infant botulism being the most common form. Diagnosis can be difficult and delayed given the broad clinical manifestations. Specific treatment consist of intravenous botulism immune globulin (BabyBIG) at early stage of the disease, however, it's highly costive and its availability is limited.

Results: We report two severe cases of infant botulism diagnosed at our reference hospital in 2008 and 2011. Both infants were feed with mix formula, none of them ingested honey and presented at 32 and 56 days of age with constipation, progressive muscle weakness, fatigue, altered cry and feeding difficulties. Physical exploration revealed poor head control, ptosis, facial weakness, decreased spontaneous movement, weak suck and cry. Initial presumed differential diagnosis included neuromuscular disorder and sepsis. Electromyogram findings were not consistent with infant botulism. Stool samples were positive for clostridium toxin whereas formula milk samples were negative, leaving the source of infection unclear. Case 1 was managed symptomatically requiring PICU admission for 10 days whereas patient 2 received intravenous immunoglobulin, IVIG (1g/kg for 2 days) on day 5 of symptoms and improved clinically within 48h post infusion. Hospital stay was 23 and 17 days respectively with complete clinical recovery in follow-up.

Conclusions: Infant botulism should be suspected in infants with constipation, muscle weakness, difficult feeding and altered cry. Mainstay of management consist of supportive care +/- infusion of BabyBIG, however IVIG might be an effective alternative when the later is not available.

FAMILY OUTBREAK OF FOOD-ASSOCIATED BOTULISM; CLINICAL AND LOCAL LABORATORY FEATURES

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Background and aims: Botulism is a neuroparalytic disease caused by a heat-labile toxin produced by *Clostridium botulinum*. We present here a case of three children of the same family, all aged under 10yrs, who presented with foodborne botulism, resulting from ingestion of commercial korma sauce which contained preformed toxin. We will present clinical features, laboratory issues, and learning outcomes from the outbreak.

Methods: The children presented at our institution with similar features of descending paralysis with diplopia, dysarthria and dysphagia. A clinical diagnosis of botulinum toxin poisoning was made, and antitoxin administered. Clinical specimens from the patients and also from food consumed confirmed the diagnosis. Two siblings required ventilation and prolonged intensive support. All three survived and continue to make slow/good recuperation.

Results:

- Liaison between clinical and laboratory staff important
- Correct specimens to be taken ; pre-treatment required for mouse bioassay/PCR
- Notifiable disease-public health involvement
- Press release and national interest
- External agency involvement (HPA; BTS)

Conclusions: Foodborne botulism is rare in the UK. This family outbreak in three children was quickly identified and supportive care and antitoxin instituted. Clinicians should be aware of the possibility of botulism in patients presenting with symmetrical descending paralysis.

RISK OF INFECTIOUS DISEASES DISSEMINATION FROM ADOPTEES

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Background and aims: One child out of every 100 in France is adopted, and 80% of adoptions are international. This study sought to evaluate the frequency of infectious diseases that the children present on arrival and that may disseminate from adoptees to their new family.

Methods: We retrospectively reviewed the chart of 128 consecutive adoptees (male: 51%; mean age: 39 months \pm 2) seen at a clinic dedicated to international adoption (Clermont-Ferrand hospital, France) since 2010. All children had a physical examination and a standardized blood test.

Results: 2% were diagnosed with acute hepatitis A. There was no familial dissemination and 44% were immunized against hepatitis A. Two had chronic hepatitis B diagnosed on arrival, whereas they were tested negative in their country of origin. None was HCV or HIV positive. All children coming from Haiti were tested negative for HTLV. 88 children were screened for *staphylococcus aureus* nasal carriage. Of these, 14% (8 SAMS, 4 MRSA) were positive, including one whose *S. aureus* was transmitted to his father, who required hospitalization. No active tuberculosis was diagnosed. 32% were diagnosed with tinea (mainly *T soudanese* and *T tonsurans*). 4 intra-familial transmissions were diagnosed at the date of consult (3 involving mothers, one involving brother and cousin). 7% had scabies diagnosed with no familial dissemination.

Conclusions: Internationally adopted children are at risk to transmit infectious diseases, which should be detected shortly after arrival. Future parents should also be informed and vaccinated before adoption.

CHILDREN ARE DISPROPORTIONATELY AFFECTED BY INFECTIOUS DISEASE IN COMPLEX HUMANITARIAN EMERGENCIES: PAKISTAN FLOODS 2010

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Introduction: Complex humanitarian emergencies (CHE), such as the 2010 floods in Pakistan are catastrophic public health emergencies, which put vulnerable population at greatest risk of disease, particularly communicable diseases. The objective of this study is to provide with field epidemiological and clinical data in a CHE setting with the objective to guide quality and effective emergency response.

Materials and methods: In 2010 a team from AECID (Spanish Agency for International Development and Cooperation) participated in coordination with the Pakistani government in a medical team response in Dera Allah Yar, Baluchistan.

1571 patients (43% female) were attended over a six-day period in a district hospital and refugee camp and data was collected on the field for surveillance.

Results: 42% of patients were under 15 years of age and 82% of them were affected by infectious diseases, as compared to 48% in adults ($p < 0,001$). Children had a significantly higher incidence of skin, gastrointestinal and eye infection (27, 25 and 7% vs 18, 4 and 5% respectively) whereas respiratory infections were as prevalent in both groups (12% in children and 9% in adults). The use of antibiotics was higher in children (70% vs 50%, $p < 0.001$), including betalactams, albendazol, cotrimoxazole and cloxaciline, whereas no difference was seen in the use of antifungals or tetracyclines.

Conclusion: Children continue to carry the highest burden of disease in communicable diseases, particularly in CHE settings. Field data, although scarce and difficult to obtain, is crucial for better guiding public health response and improving children health.

PEDIATRIC RESEARCH IN COMPLEX HUMANITARIAN EMERGENCIES (CHE): OPTIMIZING PUBLIC HEALTH APPROACHES. DERA ALLAH YAAR, BALUCHISTAN, PAKISTAN FLOODS 2010

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Background: Field epidemiological and clinical research in CHE is crucial for guiding high quality and effective public health emergency responses.

Aims: to provide with field data that quantifies paediatric morbidity and assesses medical needs in a CHE setting, the 2010 floods in Pakistan.

Materials and Methods. Members of AECID (Spanish Agency for International Development and Cooperation) participated in coordination with the Pakistani government in a medical team response in a district hospital and refugee camp. 1571 cases were attended over a six-day period and data was collected on the field for surveillance.

Results: 664 cases (42%) were under 15 years of age, 50% were below 5y (median 4y, IQR 2.8y) and 47% of paediatric cases were female. 82% suffered from an infectious disease, most common were skin (27%), gastrointestinal (25%), respiratory (12%), pharyngeal (7%) and eye infection (5%). Malnutrition was evidenced in 8% of all paediatric cases, and 2% were suspected to have anaemia. Most common medication prescribed were antibiotics (38.5%), followed by analgesics (36%), vitamins and/or iron supplements (27%), oral rehydration solutions (24%) and topic treatments or (22%). Most common antibiotics used were betalactams, albendazole, cotrimoxazole and cloxaciline. 4.5% of cases were admitted to day-hospital for intravenous treatment and one died (0.45%).

Conclusion: The principle paediatric diagnosis was infectious, with a high % of underlying chronic diseases such as malnutrition or anaemia. Such analysis depicts the need for emergency care medication kits that combine acute care as well as vitamins and dietary supplements.

PRE-TRAVEL COUNSELLING IN GREECE FOR CHILDREN**H. Maltezou**¹, A. Pavli¹, A. Spilioti¹, P. Katerelos¹, M. Theodoridou²¹*Hellenic Center for Disease Control and Prevention*, ²*University of Athens, Athens, Greece***Aim:** The aim of this study was to describe the profile of children seeking pre-travel counselling in the Health Departments of all (57) Prefectures across Greece.**Methods:** Data were collected prospectively from 1/2008 through 12/2010.**Results:** During the study-period, 4065 persons sought pre-travel services in the 57 Prefectures, including 128 (3.15%) children < 15 years old (74 boys;57.8%). Of the 128 children, 118 (92.2%) were of Greek nationality. Prevalent travel destinations were sub-Saharan Africa (54 children;42.2%), South America (18;14.1%), Middle East (16;12.5%), Indian subcontinent (12;9.4%), and Southeast Asia (7;5.5%). Regarding duration of travel, 76 children (59.4%) stayed for < 1 month, 34 (26.6%) for 1-6 months, and 10 (7.8%) for >6 months. Most children (59.4%) stayed in a hotel, while 27.3% in a local residence. Overall, 53.1% of children stayed in urban areas, 35.2% visited both rural and urban areas, and 1.6% stayed in rural areas exclusively. Purpose of travel included recreation (81 children;63.3%), work (24;18.8%), visiting friends and relatives (VFRs) (14;10.9%), and unknown (9;7%). Among the 14 children VFRs, 10 traveled to Africa and 4 to Indian subcontinent. Logistic regression analysis revealed that children more frequently stayed in local residences and traveled for recreational purposes or to VFRs (27.3%, 63.3%, and 10.9%, respectively), compared to adults (11.9%, 58.8%, and 4%, respectively). Antimalarial chemoprophylaxis was prescribed to 64.8% and 66.7% of children traveling to sub-Saharan Africa and Indian subcontinent, respectively.**Conclusions:** There is a need to increase awareness and education of professionals providing travel health services for children in Greece.

BLACKWATER FEVER AFTER INTRAVENOUS QUININE TREATMENT IN A CHILD WITH SEVERE PLASMODIUM FALCIPARUM MALARIA

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Introduction: Blackwater fever (BWF) is rarely observed in Europe. Worldwide resurgence of BWF has been described since 1990.

Case report: A 6 year old child born in Spain, started with high fever and prostration in Gambia, while visiting relatives. Antimalarial prophylaxis with mefloquine had been irregularly administered by two months. His brother died from malaria at a local hospital. Malaria was diagnosed, but no treatment was administered before arriving in Madrid. At admission, high fever, somnolence, prostration and mild respiratory distress were observed. Plasmodium falciparum parasitemia was 6% and haemoglobin 6,3 g/dl. Intravenous quinine (Quinimax®) and clindamycin were started, together with cefotaxime, fluids and a single packed red blood cells transfusion. Parasitemia dropped to 1% in 24 hours. Haemoglobinuria and renal failure, secondarily to intravascular haemolysis, appeared 24 hours after administration of first quinine dose. Pulmonary oedema worsened, requiring mechanical ventilation. Hypotension required catecholamines infusion. Quinine was discontinued, and atovaquona-proguanil added. Coombs test and cryoglobulins were negative. Artemeter was added at 48 hours of treatment, with subsequent complete resolution of the situation. Haemoglobin study showed no abnormalities and G6PDH was normal.

DISCUSSION: Resurgence of BWF confirms that aryl-amino-alcohol drugs (quinine, mefloquine, halofantrine) act like triggers in falciparum malaria when any of these drugs have been previously taken.

Conclusions: Aryl-amino-alcohol drugs should be used with caution. Risk of BWF and higher effectiveness of parenteral artemisinin derivatives suggest these drugs should replace quinine as first choice to treat severe malaria. No aryl-amino-alcohol drug should be used in patients with history of BWF.

PROGNOSIS OF THERAPEUTIC FAILURE IN PEDIATRIC PATIENTS WITH AMERICAN CUTANEOUS LEISHMANIASIS

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Background: American cutaneous Leishmaniasis (ACL) is endemic in the highland regions of Peru where children are particularly susceptible to develop deforming lesions due to high rate of failure after conventional treatment with pentavalent antimonials. Because treatment of established lesions is the cornerstone on control in several endemic regions, simple tools to evaluate risk of failure are necessary to achieve early detection and treatment of relapsing cases determining in decrease chances of disfiguring scars.

Material and methods: A cohort study was carried out at the Leishmania clinic (Cayetano Heredia Hospital - Institute of tropical medicine Alexander von Humboldt) in the period 2001 - 2009. Only patients under 15 years with confirmed diagnosis of ACL and without prior therapy were included. Patients received Sodium stibogluconate 20mg/Kg/day for 20 days according national guidelines for treatment of ACL and follow-up for 3 months or less depending of the development of signs suggestive of relapse.

Results: 80 patients coming mainly from endemic areas of *L. (V). peruviana* (85%) were included. From the multivariate model, the risk factors involved in treatment failure were: at least one facial lesion (OR:5; p=0.01), cutaneous lesion of less than 6 weeks of duration (OR: 5,6; p=0.009), a negative scraping (OR: 0,1; p=0.06) and to be a native case (OR:0,2; p=0.01).

Conclusions: Localization of lesions, duration of disease, a negative scraping and to be a native case were prognosis factors associated with treatment failure in pediatric patients from Cayetano Heredia National Hospital treated with Sodium stibogluconate during 2001-2009.

WHY DID EARLY FLUID RESUSCITATION INCREASE MORTALITY IN AFRICAN CHILDREN WITH SEVERE FEBRILE ILLNESS AND SHOCK IN THE FEAST TRIAL?

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Background: Early fluid boluses in African children with severe febrile illnesses increased absolute 48-hour mortality by 3.3% compared to controls. We explored the effect of boluses by clinical presentation at enrolment, by change in bedside observations over the first hour following randomization, and on different modes of death according to terminal clinical events (TCE).

Methods: 3141 children (median(IQR) age 24(13-38) months), presenting to African hospitals with febrile illness plus impaired consciousness or respiratory distress and signs of impaired perfusion were randomized to boluses: 20-40ml/kg 5%albumin or 0.9%saline(n=2047) or control(n=1044). Three presentation syndromes (severe acidosis/shock, respiratory, neurological) and 3 predominant TCEs (cardiovascular collapse, respiratory, neurological) were pre-defined, and adjudicated blind to randomised arm.

Results: Among 2396/3141(76%) classifiable participants, 1647(69%) had severe acidosis/shock, 625(26%) respiratory and 976(41%) neurological presentation syndromes, alone/combined. Excess mortality in bolus versus control was apparent for all syndromes and for all their component features. By one hour, shock resolved more frequently in bolus vs control (43% vs 32%, $p < 0.001$), but excess mortality in bolus arms occurred irrespective of shock resolution. 9% bolus versus 7% control children developed hypoxia de novo by one hour ($p=0.06$), but this did not explain excess mortality with boluses. Excess terminal clinical events with boluses were mainly cardiovascular collapse (123 TCEs: 4.6%bolus vs 2.6%control, $p=0.008$), then respiratory (n=61; 2.2%vs1.3%, $p=0.09$) and least, neurological (n=63, 2.1%vs1.8%, $p=0.6$).

Conclusions: Excess mortality from boluses occurred in all subgroups. Cardiovascular collapse rather than fluid overload appeared to contribute most to excess deaths with bolus fluid resuscitation.

CONTRIBUTION OF REAL-TIME POLYMERASE CHAIN REACTION FOR THE DIAGNOSIS OF LEPTOSPIROSIS IN CURITIBA (SOUTHERN BRAZIL)

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Introduction: The quality of epidemiological surveillance and the outcome of Leptospirosis depend on a correct and timely diagnosis and treatment. In the first phase of the disease, especially when isn't possible to detect specific antibodies by serological techniques, the Polymerase Chain Reaction (PCR) is a complementary tool that allows the early infection confirmation and differential diagnosis of other febrile illnesses.

Results: From Jan-July/2010, 540 patients have been reported suspected for Leptospirosis in Curitiba (Southern-Brazil), and 131(24%) confirmed. From jan-july/2011, 1228 patients were investigated, of whom 169(14%) were confirmed. The mortality rate was 18%(24/131) in 2010 and 17%(28/169) in 2011. Of the suspected cases, ~80% had symptoms for less than 7 days, 92% have a first sample for serology (ELISA IgM), but only half for the second serology (41% in 2010 and 54% in 2011). The first serology was positive in 14%(70/495) in 2010 and 8%(95/1137) in 2011. Blood sample for PCR was collected on the same date of the first serology in 33%(177) suspected cases of 2010 and 61%(748) in 2011, and was positive in 18% (31) and 9% (71), respectively. The first serology was negative and PCR positive in 24 cases of 2010 and 41 cases of 2011, indicating the contribution of PCR for early diagnosis.

Conclusion: The present study evidence an increase of Leptospirosis early diagnosis with a real-time PCR, but is essential to constant training health professionals to clinical suspicion, blood collection and early treatment of all patients with clinical and epidemiological characteristics compatible with Leptospirosis.

PLASMODIUM FALCIPARUM MALARIA CAUSES PROLONGED IMPAIRMENT OF NEUTROPHIL OXIDATIVE BURST ACTIVITY

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Background and aims: Malaria causes susceptibility to non-typhoid Salmonella (NTS) bacteremia. We have shown that in mice malarial hemolysis impairs killing of NTS by reducing the ability of circulating neutrophils to mount an effective oxidative burst. Suppression of the neutrophil oxidative burst is a consequence of induction of the cytoprotective heme degrading enzyme heme-oxygenase-1 (HO-1) in neutrophil progenitors in bone marrow. In this study we looked for evidence of impaired neutrophil function in *Plasmodium falciparum* malaria, and for associations with hemolysis and HO-1 induction.

Methods: We quantified neutrophil oxidative burst and degranulation using flow cytometric assays in acute and convalescent samples from 58 Gambian children with *P. falciparum* malaria. We assessed HO-1 expression by intracellular flow cytometry, qRT-PCR and ELISA, and we assessed the role of hemolysis in HO-1 induction by measuring parasite biomass, erythrocyte count, and plasma heme, as well as haptoglobin and hemopexin and expression of their respective receptors.

Results: In acute malaria there were two distinct populations of neutrophils, the major population having reduced oxidative burst activity. Over 8 weeks of follow-up neutrophil function progressively normalized towards a single population of neutrophils with normal oxidative burst activity. The degree of oxidative burst impairment correlated significantly with markers of hemolysis. HO-1 expression was increased in blood during acute malaria, although at a cellular level its expression was modulated by changes in expression of the haptoglobin receptor (surface CD163).

Conclusions: Neutrophil dysfunction occurs in children with *P. falciparum* malaria and may explain the associated susceptibility to NTS infection.

A SORE THROAT EVERY CLINICIAN SHOULD KNOW - LEMIERRE'S DISEASE

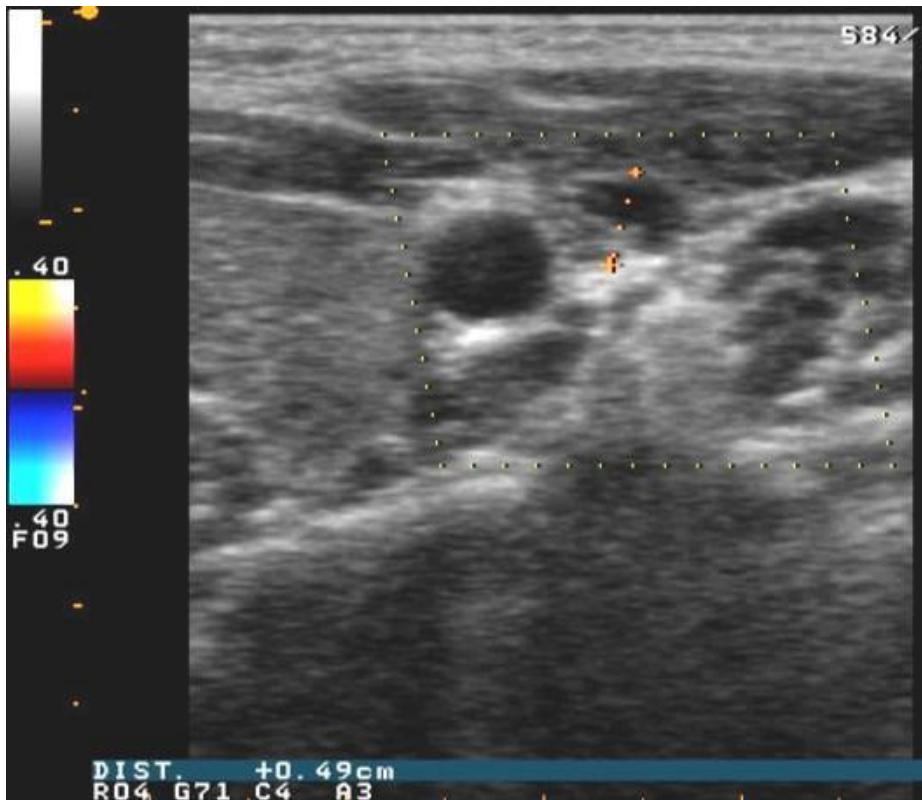
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Background and aims: Sore throat and oropharyngeal infections are common in children and are usually a self limiting condition. However, sore throat can be the presenting feature of serious pathologies and can present a diagnostic challenge. We report two cases of Lemierre's disease with an aim to make clinicians aware of this rare but serious pathology.

Methods: 2 adolescent children: 16-year-old girl and 17-year-old boy presented with a history of rigors, generally unwell, sore throat, cough and chest pain. The initial diagnosis was of sepsis and was started on IV antibiotics and IV fluids. They were admitted to the HDU for close monitoring.

Results: The initial blood culture results at 48 hours showed gram negative bacillus and a suspicion of *Fusobacterium sps.* was raised and this was confirmed later. Both the patients had CRP values of >300mg/L. The patients developed a pleural effusion and the boy needed a chest drain. The girl also developed a left internal jugular vein (IJV) thrombosis (Fig 1) and was treated with subcutaneous tinzaparin. The antibiotic regime consisted of high dose IV benzylpenicillin and metronidazole; the total duration of antibiotic therapy was 6 weeks.



[IJV thrombosis]

Discussion: Professor Lemierre described this condition in 1936 and the diagnostic criteria include:

- 1) A history of recent oropharyngeal infection.
- 2) Clinical or radiological evidence of IJV thrombophlebitis
- 3) Isolation of an anaerobic pathogen

Conclusion: These cases highlight the need for considering Lemierre's disease in patients presenting with sore throat like symptoms and show clinical deterioration.

CRIMEAN-CONGO HAEMORRHAGIC FEVER AS AN EMERGING TROPICAL DISEASE IN IRANIAN CHILDREN

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Background: Crimean Congo Haemorrhagic Fever (CCHF) is a zoonotic viral infection which causes serious threat to humans. Human infection begins with nonspecific febrile symptoms, but ends with serious hemorrhagic syndromes with a case fatality rate up to 50%. The route of transmission is through the bite of infected ticks, handling of infected blood or organs of livestock and nosocomially.

Methods: From June 2000 to December 2011, we surveyed 59 sera samples from probable children, less than 12 years old, for CCHF in 4 tropical provinces including Sistan va Baluchistan, Hormozgan, Fars and Yazd. Samples were analyzed serologically (IgM & IgG ELISA) and molecularly (gel based and Real time RT-PCR) for CCHF disease.

Results: From 59 samples, results illustrated that the number of confirmed cases were 22 and death cases were 2. Among the 22 confirmed cases, 20 were from Sistan va Baluchistan, 1 from Hormozgan, 1 from Yazd and no confirmed cases from Fars. Between the confirmed cases, 16 (72.7%) were boys and 6 (27.3%) were girls.

Conclusion: Interestingly, the most infected province was Sistan va Baluchistan in the south of Iran neighboring Pakistan and Afghanistan where CCHF is endemic. Regarding the sex ratio, CCHF infection in boys is about 3 times more than girls, which seems due to boys implication in high risk professions related to infected livestock such as slaughtering in rural areas. So in these areas, hygienic awareness and training programs could be effective in disease controlling and declining the number of infected children.

PULMONARY PARAGONIMIASIS: CASE SERIES OF MYANMAR REFUGEE CHILDREN IN MALAYSIA

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Background: Food borne trematodiasis affect about 10% of the world's population. 293 million people are at risk of paragonimus infestation. 20 million people can potentially be infected. Paragonimiasis is endemic in the Far East whilst cases had been reported in South East Asia.

Case series: We describe here, 3 cases of pulmonary paragonimiasis in Myanmar refugee children residing in Malaysia. They presented with low grade intermittent fever with either unresolving pulmonary consolidations or pleural effusions. In all cases pulmonary tuberculosis (PTB) were entertained. The two earlier cases had anti-TB treatment without any clinical resolution. All cases had eosinophilia on FBP. The first case showed eosinophilic pneumonia histological from ultrasound guided lung biopsy. The HPE findings on open lung biopsy were characteristic of pulmonary paragonimiasis with adult worm found on biopsy. The latter two cases both had eosinophilia in pleural fluid and the last case had even char-coat leydien crystals in pleural fluid cytology.

These cases depicted contrasting diagnostic and therapeutic courses that the responsible clinicians had to endeavor in managing them. A high index of suspicion following the discovery of the index case with detailed questioning on risk factors and the experience of handling the initial challenging patient proved to be really rewarding.

Oral praziquantel was prescribed for the latter two patients with resolution of signs and symptoms.

Conclusion: Pulmonary paragonimiasis must be thought of as a differential diagnosis in any person with chronic cough with eosinophilia. It can mimic PTB as both diseases are endemic in the geographical areas of concern.

CLINICIANS' PRESCRIPTION INDEX IN THE MANAGEMENT OF TROPICAL DISEASES IN A SECOND-TIER HEALTH FACILITY IN LAGOS, NIGERIA**B.M. Afolabi**¹, C. Clement², A.A. Ekundayo³¹Health, Health Environment and Development Foundation, ²Morbid Anatomy, College of Medicine, University of Lagos, Lagos,, ³Medical Research and Development, Silverwood Consult, Lagos, Nigeria

Background and aims: Infections and infestations, some of the largest causes of infant morbidity and mortality in sub-Saharan Africa, are met with prescriptions of various antibiotics, antimalarials and antimicrobials. This study aims to disentangle prescription index according to age and sex.

Method: Data from the intensive care unit (ICU) of a second-tier pediatric health facility (S-tPHF) in Nigeria was extracted from patients' medical records retrospectively and analyzed using SPSS19.

Results: The records of 225 infants, 124 males and 101 females, admitted into the ICU of an S-tPHF were retrieved retrospectively and analyzed. The diagnosis of Respiratory tract infection was significantly higher among infants aged ≥ 6.1 months than in age-group ≤ 6.0 months ($\chi^2=26.07$, $p=0.000003$) but not among the sexes. Females were 2½ times more likely to suffer gastroenteritis than males (OR=2.46, 1-29-4.70; $\chi^2=8.87$, $p=0.003$). Clinicians' prescription of antibiotics was significantly higher among age-group ≤ 6 months (OR=1.63, 1.20-2.21; $\chi^2=10.65$, $p=0.001$) but prescription of antimalarials was considerably higher among infants aged ≥ 6.1 months (OR=1.88. 1.19-2.97; $\chi^2=8.27$, $p=0.04$). There was a 15.6% increase in prescription index (Pi) for males aged ≤ 6 months (3.2) compared to those aged ≥ 6.1 months (3.7) while only 2.9% increase in Pi was noted in females aged ≤ 6 (3.4) compared to those aged ≥ 6.1 months (3.5).

Conclusion: RTI and gastroenteritis were major causes of morbidity and mortality in the first year of life. Poly-pharmacy should be reduced and treatment courses should be more specific for age and sex. Continued medical education in SSA should emphasize this.

PERSISTENT ENDOTHELIAL ACTIVATION AFTER MALARIA INFECTION IN MALAWIAN CHILDREN

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Background and aims: *Plasmodium falciparum* causes 300-500 million clinical episodes annually. Disease is characterized by microvascular sequestration of parasitized red blood cells. We hypothesized that the high burden of repeated malaria infection in endemic countries may have long-term consequences, as endothelial alterations by other acute infections are a major risk factor for cardiovascular disease. We therefore measured the evolution of plasma markers of endothelial activation, inflammation and coagulation following acute malarial infection in African children.

Methods: Plasma samples were taken at day 0, 7 and 28 from Malawian children aged 1 - 12 years with uncomplicated malaria (UM, n=90), mild non-malarial febrile illness (MF, n=89), cerebral malaria (CM, n=18) and healthy controls (HC, n=38). Levels of Intercellular adhesion molecule-1 (ICAM-1), C-reactive protein (CRP) and pro-thrombin fragment (F1+2) were determined by ELISA.

Results: On admission all markers were raised in UM and CM and all markers except F1+2 were raised in the MF group when compared with HC. At follow-up, ICAM-1 ($p < 0.05$) and CRP ($p < 0.001$) remained elevated in the CM group until day 28 and F1+2 ($p < 0.001$) remained elevated until day 7. In uncomplicated malaria and MF, ICAM-1 remained elevated until day 28 ($p < 0.05$) and CRP until day 7 ($p < 0.001$).

Conclusions: Endothelial changes induced by malaria persist beyond acute infection. The process appears more marked in those with severe disease. Studies on the effect of these changes on response to further infections and subsequent cardiovascular risk are warranted.

SUBCUTANEOUS EMPHYSEMA, NORMALLY A RARE COMPLICATION OF MEASLES. REPORT OF ALARMINGLY HIGH INCIDENCE IN SOMALI REFUGEE CHILDREN

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Drought, poverty, famine and conflict in the Horn of Africa have forced people to flee Somalia and seek refuge in Ethiopia. Medecins Sans Frontieres provides medical care to five refugee camps in the Somali area.

During an outbreak of measles between August and November 2011 nine cases of subcutaneous emphysema were diagnosed. All patients cases (age range 8 months - 18 years, 78% male) had a previous history of measles. Median duration between start of the measles rash and onset of subcutaneous emphysema was 11 (range 7-30) days. Three patients still had signs consistent with measles exanthema on presentation. In others rashes typical of measles were no longer found. Subcutaneous emphysema mostly started at the neck and later spread to the thorax. In 3 patients the emphysema extended to the face. Extension to the extremities and down to the abdomen or groin occurred in 3 and 4 patients respectively.

All patients were admitted, treated with nutritional supplements and broad spectrum antibiotics. Oxygen was not available in the camp. Five patients survived (case fatality rate 44%).

Subcutaneous emphysema is a rarely reported complication of measles. Incidence in this refugee camp was high (4.3%), but very high in children under 5 years (15.4%). The high incidence is most likely related to poor physical state of the refugee population with high rates of malnutrition. Malnutrition has a deleterious effect on immune function, leads to increased severity of measles and increased fragility of connective tissues (thought to be a factor leading to alveolar rupture).

ROLE OF TOLL-LIKE RECEPTORS 4 AND 9 IN MALARIA INCIDENCE AND SEVERITY

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Background and aims: Dysregulated innate immune response due to inappropriate signaling by toll-like receptors (TLRs) could be implicated in the disease outcome of malaria. However, data at this regard are conflicting. This study was planned to investigate the relationship between polymorphisms of genes codifying for TLR4 and 9 and susceptibility to and manifestations of malaria in children living in Burundi, a country in central Africa in which malaria is highly endemic.

Methods: Blood samples for molecular methods were drawn from 180 children admitted to the hospital of Kiremba in Burundi for an acute episode of malaria and from 337 healthy controls. The TLR4 Asp299Gly, TLR9 G1174A, TLR9 T1486C and TLR9 T1237C variants were screened by allele-specific PCR assays. Frequencies found in children with malaria and healthy controls were compared. Polymorphisms' frequency in children with mild to moderate malaria and in those with cerebral malaria was also evaluated.

Results: TLR4 polymorphism was found in more than 80% of both healthy controls and malaria children. Polymorphisms of TLR9 G1174A, T1486C and T1237C were found in more than 40% of enrolled children, independently from their clinical condition. No differences were found between mild to moderate malaria cases and cerebral malaria.

Conclusions: Polymorphisms of TLR4 and TLR9 do not seem to influence the incidence and severity of malaria. It is possible that other genetic variants or combination of these can play a role. Other studies are needed to clarify the role of genetics and innate immunity in conditioning malaria susceptibility and outcome.

OCCURRENCE AND PROGNOSTIC IMPLICATION OF THROMBOCYTOPENIA IN CHILDHOOD PLASMODIUM VIVAX MALARIA: A STUDY FROM BIKANER, NORTHWESTERN INDIAP.C. Khatri¹, G.S. Tanwar²¹Department of Pediatrics and Neonatology, ²S.P. Medical College, Bikaner, India

Background and aims: The correlation of thrombocytopenia with different types of malaria and its prognostic implications in context with severity of the low platelet count has not been evaluated. We attempted to study the platelet count in different species of malaria infection and to emphasize the usefulness of thrombocytopenia in predicting severe malaria.

Methods: This prospective study was conducted on 676 admitted children of malaria. Pediatric malaria patients with thrombocytopenia and evidence of asexual phase of malaria parasite in peripheral smear and rapid diagnostic test were included in the study. PCR confirmation was also done in children having severe thrombocytopenia (platelet count < 20x10³/mm³).

Results: Thrombocytopenia was found in 442 (65.38%). The association of thrombocytopenia was statistically significant with *P.vivax* mono-infection (73.16%) in comparison to either *P.falciparum* mono-infection (55.34%; OR=2.2[95%CI=1.6-3.1], p< 0.0001) or mixed infection (55.88%; OR=2.2[95%CI=1.1-4.4], p=0.032). In *P.vivax* mono-infection, thrombocytopenia was highest in 0-5 year age group and then subsequently decreased with advancing age whereas in *P.falciparum* mono-infection it was reverse. Severe thrombocytopenia was present in 16.52% children. The risk of developing severe thrombocytopenia was also highest in *P.vivax* mono-infection (15.79%) in comparison to *P.falciparum* mono-infection (10.59%; OR=3.6[95%CI=1.9-6.7], p< 0.0001). The association of severe malaria was significantly more amongst children having *P.vivax* mono-infection with platelet counts < 20x10³/mm³ (OR=2.6[95%CI=1.2-5.5], p< 0.014) with specificity of 88.3% and positive predictive value of 85%.

Conclusions: Till today, thrombocytopenia is not included in severe malaria criterion described by WHO but when platelet counts < 20x10³/mm³, we advocate it to include as one of the severe malaria criteria.

COMPARISON BETWEEN THE MICROBIAL RESISTANT IN URINE CULTURE OF BREAST FED VERSUS FORMULA FED FEMALE INFANTS SUFFERING FROM URINARY TRACT INFECTION**P. Yousefichaijan***Nephrology, Arak University of Medical Sciences, Arak, Iran*

Introduction: Urinary tract infection is the most common bacterial infection among children younger than 12 years old. In case of inappropriate management it may result in severe and irreversible damage to child's urinary tract; so intense and meticulous attention should be paid to treatment. It is well known that breast milk is supplied with anti microbial and immunologic factors, so we decided to assess the microbial resistance to commonly administered antibiotics in the urine culture of children fed by breast Vs formula and use the result in better management and recommendations about breast feeding.

Methods: We recruited 304 female volunteers younger than 2 years old with diagnosis of urinary tract infection, divided into two equal breast and formula feeding groups.

For each group urine analysis and culture tests were requested. Consequently microbial resistance to 9 commonly used antibiotics (including Gentamicin, Ampicillin, Amikacin, Ceftriaxone, Cefixime, Cephalexin, Nitrofurantoin, Nalidixic acid and Co-trimoxazole) was evaluated separately.

Results: Microbial resistance to all 9 antibiotics was more common in children fed by formula in comparison with breast feeding group.

Conclusion: Regarding higher prevalence of microbial resistance in children fed by formula, the role of breast feeding in prevention and management of disease is better elucidated.

THE EFFECTIVENESS OF HYDROCHLOROTHIAZIDE ON PREVENTING RECURRENT URINARY TRACT INFECTIONS IN IDIOPATHIC HYPERCALCIURIC GIRLS

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Introduction: Hypercalciuria is a common childhood disorder. Hydrochlorothiazide is another safe and effective option in this disease; we decided to assess its efficacy in preventing recurrent UTIs in hypercalciuric girls.

Methods: In this single blind randomized clinical trial, one hundred girls aged 1 to 12 years old afflicted with idiopathic hypercalciuria and recurrent UTIs were randomly divided into two equal groups. One group were instructed about general preventive measures consisting of liberal fluid intake, frequent urination, reduced salt and protein intake, washing method of genitalia, wearing loose cotton underwear and complete urination. In the second group, in addition to these measures, hydrochlorothiazide was administered (1mg/kg/day). UTI recurrence rates were compared between the two groups using Chi² test.

Results: 96% of patients who received hydrochlorothiazide became normocalciuric. In both groups the incidence of UTI recurrence was 34% (17 cases) and no difference was noted. None of the children demonstrated side-effects regarding thiazide administration and it was tolerated well.

Conclusion: A multitude of factors play roles in the host susceptibility to UTIs and it seems the relationship between hypercalciuria and UTI is more complex than what has been assumed before. Previous studies that reported reductions in UTI recurrences used adjunctive potassium citrate which could have influenced the results by altering the urinary milieu; thus, exclusive treatment of hypercalciuria might not thwart the recurrences by itself. Due to the high prevalence of IH and its eminent association with UTIs, further studies are required to resolve the controversies and establish the best management in the treatment of these children.

EVALUATION OF ADDITIONAL FLUID (1.5 TIMES THE MAINTENANCE) ON THE URINARY TRACT INFECTIONS THERAPY IN CHILDREN

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Background & Objectives: Urinary tract infection (UTI) ranges from asymptomatic bacteriuria to severe renal infection with sepsis. Urinary tract infection can cause many complications as abscess, hypertension, renal failure, renal scar, reflux and so on. Since there is no general agreement on the administration of additional fluid (1.5 times maintenance) on the early treatment of UTI on this study was conducted to see the effect of additional fluid.

Methods: 206 children with UTI, who were admitted in Amir Kabir Hospital of Arak from March 2005 to March 2006, were divided into two groups of 103. One group received the usual amount of maintenance fluid and the other 1.5 times of maintenance. The course of resolution of dysuria, frequency, malodorous urine, abdominal pain and fever were compared in the two groups. Patients' urine culture was performed on the second day, 7-10 days, and 90 days after admission. Patients were matched according to their age and sex. Those who presented with azotemia were excluded from the study.

Results: Receiving additional fluid had a significant effect on the malodorous urine dysuria. However, it had an inverse effect on the treatment of fever and urinary frequency and it made them even last longer. In other areas like abdominal pain and urine culture in 3 stages there was no difference.

Conclusion: It seems that intake of excessive amounts of water has no significant effect on the results of the UTI treatment.

RENAL ABSCESSSES AND CHRONIC RENAL FAILURE IN AN ADOLESCENT DUE TO PHIMOSIS

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Background and aim: Renal abscess is a rare complication of pyelonephritis in healthy individuals. Common predisposing factors include diabetes mellitus, renal calculi, ureteral obstruction, and vesicoureteral reflux (VUR). We describe the case of a 14-year old boy with phimosis and renal abscesses who developed chronic renal failure.

Methods: A 14-year old boy was admitted with high fever (39°C), malaise, and abdominal pain. He had been hospitalized twice for acute pyelonephritis and renal abscesses over the last two months and had received a 3-week course of IV antibiotics on each occasion. Clinical examination revealed phimosis with ballooning of the prepuce. Urine culture grew *E. coli* >10⁵ cfu/ml. He also had oliguria, hypertension and compromised renal function with elevated urea and creatinine levels. Renal abscesses were detected on renal U/S and DMSA-scanning showed relative renal function of 50% of both kidneys. The absolute renal function was low (right kidney 10% and left kidney 10%- normal values 27+/- 5%). GFR Schwartz was 72 ml/min/1,73 m² sc.

Results: After a 14-days course of antibiotics (ciprofloxacin and gentamycin), surgical correction of phimosis (preputial plasty) was performed. Remission of symptoms was achieved. Creatinine levels remained elevated (1,21 mg/dl).

Conclusions: In our case, phimosis caused intermittent VUR and urinary tract infections. Chronic renal failure was the result of renal scarring due to recurrent pyelonephritis of both kidneys and secondary formation of renal abscesses. To our knowledge, this is the first case of phimosis as a cause of chronic renal failure in an otherwise healthy adolescent.

CLINICAL AND MICROBIOLOGICAL CHARACTERISTICS OF CHILDHOOD UTI AT A UK HOSPITAL

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Background and aims: Children with urinary tract infections may present with nonspecific features that often overlap with other common childhood illnesses. We reviewed the clinical and microbiological characteristics of young children with a first documented clinical diagnosis of UTIs admitted to our hospital.

Methods: Patient casenotes were analysed and laboratory information was obtained from the laboratory system retrospectively. A structured proforma was used to collect the data.

Results: 121 patients under 5 years were identified, consisting of 30% males and 70% females. The commonest symptoms were pyrexia and vomiting. *Escherichia coli* (59%) was the commonest organism isolated from the urine, followed by other coliforms (34%).

Conclusion: In our study, the commonest symptoms associated with clinical UTI were fever and vomiting. *E. coli* and coliforms were the commonest organisms and females were the majority. This study enables clinicians to appreciate the variety of symptoms associated with UTI so that treatment can be started early.

THERAPEUTIC EFFECTS OF ZINC SUPPLEMENTATION IN CHILDREN WITH URINARY TRACT INFECTION

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Introduction: Urinary tract infection (UTI) is the most common disease of urinary tract. This disease lacks characteristic signs and symptoms and occasionally occurs with atypical presentations such as weight loss, anorexia, and growth failure. Zinc improves host immune-system response to many infections and has a significant role in immune system integrity. The aim of this was to study of zinc supplementation on treatment of UTI in children.

Materials and methods: In this clinical trial study, 200 children with UTI who were admitted to Amir Kabir hospital (Arak, Iran) were randomly divided into two control and case groups. Two groups were matched in age, gender, urine laboratory profiles, and clinical signs and symptoms such as fever, dysuria and frequency. The control group received only routine treatment of UTI. The case group, in addition to routine treatment of UTI, received oral zinc sulfate syrup.

Results: Findings showed that dysuria and frequency in zinc-supplemented subjects recovered significantly sooner than control subjects, while the abdominal pain persisted longer. There were no significant differences in onset of fever remission and negative urine culture time 48h and 7-10 days after treatment between two groups.

Conclusion: Zinc supplementation has a significant effect in ameliorating severe dysuria and frequency of urinary in UTI. When the abdominal pain is present, usage of this drug is not recommended.

DIAGNOSIS OF URINARY TRACT INFECTION IN CHILDREN: IMPACT ANALYSIS OF AN EVIDENCE BASED GUIDELINE

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Background: In young children with fever without source, presenting at the emergency department, urinary tract infection (UTI) is one of the most common serious bacterial infections. To improve reliable diagnosing UTI in young, non toilet trained children, the diagnostic strategy of the Nice guideline was nationally introduced in the Netherlands Our aim was to determine the impact of this diagnostic strategy in clinical practice.

Methods: We conducted a cross-sectional observational study, with observations before and after implementation of the guideline: catheterisation according to age, presentation and dipstick result. We prospectively collected data from all healthy children aged 1 month- 2 years, presenting with fever at the emergency room at Sophia Children's Hospital in 2008 and 2010-2011. Primary outcome measure was correct assessment of children suspected with UTI according to the guideline. Secondary outcomes included the number of contaminated cultures, hospitalisation and antibiotic treatment. For statistical testing the Chi-squared test and Fisher Exact test were used.

Results: The preintervention group consisted of 207 children (male 64.3%, median age 0.98 year(interquartile range IQR 0.77)), the postintervention group 194 children (male 55.2 %, median age 1.06 year (IQR 0.78). Correctly diagnosed UTI was observed in 41 (19.8%; 95% CI:14.3-25.3) children of the preintervention group, this significantly increased to 101 (52.1%; 95%CI: 45.0-59.2) in the postintervention group (p-value< 0.0001). We did not observe significant differences in secondary outcome parameters between the pre- and postintervention group.

Conclusion: Implementation of the guideline has lead to a significant higher frequency of correct assessment of UTI in young children.

IS SERUM PROCALCITONIN RELIABLE FOR PREDICTOR MARKER FOR VESICoureTERAL REFLUX IN CHILDREN WITH FIRST FEBRILE URINARY TRACT INFECTION?

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Among children with febrile UTI, 25 to 40% had vesicoureteral reflux (VUR). Procalcitonin (PCT) are correlated to VUR and could be used to avoid unnecessary cystography. The aim of our study was to validate the use of serum PCT as a predictor of VUR in children with a first febrile urinary tract infection (UTI).

Patients and methods: This prospective study includes 162 children less than 4 years; 34.8% males and 65.2% females. PCT was measured at admission. Cystography was performed 6 weeks after UTI diagnosis.

To compare the mean PCT concentration among children with and without VUR we use Mann-Whitney test. We analyze the relationship between PCT and grade of VUR using a logistic-regression model. We performed a ROC curve for examine potential PCT cutoff.

Results: VUR was diagnosed in 35 children (22.6%): 15 grade 2, 14 grade 3 and 6 grade 4.

The median PCT concentration in patients without VUR was 0.6 ng/ml and 0.4 ng/ml with VUR, we found no statistically significant differences. Among 35 children with VUR, 13 (37%) had PCT \geq to 0.6 ng/ml:

8 grade 3 and 1 grade 4. Sensitivity and Specificity of PCT $>$ 0.6 ng/ml for all grades VUR was 37% and 45% respectively and for high grade was 45% and 49%.

The odds ratio for grade 4: 0.166 (IC 95%: 0.019-1.462). The AUC (area under curve) is 0.504.

Conclusions: In our study, serum PCT level is not an early marker of VUR. More studies are necessary for support that PCT define strategies for cystourethrography in children after first febrile UTI

BACTEREMIC URINARY TRACT INFECTION COMPARED TO PRIMARY BACTEREMIA IN CHILDREN < 3 MONTHS. IS PYELONEPHRITIS A SERIOUS BACTERIAL INFECTION?

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Background: About 7% of febrile infants < 3 months have a serious bacterial infection (SBI), which could result in significant morbidity and mortality. Established criteria, including pyuria, identify those at higher risk for SBI, including pyelonephritis, and recommend aggressive evaluation and hospitalization for parenteral antibiotics. The purpose of this study was to evaluate if bacteremic urinary tract infection (BU) has the same risk of poor outcome (PO) defined as death, meningitis or long term sequelae than those with primary bacteremia (PB).

Methods: Multicenter retrospective chart review of bacteremic infants 2-90 days old evaluated at CHOC Children's Hospital and 7 Kaiser Permanente medical centers in Southern California between (7/1/2005-12/31/2010). Charts were reviewed for clinical, laboratory and outcome data.

Results: There were 162 patients with bacteremia; 84 BU (71 received lumbar puncture (LP)) and 78 PB (70 with LP). Average age was 35.8d and 40.2d respectively. The most common organism in PB was *S agalactiae* (49/78) whereas *E coli* (69/84) was the most common in BU group. PO was found in 19 patients in PB group (proportion = 0.24; 95% CI 0.16-0.34) and none in BU group (proportion = 0; 95% CI= 0.0-0.04). WBC count did not discriminate between BU, BP or outcome.

Conclusion: Amongst bacteremic infants, those with BU have significantly better outcomes than those with PB. Future studies are needed to evaluate if this subgroup of patients requires hospitalization, parenteral antibiotics and invasive procedures.

EVALUATION THE RELATIONSHIP OF GENITOURINARY SYMPTOMS AND FINAL DIAGNOSIS IN 6-12 YEARS GIRLS IN ISFAHAN, IRAN

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Introduction: Genitourinary signs and symptoms are important in girls around puberty time despite differences in societies due to varieties in hygiene, culture, clothing and so on.

In this study we evaluate the relation between genitourinary symptoms and final diagnosis in 6-12 years girls in Isfahan, Iran.

Materials and methods: It is a descriptive - prospective study with convenience sampling in Shariati hospital from 49 girls with genitourinary symptoms from June to September 2010. A 47 part questionnaire completed for chief complaint, present and past medical history , physical examination and Paraclinic studies like urinary exam and culture, vaginal smear and culture, stool exam, sonography and VCUG as indicated. We used SSPE ver.16 , chi-square, t-test... for datae analysis.

Results: For symptom frequency nocturnal enuresis 28.6%, vaginal itching42.9%,urgency51%, frequency 63%, urine malodor30.6%, dysuria46%, daytime enuresis22.4%, urine color change16.3%, polydipsia44.9%,chronic constipation34.7%, fever6.1%, vaginal discharge30.6%, polyuria46.9%,hematuria4.1%,vomiting6.1% anal itching4.1% and sleep disorders22.4% were detected. None of them had diarrhea, and oliguria. In laboratory data 50% had positive urine culture(half with constipation), 30% positive vaginal smear(half with UTI) and one CRF. 95.9% of 49 patients had water washing after each urination and 73.5% sometimes used restrict clothes. P value measured for UTI relation to frequency0.026, abnormal U/A 0.00, constipation.090, nocturnal enuresis0.29, daytime enuresis0.072,vaginal itching 0.385 and urgency0.063.

Conclusion: Although UTI is the most frequent diagnosis of genitourinary classic symptoms and signs, other symptoms like chronic constipation and other diagnosis like vulvovaginitis should be recalled in 6-12 years girls along enough education for appropriate clothing and hygiene.

RELATIONSHIP BETWEEN PREVALENCE OF UROPATHOGENS, AGE AND GENDER IN PEDIATRIC URINARY TRACT INFECTION

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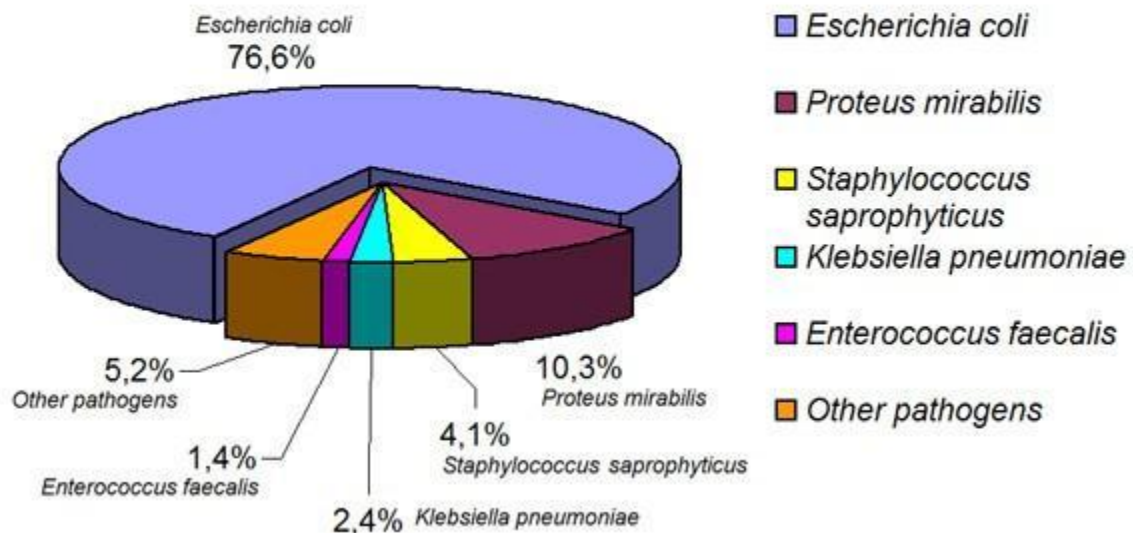
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Backgrounds and aims: Effective treatment of urinary tract infection (UTI) requires prompt initiation of antimicrobial agents to which the causative pathogen is susceptible. The aim of this study is to provide the uropathogens frequencies and the relationship between bacterial species, gender and age.

Methods: Cross-sectional study, performed at Hospital Universitário da Universidade de São Paulo, Brazil, from January to December 2010, children aged 0 to 15 years, who present to the emergency department with UTI. We defined UTI by growth of a single pathogen of $\geq 50,000$ colony-forming units(CFU)/mL of a specimen collected by transurethral bladder catheterization or $\geq 100,000$ CFU/mL of a specimen obtained by clean void.

Results: 2577 urine samples were analyzed, of which 291(11.3%) were culture-positive, the majority was female(72.8%), aged 3 months to 10 years(78.3%). *E.coli* was the predominant organism(76.6%), followed by *Proteus mirabilis*(10.3%) and *Staphylococcus saprophyticus*(4.1%).

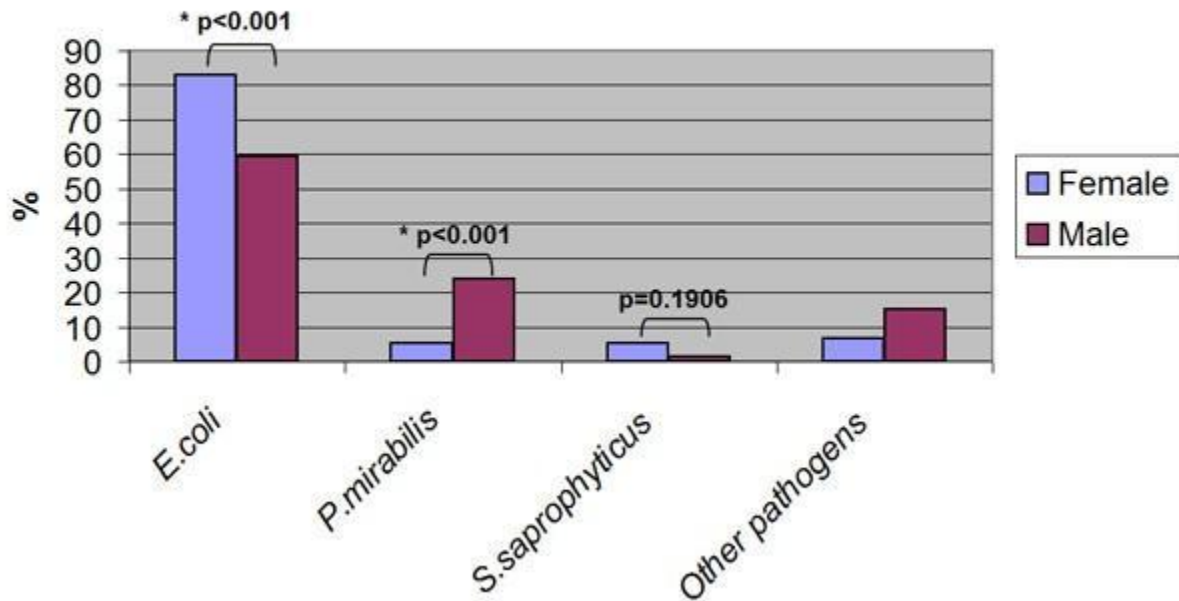
Frequency of uropathogens at Hospital Universitário da USP, São Paulo, Brazil, 2010



[Frequency of uropathogens]

Analysis by age group revealed statistically significant lower prevalence rates of in infants < 3 months (50% vs 78.4%, OR=0.276; 95%CI= [0.105-0.726], p=0.006); increased prevalence of *Staphylococcus saprophyticus* in patients >10 years (24.4% vs 0.4%, p< 0.0001). Among the males, *Proteus mirabilis* is more frequent than in females (24.0% vs 5.2%, p< 0.001).

Frequency of uropathogens according to patient gender, at Hospital Universitário da USP, São Paulo, Brazil, 2010



[Frequency of uropathogens according to gender]

Conclusions: *E.coli* was the most common uropathogen identified. Nevertheless, initial empiric antimicrobial selection should consider other non-*E.coli* species in infants < 3 months, male preponderance of *Proteus mirabilis* and the significance of *Staphylococcus saprophyticus* in patients >10 years.

PREVENTION OF RECURRENT URINARY TRACT INFECTIONS (UTIS) IN CHILDREN: CO-TRIMOXAZOLE (SXT) VERSUS SECOND-GENERATION CEPHALOSPORINS (2NDGC)

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Background and aims: Chemoprophylaxis is recommended for children at high risk for recurrent UTIs. Our aim was to prospectively compare SXT and 2ndGC as chemoprophylaxis for UTI in children, in terms of efficacy and emergence of bacterial resistance.

Methods: During 2007-2010 after the first UTI episode children (1mo-6yrs) were randomized on 1:1 to receive SXT or 2ndGC. Every 6 months (1 course) antibiotics were switched to each other in each patient and urethral orifice cultures (UOC) were taken. The incidence of breakthrough UTIs as well as species and susceptibility pattern of isolated bacteria from both urine and UOC were recorded.

Results: Among 97 children [median age 7.7mo], breakthrough UTIs occurred in 10/75 (13.3%) and 8/78 (10.3%) SXT and 2ndGC courses, respectively (p=NS). All but one breakthrough UTIs occurred during the first 6-mo courses. *Enterobacteriaceae* colonized more likely children receiving SXT (90% vs 53%, p< 0.001), whereas *Pseudomonas aeruginosa* predominated in children receiving 2ndGC (23% vs 5%, p=0.002). At the end of SXT courses 94% of isolates were resistant to SXT, while at the end of 2ndGC courses 93% were resistant to 2ndGC. Comparing susceptibilities of pathogens isolated before and after the first course, administration of SXT significantly increased resistance to SXT (p=0.0007) but not to beta-lactams (p=NS); whereas, administration of 2ndGC significantly increased resistance to both SXT (p=0.0027) and beta-lactams (p< 0.01).

Conclusions: SXT and 2ndGC demonstrated comparable efficacy in preventing UTIs in children. Notable differences were recorded in species and susceptibility pattern (cross-resistance) of colonizing/infecting bacteria following prophylaxis with these antibiotics.

EXTENDED SPECTRUM BETA LACTAMASE (ESBL)-PRODUCING ENTEROBACTERIACEAE FROM URINARY TRACT INFECTIONS IN A PAEDIATRIC HOSPITAL

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Background and aims: Enterobacteriaceae are major pathogens in childhood and the leading cause of urinary tract infections (UTIs) in this age group. There have been significant changes in the antimicrobial resistance patterns of uropathogens over the years including resistance due to extended spectrum beta lactamase (ESBL). The aim of this study was to investigate the frequency, demographics, trends, susceptibility patterns and clinical outcome of children with UTI caused by ESBL-producing enterobacteriaceae.

Methods: The study took place between 01/01/2009 and 31/12/2011. After culture, enumeration and identification by API system, the antibiogram was carried out by disk method.

Results: In a total of 347 positive urine cultures, 36 (10.4%) were ESBL-producing enterobacteriaceae, coming from 29 patients (23 boys). Two patients had 3 episodes and 3 had 2 episodes. The mean age was 17.8 months (0.2-132), with 65.2% younger than 12 months. *Escherichia coli* was the predominant specie (23 isolates, 63.9%) followed by *Klebsiella spp.* (10 isolates, 27.8%), *Enterobacter cloacae* (2 isolates: 5.6%) and *Citrobacter freudi* (1 isolate: 2.8%). The total susceptibility results of the 36 ESBL-producing enterobacteriaceae showed a sensitivity for imipenem (91.7%), ciprofloxacin (75%), ofloxacin (77.8%), norfloxacin (77.8%), amikacin (80.6%), gentamycin (52.8%), tobramycin (30.6%), nalidixic acid (69.5%) and co-trimoxazole (36.1%). Hospitalization was needed for 66.7% of patients with a mean duration of 7.4±5.5 days. All patients had a favorable outcome.

Conclusion: The most common ESBL-producing pathogen of UTI was *E. coli*. The isolated ESBL-producing pathogens were highly sensitive to carbapenems, quinolones and amikacin. Despite antibiotic resistances, all patients did well.

URINARY TRACT INFECTIONS AFTER KIDNEY TRANSPLANTATION IN CHILDREN

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Background and aims: Urinary tract infection (UTI) remains one of the main complications after kidney transplantation and it has serious consequences. The purpose of this study was to evaluate the prevalence of UTI in children with kidney transplantation.

Methods: The period of the study enrollment extended from 01/01/2009 to 31/12/2011. Confirmed episodes of UTI after the 1st month of kidney transplantation were reviewed.

Results: In a total of 347 positive urine cultures, 20 (5.8%) were coming from 6 kidney transplant patients (4 girls), of whom 3 experienced 1 episode, 1 had 2 episodes, and 2 had more than 6 episodes. Of the patients with UTI, 2 had urinary reflux-obstruction disorders as the primary kidney diseases, 2 had suffered reflux nephropathy, 1 had metabolic disease and 1 had end stage renal disease of unknown origin. *Escherichia coli* was the predominant specie (11 isolates, 55%) followed by *Staphylococcus* spp. (3 isolates, 15%), *Citrobacter freudi* (2 isolates, 10%), *Klebsiella pneumoniae* (2 isolate: 10%), *Enterobacter cloacae* (1 isolate, 5%) and *Pseudomonas aeruginosa* (1 isolate, 5%). The total susceptibility results of the 17 gram-negative pathogens showed that the sensitivity was: ampicillin (11.8%), co-trimoxazole (17.6%), amoxicillin/clavulanic acid (41.2%), cefoxitin (58.8%), ciprofloxacin (70.6%), imipenem (100%) and amikacin (100%). Two enterobacteriaceae were found to be extended spectrum beta lactamase- producing pathogens.

Conclusion: The most common pathogen of UTI in kidney transplant patients was *E. coli*. The increased resistance of uropathogens could be explained by the frequent UTI relapses in the same patient.

FREQUENT CAUSES OF URINARY INFECTION DUE TO OBSTRUCTIVE UROPATHIES IN CHILDREN OF 2-6 YEAR OF AGE

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Obstructive uropathies present changes in anatomy and function of urinary tract, localized in the upper parts from the place of obstruction.

Aim of study: Presentation of the most frequent causes of urinary tract infections in most frequent types of obstructive uropathies in children 2-6 years of age.

Materials and methods: There were 55 children of the ages 2-6 included in our study; they were diagnosed in the Pediatric Clinic during the period of time 2007-2009.

Results of study: 52.24% of the children were females and 47.76% males. Ureteropelvic junction obstruction was the most common obstructive uropathy, present in 42.7% of all cases, vesicoureteral reflux (VUR) in 20.8% and urether duplex in 10.2% of the cases. Results of bacteriological examination show that ureteropelvic junction obstruction was connected with E.coli infection in 65.1% of the cases, Klebsiella pneumonia in 14% of the cases, Proteus spp. in 9.3% of the cases and in 11.6% of the cases urinoculture was sterile. At VUR, the most frequent cause of infection was Ecoli in 61.8% of the cases, Klebsiella in 17.6%, Proteus spp. in 17.6%, Pseudomonas aeruginosa in 2.9%, Citrobacter in 5.9% and in 5.9% of the cases urinoculture was sterile. At urether duplex, E.coli was the most frequent cause of infection in 56.3% of the cases, Klebsiella in 16.7% and Proteus spp. was isolated in 25% of the cases.

Conclusion: According to the results of the study, we can conclude that the most frequent cause of urinary tract infection in obstructive uropathyes is E.coli.

URINALYSIS FROM VOIDED VS. CATHETERIZED URINE FOR THE DIAGNOSIS OF URINARY TRACT INFECTIONS IN PAEDIATRIC PATIENT

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Background and aims: Diagnosis of urinary tract infection (UTI) should be based on positive urine culture. In routine, urinalysis (leucocyturia, nitrituria) is important for the decision to obtain urine culture and to start antibiotic treatment while culture results are pending. We questioned how reliable voided urine can predict results of sterilely obtained urine.

Methods: At our institution, pathological urinalyses of spontaneous voided urine (voidU, plastic bag or midstream urine) are rechecked by urine obtained by urethral catheterization (cathU) in selected cases. We retrospectively compared urinalyses of voidU with cathU from the same patient and the same day. Leucocyturia was defined as >10 leucocytes/ml.

Results: 278 pairs of urinalyses were analysed (age 1 day to 22 years, median 3.4 years, 80.2% female). When compared with cathU, leucocyturia in voidU was false positive in 21.6% and false negative in 1.4%. However, leucocyte counts were significant lower ($p=0.015$) in false positive voidU (20 to 2280/ml, median 100/ml) than in true positive (20 to 19,200/ml, median 340/ml).

Nitrituria was false positive in 14.0 and false negative in 1.1%. Taken both parameters together, voidU was false positive in 32.7% (38.1% in female vs. 10.9 % in male, Chi-square-test $p < 0.001$).

In 7 episodes (2.5%) voidU was negative for both parameters despite one positive parameter (4x leucocyturia, 3x nitrituria) in the corresponding cathU.

Conclusions: In selected cases, pathological urinalysis of voidU should be proven by cathU to avoid unnecessary examinations (ultrasound, miction cystography, scintigraphy) and antibiotic treatment in paediatric patients.

IDIOPATHIC URETHRITIS IN CHILDHOOD: PRESENTATION OF FIVE CASES

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Introduction: Idiopathic urethritis (IU) in childhood is a rare disease with very few cases reported so far.

Materials and methods: The medical records of the patients diagnosed with IU were retrieved and their clinical course is presented herein.

Results: During the last 3 years (September 2008 till August 2011) five male patients (mean age: 8.2, range: 3-14 years) presented with blood spotting of the underwear or urethral discharge, with or without dysuria. 3 of them had a pale colored, low-viscous, purulent -like urethral discharge. Investigation for the presence of bacteria was negative. All were treated in an outpatient basis with favorable clinical course (follow up: 15.8 months, range: 7-26). The mean duration of symptoms was 21.4 weeks (range: 3-53 weeks). Antibiotics were not prescribed. Instructions for timed voiding and pelvic floor relaxation were provided accompanied by antiinflammatory regimens. If constipation was referred, dietary instructions with or not laxatives were administered. After one month, 2 patients were symptoms free and after 3, all of them were in a good health condition. 2 patients recurred at 8 and 12 months respectively. The ultrasound examination of the urinary tract was normal. So far, the need for more invasive urinary studies is not justified to anyone.

Conclusions: IU is a rare disease with benign clinical course. Should bacterial infection, lithiasis, tumor and Reiter's syndrome have been excluded, the treatment must be tailored to symptomatic relief. An aggressive diagnostic workup should be reserved to those with persistent symptoms or frequent recurrences.

DIAGNOSTIC ACCURACY OF STERILE BAG URINE SAMPLING FOR THE DIAGNOSIS OF URINARY TRACT INFECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Urinary tract infections (UTI) are the most common source of bacterial infections among young children. Making a proper diagnosis is important but requires invasive urine collection techniques, such as urethral catheterization (UC) or suprapubic aspiration (SA). Sterile bag (SB) is a less invasive method of urine collection, but is thought to have a higher risk of contamination and thus a lower diagnostic accuracy. We aimed to perform a systematic review and meta-analysis of the diagnostic accuracy of SB urine sampling for UTI diagnostic.

Methods: All studies identified by a systematic electronic search in usual databases until 2011 were included, and meta-analysed.

Results: From the 686 identified articles, 7 articles were included, where SPA (in 5 studies) or UC (in the left 2) were considered as the reference standard. 1056 children < 2 years-old were included, 435 (41%) had a proven UTI. SB had a pooled sensitivity of 74% [70-77], and a pooled specificity of 84% [81-87], both with a significant heterogeneity ($p < 0.001$). The pooled LR+ was 5.7 [2.9-11.2] and the LR- was 0.4 [0.2-0.7], without significant heterogeneity. Based on a 7% pooled prevalence of UTI in febrile children, the use of SB for urine collection led to a post-test probability of 0.02%, meaning that 1/5,000 child with UTI would be missed.

Conclusion: The diagnostic accuracy of SB urine sampling could be of interest, as an intermediate step in a selective strategy for SPA and UC.

VESICO-URETERAL REFLUX AS A RISK FACTOR FOR ACUTE PYELONEPHRITIS AND RENAL DAMAGE IN CHILDREN WITH UTI: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Urinary tract infection (UTI) is one of the most common bacterial infections in childhood. UTI may result in renal scarring (RS) predisposing to long-term complications. Vesicoureteral reflux (VUR) is thought as a risk factor for both acute pyelonephritis (APN) and RS, but with conflicting results according to recent meta-analyses that presented with methodological weaknesses. We aim to study if VUR is a risk factor for APN and RS, using a methodologically robust and updated systematic review and meta-analysis.

Methods: All studies of children with UTI, DMSA scan and cystography, were identified by a systematic electronic search in usual databases until 2011, and meta-analysed using DerSimonian and Laird random-effects model.

Results: From the 1558 identified articles, 80 were included, representing 11410 children; children had a first UTI in 53 (66%) studies; 48 (60%) studies were prospective, and in 15 (19%) children underwent both early and late DMSA scan. At all, 6681 children with an early scan were included, and 5879 with a late scan. All-grade VUR was significantly associated to both APN (OR=2.0 ; 95%CI: 1.8-2.3) and RS (OR=4.8; 95%CI: 4.3-5.5). High-grade (≥ 3) was also significantly related to APN (2.4; 95%CI: 1.9-3.1) and RS (OR=5.7; 95%CI: 4.5-7.3). Pooled estimates were found with heterogeneity due to the variability of delay between UTI and late scan within studies.

Conclusions: Children with VUR had a higher risk of APN and RS. These data suggest that identification of VUR can be a practical method of identifying children who are at risk for renal scarring.

INCREASING RESISTANCE OF ESCHERICHIA COLI TO ANTIBIOTICS IN URINARY TRACT INFECTIONS IN CHILDREN IN JORDAN**A.A. Almatti***Pediatric and Neonatology, Islamic Hospital, Amman, Jordan***Introduction:** Escherichia coli (Esch. coli) is the commonest pathogen worldwide. Resistance to many antibiotics is increasingly reported.**Objectives:** *To study the frequency of E. coli resistance to antibiotics.**Settings and method:** A prospective study of all cases of UTI presented to our pediatric department both in-patient and out-patient over two years (2010 and 2011). Studying the age and sex, the causative pathogens and their sensitivity and resistance to antibiotics.**Results:** Age: Under 1 year of age 26 cases (21%), 1-5 years: 51 cases (42%). Above 5 years: 37 cases (32%).

SEX: Females 94 cases (82%), Males 20 cases (18%). The ratio of 4.7 : 1

A total number of 123 episodes of UTI were recorded over 24 months from Jan, 2010 to Dec, 2011.

The total number of cases was 114 including: 79 cases of Esch. Coli (64%), 29 cases of Klebsiella sp. (23%), 7 cases of Enterobacter sp. (6%), 5 cases of Proteus sp. (4%), 2 cases of Staphylococcus aureus (2%) and 1 case of Pseudomonas sp. (1%).

The following antibiotics were administered according to the sensitivity of Esch. Coli and other factors related to the drug and the patient and his family:

Amikacin in 29 cases (36%), Cefixim 27 cases (34%), Amoxy-clav. 13 cases (17%)

Cephtriaxone 4 cases (5%), Cefpodoxime 3 cases (4%), Cefuroxime 3 cases (4%)

Conclusion: *Esch. coli is the commonest cause of UTI in children in Jordan.

*36% of cases were sensitive to Amikacin but resistant to other commonly used antibiotics. *Cefixim is the best oral antibiotic followed by Amoxy-clav.

THE FREQUENCY OF RECURRENCE OF URINARY TRACT INFECTION (UTI) IN 1 MONTH TO 12 YEAR OLD CHILDREN WITHOUT CONGENITAL ABNORMALITIES

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Background and objective: Urinary Tract Infection (UTI) is one of the most common diseases of childhood which may cause serious morbidity. We evaluated recurrence rate of UTI in children without congenital abnormalities who were at the age of 1 month to 12 years old.

Materials and methods: This cross-sectional study was carried out for three months after the termination of the treatment in order to determine the rate of recurrence and re-infection in children (sex segregation) at the age of 1 month to 6 years and 6 to 12 years who did not have any anatomical or functional urinary abnormalities at Arak Amir kabir Hospital.

Results: In total, 250 patients (224 girls and 26 boys) were evaluated. 17 girls had recurrences, of whom, 2 cases (11.7%) were under 1 year old, 14 cases (82.2%) had 1 to 6 years old and 1 case (5.8%) was in the 6 to 12 years old group. In the first month there was no relapse and most recurrences occurred through the third month (65%). All recurrences were symptomatic.

Conclusion: Due to low rate of recurrence of urinary infection in our study group, repeated cultures and prophylactic treatments is not recommended in children and infants without underlying congenital renal abnormalities. In such cases, UTI can be prevented by effective trainings.

IMMUNOLOGICAL HYPORESPONSIVENESS TO PNEUMOCOCCAL CONJUGATE VACCINES (PCV) ASSOCIATED WITH REPEATED USE OF PPV23 IN ASPLENIC β -THALASSEMICS: A 7-YEAR FOLLOW-UP**I. Papadatou**¹, K. Alexandraki², G. Orthopoulos¹, A. Kattamis³, M. Theodoridou¹, V. Spoulou¹¹*Department of Infectious Diseases, Aghia Sophia Children's Hospital, University of Athens,* ²*Endocrine Division, Department of Pathophysiology, University of Athens,* ³*Thalassemia Unit, Aghia Sophia Children's Hospital, University of Athens, Athens, Greece*

Background and aims: PPV23-induced protection against invasive pneumococcal disease is of limited duration and frequent revaccinations are required for life-long protection of high-risk individuals. However, repeated PPV23s have been associated with suboptimal immune response to subsequent immunizations with PCV. We evaluated the effect of PPV23 on PCV immunogenicity by comparing immune responses to PCV7 and PCV13 given with a 7-year interval in a group of asplenic β -thalassemics who had been previously exposed to repeated PPV23s.

Methods: 24 subjects (11male, mean age 36years), who had received PCV7 7 years earlier, were vaccinated with 1 dose of PCV13. All subjects had been exposed to PPV23 in the past and received 1-2 additional PPV23s in the 7-year interval. Blood samples were obtained before and one month after both PCV7 and PCV13 vaccinations. Antigen-specific antibodies for serotypes 9V, 19F and 23F, included in both PCV7 and PCV13, were quantified using a double-absorption (CPS and 22F) ELISA.

Results: Baseline antibodies before PCV13 vaccination were lower than those pre-PCV7 for all studied serotypes: Geometric Mean Titers (GMTs) for 9V 23F and 19F were 2,16vs9,23 μ g/ml ($p < 0,001$); 4,76vs7,91 μ g/ml and 6,98vs13,7 μ g/ml respectively. One month post PCV13, antibody GMTs were lower than those one month post PCV7: 5,12vs13,95 μ g/ml ($p < 0,001$); 9,68vs25,36 μ g/ml ($p = 0,026$) and 11,86vs9,68 μ g/ml ($p = 0,124$) for 9V, 23F and 19F respectively.

Conclusion: PCV13 failed to elicit responses similar to a PCV7 administered 7 years earlier in asplenic β -thalassemics. These findings suggest a persisting state of PPV23-induced immune hyporesponsiveness, which cannot be overcome by vaccination with conjugate vaccines.

10 YEARS OF A SINGLE DOSE MENINGOCOCCAL C VACCINATION PROGRAMME IN FLANDERS: PERSISTENT HERD IMMUNITY WITHOUT ANY VACCINE FAILURES

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Background and aims: In 2001 an epidemic increase in invasive meningococcal C infections was seen in Flanders. In 2002 a vaccination campaign with conjugated meningococcal C vaccines was targeting preschool children older than 12 months and adolescents. Single dose meningococcal C vaccination at the age of 1 year was added to the vaccination programme. The impact of the vaccination campaign and programme was evaluated based upon epidemiological data of invasive meningococcal diseases.

Methods: Data from all notifications of meningococcal infections in Flanders since 1999 were examined, including data from the national meningococcal reference laboratory. For meningococcal C infections in children, adolescents and young adults vaccination data were checked systematically to exclude vaccine failure.

Results: The vaccination campaign for preschool children and adolescents and systematic vaccination of babies at 12 months resulted in a rapid decrease in incidence of invasive meningococcal C infections. Herd immunity was seen in younger and older age groups. No cases of vaccine failure could be documented so far, unlike in the UK. For the whole period the same tetanus toxoid conjugated meningococcal C vaccine was used in the vaccination programme. The systematic vaccination above the age of 12 months and the type of vaccine might be reasons why no vaccine failure was seen.

Conclusions: The vaccination programme with systematic single dose vaccination at the age of one year seems to maintain herd immunity for meningococcal C infections. In the current epidemiological situation in Flanders there is no reason to add a booster vaccination in adolescence.

DIFFERENCES OF IGG-ANTIBODY-AVIDITY AFTER AN ACELLULAR PERTUSSIS-AP BOOSTER IN ADOLESCENTS WITH A PREVIOUS WHOLE CELL-WCP OR AP PRIMARY VACCINATION

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Antibody concentrations alone do not sufficiently differentiate between recent exposure or previous immunization and do not necessarily correlate with protection against diseases.

Therefore, the aim of the study was to assess the IgG-antibody-avidity and the IgG-concentrations against pertussis antigens, such as filamentous hemagglutinin-FHA and pertussis toxin-PT in a cohort of 78 adolescents before and after tetanus-diphtheria-pertussis (Tdap) booster vaccination. We defined three groups of individuals who had received either four (4aP; last dose age 18-24 months) or five doses (5aP; last dose age 4-6 years) of aP or four doses of wcP vaccine (last dose age 18-24 months), previously. The relative avidity index (RAI) was evaluated by an adapted ELISA.

RAI positively correlated with IgG-concentrations in all groups ($p < 0.001$). A significant increase of RAI of IgG-anti-PT was found after Tdap in all groups ($p < 0.01$). After booster, RAI of IgG-anti-FHA was significantly higher in the wcP group (mean: 69%) compared to 5aP (mean: 49%, $p < 0.05$). Interestingly, before Tdap, reverse cumulative distributions of the RAI of IgG-anti-PT showed significantly higher proportions of individuals of the wcP group (38%) which showed low RAI ($< 30%$) compared to the 5aP and 4aP group (8% and 22%, respectively, $p < 0.01$), but a similar response after Tdap booster in all groups.

In the case of pertussis vaccines, RAI clearly reveals differences of antigen-specific-IgG responses and the influence of different vaccine preparations and booster intervals. Differences in RAI may be influenced by exposure to Pertussis within the community. Assessment of RAI may help to interpret the quality of antigen-specific-IgG-antibodies and allows estimating the long-term affinity maturation and long-term protection against disease.

PECULIARITIES OF SUBSTRAIN BCG RUSSIA 368

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Background and aims: Region of difference (RD) and tandem duplication (DU) are the markers of substrains of BCG. Earlier substrains BCG Russia, Tokyo, Moreau distinguish oneself by two copies of IS6110. BCG Russia, Tokyo have three copies of DU2-I according to Brosch R.. Some genomic differences determine protective efficacy of vaccines. Data of genomes sequencing can explain what features are retained when daughter strains are passaged.

Methods: Whole genome sequencing of substrain BCG Russia 368 by using the GS Junior pyrosequencing system (Roche 454 Life Sciences, Branford, CT, USA).

Results: Shotgun sequence reads from the GS Junior Systems were assembled de novo and by reference strains. Assembled contiguous sequences were queried against the GenBank database. One region of major rearrangements was identified. Genome of substrain BCG Russia 368 had only one copy of 20740 bp region which in BCG Pasteur has one tandem duplication DU2 and two it in BCG Tokyo. Therethrough DU2 is deleted in the genome of BCG Russia 368 without influence on protective efficacy of vaccine.

Conclusions: Investigation of Russian passages of BCG strains of different years will permit understand what rearrangements are allowable at *maintenance vaccine efficiency*.

UNIVERSAL HEPATITIS B VACCINATION IN BELGIUM: REPERCUSSION ON SEROLOGY IN UP TO 19 YEAR-OLDS AT TWO DIFFERENT TIMEPOINTS

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Background: Hepatitis B virus (HBV) can be eliminated by effective universal vaccination programs, as recommended by WHO. In Belgium, large scale free of charge HBV vaccination in infants and 12 year-old adolescents (catch-up) started in 1999. To evaluate the effects of this campaign, seroprotection and breakthrough infection in < 20 year-olds were assessed through a serosurvey.

Methods: Seroprotection (anti-HBs > or = 10 mIU/ml) and markers of breakthrough infection (anti-HBc, HBsAg) were assessed by ELISA in 2443 sera (left-over from diagnostic testing) of < 20 year-olds (°1987-2005) collected in 2006-2007, and compared with 1) the results of an earlier serosurvey conducted in 2002-2003 (°1983-2001) and with 2) vaccination coverage data.

Results: In 2006, the maximal prevalence of solely anti-HBs seropositivity ('vaccinated' serostatus) was 82.9% at one and 60.5% at thirteen years of age. A clear increase of the 'vaccinated' serostatus was found in age cohorts that had been targeted by the campaign after the previous serosurvey. Regional differences in young children mirrored differences in available regional coverage data. In adolescents coverage data were scarce but serological data suggested significant regional differences as well. The prevalence of markers of HBV-infection (anti-HBc, HBsAg) remained stable despite universal vaccination, at a low level (2.2% in 2002 and 1.8% in 2006) similar to pre-vaccination data.

Conclusion: These findings demonstrate that universal infant and catch-up HBV vaccination was well implemented in Belgium, though with regional differences that might impact on adult prevalence in the future.

MEDICAL STUDENT ATTITUDES AND PRACTICES ASSOCIATED WITH RECEIVING HEPATITIS A VACCINE AND ALSO VACCINE ADVERSE EVENT AND EFFECT ON ACCEPTABILITY

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Objective: Hepatitis A is the most frequently reported vaccine-preventable diseases . In this study we aimed to assess the attitudes and practices of medical students regarding hepatitis A immunization and also adverse reactions of associated with vaccine and effect on acceptability.

Methods: One hundred tree fourth- to sixth- year medical students with ages ranging from 20 to 26 years were vaccinated with a hepatitis A vaccine on 14 days in the 2rd and 3rd week of December by the same nurse at Hacettepe University Faculty Of Medicine. Each subject was asked to complete a questionnaire and follow-up form.

Results: One hundred tree fourth- to sixth- year medical students were enrolled to this study. These participants included 67 females and 36 males. The mean student age was 21.69 ± 0.97 years. Complaints related to the injected site predominated; pain (58.3%) and sensibility (38.8%) were the most common side effects of the vaccination site. Despite the side effects all of the vaccinated students wanted to receive the following dose of vaccine because of hepatitis A is a vaccine preventable disease. Twelve students (11.7 %) said that our immunization recommendations because of to become a pediatric infectious disease department was very important to receive vaccination. The cost of vaccination was also one of the major reason not to vaccinate for 60 (58.3%).

Conclusions: The cost of vaccination and recommendation who said may have been important to receive hepatit A vaccination for medical students and also may be for other healt care workers.

COMBINED HEPATITIS B IMMUNIZATION OF NONRESPONDER HEALTH CARE WORKERS IN A HOSPITAL FOR INFECTIOUS DISEASES IN HUNGARY**Z. Meszner**^{1,2}, P. Veres³, I. Mihaly⁴

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Background and aims: Health care workers, especially in a hospital specialized for infectious diseases, worry more and are at greater risk of contacting hepatitis B than members of the normal population. Nonresponders - less than 10 IU/ml anti-hbs after two complete series of a hepatitis B vaccine - could, according to some observations, benefit from a combined - hepatitis A+B immunization. In our hospital altogether 35 health care workers, as nonresponders, were offered this opportunity with the hope of seroconversion.

Methods: 31/35 nonresponder health care workers accepted the three doses (schedule: 0, 1 and 6-12 mo) of the combined hepatitis, A+B vaccine. 29/35 completed the three doses and returned for the serology 30-60 days after the 3rd dose. Anti-hbs and anti-HAV IgG testing was done in each case.

Results:

1. anti-HAV IgG seroconversion was seen in each of the 29 cases.
2. 28/29 had anti-hbs titers above 10 IU/ml
3. no adverse events to vaccination was seen.
4. the success of the vaccination program improved influenza vaccination attitudes in all health care workers as an unexpected benefit

Conclusion: For nonresponder health care workers the use of a combined hepatitis A+B vaccine could be a beneficial approach, as was seen in our experience. The possible mechanisms of action is briefly discussed through available data in the literature..

WHO CAUSES PERTUSSIS DISEASE IN THE YOUNGEST INFANTS?

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Background and aims: Case contacts of pertussis in infancy have been evaluated in a Swedish surveillance study in the period January 1, 2009 - December 31, 2010. The aim was to disentangle the path of infection for infants with pertussis disease. This knowledge is needed in the planning of pertussis prevention strategies for infants.

Methods: The parents were asked if someone who had been coughing for over a week had been in close contact with the infant with pertussis disease in the month prior to symptoms in the infant.

Results: When the mother was the case-contact, the infected infant had more breathing problems ($p=0.015$) and a trend to more hospitalizations ($p=0.068$) than infants with other persons as the case-contact. The median age of the infant at the onset of pertussis symptoms when the mother was the case-contact was 25 days. For other case contacts the age was 91 days ($p=0.003$). Also, when the mother was the case-contact, there was a tendency towards shorter time intervals between the start of pertussis symptoms and both the diagnostic test for pertussis and antibiotic treatment.

Conclusions: Pertussis in early infancy is a serious disease and the mother may be an important source of disease transmission. According to the literature, prevention with the cocoon strategy has shown to be challenging to implement. A high coverage rate, timeliness to vaccination schedule, and probably, vaccination in the third trimester of pregnancy could decrease pertussis and its complications in infancy through maternal transmission of antibodies.

IMPROVING SECURITY AND ADHERENCE TO IMMUNIZATION**H.I.G. Giamberardino, A. Hoinski***Hospital Pequeno Principe, Curitiba, Brazil*

Background and aims: Misconceptions and false contraindications to immunization can discourage parents of children and adolescents to following their vaccination schedules. Since 2008, the Immunization Center of a paediatric referral hospital, implemented a service screening and pre-vaccination medical advice and monitoring the adverse reactions (AR). The aim of this study is to describe its experience, the main AR observed and improving vaccinations coverage.

Methods: For each child without medical prescription attended in the Centro de Vacinas Pequeno Principe, Curitiba city, Brazil, a pre-vaccination form is applied with questions about the current conditions and health history. Information about use or nonuse of medications, chronic diseases, previous AR, presence of allergy and fever in the past 72 hours, were verified. After the medical consultation is applied or not the vaccine

Results: An average of 1800 doses/month of vaccines was applied. The main cause of vaccine contraindication is the presence of fever in the past 24 hours. Between January/2008 to December/2011, 89003 doses have been applied, 163 AR(0.18%) were observed: redness and swelling 50.92%(83), fever 26.99%(44) local pain 11,04%(18), syncope 4.90% (8), continuous crying 4.90%(8) and convulsive seizures 1,22%(2). The AR was more associated with the following vaccines: pneumococcal conjugate vaccine (31.03%), meningococcal C conjugate vaccine (17.92%), acellular pertussis vaccine (15.17%), pentavalent (6.89%) and 23 valent pneumococcal polysaccharide vaccine (6.2%).

Conclusions: Most AR observed was mild and well tolerated. This screening tool helps correct indication and maintenance of the opportunity and adherence to the vaccines.

IMMUNOPROPHYLAXIS FOR RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS AMONG INFANTS WITH SEVERE OSTEOGENESIS IMPERFECTA: NEW INDICATION AND NATIONAL AUDIT IN IRELAND

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Background and aims: Respiratory illnesses could be very serious, even life threatening among neonates and infants with severe forms of osteogenesis imperfecta (OI). Respiratory syncytial virus (RSV) bronchiolitis could deteriorate the respiratory status of infants with severe OI increasing length of stay (LOS) and often needing paediatric high dependency unit (PHDU) or paediatric intensive care unit (PICU) care. Immunoprophylaxis using Palivizumab - a monoclonal antibody to RSV F protein could prevent RSV bronchiolitis for severe OI infants. We aimed to audit our local practice and national data.

Methods: We conducted a retrospective chart review of infants with severe OI in the Mid-West of Ireland from 2005 to 2010, all of whom received Palivizumab in addition to the standard care for OI with early bisphosphonates. From national computerised Hospital In-Patient Enquiry (HIPE) data information all infants in Ireland with OI admission and RSV positive bronchiolitis was tabulated for study period. LOS and bed days use nationally were determined. Information of immunoprophylaxis for national OI cohort was obtained from the national provider of Palivizumab. Hospital audit committee approval was sought.

Results: No infant in the Mid-West of Ireland with severe OI who have received Palivizumab developed RSV bronchiolitis (n=5). Nationally 17% of non-prophylaxed infants with OI developed RSV positive bronchiolitis among the 121 admissions. Increased LOS, bed days consumption and PICU admission were observed among those with dual pathology of severe OI and RSV infection.

Conclusion: Infants with severe forms of Osteogenesis Imperfecta (OI) seems to benefit from RSV immunoprophylaxis with Palivizumab

FOUR YEARS PNEUMOCOCCAL CONJUGATE INFANT VACCINATION IN GERMANY: IMPACT ON INCIDENCE OF INVASIVE INFECTIONS AND SEROTYPE DISTRIBUTION IN CHILDREN

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Background: Vaccination of infants with pneumococcal conjugate vaccine (PCV7) was recommended in Germany in July 2006. Additionally, PCV10 was available from April 2009 and PCV7 was replaced by PCV13 in December 2009.

Objective: To compare the incidence and serotype distribution of invasive pneumococcal disease (IPD) in children from 2007 to 2010 with reference to the pre-vaccination period (1997-2002).

Methods: Nationwide surveillance of IPD for children < 16 years in Germany was based on two independent reporting sources: active surveillance in paediatric hospitals and passive web-based sentinel surveillance through microbiological laboratories. Serotyping was performed using the Neufeld Quellung reaction. Case definition: isolation of *Streptococcus pneumoniae* from a normally sterile body site. IPD incidence was estimated by capture-recapture analysis. Rate ratios comparing post- to pre-vaccination incidence were calculated.

Results:

Table: IPD incidence rate ratios post- vs. pre-vaccine introduction

age	2007	2008	2009	2010 (95% CI)
0-1y	0.58	0.58	0.63	0.64 (0.35-1.06)
0-4y	0.77	0.66	0.89	0.75 (0.45-1.15)
5-15y	1.22	1.23	1.72	1.77 (0.50-4.28)
0-16y	0.87	0.78	1.06	0.94 (0.59-1.39)

[Table]

The incidence of PCV7 serotypes decreased from pre-vaccination years to 2010 (< 2y: -91% from 13.25 to 1.16 per 100.000), < 16y: -88% from 2.41 to 0.29), while the incidence of non-PCV7 serotypes increased (< 2y: +72% from 6.84 to 11.74 per 100.000), < 16y: +123% from 0.78 to 1.74).

Conclusion: Infant PCV7 vaccination in Germany prompted a decrease in the incidence of IPD in infancy, but no significant overall IPD reduction in children < 16.

COMPARISON OF IMMUNOGENICITY AND REACTOGENICITY OF SPLIT VERSUS SUBUNIT INFLUENZA VACCINE IN KOREAN CHILDREN 6 THROUGH 35 MONTHS OF AGE

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Trivalent inactivated subunit and split vaccines are the two most common formulations against influenza for Korean. We compared the safety and immunogenicity in children 6-35 months of age in Korea of influenza subunit vaccine and split vaccine in 2008.

In our randomized, parallel-group, controlled trial, healthy children received split or subunit vaccine before influenza season (from Oct to Dec, 2008) at six hospitals in Korea. We measured antibody titers with a haemagglutination-inhibition assay at baseline and 30 days after 1st or 2nd flu shot depending on vaccinee's influenza vaccine history. Primary outcome was vaccine immunogenicity of the full analysis set by the EU Committee of Human Medicinal Products licensing criteria.

Out of the total 106 participants aged 6-35 months, 47 received split vaccine (SPL) and 59 received subunit vaccine (SU). The two groups shared similar demographic characteristics. After vaccination, 41 out of 47 (87%) with SPL and 42 out of 59 (71%) SU had titers of 1:40 or greater against H1N1. 40 out of 47 (85%) in SPL group and 34 out of 59 (58%) in SU group had titers of 1:40 or greater against H3N2. Seventy percent in SPL group and 37% in SU group had titers of 1:40 or greater against B. There were no vaccine-related serious adverse events. Subunit vaccine was associated with fewer local reactions than split vaccine.

This study demonstrated that split vaccine showed better immunogenicity than subunit vaccine in children 6-35 months of age in Korea.

OPEN-LABEL RANDOMISED CONTROLLED STUDY TO EVALUATE INDUCTION OF IMMUNE MEMORY FOLLOWING INFANT VACCINATION WITH GLYCO-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 subsequently receive a *Haemophilus influenzae* type b (Hib)-MenC booster at 12 months. DTaP-IPV-Hib, pneumococcal conjugate and MMR vaccines are administered to all children according to routine schedule. Blood samples are drawn at 5, 12, 12 months+6 days, 13 and 24 months.

Results: Results were available from 74, 71, 48 and 30 children from each group respectively at 5 months. Visits for 12-13 month old toddlers are ongoing. More MenC-specific memory B-cells were measured at 5 months following single-dose MenC-TT at 3 months, compared to other schedules. These children also produced the greatest response to the Hib-MenC-TT booster. There was a faster and greater booster response in children primed with single-dose MenC-CRM compared to 2 doses. By 13 months, un-primed children had a similar number of memory B-cells following Hib-MenC-TT when compared to 2-dose MenC-CRM-primed children.

Conclusions: Fewer doses of MenC conjugate vaccine in early infancy prime for a stronger memory B-cell response following Hib-MenC-TT booster. MenC-TT priming appears to induce more memory B-cells than MenC-CRM, which may explain improved persistence of bactericidal antibody documented with this combination of vaccines.

PRIMARY VACCINATION WITH 10-VALENT PNEUMOCOCCAL NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* PROTEIN-D CONJUGATE VACCINE [PHiD-CV] IN HIV-EXPOSED-INFECTED, EXPOSED-UNINFECTED AND UNEXPOSED-UNINFECTED SOUTH AFRICAN INFANTS

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Aims: HIV-infected (HIV+) infants are at increased risk of mortality and invasive pneumococcal disease. This study evaluated immunogenicity, reactogenicity and safety of PHiD-CV (GlaxoSmithKline Biologicals) in HIV+, HIV-exposed (*in utero*) but uninfected (HEU) and HIV unexposed-uninfected (HUU) infants following primary vaccination.

Methods: In this Phase III, open-label, single-centre, controlled study in South Africa, infants stratified by HIV status received PHiD-CV primary vaccination at age 6, 10 and 14 weeks, co-administered with Expanded Programme on Immunisation (EPI) vaccines. Immune responses were assessed pre- and 1-month post-primary using GSK's 22F-ELISA and opsonophagocytic activity (OPA) assays. Baseline CD4⁺ cell percentages were evaluated in HIV+ infants.

Results: Of 384 vaccinated infants, 349 were included in the according-to-protocol immunogenicity cohort. At baseline, all HIV+ infants were classified in WHO clinical stage 1; median (interquartile range) CD4⁺ cell percentage was 35.9% (28.7-41.0%). ELISA, but not OPA responses, in HIV+ infants seemed similar to HUU infants; ≥97.2% HIV+ infants had antibody concentrations ≥0.2 µg/mL for all vaccine pneumococcal serotypes except for 6B and 23F (Table). Incidences (overall/dose) of solicited local/general adverse events within 4 days post-vaccination in HIV+ and HEU infants were not higher than in HUU infants.

Table. Immune responses to PHiD-CV vaccine pneumococcal serotypes

1 month post-dose 3 (according-to-protocol cohort for immunogenicity)

Serotype	Infants with antibody concentrations ≥0.2 µg/mL (%)		
	HIV+ n=72	HEU n=90	HUU n=187
1	98.6	98.9	100
4	98.6	98.9	100
5	100	98.9	100
6B	87.5	88.9	84.4
7F	98.6	98.9	100
9V	97.2	98.9	100
14	98.6	98.9	100
18C	100	98.9	100
19F	97.2	98.9	100
23F	90.3	92.2	89.8
	Infants with OPA titres ≥8 (%)		
1	80.0	87.8	88.1
4	92.8	98.9	100
5	90.0	95.6	95.7
6B	71.4	82.0	85.8
7F	98.6	100	100
9V	94.3	96.6	98.9
14	95.7	100	97.8
18C	91.4	98.9	99.5
19F	82.9	94.4	98.9
23F	75.7	85.2	87.2

N=maximum number of infants with available data; OPA=opsonophagocytic activity

[Table]

Conclusions: PHiD-CV was immunogenic and well tolerated in HIV+, HEU and HUU infants following 3-dose primary vaccination co-administered with EPI vaccines. PHiD-CV could potentially provide benefit against pneumococcal disease in HIV+ infants.

IMMUNISATION WITH 10-VALENT PNEUMOCOCCAL NTHI PROTEIN D CONJUGATE VACCINE (PHID-CV) ACCORDING TO DIFFERENT SCHEDULES IN HIV UNEXPOSED/UNINFECTED SOUTH AFRICAN INFANTS

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Aims: To evaluate the immunogenicity of different immunisation schedules of PHiD-CV in healthy, HIV unexposed/uninfected (HUU) South African infants.

Methods: In this Phase III, open-label, single-centre, controlled study, HUU infants were randomised (1:1:1) to receive PHiD-CV in 1 of 3 schedules: **3+1** (aged 6, 10 and 14 weeks [primary] and 9-10 months [booster]); **3+0** (aged 6, 10 and 14 weeks [primary], no booster); **2+1** (aged 6 and 14 weeks [primary] and 9-10 months [booster]). Immune responses were assessed pre- and 1 month after priming and booster vaccination (3+1 and 2+1 groups) using GSK's 22F-ELISA and OPA assays.

Results: 300 infants were enrolled (total-vaccinated-cohort, 100 per group). Immune responses for the according-to-protocol cohort (n=284) are shown in the table. Post-priming antibody levels tended to be lower in the 2+1 group. At 6 months post-priming, antibody GMCs and OPA GMTs were generally within the same ranges after 3- or 2-dose priming. Robust increases in responses were observed pre- to post-booster in the 3+1 and 2+1 groups; 2.80-9.61 and 3.63-9.88-fold, respectively, for antibody GMCs and 4.95-71.97 and 4.42-74.68-fold, respectively, for OPA GMTs.

Table: Immune responses to PHiD-CV pneumococcal serotypes 1 month post-primary and post-booster vaccination (ATP cohort for immunogenicity)

Serotype	Post-primary			Post-booster	
	3 (+1) n=93	3 (+0) n=94	2 (+1) n=97	3+1 n=93	2+1 n=97
	% infants with antibody concentrations ≥0.2 µg/mL				
1	100	100	99.0	100	100
4	100	100	99.0	100	100
5	100	100	97.9	100	100
6B	79.6	89.2	82.5	93.5	97.9
7F	100	100	99.0	100	100
9V	100	100	94.8	100	96.9
14	100	100	97.9	98.9	96.9
18C	100	100	97.9	100	100
19F	100	100	97.9	98.9	99.0
23F	89.2	90.3	86.6	92.5	96.9
	% infants with OPA titres ≥8				
1	82.8	93.5	90.6	100	98.9
4	100	100	97.9	98.9	100
5	94.6	96.7	94.8	100	98.9
6B	79.3	92.3	81.5	92.0	94.7
7F	100	100	98.9	100	100
9V	97.8	100	94.8	100	96.8
14	95.7	100	80.0	100	100
18C	98.9	100	97.8	100	98.9
19F	98.9	98.9	92.6	95.5	92.6
23F	86.4	88.0	83.5	90.0	91.6

N=maximum number of infants with available results;
OPA=opsonophagocytic activity

[Table]

Conclusions: PHiD-CV was immunogenic when administered in different schedules to healthy HUU infants. The post-booster responses suggest effective immunological priming with both the 3-dose and 2-dose primary series.

POPULATION IMMUNITY TO POLIOVIRUSES IN THE CONTEXT OF A LARGE-SCALE OUTBREAK OF POLIOMYELITIS - TAJIKISTAN, 2010

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Background: A nationwide serosurvey was conducted in Tajikistan to better understand population immunity to polioviruses (PV) before and after the poliomyelitis outbreak in 2010 caused by imported wild PV type 1 (PV1) (460 confirmed cases among children and young adults). The serosurvey was conducted after mOPV1 and before tOPV immunization rounds implemented to control the outbreak.

Methods: Serum specimens from a nationwide sample of persons aged 1-24 years selected through stratified cluster sampling (n=2447) were tested for neutralizing antibodies to all three PV types. Samples with titers < 1:8 were considered seronegative.

Results: Proportion of seronegatives was 1.1% (95% CI, 0.7-1.8) to PV1, 1.2% (95% CI, 0.9-1.7) to PV2, and 13.1% (95% CI, 11.5-14.9) to PV3. Seronegativity to PV3 exceeded 10% in all age groups except 15-19 years (8.3%), and was highest (17.3%) among 1-4 year-olds. Seronegativity to PV3 was $\geq 10.0\%$ in all regions, and was highest (20.0%-23.7%) among 1-4 year-olds in the two regions where the outbreak began among young children in early 2010.

Conclusions: Based on a high seronegativity to PV3 across wide age range (used, in the absence of pre-outbreak specimens, as a proxy for pre-outbreak PV1 immunity), the outbreak in Tajikistan resulted from accumulation of susceptibles due to historic weaknesses in immunization program, particularly where early cases occurred. Low current PV1 seronegativity indicates that mOPV1 rounds with expanded target age (≤ 15 years) succeeded in closing the immunity gap. To accelerate control of outbreaks in areas polio-free for >10 years, expanding SIA target age groups should be considered.

ANTIBODY PERSISTENCE 66 MONTHS AFTER A BOOSTER DOSE OF COMBINED *HAEMOPHILUS INFLUENZAE* TYPE B-*NEISSERIA MENINGITIDIS* SEROGROUP C-TETANUS-TOXOID (HIB-MENC-TT) CONJUGATE VACCINE

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Background and aims: Persisting antibodies play a critical role in long-term protection against Hib and MenC disease. Long-term antibody persistence was assessed 66 months after a booster dose of Hib-MenC-TT given at 13-14 months of age.

Methods: Previously (NCT00352963) subjects were randomised 1:2:1 to

- 1) Hib-MenC group: primed with 3 doses (2,4,6 months) Hib-MenC-TT+DTPa-HBV-IPV, boosted with Hib-MenC-TT at age 13-14 months;
- 2) Neis_HibMenC group: primed with 2 doses MenC-TT and 3 doses of DTPa-HBV-IPV/Hib containing vaccines, boosted with Hib-MenC-TT at age 13-14 months;
- 3) MenC-CRM group: primed with 3 doses of MenC-CRM₁₉₇+DTPa-HBV-IPV/Hib, boosted with DTPa-HBV-IPV/Hib at age 13-14 months (plus a 4th dose of MenC-CRM₁₉₇ after completion of the booster study).

Blood samples were taken 1, 18, 30, 42, 54 and 66 months post-booster. Serum bactericidal activity was measured using rSBA-MenC and anti-PRP (Hib) was measured using ELISA. Serious adverse events (SAEs) occurring since the booster and considered possibly vaccine-related were recorded.

Results: Protective antibodies against Hib and MenC persisted in 100% and >82% of Hib-MenC-TT boosted children, respectively, up to 66 months post-booster vaccination. No vaccine-related SAEs were captured retrospectively.

Conclusions: One booster dose of Hib-MenC-TT given to toddlers after a Hib-MenC-TT or MenC-TT priming course induced protective antibody levels to Hib and MenC, persisting up to 66 months post-booster, regardless of the priming schedule used.

Table rSBA-MenC and anti-PRP immunogenicity one and 66 months after booster vaccination (ATP cohort for persistence, 66 months post-booster)

Group	Post-booster timepoint ^a	n	rSBA-MenC [95% CI]		n	Anti-PRP antibodies [95% CI]	
			% ≥1:8	GMT		% ≥0.15 µg/mL	GMC, µg/mL
1) Hib-MenC group: (N=47)	Month 1	40	100 [91.2–100]	5217.1 [3781.6–7197.4]	47	100 [92.5–100]	56.88 [40.34–80.20]
	Month 66	46	82.6 [68.6–92.2]	121.5 [71.0–207.9]	47	100 [92.5–100]	1.60 [1.11–2.32]
2) Neis_HibMenC group: (N=103)	Month 1	89	100 [95.9–100]	9739.2 [7132.9–13297.8]	102	100 [96.4–100]	67.94 [51.23–90.09]
	Month 66	101	94.1 [87.5–97.8]	227.6 [160.2–323.3]	101	100 [96.4–100]	2.63 [2.11–3.26]
3) MenC-CRM group: (N=47)	Month 1	41	*	*	47	100 [92.5–100]	43.60 [30.12–63.12]
	Month 66	46	60.9 [45.4–74.9]	42.7 [22.3–81.8]	47	97.9 [88.7–99.9]	1.76 [1.17–2.66]

^aAll timepoints will be reported in the poster

* Because Spain did not recommend a booster dose of MenC vaccine at the time of the study, a post-booster sample was not planned for the MenC-CRM₁₉₇ group. Subjects were subsequently offered a dose of MenC-CRM₁₉₇ at 14–15 months of age, and subjects who received this fourth dose were invited to enter the long-term persistence phase at Month 30.

ATP = according-to-protocol; n = number of subjects with available results; GMC = geometric mean concentration
GMT = geometric mean titre

[Table]

IMPACT OF THE PNEUMOCOCCAL CONJUGATE VACCINES PCV-7 AND PCV-13 ON THE BURDEN OF INVASIVE PNEUMOCOCCAL DISEASE IN KUWAIT: 8-YEAR OVERVIEW**J.M. Albert**¹, N. Aleyadi²¹*Microbiology, Faculty of Medicine, Kuwait University,* ²*Public Health Department, Ministry of Health, Kuwait, Kuwait***Introduction:** Pneumococcal conjugate vaccine PCV-7 and PCV-13 were introduced in Kuwait in August 2006 and June 2010 respectively.**Objectives:** The impact of both the vaccines on the burden of invasive pneumococcal disease (IPD) and prevalence of resistance to penicillin were evaluated.**Methods:** Two periods from January 2004-July 2006 (pre-PCV era) and from August 2006-September 2011 (post-PCV era) were reviewed. The age distribution and source of infection were determined. The susceptibility of *S.pneumoniae* to penicillin using E test were determined.**Results:** In the pre-PCV era, out of 250 *S.pneumoniae* isolates, seventeen percent and 50% were from children ≤ 5 years and adults > 50 years causing IPD in 36% and 27% of them, respectively. In the post-PCV era, out of 395 *S.pneumoniae* isolates 24% and 46% were from children ≤ 5 years and adults > 50 years causing IPD in 50% and 27% of them, respectively. A year-wise analysis of data showed that there was a significant decline in the burden of IPD in children ≤ 5 years from 75% in 2007 to 26% in 2011 ($p < 0.01$) and in adults > 50 years, from 39% in 2007 to 18% in 2011 ($p < 0.01$). Full resistance to penicillin dropped from 9.1% in the pre-PCV era to only 1.6% in the post PCV era ($p < 0.05$).**Conclusion:** In Kuwait, the impact of PCV's on IPD and penicillin resistance is well noted. Also the new recommendation for introduction of PCV-13 for adults > 50 years is validated by our data.

ASSOCIATION BETWEEN HPV VACCINE UPTAKE AND CERVICAL CANCER SCREENING IN THE NETHERLANDS; IMPLICATIONS FOR FUTURE IMPACT OF PREVENTION

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An increasing number of countries has introduced HPV vaccination additionally to cervical cancer screening. Information on the association between participation in either programme and on potential risk groups for non-participation, is essential for estimating the future impact of cervical cancer prevention. We studied the association between participation in screening (mothers) and in vaccination (girls) and studied the impact of this association on the effectiveness of cervical cancer prevention. Furthermore, we investigated risk groups for non-participation and calculated population attributable fractions.

Girl's vaccination status (from the vaccination registry) was matched by houseaddress with her mother's screening participation (from the cervical cancer screening database). We performed multivariable multilevel logistic regression.

Our results, based on 89% of all girls invited for HPV vaccination (n=337,368), show that vaccination status was significantly associated with mother's screening participation (OR: 1.54 (95%CI 1.51-1.57)). If mother's screening participation is taken as proxy of a girl's future screening behaviour, only 13% of the girls will not participate in any prevention programme compared to 23% non-participation if only screening is available. The positive association between vaccination and screening participation resulted in slightly lower model estimates of the impact of vaccination on cervical cancer incidence compared to estimates based on random participation.

Girls with non-western ethnicities, with young mothers, who live in urban areas with low SES are at risk for non-participation. A significant part of potential non-screeneres may be reached through vaccination.

The association between vaccination and screening participation has almost no bearing on the effectiveness of the vaccination programme.

AN OVERVIEW OF POTENTIAL PUBLIC HEALTH IMPACT OF DELAYING UNIVERSAL ROTAVIRUS VACCINATION IMPLEMENTATION IN WESTERN EUROPEAN COUNTRIES IN 2011

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Background and aims: In 2006, 2 rotavirus (RV) vaccines were licensed in Europe for prevention of RV gastroenteritis (RVGE) in infants. Up to December 2011, universal RV vaccination was recommended, funded, and implemented in 4 European countries (Austria, Belgium, Finland, and Luxembourg) although evidence concludes that such vaccination policy would have significant impact in reducing RV burden. This study aims to estimate the potential public health consequences of delaying universal RV vaccination implementation in terms of non-avoided burden in Western Europe.

Methods: A comprehensive literature search has identified evaluations performed by European independent bodies regarding health and economic impact of universal RV vaccination in their countries. Countries for which evaluation was available, but where no universal RV vaccination was implemented, were then selected for analysis. The cumulative non-avoided RV burden (defined as non-avoided RVGE-related hospitalizations) was estimated for a 5-year period following RV vaccines license (2007-2011).

Results: In December 2011, evaluations of the RV vaccination were available for 8 European countries, and 6 of them had not yet implemented universal RV vaccination: France, Ireland, Italy, the Netherlands, Norway, and the UK. The cumulative non-avoided number of RVGE-related hospitalizations over a 5-year period in children under 3-5 years of age was estimated to be around 4,000 in Norway, 10,000 in Ireland, 12,000 in the Netherlands, and over 50,000 in France, Italy or the UK.

Conclusions: Delaying the implementation of universal RV vaccination in Western European countries has substantial public health impact and should be taken into account by decision makers.

COMMUNITY INTERVENTION TO AN OUTBREAK OF VACCINE-PREVENTABLE DISEASE. RISK STRATEGY

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Background and aims: There is evidence of a relationship between health and social inequalities in Public Health. In this sense, the Romani communities are socially vulnerable to health issues; and they are especially vulnerable to vaccine-preventable diseases. For this reason, Evangelical Churches offer the Romani communities crucial support during health crises. After detecting cases of measles in a predominantly Romani neighbourhood, a vaccine intervention under a risk strategy was proposed.

Methods: Qualitative methodology. A community-scale intervention was performed with technical consensus between health workers, the Romani Association ENSAYE-KALO and pastors of Evangelical Churches.

Results: 5 cases of measles were detected in Romani children with family ties to people living in two specific streets (5 and 6 blocks of flats). The "La Banda" Health Centre located in Chiclana de la Frontera, Cadiz (Spain), carried out an immunization survey in under 40 year-olds, and contacted the Romani Collective ENSAYE-KALO informing them of the importance of vaccination to prevent the spread of the measles outbreak. In turn, this collective together with the pastors of evangelical churches published and informed during their religious service that, after the service, everyone had to go to the "La Banda" Health Centre for vaccination. 75 people under 40 attended, and all 46 susceptible were vaccinated (100%). Following the intervention, there have not been new cases of measles in the area.

Conclusions: The use of a risk strategy in vaccines and the involvement of community agents and leaders together with the health team, is highly efficient in vaccine-preventable outbreaks.

THE BURDEN OF GENITAL WARTS IN THE BALEARIC ISLANDS: A FIRST APPROACH

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Background and aims: Genital warts are the most frequent sexually transmitted infection, particularly in youngsters. In Spain, in two different studies there were an incidence of 118 and 160 cases out of 100.000 in the 15-64 year-old population. The estimated health cost is of €833 per patient. Since 2010 the HPV vaccine is offered to the 14 year-old females. Our aim was to make a first approach of the burden of the disease in our region.

Methods: Ecological, descriptive study of the cases recorded in the primary care electronic records as Condyloma acuminatum or Other specified viral warts in the years 2006 to 2010. Estimated incidence (incident rates -IR- per 100,000) by age and gender. Evolution over years.

Results: 6,804 cases were recorded (annual average IR of 128; 166 in 15-64 year-old group), half of them male. The higher IR was for the 20-29 year-olds (316), followed by 15-19 year-olds (145). In male, IR was lower in teenagers (rate ratio 0.65, 95% CI 0.53-0.79) and higher in young adults (20-29 year-old: 1.14 95% CI 1.05-1.23; 30-39 year-old: 1.22 95% CI 1.11-1.35). The linear trend shows a significant rise (Chi-square 57.7; $p < 0.01$) over the period.

Conclusions: Some possible biases (misclassification, under-recording, lack of use of primary care services) need further analysis. Nevertheless, the burden of genital warts is high and rises each year, claiming for specific control programmes. Better knowledge about the populations at higher exposure risk (especially teenagers) is needed, as well as monitoring the post-vaccination trends.

IMMUNOGENICITY REVIEW OF A NEW DTAP-IPV-HEP B-PRP-T VACCINE (HEXAXIM™) FOLLOWING PRIMARY SERIES ADMINISTRATION AT 2-4-6 MONTHS IN LATIN AMERICA

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Background and aims: To provide an overview of the primary series immunogenicity of a new fully liquid DTaP-IPV-Hep B-PRP-T hexavalent vaccine, Hexaxim™.

Methods: Immunogenicity 1 month following a primary series at 2-4-6 months of age was investigated in four randomized clinical trials in Argentina, Mexico, and Peru. In total, 1279 subjects were assessed and the data from the four trials were pooled. Hepatitis B vaccine was not administered at birth. Immunogenicity was determined 1 month post-3rd vaccination.

Results: Seroprotection (SP)/seroconversion (SC) rates (% subjects):

	Argentina N=260	Mexico N=192	Mexico N=695	Peru N=132	Pooled
Anti-Hep B ≥ 10 mIU/mL	99.2	100	98.3	99.2	98.8
Anti-Diphtheria ≥ 0.01 IU/mL	100	NA	96.4	95.5	97.1
Anti-Tetanus ≥ 0.01 IU/mL	100	NA	100	NA	100
Anti-Polio 1 ≥ 8 (1/dil)	100	NA	99.9	NA	99.9
Anti-Polio 2 ≥ 8 (1/dil)	100	NA	100	NA	100
Anti-Polio 3 ≥ 8 (1/dil)	100	NA	99.9	NA	99.9
Anti-PRP ≥ 0.15 μ g/mL	94.6	NA	98.8	100	98.0
Anti-PT titer ≥ 4 -fold increase	91.8	NA	97.4	NA	96.0
Anti-FHA titer ≥ 4 -fold increase	93.2	NA	98.4	NA	97.0

NA=not assayed

[Table 1]

For each antibody and country (when tested) SP/SC rates were high. The SP/SC rates following Hexaxim were similar to licensed comparator(s). Non-inferiority to licensed comparators was demonstrated in Argentina (each antigen) in Mexico (anti-D) and in Peru (anti-Hep B) (not tested elsewhere). There were no safety concerns.

Conclusions: Each antigen contained in this new hexavalent vaccine (Hexaxim™, an AcXim family vaccine) in Latin American countries induced a high immune responses following primary series administration at 2-4-6 months.

COST-EFFECTIVENESS OF 13-VALENT RELATIVE TO 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN THE UNITED KINGDOM

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Background and aims: Seven-valent pneumococcal conjugate vaccine (PCV7) has had a profound public health impact by preventing disease caused by seven *Streptococcus pneumoniae* serotypes. PCV13 covers six additional serotypes while PCV10 covers an additional three. The study objective was to assess the cost-effectiveness of PCV13 versus PCV10 paediatric vaccination in the United Kingdom (UK).

Methods: A static steady state model was developed to estimate the impact of PCV13 and PCV10 on invasive pneumococcal disease (IPD), pneumonia, and acute otitis media (AOM). Pneumococcal disease cases were estimated based on 2009/10 UK incidence and serotype coverage, vaccine effectiveness, and indirect effects. Direct effects for PCV13- and PCV10-covered serotypes were assumed to be similar to PCV7. IPD serotype distribution was used for pneumonia and AOM. Indirect "herd" effects were assumed only for PCV13 as PCV10 has not demonstrated significant reduction in nasopharyngeal carriage in vaccinated individuals. Assumptions were tested in sensitivity analyses.

Results: It is estimated that PCV13 will have a greater impact than PCV10 on all forms of pneumococcal disease under base-case assumptions due to higher serotype coverage. Compared with PCV10, PCV13 is expected to further reduce direct medical costs by over £60 million and add 30,000 QALYs annually. For all scenarios tested, PCV13 was either cost-saving or cost-effective with an ICER < £1,000 per QALY gained when indirect effects were included.

Conclusions: Continuing national PCV13 paediatric vaccination in the UK is expected to be cost-saving or cost-effective by providing a substantial further reduction in pneumococcal disease cases when compared to PCV10.

TIMING OF MEASLES VACCINATION FOR PRE-SCHOOLERS: TIME POINT OR PERIOD?**J.A. Bielicki**^{1,2}, R. Achermann^{3,4}, C. Berger¹

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Background and aims: Structural aspects of immunization schedules may impact on vaccine delivery and coverage. We assessed what information could be derived from statutory health insurance data in describing measles vaccination levels in Switzerland, a country with near universal health insurance coverage.

Methods: A dynamic cohort study evaluating measles immunizations in children born between 2006 and 2008 insured with a single health insurer was conducted. Age at first (MCV1) and second (MCV2) measles immunization was identified through a time-to-event analysis of claims data submitted until December 2010.

Results: 42950 infants (52% males) were included. In our cohort only 62.6% of 13 month-olds and 59.4% of 25 month-olds were up-to-date for MCV1 and MCV2, respectively. For 24 to 35 month-olds vaccination levels (85.7% MCV1, 66.7% MCV2) corresponded well with nationwide official estimates (86.9% MCV1, 70.8% MCV2). Most MCV1 doses were administered in the 12th month of life as recommended in the Swiss schedule. Most MCV2 doses were administered during the recommended interval (15 to 24 months of age) with delivery spread out across the interval and accelerations at 18 and 24 months of age corresponding to time points for recommended well-child visits.

Conclusions: Use of health insurance data allows timing to be evaluated in addition to vaccination levels in a given age group. From our data, it appears that recommending a narrower period for measles vaccination may facilitate vaccine delivery. Structural aspects of an immunisation programme should be taken into account when trying to optimise measles vaccine coverage.

REGIONAL DIFFERENCES IN MEASLES IMMUNIZATION PATTERNS IN SWITZERLAND**J.A. Bielicki**^{1,2}, R. Achermann^{3,4}, C. Berger¹

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Background: Nationwide vaccination coverage reporting may hide important regional variations in immunisation levels. We aimed to explore regional differences in measles vaccination levels in Switzerland.

Methods: A dynamic cohort study evaluating first (MCV1) and second (MCV2) measles immunizations in children born between 2006 and 2008 registered with a single health insurer was conducted. Time-to-event analysis of claims data was used to analyse measles vaccination levels by age and region. The Swiss Federal Office for Statistics definitions of Swiss regions were used.

Results: 42950 infants were included. In our cohort 62.6% of 13 month-olds and 59.4% of 25 month-olds were up-to-date for MCV1 and MCV2, respectively. For 24 to 35 month-olds MCV1 vaccination levels (85.7%) accorded with nationwide official estimates (86.9%). However, these ranged from 81.1% (95%CI 80.0%-82.2%) for Lake Geneva region to 87.9% (95%CI 87.0%-88.8%) for Zurich region. When timing of MCV1 administration was considered, almost 20% of children were vaccinated with MCV1 before 365 days of age in Lake Geneva region compared to maximally 10% in other regions. However, with 81.1% at 24 to 35 months of age MCV1 immunisation levels were lower than for other regions (83.8-87.9%) and lower than previously reported for this region and age group.

Conclusions: Time-to-event analysis using health insurance data can identify regional differences in measles vaccination beyond variations in immunisation level at a given age. In our cohort MCV1 was administered at younger ages, but to a lower overall level for the region of Lake Geneva compared with other parts of Switzerland.

EFFECT OF SECOND VARICELLA VACCINE DOSE ON BREAKTHROUGH CASES IN GERMANY - PRELIMINARY RESULTS FROM SENTINEL SURVEILLANCE**A. Siedler**¹, A. Grueber²¹*Infectious Disease Epidemiology, Robert-Koch-Institute, Berlin,* ²*German Green Cross, Marburg, Germany*

Background: In Germany, varicella vaccination was recommended for children >11 months in 2004 with one dose of monovalent or two doses of combined varicella vaccine (since 2006). Since 2009 two doses are generally recommended.

We investigated the acceptance of a 2-dose schedule and its effect on breakthrough varicella cases (BTC) by sentinel surveillance.

Methods: About 650 physicians sent monthly aggregated reports on numbers of cases and varicella vaccinations administered, and case-based questionnaires for all vaccinated cases from April 2005 to March 2011. BTC was defined as varicella ≥ 42 days after vaccination. Cases and vaccine doses were calculated as mean number per sentinel-physician and month (NPM).

Results: Varicella cases decreased from 3.6 to 1.1 NPM. Monovalent first vaccine doses increased from 7.4 to 9.8 NPM in 2006 and decreased to 1.2 in 2011. Monovalent second doses increased from 0.2 to 5.1 NPM in 2009 and decreased slightly to 3.0 NPM in 2011. Combined first (second) doses steadily increased from 5.3 (2.8) NPM in 2007 to 7.0 (6.0) NPM in 2011.

Case-based reports included 2,615 and 135 cases of breakthrough varicella after one (BTC1) or two (BTC2) vaccine doses, respectively. BTC1 increased from 1.2 to 9.4 NPM in 2008 and dropped to 4.1 in 2011. First BTC2 appeared in 2007, growing to 1.1 NPM in 2011. Severity did not differ between BTC1 and BTC2.

Conclusions: In Germany, combined vaccines and monovalent second doses were preferred for varicella vaccination. Breakthrough cases of varicella can be diminished but not avoided with a 2-dose schedule.

ANALYSIS OF THE AEFI ASSOCIATED WITH THE DTAP VACCINE. VALENCIAN COMMUNITY

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Background: The vaccination against diphtheria-tetanus-pertussis in Spain and in the Valencian Community (VC) is established in a 5 doses schedule. In children who have received previous doses of acellular vaccine in primary vaccination, adverse reactions increases with successive booster. The substitution of a DTaP vaccine for dTap in the schedule for the administration of the fifth dose, done in 2010 in the VC, keep the immunogenicity and also reduce the reactogenicity of the fifth dose.

Aim: To analyze adverse events following immunization (AEFI) of the DTaP and dTap vaccine reported in the SIV, in children aged 5 and 6, from July 2009 to July 2011.

Methods: A retrospective descriptive analysis of the AEFI of DTaP and dTap reported via SIV has been done. Target population: children aged 5 and 6. Study period: from July 2009 to July 2011.

Results: 98,398 children vaccinated with fifth dose against diphtheria-tetanus-pertussis during the study period, 59,629 were vaccinated with DTaP and 38,769 with dTap. 66 suspected reactions reported for DTPa (rate 1.11 per thousand) and 20 for the dTap (rate 0.52 per thousand). For both vaccines, 100% of the reactions were classified as general and administration site disorders by System Organ Class. The most notified reaction for the DTPa was the swelling 29.63% [95% CI (19.69, 39.57)] and the inflammation at the point of injection for the dTap vaccine, 23.53% [95% CI (9.27, 37.59)].

Conclusions: The rate of reporting of suspected adverse reaction to DTaP is less than dTap. The reactions reported are mild.

THE VACCINE REFUSAL RECORD. NEW UTILITY OF THE VACCINE INFORMATION SYSTEM OF THE VALENCIAN COMMUNITY

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Background and aim: Today is increasing the number of people who refuse vaccination. This rejection may be due to the high vaccination coverage achieved, for these reason the incidence of preventable diseases is very low which leads to a decrease in the perception of risk in society against the immunopreventable illnesses and increased concern potential adverse effects.

In Valencian Community, it was considered necessary to know the reasons for rejection, and data are recorded on the vaccination history of each person through the Vaccine Information System. The aim of the study is to describe the new utility of vaccine refusal record.

Methods: A description of the utility has been done.

Results: Once Nominal Vaccine Registry is accessed by selecting the vaccine to administer, the application allows you to reject a specific vaccine or a particular dose or all vaccines that would be dealt to the person administering the vaccine act. When the rejection of the vaccination is given in people less than 16 years, the application requires complete NIF, full name of legal representative. In any refusal to complete the application requires the reasons for non-vaccination (allergic, religious, as opposed to vaccination or other). Through the history of rejection icon is available the data of vaccines that have been rejected.

Conclusions: The new utility is a powerful tool to help you understand more accurately the population of unvaccinated and reasons, in order to plan specific strategies aimed at this population.

ANALYSIS OF THE REJECTION OF VACCINES VIA THE VACCINE INFORMATION SYSTEM OF THE VALENCIAN COMMUNITY

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Background: It seems that the number of people who reject vaccines for their children and themselves is increasing, probably due to the low incidence of preventable diseases and a major concern for adverse effects. The reasons for rejection are often grounded in decisive philosophical, religious, cultural or political. In Valencian Community, data of vaccination's rejection are recorded on the vaccination history of each person through the Vaccine Information System.

Aim: To describe and quantify the data of the vaccination rejection recorded in the Vaccine Information System (SIV) of the Valencian Community.

Methods: A retrospective study of data of rejection of vaccines in the Nominal Vaccine Registry (RVN) of SIV from 27th September to 15th December 2011 has been done. Study variables: age, sex, rejected vaccine and reasons for refusal.

Results: 7,246 vaccines on 931,398 vaccine acts recorded have been rejected (0.77% rejection rate). 3,597 people, 39.2% men. 123 people reject all vaccines (52% men). For reasons of rejection, 1,833 people contrary to the vaccine (50.9%). The most rejected vaccine has been influenza vaccine, 3,364 rejections (0.49% rejection rate), but 23-valent pneumococcal disease is one who has a higher rate of rejection (2.49%). 67.8% of the rejections were recorded in people aged 60 years or older.

Conclusions: The most rejected vaccine has been influenza vaccine, according to the date of the utility implementation. The highest percentage of rejections is in the group of age 60 years and over. The highest percentage of rejections is for reason opposed to vaccination.

LASTING IMMUNE MEMORY AGAINST HEPATITIS B 10 YEARS AFTER THE 2+1 PRIMARY VACCINATION SCHEDULE WITH DTPA-HBV-IPV/HIB OR DTPA-IPV/HIB+HBV

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Background: A 2+1 infant vaccination schedule has been adopted in countries with low infectious pressure and good booster dose coverage (e.g. Scandinavia, Italy and Slovakia). This study evaluated long-term immune memory towards hepatitis B in children aged 11-12 years who had received 3 doses (2+1) of either DTPa-HBV-IPV/Hib or DTPa-IPV/Hib+HBV vaccines in infancy.

Methods: Phase IV, open study [NCT01138098] conducted in 12 Slovakian centres, including children aged 11-12 years previously vaccinated at 3, 5 and 11-12 months-old with either DTPa-HBV-IPV/Hib or DTPa-IPV/Hib + HBV (all vaccines from GSK Biologicals). All subjects received a single challenge dose of monovalent HBV vaccine. Anti-HBs antibodies were measured before and 1 month post-vaccination using ELISA.

Results: 185 subjects were enrolled and vaccinated, of which 184 were included in the according-to-protocol cohort (mean age 11.3 years, SD 0.46 years; DTPa-HBV-IPV/Hib [95]; DTPa-IPV/Hib+HBV [89]). Pre-challenge, 53.7% DTPa-HBV-IPV/Hib and 56.2% DTPa-IPV/Hib+HBV vaccinees retained status of anti-HBs antibodies concentration ≥ 10 mIU/ml, increasing to 95.8% and 98.9%, respectively, after HBV challenge. Subjects with anti-HBs antibodies ≥ 100 mIU/ml increased from 11.6 to 92.6% and 7.9 to 96.6%, respectively post-challenge. An anamnestic response to the HBV challenge dose was mounted by 95.8% and 97.8% of subjects, respectively.

No more than 7.8% subjects in either group reported at least 1 unsolicited symptom after the challenge dose.

Conclusion: 2+1 primary vaccination with DTPa-HBV-IPV/Hib in infancy induces lasting immune memory against hepatitis B up to 11 years post-vaccination, and a strong anamnestic response to HBV challenge dose, which was well tolerated.

INFLUENCE OF UNDERLYING HEALTH STATUS ON RV DISEASE BURDEN AND HOSPITAL RESOURCE UTILIZATION

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Background: Each year rotavirus (RV) causes numerous episodes of acute gastroenteritis and related hospitalizations. Although RV vaccination can generate important reductions, budget constraints and competition in allocation of funds hamper the introduction of universal RV vaccination in many European countries. To identify those children that would benefit most from vaccination, we performed an observational study of RV hospitalizations assessing disease burden and health resource utilization in relation to patients' underlying health status.

Methods: RV positive cases were identified by screening laboratory reports from four participating hospitals between 2006-2010. Data on RV disease course and patients health characteristics were obtained by detailed review of medical records.

Results: Among 936 RV related hospitalizations, 219 patients (23%) suffered from an underlying complex chronic condition (CCC). Intravenous rehydration was needed more frequently in patients with CCC compared to healthy children (OR: 2.1, 95%CI: 1.4; 3.0) and mean hospital-stay was prolonged by 2.6 days (95%CI: 1.9; 3.2).

ICU admission was required in 3% of CCC-patients compared to 1% of healthy children (OR: 2.5, 95%CI: 0.81; 7.58). Six out of seven severe complications ($p < 0.001$) and two RV related deaths occurred among patients with CCC. In a nested-case control study of nosocomial RV infections, cases were shown to suffer more frequently from CCC's than hospital controls (OR: 3.4, 95%CI: 1.8-6.4).

Conclusion: Complex chronic conditions are common among RV hospitalizations and increase resource utilization and the rate of complications. The results suggest important health benefits could be generated by selective RV vaccination limited to children with CCC.

ROTAVIRUS RELATED HOSPITALIZATIONS: INCIDENCE AND CONTRIBUTION TO SEASONAL PEAKS IN PEDIATRIC HOSPITAL ADMISSIONS

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Background: The seasonal Rotavirus (RV) epidemic partly overlaps with those of other common childhood infections and generates enormous pressure on hospital resources during winter and early spring. We performed an observational study of RV related hospitalizations to determine incidence rate and to assess its relative contribution to all-cause pediatric hospitalizations.

Methods: Laboratory confirmed RV hospitalizations and hospital administrative data (Dec 2005-Nov 2010) were collected retrospectively for 3 general hospitals and one tertiary care pediatric hospital. Subsequent prospective active surveillance was performed among symptomatic hospital-patients during the 2011 RV season to quantify RV under-reporting. Rates of RV hospitalizations in the population and 95% Confidence Intervals (CI) were calculated with under-reporting adjustment based on surveillance results. RV's contribution to seasonal peaks in all-cause pediatric hospitalizations was determined.

Results: The estimated rate of RV hospitalizations in the population was 17 per 1000 child-years under 15 (95%CI: 15-19) and 51 per 1000 under five (95%CI: 47-58). RV was responsible for 6.3% of all-cause pediatric hospitalizations per year among general hospitals and 3.5% at the tertiary care centre. Among general hospitals, RV was responsible for 30% of winter excess in all-cause pediatric hospitalizations and peaked between January and May when 67% of winter excess was due to RV.

Conclusion: RV causes an estimated 5000 pediatric hospitalizations per year in the Netherlands. The seasonal pressure on pediatric hospital beds is greatly enhanced by RV, especially in general hospitals, a phenomenon not routinely taken into account in decisions on RV vaccination policies.

DIPHTHERIA AND TETANUS SEROEPIDEMIOLOGY AMONG CHILDREN AND YOUNG ADULTS IN TAJIKISTAN, 2010

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Background: Tajikistan experienced a major diphtheria outbreak during 1993-1998 (~10,000 reported cases, 800 deaths), controlled after nationwide immunization campaigns targeting 3-50 year-olds. During 2000-2010, only 52 diphtheria cases and 7 tetanus cases were reported, but surveillance quality is uncertain. Estimated DTP3 coverage since 2000 ranged from 84% to 86%.

Methods: To assess population immunity to diphtheria and tetanus, serum specimens from a nationwide sample of persons aged 1-24 years, selected through stratified cluster sampling for the serosurvey after a large-scale poliomyelitis outbreak in 2010, were tested for anti-diphtheria antibodies (VERO cell neutralization assay) (n=2325) and anti-tetanus IgG (ELISA) (n=2319). Antibody levels < 0.1 IU/ml were considered seronegative.

Results: Overall, 51.4% (95% CI, 48.5%-54.3%) of participants were seronegative for diphtheria and 21.1% (95% CI, 18.8%-23.7%) were seronegative for tetanus. The highest prevalence of seronegatives was observed among 10-14 and 15-19 year-olds (62.9% and 64.7% for diphtheria; 34.7% and 29.9% for tetanus, respectively). Kulyab and Rayons of Republican Subordination (RRS) regions had highest prevalence of seronegatives (61.2% and 55.1% for diphtheria; 32.8% and 29.1% for tetanus, respectively).

Conclusions: In Tajikistan, population immunity for diphtheria is suboptimal, particularly among 10-19 year-olds, and in Kulyab and RRS regions. Immunity to tetanus is moderately high, but is suboptimal in the same age groups and regions as for diphtheria. These findings highlight the need to improve routine immunization delivery, and support a proposal by the Tajikistan Ministry of Health for a one-time diphtheria-tetanus supplementary immunization campaign to rapidly close immunity gaps and prevent diphtheria outbreaks.

POSTMARKETING SURVEILLANCE OF INTUSSUSCEPTION FOLLOWING MASS INTRODUCTION OF THE ATTENUATED HUMAN ROTAVIRUS VACCINE IN MEXICO

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Background and aims: Mexico initiated mass vaccination with the attenuated human rotavirus vaccine (Rotarix™; GlaxoSmithKline Biologicals) in 2006. This postlicensure study aimed to assess any potential temporal association between vaccination and intussusception in Mexican infants.

Methods: Prospective, active surveillance for intussusception among infants aged < 1 year was conducted in 221 hospitals across Mexico from the Mexican Institute of Social Security from January 2008-October 2010. The temporal association between vaccination and intussusception was assessed by self-controlled case-series analysis.

Results: Of the 753 episodes of intussusception reported in 750 infants, 701 were in vaccinated infants (34.5% post-dose 1, 65.5% post-dose 2). The relative incidence of intussusception within 31 days of vaccination was 1.75 (95.5% CI: 1.24-2.48; P=0.001) post-dose 1 and 1.06 (95.5% CI: 0.75-1.48; P=0.75) post-dose 2. The relative incidence of intussusception within 7 days of vaccination was 6.49 post-dose 1 (95.5% CI: 4.17-10.09; P< 0.001) and 1.29 post-dose 2 (95.5% CI: 0.80-2.11; P=0.29). Clustering of intussusception within 7 days of vaccination was observed post-dose 1. An attributable risk of 3-4 additional cases of intussusception per 100000 vaccinated infants was estimated.

Conclusions: This is the largest surveillance study for intussusception following rotavirus vaccination to date. A small temporal increase in risk for intussusception was seen within 7 days of administration of the first vaccine dose. This finding should be put in perspective with the well-documented substantial benefits of rotavirus vaccination. It is still uncertain whether rotavirus vaccination has any impact on the overall incidence of intussusception.

VACCINE DERIVED BOVINE ROTAVIRUS G1P[8] REASSORTANT IN INFANTS WITH ACUTE GASTROENTERITIS**M. Hemming**¹, T. Vesikari^{1,2}¹*Vaccine Research Center, University of Tampere School of Medicine, ²Department of Pediatrics, Tampere University Hospital, Tampere, Finland*

Background: RotaTeq® (Merck) is a live human-bovine reassortant rotavirus vaccine containing five reassortant strains G1P[5], G2P[5], G3P[5], G4P[5] and G6P[8]. RotaTeq® is generally considered to be a very safe vaccine, but a low rate of diarrheal symptoms after dose 1 was described in the safety and efficacy trials prior to licensure. Recently cases of diarrhea associated with a new vaccine derived double reassortant G1P[8] have been reported in the USA and Australia. We describe three such cases from Finland. Finland has had universal rotavirus vaccination program with RotaTeq® since 2009.

Materials and methods: Stool specimens were collected from 316 children with acute gastroenteritis seen in 2009-2011 at the Tampere University Hospital outpatient clinic or ward and examined for gastroenteritis viruses by RT-PCR. Specimens from exclusively rotavirus positive children (N=79) who had received RotaTeq® vaccine were analyzed to determine the VP7, VP4 and VP6 types by RT-PCR and sequencing.

Results: Three immunocompetent infants with gastroenteritis symptoms after their first or second immunization with RotaTeq® were found to shed a G1P[8] human-bovine double reassortant virus. The VP7, VP4 and VP6 gene segments were 100% identical to cognate gene segments from the corresponding vaccine viruses G1P[5] and G6P[8] in RotaTeq®.

Conclusion: Formation of G1P[8] double reassortants may explain diarrheal symptoms in a small percentage of RotaTeq® recipients. The reassortment between two vaccine strains may occur during intestinal replication even in immunocompetent infants. Such a double reassortant virus might also be transmitted to contacts in the environment.

ESTIMATED REDUCTION IN MENINGOCOCCAL DISEASE BY 4CMENB VACCINATION

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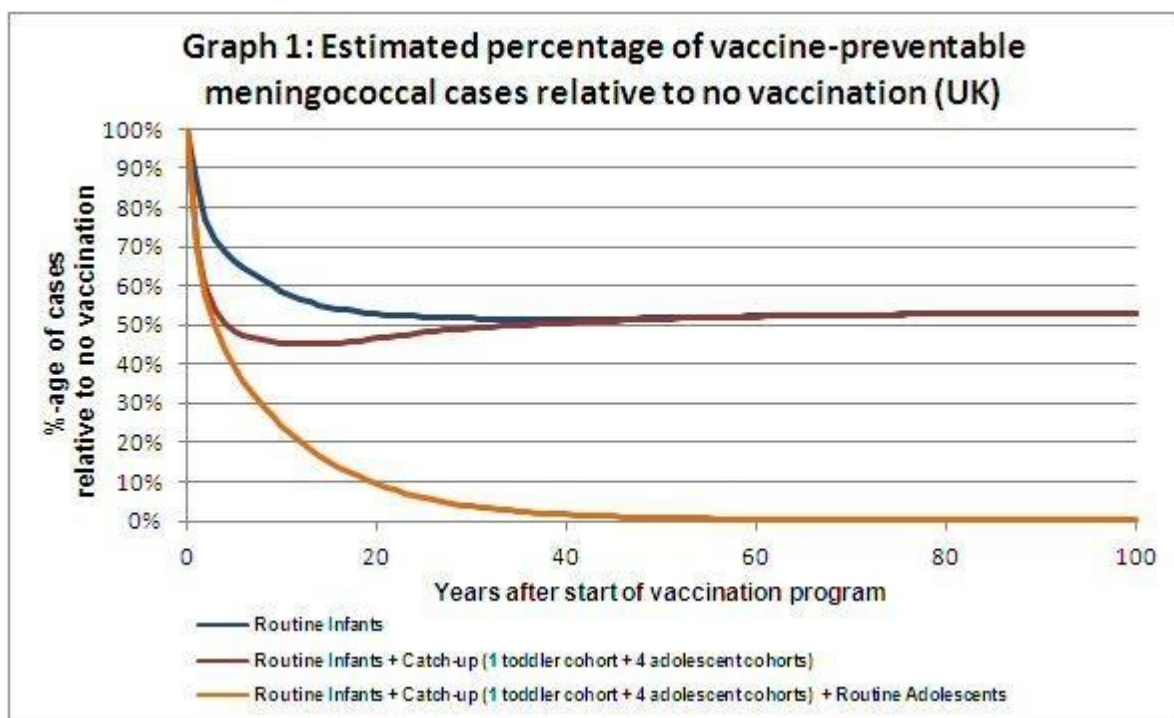
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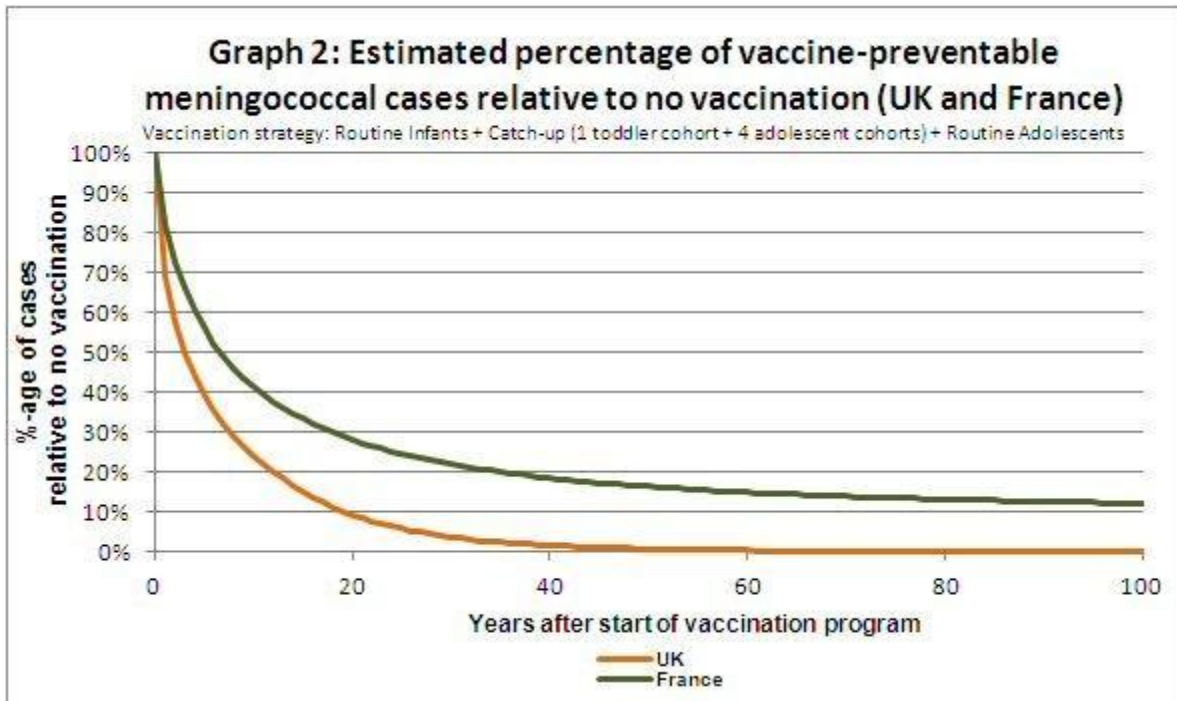
Background and aims: >70% of invasive meningococcal cases in the EU27 (2009) and nearly all infant cases are attributable to serogroup B. Adolescents are the main carriers; 72% and 80% of all tested circulating disease-causing strains (all serogroups) were estimated to be vaccine-preventable with 4CMenB vaccine in the UK and France, respectively. We evaluated the reduction potential in meningococcal disease after 4CMenB introduction.

Methods: A published transmission model was adapted, applying a model horizon of 100 years. Three vaccination strategies were evaluated, realistically assuming lower vaccination rates for France than the UK. All model inputs were derived from published literature or governmental databases.

Results:



[Figure 1]



[Figure 2]

Conclusion: Routine infant vaccination ensures direct protection against meningococcal disease in infants. Catch-up programs support a faster reduction of cases. Elimination of vaccine-preventable disease requires high vaccination rates in both, infants and adolescents. A vaccination program targeting fast onset of protection and long-term elimination of vaccine-preventable cases should comprise a routine vaccination of infants and adolescents, combined with a reasonably sized catch-up program. Examples from France and the UK show a potential for long-term reduction of vaccine-preventable cases from 88% to nearly 100%.

ROTAVIRUS VACCINATION: A RISK FACTOR FOR INTUSSUSCEPTION?**D.F. Oberle**¹, A.C. Jenke², R. von Kries³, D. Mentzer¹, B. Keller-Stanislawski¹

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Background and aims: Studies conducted in Mexico and Australia associate the currently authorized Rotavirus (RV) vaccines with intussusception (IS). Aim of this study was to investigate whether, in Germany, there is evidence for excess IS cases in RV vaccinees compared to the background incidence before market authorization in 2006.

Methods: Individual case safety reports (ICSR) of IS following receipt of RV vaccines submitted to the German Federal Institute for Vaccines and Biomedicines from 2006 to 2010 were reviewed and validated according to the criteria of the Brighton Collaboration's definition for IS. An observed versus expected analysis was conducted based on confirmed IS cases using standardized morbidity ratio (SMR) methods.

Results: A total of 27 ICSR of suspected IS in RV vaccinees were obtained. A significantly increased SMR for IS was found in a time window of 1-7 days after the 1st dose of Rotarix (4.6; 95% CI: 1.5-10.7) in infants aged 4-6 months of life. With respect to RotaTeq, there was also a significantly elevated SMR within 1-7 days following the 1st dose in children aged 4-6 months (5.8, 95% CI: 1.2-17.1). However, when combining all doses administered in the 1st year of life there was no evidence for excess IS cases 1-7 days after receipt of either RV vaccine.

Conclusions: Subgroup analyses revealed that infants aged 4-6 months are at increased risk to develop IS 1-7 days after the 1st dose of either RV vaccine. It might therefore be advisable to avoid starting RV immunization at this vulnerable age.

EFFECTS OF IMMUNIZATION WITH HIGHER VALENT PNEUMOCOCCAL CONJUGATE VACCINES IN GERMAN CHILDREN ON NUMBERS OF REPORTED IPD CASES (1997-2012)

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Background and aims: A general recommendation for vaccination with pneumococcal conjugate vaccine (PCV) was issued for German children up to the age of 2y in July 2006. In 2009, two higher valent PCVs were licenced in Germany: PCV10 in April 2009, PCV13 in December 2009. Here, we present data on cases of IPD sent in for serotyping in the six 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 diseases (IPD) were sent to the National Reference Center for Streptococci. Identification of the isolates was confirmed and serotyping was performed using the Neufeld-Quellung-reaction.

Results: In 2010-2011, IPD cases in children < 2y with PCV7 serotypes had decreased by over 90%, while cases with non-PCV7 serotypes almost doubled. The six new serotypes increased after PCV7 introduction but decreased after higher-valent vaccine introduction. From July-December 2011 only 6 cases were reported (1:n=1, 3:n=2, 5:n=0, 6A:n=1, 7F:n=1, 19A:n=1). From July-December 2010, 28 cases were reported (1:n=3, 3:n=3, 5:n=1, 6A:n=1, 7F:n=5, 19A:n=15). This represents a 78% reduction. Remarkably, the number of 19A cases, which still increased in 2010 as compared to 2009, was strongly reduced in 2011.

Conclusions: Six years after the general vaccination recommendation reported cases caused by PCV7 serotypes have almost disappeared. Two years after the introduction of higher valent PCVs strong effects are visible, among children < 2y due to all six new serotypes. The reduction of 19A cases was 93%.

IMMUNIZATION CARDS VALIDITY WITH RESPECT TO BACILLE CALMETTE-GUÉRIN IN A POPULATION OF IMMIGRANTS AND ADOPTED CHILDREN

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Background and aims: Spain is the second country in the world in number of adopted children. Medical reports submitted often provide flawed and incomplete information. It should be always considered validity of immunization cards. The main objective was to assess the correlation between cards submitted and existence of BCG scars in a population of immigrants and adopted children coming from several geographic areas.

Methods: Cross-sectional observational study. Adopted children or immigrants evaluated in our hospital between January 2003 and December 2008 were included.

Results: 1074 children were included, 69.6% girls. Origin: China (34.7%), Latin America (20.8%), India and Nepal (19.4%), Eastern Europe (15.7%) and Africa (9.3%). Valid cards with vaccine administration in 72% of children, but BCG scar was found in 79%. Concordance between valid cards and BCG scar was 87%, so 13% of children had a valid card with respect to BCG but they really were not immunized. However, in 63% of children without an immunization card or with a non-valid one, a BCG scar was found.

Conclusion: This finding should be taken into account when assessing immigrants or adopted children. Only the BCG scar should be considered to check BCG immunization status. Published articles evaluating immunization cards with respect to BCG vaccine are rare. It is important to further deepen this aspect in future studies.

RETROSPECTIVE COST-EFFECTIVENESS ANALYSIS OF PAEDIATRIC PNEUMOCOCCAL VACCINATION WITH PCV7 IN THE UNITED KINGDOM**A. Charos, P. Balmer***Pfizer Ltd, Walton Oaks, UK*

Background and aims: Seven-valent pneumococcal conjugate vaccine (PCV7) has had a profound public health impact by preventing disease caused by seven *Streptococcus pneumoniae* serotypes. The study objective was to retrospectively assess the cost-effectiveness of PCV7 paediatric vaccination in the United Kingdom (UK).

Methods: A cohort model was developed to estimate the costs and the number of Quality adjusted life years (QALYs) that were associated with the PCV7 program using the observed patterns of pneumococcal disease epidemiology. The study cohort was the UK population from September 2006, when PCV7 was introduced, to April 2010 when PCV7 was replaced by PCV13. Pneumococcal disease levels (invasive pneumococcal disease, pneumonia, and acute otitis media) after the introduction of PCV7 (2006-10) were compared to disease prior to vaccine introduction (2000-06) to estimate the effect of vaccination. The analysis used a UK NHS payer perspective, therefore only direct costs and outcomes were included.

Results: Paediatric vaccination with PCV7 is estimated to have reduced direct medical costs by £195 million, prevented approximately 10,000 deaths and added 75,000 QALYs by reducing cases of pneumococcal disease in young children directly and in older age groups indirectly via herd effects. The estimated cost of the programme based on the NHS list price was £340 million, resulting in an incremental cost of £1,930 per QALY gained.

Conclusions: The introduction of the paediatric pneumococcal vaccination program with PCV7 in the UK was a highly cost-effective use of NHS resources.

IMMUNIZATION COVERAGE AND PREDICTIVE FACTORS FOR COMPLETE AND AGE- APPROPRIATE VACCINATION AMONG PRESCHOOLERS IN ATHENS, GREECE

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Background and aims: To assess immunization coverage and identify factors influencing complete and age-appropriate vaccination among children attending public nurseries in the municipal Athens area, following a full reimbursement policy (since 2008 for MenC, PCV7, varicella and hepatitis A vaccines).

Methods: A cross-sectional study, using stratified sampling was performed during 2010-2011. Immunization history was obtained from vaccination booklets while demographic and socioeconomic characteristics along with parental attitudes towards immunization by telephone interviews. Percentages of vaccination were estimated by sample weighted proportions while associations between complete and age-appropriate vaccination and possible determinants by logistic regression analysis.

Results: A total of 731 children (mean age: 46, median: 48, range: 10-65 months) were included (participation rate: 90%). Complete vaccination coverage was satisfactory overall, exceeding 90% for traditional antigens (DTP, polio, Hib, hepatitis B, 1st dose of MMR) but ranging between 61-92% for newly reimbursed vaccines. However, immunization was significantly delayed for new vaccines, as well as for hepatitis B (only 28% were vaccinated at 12 months of age), and 2nd dose of MMR (65% at 60 months of age). Child's increasing age as well as belonging to immigrant group were significantly associated with under- or delayed immunization status while use of multivalent vaccines had a positive impact on complete and age-appropriate immunization with most vaccines.

Conclusions: Our results highlight the need to monitor uptake of new vaccines and reinforce appropriate administration of booster doses and hepatitis B vaccine. Immigration was identified as risk factor for suboptimal immunization that may warrant targeted intervention.

IMMUNOGENICITY AND TOLERABILITY OF AS03 ADJUVANTED H1N1 VACCINE IN HIV INFECTED CHILDREN

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A two dose schedule of AS03-adjuvanted H1N1 vaccine (Pandemrix) was assessed in HIV infected children. Hemagglutination-inhibition antibody titres (HIA) [GSK Biologicals laboratories, Belgium] were determined days 0, 28, & 60. Primary endpoints: proportion seroprotected (SP) (HIA $\geq 1:40$) or with seroconversion (SC) (HIA $< 1:10$ prevaccination to $\geq 1:40$ post vaccination or fourfold increase). VL & CD4 at baseline and study end were compared by Mann Whitney U test. Adverse events were sought by telephone questionnaire.

25 children; median 10 yrs enrolled. 20 on HAART; 85% VL < 40 cpm. Median CD4 861 cells $\times 10^6/L$. HIA determined days 0, 28 (range D21-28) and D 84 (range D56 -140) yielded SP rates of 16, 76 & 72% respectively. 14/21 (66%) unprotected children (pre-vaccine HIA < 40) met the primary endpoint after dose 1; 4 additional children after dose 2 (86% overall). Decline in HIA to < 10 after initial SC was observed in one 84D post dose 2. 21(84%) & 17(68%) had injection site pain after dose 1 & 2. One had T $>38^{\circ}C$ within 72 hrs of dose 1. No SAE were found. One naïve patient with prevaccine HAI < 10 , had H1N1 infection on the day of 2nd vaccine administration when his HAI was 40. 5/17 with VL < 40 at entry had detectable HIV viraemia post vaccine; 4/5 adherence related, 1 transient blip to < 100 cpm. No change in CD4 counts was found.

AS03 adjuvanted H1N1 vaccine, immunogenic in 72 - 86%, was well tolerated. Narcolepsy was not encountered subsequently.

REACTOGENICITY OF A 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV) BOOSTER AT PRE-SCHOOL AGE FOLLOWING INFANT IMMUNISATION WITH PCV-7 OR PCV-13

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Background: In a previous multi-centre study UK children were randomised to receive a 7-valent (PCV-7) or 13-valent (PCV-13) pneumococcal conjugate vaccine at 2, 4 and 12 months of age. We previously reported the persistence of antibodies to pre-school years and the immunogenicity of a PCV-13 booster at this age. We here report on the reactogenicity of this dose.

Methods: One hundred and eight children from the original study were followed-up at approximately 3.5 years of age and received the PCV-13 booster. Reactogenicity data were available for 104 participants. Local reactions and systemic events were recorded for 4 days following vaccination.

Results: No serious adverse events were recorded following the PCV-13 booster at approximately 3.5 years of age. Local reactions such as redness, hardness, swelling and tenderness were either absent or mild in most cases. However, moderate or severe tenderness was experienced by 18% of participants and moderate or severe redness by 9%. Decreased appetite and irritability were recorded in 18% and 41% of participants respectively with moderate or severe reactions being present in 4% and 13% of these children. Low-grade fever (38-39°C) was noted in 3% of the participants and none of the children had a temperature >39°C. The reactogenicity profile of this PCV-13 booster was similar regardless of whether participants had previously been immunised with PCV-7 or PCV-13.

Conclusions: A pre-school booster with the 13-valent pneumococcal conjugate vaccine is well tolerated with low rates of local and systemic side effects after priming with either PCV-7 or PCV-13.

PARENTS OF CHILDREN PARTICIPATING IN A VACCINE CLINICAL TRIAL OPINIONS REGARDING ROUTINELY RECOMMENDED VACCINES: CONVINCED BUT NOT FULLY

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Background and aims: Anecdotal data allow supposing that participants in vaccine clinical trials are supporters of vaccination and have strong conviction about vaccines usefulness, safety, and effectiveness. However, little data is available on this issue. The objective of this report was to assess participants' in a vaccine clinical trial opinions regarding vaccination in general and specifically about different routinely recommended vaccines.

Methods: Data were collected from parents of children participating in an influenza vaccine immunogenicity clinical trial. Parents of 153 15-120 month-old children were asked to complete an anonymous, self-administered questionnaire. A five-point Likert scale was used. Descriptive statistics were generated for all variables.

Results: 113 out of 136 parents (83%) who returned for the second visit completed the questionnaire. 97% were convinced that vaccines are safe and generally useful, and 95% that vaccines ensure a good protection. However, only 64%, 57% and 56% were strongly convinced, respectively. Specific vaccine perceived usefulness varied from 87% for varicella and hepatitis A&B to 99% for DCaT-Polio-Hib and MMR vaccines. For each of routinely recommended vaccine: 89-97% of parents thought that it is safe (66-76% strongly convinced) and 89-100% that vaccines ensure a good protection. Depending on vaccine, 87%-100% were ready to recommend it to other parents.

Conclusions: Generally, parents were convinced about the usefulness, safety and protectiveness ensured by routinely recommended vaccines. However, less than 2/3 of them were strongly convinced. The heterogeneity observed in perceived safety, effectiveness and intention to recommend different vaccines to other parents warrant further investigation.

CELLULAR RESPONSES AND ANTIBODY KINETICS INDUCED BY PCV7 IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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Aim: Memory B cells (MBCs) have been associated with establishment of immunological memory and antibody (Ab) persistence. We evaluated the kinetics of PCV7-induced pneumococcal serotype (PS)-specific MBCs and Abs in children with idiopathic nephrotic syndrome (INS) in remission compared to controls.

Methods: 32(17 male) children with INS [median age(range): 9(4-17)yrs] and 16(10 male) controls [14(7-20)yrs] (no history of pneumococcal vaccination/infection) received PCV7. PS-specific IgM MBCs (d0, d6-8, d28) and IgG Abs (d0, d28, m12) were analysed by ELISPOT (peripheral blood mononuclear cells (PBMCs) stimulation with SAC, PKW and CpG2006) and ELISA, respectively.

Results: At d6-8, MBC frequencies increased significantly over baseline for all PS in patients and controls ($p < 0.05$) and remained elevated ($p < 0.05$) at d28 after PCV7. MBCs were similar between groups for all PS at detected time points (median spot counts/ 10^5 PBMCs at d0vsd6-8vsd28: 58vs64vs58, 46vs57vs58, 35vs63vs48 in patients and 30vs65vs53, 35vs57vs49, 33vs61vs68 in controls for PS 6B, 14, 23F, respectively). Despite lower GMCs in INS subjects for PS 6B and 23F before PCV7 ($p=0.02$), both groups achieved significant increase in Abs at d28 for all PS, which persisted at 12 months after vaccination (GMCs at d0vsm1vsm12: 0.04vs3.62vs1.23, 0.12vs6.68vs3.15, 0.19vs7.33vs3.20 $\mu\text{g/ml}$ in patients and 0.42vs9.22vs3.74, 0.51vs11.64vs4.93, 0.44vs10.09vs4.20 $\mu\text{g/ml}$ in controls for PS 6B, 14, 23F, respectively, $p < 0.01$, comparisons with baseline). No significant differences in GMCs were observed between patients and controls after vaccination.

Conclusions: Similar cellular responses in patients and controls and Ab persistence up to 1 year after PCV7 suggest successful induction of immunological memory in INS children.

PRO-VACCINATION PARENTS' SELF-ESTIMATED KNOWLEDGE AND PRACTICE REGARDING DIFFERENT VACCINES, MULTIPLE INJECTIONS AND PROPHYLACTIC USE OF ANTIPYRETICS

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Background and aims: Parents' opinion/acceptance is crucial when vaccinating children. The objectives of this study were to assess: parents' self-estimated sufficiency of knowledge and practices regarding routinely recommended vaccines, acceptability of multiple injections, and vaccination related use of antipyretics.

Methods: Parents of 153 15-120 month-old children participating in a vaccine clinical trial were invited to complete an anonymous, self administered questionnaire. No specific information about 7 routinely recommended vaccines was delivered and participants were encouraged to base their answers on own opinions.

Results: 111 (72.5%) questionnaires were included in this analysis. 94% of respondents estimated to be sufficiently informed about the vaccination of their child. The satisfaction level with the knowledge they have about recommended vaccines varied from 71-73% for HA&HB to 90-92% for pneumococcal and meningococcal vaccines. 88% gave their preference to combined vaccines. Two, three and four injections during one vaccination session were judged acceptable by 82%, 36% and 22% of parents; 42% thought that multiple injections increase the risk of adverse events. Unexpectedly, 85% of parents reported the use of antipyretics just before or during the first hour post-vaccination. 2/3 of parents thought their child's health will be at risk if vaccination is delayed.

Comments: The majority of parents estimated their knowledge about recommended vaccines as sufficient and gave their preference to combined vaccines. Acceptability of more than two injections during one vaccination session seems to be low. Multiple injections practice and antipyretics' use warrant further assessment.

VIROSOMAL INFLUENZA VACCINE IN PRETERM INFANTS (BIRTH WEIGHT < 1500 G AND GESTATIONAL AGE < 32 WEEKS OF PREGNANCY)

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Background: Preterm infants with chronic lung or heart disease have a high risk of influenza morbidity and hospitalization. Influenza vaccines are approved only after 6 months.

Question: Can a virosomal split virion influenza vaccine (0.25 ml Inflexal V) given at the same time as routine immunization induce a sufficient immunological response in very premature infants?

Methods: Peripheral blood was collected from 9 preterm infants (GA 23+6 - 27+5 weeks) one month after influenza vaccination (8x after second, after first 3x) in years 2006 to 2010 at an infants age of 85 (56-156) and 132 (88-173) days (mean, range). Mononuclear cells were incubated with each of the seasonal influenza vaccine for 13 hours.

CD3+ / CD4+ T helper cells reacting specific to the vaccine were determined by measuring the cytokines interferon (IFN)- γ and tumor necrosis factor (TNF)- α using intracellular cytokine staining (ICC) in a flow cytometer FACSCalibur.

Haemagglutination inhibiting antibodies were determined.

Results: In none of the nine (out of 15 planned by biometrician) blood samples CD3+ / CD4+ T helper cells showed a measurable cytokine stimulation with influenza antigens.

Specific antibodies against influenza in hemagglutination inhibition (HI) assays were only detectable (1:15 and 1:60) after 2 infant's additional vaccination with Pandemrix fortified with AS03 containing squalen, tocopherol and polysorbate.

Conclusion: Influenza vaccination with virosomes as an adjuvant simultaneously to the routine immunization in very preterm infants didn't induce a measurable cellular immunity nor a protective antibody titer.

Adjuvanted influenza vaccines might have the potential for improved immunogenicity in young infants.

HOW WELL PARENTS DECLARE INFLUENZA VACCINATION IN THEIR CHILDREN: RESULTS AFTER PANDEMIC INFLUENZA CAMPAIGN IN QUEBEC, CANADA

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Background and aims: Little is known about the validity of data on vaccination in children as reported by their parents when vaccination is given during the course of an epidemic. We validated vaccination status and date of pandemic influenza vaccination (PIV) in children 6 months to 9 years of age during the fall 2009 campaign such as declared by their parents in Québec, Canada.

Methods: As part of a case-control study assessing effectiveness of PIV in children, trained interviewers administered a standardized phone questionnaire to parents 3-7 months after vaccination campaign. Data were validated through linkage to the provincial electronic pandemic vaccination registry.

Results: Among the 884 participants, parents reported PIV for 688 children compared to 676 entries in the registry (positive predictive value 98%); 196 parents said that their child did not receive the vaccine, 189 of these reports were exact (negative predictive value, 96%). Among the 325 (47%) participants who were able to provide the date of vaccination, 164 (50%) provided the exact date; for 93 (29%) the difference was of +/-1-4 days. Reporting the exact date of vaccination was significantly associated with younger age of the child, fewer siblings of ≤5 years in the household, and higher level of education of the mother.

Conclusions: Shortly after pandemic influenza vaccination campaign, reliability of true vaccination status of children declared by their parents was very high. However, uncertainty was important for the date of vaccination. This uncertainty should be acknowledged when estimating vaccine effectiveness based on survey data.

EFFICACY OF 13-VALENT VERSUS 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13; PCV7) IN PREVENTING NASOPHARYNGEAL COLONIZATION: A RANDOMIZED DOUBLE-BLIND TRIAL IN ISRAEL

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Background and aims: This double-blind study assessed the efficacy of PCV13 versus PCV7 in preventing nasopharyngeal (NP) colonization in infants; serotype 6C, a serotype with similar structure to 6A, was also assessed.

Methods: Healthy infants were randomly assigned to receive PCV13 (n=932) or PCV7 (n=934) at ages 2, 4, 6 and 12 months (m). Eight NP-swabs were collected between ages 2-24m. New NP-acquisitions (rate ratio; RR) within ages 7-24m, and prevalence (odds ratio; OR) at 5 age points were evaluated.

Results: For the 7 common serotypes, NP-acquisition and prevalence with 19F was lower in PCV13 recipients and did not differ for the other 6 serotypes (Table 1). For the 6 additional PCV13-serotypes grouped, 6A/6C grouped, and single serotypes 1, 6A, 6C, 7F and 19A NP-acquisition were reduced in PCV13 recipients (Table 2); there was a similar impact on the prevalence of colonization.

Conclusions: PCV13 should be more effective than PCV7 in preventing vaccine-type pneumococcal disease, in particular for the 6 additional serotypes, and non-vaccine serotype 6C, and perhaps 19F.

Serotypes Grouped or Single Serotype	PCV13	PCV7	PCV13:PCV7 Rate Ratio	95% CI
	N=833-881 %	N=831-873 %		
PCV7/PCV13 serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F	23.6	27.4	0.86	0.73, 1.01
19F	7.9	12.2	0.65	0.48, 0.87

[New Acquisitions Age 7-24 Months: PCV7-serotypes]

Single Serotype	PCV13	PCV7	PCV13:PCV7 Rate Ratio	95% CI
	N=832-880 %	N=806-872 %		
1	0.0	0.9	0.00	NE, 0.44
3	1.8	1.9	0.99	0.48, 2.06
5	0.1	0.2	0.50	0.02, 5.54
6A	7.7	13.2	0.58	0.43, 0.78
6C	2.7	6.0	0.44	0.27, 0.71
7F	0.3	1.3	0.27	0.04, 0.90
19A	12.6	22.9	0.55	0.44, 0.68

[New Acquisitions Age 7-24 Months: PCV13-unique, 6C]

BACTERICIDAL ANTIBODY PERSISTENCE TWO YEARS FOLLOWING MENINGOCOCCAL B VACCINATION AT 6, 8 AND 12 MONTHS IN 40 MONTH OLD CHILDREN

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Background and aims: In a previous study 60 infants receiving a serogroup B meningococcal vaccine containing recombinant-proteins alone (rMenB) or the proteins with an outer-membrane vesicle (4CMen B) at 6, 8 and 12 months of age produced serum bactericidal antibody (SBA) responses against multiple meningococcal strains. We studied persistence of the response.

Methods: In this extension study, rMenB and 4CMenB recipients had SBA titres evaluated before and after booster doses of their respective vaccines at age 40 months. Men B naïve age-matched children served as a control group.

Results: Prior to the booster, the proportions of 4CMenB recipients with SBA titres $\geq 1:4$ were 36% (n=14, 95% C.I. 13-65%) for strain 44/76-SL, 100% (77-100%) for 5/99, 14% (2-43%) for NZ98/254 and 79% (49-95%) for M10713. These percentages were 14 to 29% for rMenB recipients (n=14), except for strain 5/99 (93%, C.I. 66-100%). For controls (n= 40) these proportions were $\leq 3\%$ for all strains except M10713 (53%, C.I. 36-68%).

One month after the booster, $\geq 93\%$ of 4CMenB recipients had SBA titres $\geq 1:4$ for all 4 strains.

For controls receiving their first dose of 4CMenB, 23% (11-39%) had SBA titres $\geq 1:4$ for NZ98/254, compared with 62% to 87% for the remaining strains.

Conclusion: These data suggest waning of bactericidal antibodies following infant immunisation with rMenB or 4CMenB, but an anamnestic response to a booster-dose. Booster doses of 4CMenB may be required to maintain immune protection through childhood and adolescence.

SURVEILLANCE OF PERTUSSIS IN THE NETHERLANDS: MONITORING THE IMPACT OF RECENT CHANGES IN THE VACCINATION PROGRAM

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Background and aims: Because of a pertussis-upsurge since 1996, an acellular booster was added to the NIP in late 2001. Furthermore, an acellular vaccine replaced the whole-cell vaccine at infancy in 2005. We aimed to measure the impact of these interventions on the Dutch pertussis-epidemiology.

Methods: Disease-, immuno- and pathogen-surveillance were used for monitoring. The 'screening'-method was used to calculate age-specific vaccine-effectiveness.

Results: Overall mean incidence of notifications per 100,000 increased from 32 (1996-2004) to 37 (2005-2010).

Mean incidence in 0-year-olds decreased from 123 (1996-2004) to 88 (2005-2010). Likewise, mean incidence in 1-4-year-olds decreased from 123 to 52. In 5-9-year-olds mean incidence decreased from 174 (1996-2001) to 112 (2002-2010).

In persons ≥ 10 years, mean incidence increased from 15 (1996-2004) to 33 (2005-2010). Likewise, immunosurveillance data showed an increase of pertussis-specific antibodies from 4% (1996-1997) to 9% (2006-2007).

Mean vaccine-effectiveness in 1-3-year-olds increased from 31% (1996-2004) to 81% (2005-2010).

In the cohorts targeted for the booster vaccination vaccine-effectiveness remained high (mean 64%) with still 28% in the first two cohorts vaccinated, i.e. 8-9 years after introduction of vaccination.

Conclusions: Due to changes in the vaccination program, the incidence of pertussis is decreasing in children. Vaccine-effectiveness considerably improved after introduction of an acellular vaccine. More than 5 years after its implementation, vaccinated cohorts still benefit from the introduction of a preschool booster dose.

In contrast, the incidence of pertussis in adults is increasing, probably due to increased circulation following pathogen adaptation. Further optimization of the vaccination strategy should be addressed.

PERSISTENCE OF IMMUNE RESPONSE TO A CANDIDATE MENINGOCOCCAL TETRAVALENT TETANUS TOXOID-CONJUGATE VACCINE (MENACWY-TT) IN TODDLERS, 2 YEARS AFTER VACCINATION

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Background and aims: Invasive meningococcal disease is a serious infection that is vaccine-preventable; long-term protection relies on antibody persistence. Here we report the persistence of immune response 2 years post-vaccination with a meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (MenACWY-TT), compared with a conjugate MenC vaccine (MenC-CRM₁₉₇), in Finnish toddlers aged 12-23 months.

Methods: This persistence study (NCT00955682) included toddlers who previously (study NCT00474266) received MenACWY-TT (N=253) or MenC-CRM₁₉₇ (N=42). Immunogenicity was measured using rabbit and human complement serum bactericidal assays (rSBA; hSBA) with cut-offs of 1:8 and 1:4, respectively. Vaccine-related serious adverse events (SAEs) occurring since the end of the primary vaccination study were recorded retrospectively.

Results: At Year 2, ≥88.2% of subjects receiving MenACWY-TT had persisting rSBA antibody titres ≥1:8 against each serogroup (table). More than 87% retained hSBA titres ≥1:4 for serogroups C, W-135, and Y; persistence against MenA was low, consistent with other reports (Gill *et al. Hum Vaccin.* 2010;6:881-7). MenC antibody persistence was significantly higher (exploratory analysis) in the MenACWY-TT group than in the MenC-CRM₁₉₇ group in terms of rSBA titres ≥1:8, hSBA titres ≥1:4 and ≥1:8, and hSBA GMT. No vaccine-related SAEs were reported up to 2 years after the primary vaccination.

Table. Subjects with meningococcal rSBA titres ≥1:8, hSBA titres ≥1:4 and GMTs 42 days and 2 years post-vaccination (According-to-Protocol cohort for persistence at Year 2; MenACWY-TT [N=188], MenC-CRM₁₉₇ [N=30]).

Antibody	Group	Time point	rSBA			hSBA		
			N	% ≥1:8	GMT	N	% ≥1:4	GMT
MenA	MenACWY-TT	Day 42	186	100 [98.0–100]	1924 [1698–2181]	179	83.2 [76.9–88.4]	23 [19–29]
		Year 2	181	97.8 [94.4–99.4]	420 [356–496]	183	25.1 [19.0–32.1]	4 [3–5]
	MenC-CRM ₁₉₇	Day 42	14	50.0 [23.0–77.0]	22 [7–66]	23	0 [0–14.8]	2 [2–2]
		Year 2	28	82.1 [63.1–93.9]	91 [46–178]	23	8.7 [1.1–28.0]	2 [2–2]
MenC	MenACWY-TT	Day 42	184	100 [98.0–100]	447 [397–503]	179	98.3 [95.2–99.7]	170 [143–202]
		Year 2	186	88.2 [82.6–92.4]	98 [78–124]	175	88.0 [82.2–92.4]	50 [39–65]
	MenC-CRM ₁₉₇	Day 42	30	93.3 [77.9–99.2]	146 [84–255]	23	82.6 [61.2–95.0]	46 [21–100]
		Year 2	29	69.0 [49.2–84.7]	54 [26–112]	19	57.9 [33.5–79.7]	10 [5–23]
MenW-135	MenACWY-TT	Day 42	186	100 [98.0–100]	2241 [1999–2512]	176	81.8 [75.3–87.2]	42 [32–55]
		Year 2	188	98.9 [96.2–99.9]	397 [342–461]	180	92.8 [88.0–96.1]	78 [62–98]
	MenC-CRM ₁₉₇	Day 42	16	50.0 [24.7–75.3]	22 [7–65]	23	4.3 [0.1–21.9]	2 [2–3]
		Year 2	29	58.6 [38.9–76.5]	42 [19–96]	23	0 [0–14.8]	2 [2–2]
MenY	MenACWY-TT	Day 42	185	100 [98.0–100]	2550 [2213–2937]	169	79.3 [72.4–85.1]	30 [23–38]
		Year 2	188	97.9 [94.6–99.4]	397 [324–486]	154	87.0 [80.7–91.9]	58 [45–76]
	MenC-CRM ₁₉₇	Day 42	16	75.0 [47.6–92.7]	88 [30–262]	23	4.3 [0.1–21.9]	3 [2–4]
		Year 2	30	80.0 [61.4–92.3]	151 [69–331]	22	22.7 [7.8–45.4]	5 [2–11]

[] = lower and upper limits of 95% confidence interval; N, number of subjects with available results; GMT, geometric mean titre.

[table]

Conclusions: Two years post-vaccination, >88% of toddlers receiving MenACWY-TT had rSBA titres ≥1:8 for each serogroup.

IMPACT OF CONJUGATE VACCINES ON INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN < 2 YEARS IN NAVARRA, SPAIN (2007-2011)

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Background and aims: 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in Spain in 2001; 10-valent (PCV10) in November 2009 and 13-valent (PCV13) in June 2010. This study assesses the impact of new conjugate vaccines on the incidence of invasive pneumococcal disease (IPD) in children aged < 2 years in Navarra, Spain.

Methods: Vaccination data was obtained from the regional vaccination registry. IPD diagnosed by pneumococcal isolation, PCR or antigen detection in normally sterile samples were considered. We analysed incidence in two periods: pre-introduction of PCV10 (week 40/2007 - week 39/2009) and post-introduction (week 40/2009 - week 39/2011).

Results: 60.1% children born in 2009 received a 4th dose (12.5% with PCV10 and 33.1% with PCV13); 67.6% of born in 2010 received a 3rd dose (10.1% with PCV10 and 50.1% with PCV13).

Twenty six IPD cases (none caused by serotypes (stp) included in PCV7) were diagnosed: 16 (61.5%) in PCV7-vaccinated, one (3.8%) in PCV10-vaccinated and one (3.8%) in PCV13-vaccinated. None of IPD in vaccinated was due to stp included in the administered vaccine.

	2007-2009	2009-2011	p	% decrease
IPD by any stp	74.6	25.5	0.018	65.8
IPD by stp in PCV10/PCV13 but not in PCV7 (1, 5 and 7F)	19.6	0.0	0.025	100
IPD by stp exclusively in PCV13 (3, 6A and 19A)	35.3	7.3	0.025	79.3
IPD by stp in PCV13 but not in PCV7 (1, 3, 5, 6A, 7F and 19A)	54.9	7.3	0.001	86.7

[Incidence of IPD (per 100000 inhabitants)

Conclusion: IPD incidence in young children sharply decreased after introduction of new pneumococcal conjugate vaccines.

PERSISTENCE OF IMMUNE RESPONSE TO A CANDIDATE MENINGOCOCCAL TETRAVALENT TETANUS TOXOID-CONJUGATE VACCINE (MENACWY-TT) IN HEALTHY ASIAN ADOLESCENTS, 2-YEARS AFTER VACCINATION

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Background and aims: Invasive meningococcal disease is a serious infection that is vaccine-preventable; long-term protection relies on antibody persistence. Here we report the persistence of immune response 2 years post-vaccination with a meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (MenACWY-TT), compared with a MenACWY polysaccharide vaccine (MenACWY-PS), in Asian adolescents aged 11-17 years.

Methods: This persistence study (NCT00974363), conducted in India and the Philippines, included subjects who previously (study NCT00464815) received MenACWY-TT (N=521) or MenACWY-PS (N=168). Persistence of functional antibodies was measured 2 years post-vaccination using a rabbit complement serum bactericidal assay (rSBA) with a 1:8 cut-off. Vaccine-related serious adverse events (SAEs) occurring since the end of the primary vaccination study were retrospectively recorded.

Results: Two years post-vaccination, ≥99.3% of subjects receiving MenACWY-TT had persisting antibody titres ≥1:8 against each serogroup (table). Antibody persistence was significantly higher (exploratory analysis) in the MenACWY-TT group than the MenACWY-PS group in terms of rSBA titres ≥1:8 for serogroups W-135 and Y; rSBA titres ≥1:128 for serogroups A, W-135 and Y; and rSBA GMTs for serogroups A, W-135 and Y. No vaccine-related SAEs were reported.

Table. Subjects with meningococcal rSBA titres ≥1:8, ≥1:128 and GMT 1 month and 2 years post-vaccination (According-to-Protocol cohort for persistence at Year 2; MenACWY-TT [N=447], MenACWY-PS [N=145]).

Antibody	Group	Time point	N	% rSBA ≥1:8	% rSBA ≥1:128	GMT
MenA	MenACWY-TT	Month 1	443	100 [99.2–100]	99.8 [98.7–100]	5649 [5200–6136]
		Year 2	445	99.8 [98.8–100]	99.6 [98.4–99.9]	1517 [1400–1645]
	MenACWY-PS	Month 1	144	99.3 [96.2–100]	99.3 [96.2–100]	2901 [2459–3421]
		Year 2	144	100 [97.5–100]	97.2 [93.0–99.2]	811 [696–944]
MenC	MenACWY-TT	Month 1	444	99.5 [98.4–99.9]	99.3 [98.0–99.9]	13071 [11544–14801]
		Year 2	447	99.3 [98.1–99.9]	97.1 [95.1–98.4]	1122 [997–1263]
	MenACWY-PS	Month 1	144	100 [97.5–100]	99.3 [96.2–100]	8736 [6904–11054]
		Year 2	145	98.6 [95.1–99.8]	94.5 [89.4–97.6]	1499 [1120–2007]
MenW-135	MenACWY-TT	Month 1	446	99.8 [98.8–100]	99.8 [98.8–100]	7859 [7112–8685]
		Year 2	447	99.6 [98.4–99.9]	99.1 [97.7–99.8]	2071 [1870–2293]
	MenACWY-PS	Month 1	144	100 [97.5–100]	99.3 [96.2–100]	2559 [2128–3077]
		Year 2	143	95.1 [90.2–98.0]	86.7 [80.0–91.8]	443 [342–573]
MenY	MenACWY-TT	Month 1	446	99.8 [98.8–100]	99.8 [98.8–100]	12515 [11434–13697]
		Year 2	447	100 [99.2–100]	100 [99.2–100]	3716 [3409–4050]
	MenACWY-PS	Month 1	144	100 [97.5–100]	100 [97.5–100]	4947 [4214–5806]
		Year 2	142	97.2 [92.9–99.2]	95.1 [90.1–98.0]	1090 [858–1386]

[] = lower and upper limits of 95% confidence interval; N, number of subjects with available results; GMT, geometric mean titre.

[Table]

Conclusions: Two years post-vaccination >99% of subjects in the MenACWY-TT group retained rSBA titres ≥1:8 for all serogroups, indicating that immunogenicity following a single dose in adolescents persists for at least 2 years.

PREVALENCE OF GENOTYPES OF INFLUENZA IN THE POPULATION OF POLAND DURING THE 2010/2011 SEASON

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Background and aims: Poland participated in I-MOVE network with a view to monitor influenza vaccine effectiveness (IVE), which enabled to investigate genotypes of influenza among specific age groups. In Poland vaccination campaign in the 2010-2011 influenza season commenced in week 36 and achieved 5.2% vaccination coverage.

Methods: During the study period (20 weeks) 33 sentinel GPs enrolled patients with ILI/ARI symptoms adhering to the European ILI case definition, interviewed them and collected nasopharyngeal samples for laboratory RT-PCR testing. ILI-positive patients were defined as cases. The distribution of influenza genotypes by age group and date of onset (week number) among them was compared.

Results: Of the 99 influenza cases, 54 (54.5%) were positive for influenza B and 45(45,5%) for influenza A, with 30(30.3%) being A(H1N1) and 15(15.2%) another type A. Influenza A was predominant in the 0-4 and 15-64 age group with their respective shares being (75%;3/4) and (57%;37/65). Influenza B was confirmed in 84.6%(22/26) of cases aged 5-14 years old and in 75.0%(3/4) of those aged 65 or over. Influenza A was dominant from the beginning of influenza season (week 48, 2010) to its peak (week 5-6, 2011), while influenza B became dominant at the end of the season (week 7-15, 2011).

Conclusions: The results confirmed that the vaccine was a good match for the virus circulating in the environment. In order to achieve more reliable results, more samples should be collected in 2011/12 season.

MANAGEMENT OF PATIENTS WITH PROLONGED COUGH IN GP PRACTICE SUSPECTED OF PERTUSSIS IN POLAND, 2009-2011

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Background and aims: Effective vaccination against pertussis which affected the perception of the disease as eliminated and high underreporting rate of pertussis observed in Poland may contribute to the misdiagnosis of pertussis cases. The aim of the analysis was to determine diagnosis and treatment of patients with prolonged cough, enrolled in surveillance of pertussis in Poland.

Methods: The study was conducted from July 2009 to April 2011 in the population served by 78 randomly selected GPs. Inclusion criteria were: age > 3 years old, cough lasting 2-15 weeks and one of the following symptoms: paroxysms of coughing, inspiratory whooping, post-tussive vomiting. GPs inquired each eligible patient about utilization of healthcare services, diagnostic tests and medications regarding period from appearance of the first symptoms to GP visit.

Results: Of the 1232 included patients, 288 (23,4%) were confirmed as pertussis. As many as 787 patients (63,9%) used healthcare services (1.0 -3.7 visit per patient). Out of 581 (47,6%) patients tested, 78 (13,4%) patients had test directed to identify specific etiological factor, including only 2 tests aimed at *Bordetella pertussis* identification. Out of 960 (78%) patients who received medications, 610 (49,5%) received antibiotics, 360 (30,4%) received antibiotics effective for pertussis including 99/288 (34,3%) pertussis-positive patients.

Conclusion: The differential diagnosis of coughing patients do not include pertussis, which leads to its underascertainment. Symptomatic instead of etiologic treatment contribute to the maintained transmission of *Bordetella pertussis* and other pathogens in the society.

COST-EFFECTIVENESS OF PERTUSSIS BOOSTER VACCINATION IN ADOLESCENTS AND ADULTS: A REVIEW

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Background and aims: Following childhood implementation of vaccination against pertussis with achievement of high coverage, the disease incidence decreased significantly. However re-emergence of pertussis was observed in young infants, adolescents and adults, which may be mitigated with booster vaccination. Economic evaluations have been performed, to assess the cost-effectiveness of different booster strategies. The objective of this literature review was to assess the level of cost-effectiveness of evaluated strategies.

Methods: The literature search covered worldwide cost-effectiveness models of pertussis booster vaccination published before November 2010. We extracted information on models, inputs and results. This analysis focuses on adolescents, adults and cocoon strategy.

Results: We identified 13 publications (4 Europe, 8 North America, and 1 Australia). In most studies, adolescent pertussis booster vaccination was found to be cost-effective or cost-saving when compared to no booster vaccination. Two studies compared adolescent strategy with others; it was found to be cost-saving compared to adult strategies in one study, dominated by combined adolescent, adult vaccination at 40 and cocoon strategy in another study. One-time adult strategy was also cost-effective vs. no booster, under certain conditions on prevalence. Cocoon strategy results were found to be cost-effective in 4 out of 5 studies. Decennial vaccination was found to be cost-effective vs. no booster, but dominated by adolescent strategy.

Conclusion: Most publications concluded that implementing pertussis booster vaccination in adolescents, adults and/or cocoon strategy would be cost-effective. However, further research is needed to determine the optimal strategy for each country considering local epidemiological/economic parameters and vaccination schedule.

CURRENT PERTUSSIS EPIDEMIOLOGY IN POLAND - RESULTS OF 2009-2011 PROSPECTIVE COHORT STUDY

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Background and aims: Adult pertussis is an important and underascertained problem in Poland especially in contexts of infection's transmission from adult to infant. The objective of the study was to estimate the incidence of pertussis among patients with cough lasting > 2 weeks visiting the GP in Poland and to compare it with national pertussis notifications.

Methods: The prospective cohort study was performed from 2009 until 2011 in the 158.863 population served by 78 randomly selected general practices. GPs interviewed two times each eligible patient, collected a blood sample, and a nasopharyngeal swab. Confirmed pertussis cases were defined as patients meeting the clinical criteria confirmed by laboratory.

Results: The 3,865 patients with cough consulted the participating GPs, of whom 288 cases were confirmed as pertussis. The highest incidence was found among persons aged 15-25 years (181.4) and 55-69 years (222.2). During corresponding period 1,248 pertussis cases were reported to national surveillance by GPs and 800 by hospital physicians. Reporting ratio was 77.3 for GPs and 4.2 for hospital physicians, and ranged from 5.2 among 3-5 year olds, to 298.3 among persons age 70 years or more.

Conclusions: The present study confirmed the high circulation of B.pertussis in all age groups in the general population. Our findings indicate that the oldest age group play an important role of disease transmission, not appropriately documented by existing surveillance system.

EFFICACY OF RSV PROPHYLAXIS IN CONGENITAL HEART DISEASE: A SINGLE CENTER EXPERIENCE

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Background: Infants or children with congenital heart disease (CHD) hospitalized for RSV infection have a more complicated clinical course with a high risk of fatal issue. The infection can increase post-operative complications after cardiovascular surgery. Moreover, some studies have shown an increased risk of RSV - related mortality in patients with CHD. RSV prophylaxis with Palivizumab is recommended in infant up to 24 months of age with hemodynamically significant CHD. We value retrospectively the efficacy of RSV prophylaxis in our institution.

Material and methods: From 2004 to 2011 28 consecutive patients with CHD eligible for RSV prophylaxis, were seen in our Institution. This group was valued for the number of RSV infections (documented by laboratory studies), and compared, for clinical score on admission, length of continuous oxygen therapy and hospitalisation, with a group of 10 healthy children admitted in our ward for bronchiolitis. Statistical analysis was made using the Mann-Whitney test.

Results: In the group of patients with CHD, 6 patients (initially followed in others institution) didn't underwent RSV prophylaxis and 5 patients (83%) contracted RSV infection. The other 22 patients had RSV prophylaxis and 1 patient (who received only a single dose) contracted RSV infection. The clinical score on admission ($p = 0.0021$), the length of continuous oxygen therapy ($p = 0.0014$) and the length of hospitalization ($p = 0.0084$) were significantly higher in patients with CHD.

Conclusion: Our experience confirms that RSV prophylaxis, correctly performed, is effective and thus mandatory in infants with hemodynamically significant congenital heart disease.

POST-IMMUNIZATION FEVER AND ANTIPYRETIC USE FROM THE POINT OF VIEW OF PARENTS AND HEALTHCARE PROVIDERS (HCPs): AN ONLINE SURVEY

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Background: Introducing new infant vaccines to established programs may increase concerns about side effects (e.g., fever). Using antipyretics to prevent post-immunization fever might impact some vaccine immune responses.

Methods: A survey was conducted online in Australia, Canada, France, Germany, Spain, Sweden, and UK to investigate parental and HCPs knowledge and opinions about vaccination.

Results: Among 2460 parent respondents, 1173 (48%) believed that vaccines could cause fever and 1059 (43%) wanted to limit fever risk due to multiple vaccines. Most parents whose children received vaccines (1652/2322; 72%) stated that HCPs sometimes recommend preventative antipyretics; of these, 923/1652 (56%) would administer them. Among those previously recommended to do so by an HCP, 82% (628/768) had administered antipyretics to treat post-vaccination fever in their infants. Most HCPs (612/725; 84%) responded that fever does not influence their vaccination decisions. Few (36/725; 5%) HCPs found post-vaccination fever concerning, but 34% (248/725) thought it worries parents. Most (463/725, 64%) HCPs recommended antipyretics for active fever, and some (206/725; 28%) recommend antipyretics prophylactically, most commonly to avert febrile seizure risk. Relatively few HCPs (195/725; 27%) believe that use of pre-vaccination antipyretics impacts immunogenicity, while most (390/725; 54%) believe that it does not.

Discussion and conclusions: HCPs and parents rate concerns about postimmunization fever differently. Without conclusive evidence that antipyretics prevent febrile seizures, HCPs state that the possibility of febrile seizures may influence co-medication decisions. Most parents would follow HCP recommendations for fever management with antipyretics. Further education could enhance the understanding of vaccination among parents and HCPs.

REGULAR IMMUNIZATION AS A PRECONDITION FOR CHILDREN'S INFECTIOUS DISEASE ERADICATION

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Introduction: Immunization has proved as a good method to eradicate the children's infectious disease around the world.

Aim: Influence of the immunization over the reduction and eradication of the infectious disease.

Materials and methods: Data from registered infectious disease and immunization reports or a period of 5 years (2007-2011 year) Analytic and descriptive methods have been used for data processing.

Results: Out of the total number of the treated 1097 children at the age of 0 to 6 years, successfully vaccinated are 98 % of the children from the immunization program of the Republic of Macedonia. In a period of 5 years (2007-2011) we have registered 5 cases with Morbilli, 1 case of Rubella, 7 of Parothisis and 453 cases of Varicella. The results clearly show significant number of Varicellas against which immunization hasn't been performed, while the rash children's fever have been registered only sporadically. Other children's disease such as Poliomyelitis, Tetanus and Pertussis are considered to be eradicated in Republic of Macedonia. A child infected by Tuberculosis hasn't been registered in our institution during this period.

Conclusion: The results clearly show the benefit of a successfully completed immunization which saves money to be spent on treating the disease and dealing with the consequences of the same.

PARENT AND HEALTHCARE PROVIDER (HCP) ATTITUDES TOWARD INTRODUCTION OF NEW VACCINES INTO NATIONAL IMMUNIZATION SCHEDULES: ONLINE SURVEY RESULTS

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Background: Adding new vaccines into immunization schedules, such as a MenB vaccine, may increase co-administrations or physician visits.

Methods: The New Vaccinations of Infants in Practice survey conducted online in Australia, Canada, France, Germany, Spain, Sweden, UK evaluated the importance of vaccination-related concerns for parents and HCPs.

Results: Overall 2460 parents and 725 HCPs responded. Most parents (1869/2460, 76%) accepted the vaccines included in national schedules and 75% (1853/2460) trusted HCP judgments about vaccine choices. Some parents (680/2460; 28%) were comfortable with doctor recommendations for maximum number of injections at a single visit; key factors influencing parental decision-making included minimizing discomfort and ensuring their child received all needed vaccines. Disease severity, lethality and national immunization schedules were key HCP considerations for pediatric vaccine recommendations. Most HCPs (601/725; 83%) would co-administer vaccines to follow established immunization schedules. Both parents and HCPs preferred the number of injections per visit that correspond to current recommendations (2-3, depending on the country). After exposure to MenB disease information, most (1672/2460; 68%) parents predicted vaccine acceptance if a new vaccine was approved and recommended by an HCP. The vast majority of parents would accept the new vaccine with co-administration or during an additional office visit. The primary factor influencing parental decisions about MenB vaccination for 0-6 month-olds was disease protection; post-vaccination fever was 7-fold less influential (ratio-scaled probability 96/100 vs. 14/100).

Conclusions: Parents strongly value HCP recommendations, and HCPs consider national immunization schedules when considering administering new vaccines to infants; recommending bodies should realize this.

ABSOLUTE LYMPHOCYTE COUNT PREDICTS RESPONSE TO NOVEL H1N1 VACCINE IN CHILDREN WITH A HEMATOLOGIC MALIGNANCY

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Background: The determinants of response to influenza vaccination in children with a hematologic malignancy are still debated. We studied the effect of a decreased absolute lymphocyte count on development of seroprotection.

Methods: We measured vaccination responses to the new swine-origin influenza A H1N1 in 20 children (11 girls and 9 boys; median age 6 years range 2-16) with a hematologic malignancy (Acute Lymphatic Leukemia (n=16); Acute Myeloid Leukemia (n=2); Non-Hodgkin Lymphoma (n=1); Langerhans Histiocytosis (n=1); 16 children were on chemotherapy, 4 were < 6 months after chemotherapy. Absolute lymphocyte count (ALC) was measured 1-10 days preceding vaccination. Lower normal limits (LNL) for ALC were defined as 1700/microL for age 2-4 years; 1100/microliter for age 5-9 years; 1000/microliter for age 10-adult. All patients were vaccinated twice with an intramuscular injection with inactivated split-virion preparation of the A/California/07/2009(H1N1)v like strain (X-179A), which contained 7.5µg of hemagglutinin per dose of 0.5 ml. A protective response was defined as achieving a hemagglutination inhibition (HI) antibody titer ≥ 1:40 following vaccination. Children with positive prevaccination HI titers or natural H1N1 infection were excluded. Statistical differences were tested by Fisher's exact test. A P < 0.05 was considered statistically significant.

Results: 11/20 (55%) of children had a protective immune response. In children with ALC < LNL for age 4/12 (33%) showed seroprotection and in children with ALC > LNL for age 7/8 (87%) showed seroprotection (p < 0.028).

Conclusion: Absolute lymphocyte count predicts the response to influenza vaccination in children with a hematologic malignancy.

POTENTIAL IMPACT OF THE BIVALENT RLP2086 VACCINE ON *NEISSERIA MENINGITIDIS* INVASIVE DISEASE AND CARRIAGE ISOLATES IN TWO ADOLESCENT POPULATIONS

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Background: Invasive disease caused by *Neisseria meningitidis* serogroup B (MnB) is preceded by acquisition and carriage. Understanding the molecular epidemiology of carriage isolates and invasive strains should help predict the breadth of coverage provided by MnB vaccines. Factor H-binding protein (LP2086) is a lipoprotein expressed on the surface of all meningococcal serogroups as 1 of 2 serologically distinct subfamilies (A and B). A bivalent vaccine including lipidated, recombinant subfamily A and B antigens (rLP2086) is in late-stage clinical development.

Methods: Amino acid sequences of LP2086 variants from carriage isolates and invasive MnB strains were analyzed and compared. Serum samples from healthy individuals aged 11 to 40 years immunized with the bivalent rLP2086 vaccine during 2 clinical studies conducted in Poland, Spain, and Australia were assayed for serum bactericidal activity using human complement (hSBA).

Results: Nearly all ($\geq 97\%$) LP2086 variants expressed by carriage isolates from all serogroups were expressed by our collection of 1841 invasive MnB strains. Robust bactericidal activity was demonstrated against diverse MnB hSBA test strains representing $\approx 90\%$ of LP2086 variants responsible for invasive MnB and $>75\%$ of LP2086 variants from carriage isolates. High hSBA responses were observed regardless of LP2086 subfamily, subgroup, variant, or other epidemiologic markers.

Conclusions: Clinical evidence of bactericidal activity elicited by the bivalent rLP2086 vaccine demonstrated broad protection against invasive MnB strains. Comparison of LP2086 variants among carriage and invasive disease strains indicated the potential impact of the bivalent rLP2086 vaccine against the major meningococcal serogroups.

This study was sponsored by Pfizer Inc.

THE IMPACT OF ROTAVIRUS MASS VACCINATION ON HOSPITALIZATION RATES, NOSOCOMIAL ROTAVIRUS GASTROENTERITIS AND SECONDARY BLOOD STREAM INFECTIONS

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Background and aims: Since July 2007 oral rotavirus vaccination is part of the routine vaccination funded by the Austrian national vaccination program. Previous studies have shown that, a secondary blood stream infection can be one major complication of a rotavirus gastroenteritis.

Methods: The aims of our retrospective study were to evaluate the effects of a routine mass vaccination on the frequency of hospitalisation, the duration of hospitalisation and the frequency of secondary blood stream infections.

Results: We detected a significant reduction of rotavirus gastroenteritis cases in the vaccination period ($p=0.041$). No shift in the seasonal distribution was detected in the vaccination period compared to the prevaccination period. In the vaccination period a highly significant reduction of duration of hospitalisation was detected ($p < 0.001$), especially in the age group of children between 6-24 months of age ($p=0.013$). In 20 patients a secondary blood stream infections occurred while treated because of a rotavirus gastroenteritis. The most commonly detected bacteriae were *Staphylococci*, followed by Enterobacteriaceae.

Conclusion: In conclusion, the first 2.5 years of the vaccination had led to a reduce of disease burden and of costs due to cases of rotavirus infections. When a secondary blood stream infections follows a rotavirus gastroenteritis, prompt initiation of wide-spectrum antibiotic treatment is crucial, because intestinal and non-intestinal bacteria can be the causative agents of secondary blood stream infections.

IMPACT OF INTRANASAL LIVE ATTENUATED INFLUENZA VACCINE ON SOCIETAL AND ECONOMIC BURDEN OF INFLUENZA IN EUROPEAN/ISRAELI CHILDREN 2-17 YEARS

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Background and aims: Few data exist regarding the impact of influenza vaccination on the societal/economic burden of influenza illness in children. This analysis describes the impact of live attenuated influenza vaccine (LAIV) versus placebo or trivalent inactivated influenza vaccine (TIV) in children 2-17 years.

Methods: In 3 randomized studies conducted in Europe and Israel in 2000-2003 (2-year, placebo-controlled study in children < 48 months attending daycare [N=846-973]; TIV-controlled studies in children < 72 months with recurrent respiratory infections [N=1609] and 6-17 years with asthma [N=2211]), multiple societal/economic burden outcomes were prospectively collected for respiratory illnesses following illness resolution. Influenza was detected by viral culture; all cases were evaluated, regardless of match to vaccine. Incidence among LAIV versus placebo or TIV recipients was compared for each endpoint.

Results: Influenza illness commonly resulted in missed school/daycare (55%-91% of subjects), medication use (45%-89%), parental missed work (30%-55%), antibiotic use (17%-55%), additional provider visits (11%-62%), and acute otitis media (8%-28%). LAIV reduced the incidence of these outcomes consistent with reductions in culture-confirmed illness (85%-88% versus placebo; 32%-48% versus TIV). LAIV recipients had 324-902 fewer days ($P < 0.01$) of missed school/daycare per 1000 children relative to placebo in children 24-47 months and 150 and 76 fewer days ($P \leq 0.02$) per 1000 relative to TIV recipients in children 24-71 months and 6-17 years, respectively.

Conclusions: In studies of European and Israeli children 2-17 years, influenza resulted in significant societal and economic burden, which was reduced by vaccination with LAIV relative to placebo or TIV. Sponsored by MedImmune.

EPIDEMIOLOGY OF HEPATITIS A IN TWO NEIGHBOUR CANADIAN PROVINCES: ONE WITH UNIVERSAL AND ANOTHER WITH TARGETED VACCINATION

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Background: In 2008, Quebec implemented a two dose universal school-based program with bivalent HA/HB vaccine, in place of the 3 doses of HB vaccine. The main objective of this study was to assess the short term impact of this program/policy change by comparing the epidemiology of HA to a targeted hepatitis A strategy.

Methods: Vaccine uptake of the bivalent vaccine in Quebec was retrieved from Public Health reports. Hepatitis A data for Quebec was obtained from notifiable diseases registry (MADO) and for Ontario from the integrated Public Health Information System (iPHIS) for the years 2002 to 2011.

Results: Since the start Quebec's universal school-based HA/HB program in 2008 bivalent vaccine uptake for grade 4 students, aged 9-10 years was ~85%. Overall incidence of HA following the universal immunization strategy (2009 to 2011) compared to prior to program implementation (2002 to 2007) has decreased by 46% (0.7 vs. 1.3. per 100,000). A decline of 81% was observed among the same time period for children aged 10-14 years who would have been eligible for the school based vaccination. This is a significant decrease in HA when compared to Ontario, where only a 36% decline was observed among children aged 10-14 years over the same time period.

Conclusion: Preliminary data indicate that two doses of HA/HB vaccine given to 9-10 year-old children have the potential to rapidly reduce the incidence of HA in low endemic regions. Further monitoring of HA epidemiology is warranted.

LONG-TERM IMMUNOGENICITY AND SAFETY OF THE HPV-16/18 AS04-ADJUVANTED VACCINE IN ADOLESCENT GIRLS AGED 10-14 YEARS: 6-YEAR FOLLOW-UP

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Background and aims: The HPV-16/18 AS04-adjuvanted vaccine was shown to induce high and sustained immunogenicity for 5 years after vaccination of girls aged 10-14 years. We present antibody persistence and safety results of the HPV-16/18 vaccine 6 years after the first dose.

Methods: Girls who received three doses of HPV-16/18 vaccine at 10-14 years of age and participated in a 4-year follow-up study (NCT00316706) were invited for an extended follow-up, up to 10 years. Serum antibody responses (determined by ELISA) were analysed at Month 72. Serious adverse events (SAEs) reported between Months 0 and 72 were analysed in the total vaccinated cohort.

Results: At Month 72, all subjects (mean age 18.0 years) in the according-to-protocol (ATP) cohort for immunogenicity (N=505) were seropositive for both HPV-16 and HPV-18 antibodies. Geometric mean antibody titres at Month 72 were 1962.0 EL.U/mL [95% CI: 1811.3-2125.3] for HPV-16 and 749.6 EL.U/mL [95% CI: 687.7-817.0] for HPV-18 (subjects initially seronegative, ATP cohort). HPV-16 and HPV-18 antibody titres were 65.8- and 33.0-fold higher, respectively, than natural infection levels (study NCT00122681), and 4.9- and 2.5-fold higher, respectively, than the plateau level (study NCT00518336), wherein vaccine efficacy was demonstrated in women aged 15-25 years. During the entire study period, a total of 74 subjects (7.1%) reported 110 SAEs; none of them were determined to be vaccine-related.

Conclusions: Persistent high antibody response of the HPV-16/18 vaccine was demonstrated in adolescent girls up to 6 years after their first vaccination, with an acceptable safety profile.

IMPACT OF CHANGES TO THE ROUTINE CHILDHOOD IMMUNISATION SCHEDULE SINCE THE MID-1990S ON IMMUNITY TO TETANUS AND DIPHTHERIA, ENGLAND 2009

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Background and aims: In 1996, 85% of the population in England were estimated to be protected against tetanus and 73% had at least basic diphtheria protection. The impact of changes to the routine childhood immunisation schedule since the mid-1990s on immunity to tetanus and diphtheria in paediatric and adult populations in England was assessed by a seroprevalence study, undertaken in 2009.

Methods: A panel of sera collected in England in 2009 were selected from 18 age groups and tested for tetanus and diphtheria immunity. Results were standardised by testing a panel of sera to enable comparison with the previous (1996) serosurvey.

Results: In 2009, tetanus immunity in the sampled population increased by 1% compared to 1996 data whereas diphtheria immunity increased by 12% to 86%. The immunity pattern for diphtheria now more closely mirrors that for tetanus. The addition of diphtheria to the school leaver booster in 1994 significantly increased immunity observed in 16 to 34 years olds in 2009 compared to 1996. Polysaccharide-protein conjugate vaccines (meningococcal C, pneumococcal and *Haemophilus influenzae* type b) containing tetanus or diphtheria carrier proteins, appear to have increased immunity in pre-school age groups, in particular for diphtheria.

Conclusions: The current schedule appears to protect well; increases in the proportions protected are observed for the ages scheduled to receive vaccinations according to the UK schedule for both tetanus and diphtheria. These findings are supported by vaccine coverage data and the observed rarity of both these diseases which predominately occur in older individuals.

BURDEN OF VARICELLA AND HERPES ZOSTER IN QUEBEC: IMPACT OF A UNIVERSAL IMMUNISATION PROGRAM

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Background and aims: In the province of Quebec (Canada), a publicly funded varicella immunisation program was launched in 2006 for children aged one year with catch-up program targeted susceptible children at 4-5 years old and grade 4 and 9 students. We estimated the impact of the universal immunisation program by examining changes in varicella-related morbidity, mortality and medical consultations from 1990 to 2008.

Methods: Incidence rates for hospitalisations, medical consultations and deaths were compared between three different periods: 1990-2000 (before vaccine use in the province), 2001-2005 (vaccine available only on the private market) and 2006-2008 (publicly funded program). Data came from three sources according to the International classification of diseases (ICD-9 and ICD-10): Hospitalisations from the Quebec hospital discharge database,, medical consultations from the provincial health insurance registry and mortality from the death registry. Age-standardized rates, age-specific rates and rate ratios were calculated.

Results: There was a significant decline of 59% in hospitalisations and 83% in medical consultations related to varicella between 2006-2008 and 1990-2000 and 61% and 69%, respectively, between 2006-2008 and 2001-2005. This decline was larger in children aged 1-4 years. Only 18 deaths occurred over the study period: 11 before 2001 and 7 between 2001-2005. No death related to varicella was observed since 2006. No significant changes in zoster-related hospitalisation, consultation or mortality rates were observed during the study period.

Conclusion: Universal immunisation program is associated with an important short-term reduction of varicella-related hospitalisations, consultations and mortality.

EVALUATION OF HOUSEHOLD IMMUNIZATION AGAINST BORDETELLA PERTUSSIS ACCORDING TO THE COCOON STRATEGY IN THE MATERNITY WARD

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Background and aims: Targeted household immunization against pertussis (cocooning) is an effective indirect strategy to protect very young infants, however reaching adults for vaccination is challenging. The birth of a child presents an opportunity to offer dTap vaccine to new parents. Our objectives were to evaluate the impact of a cocoon strategy in a maternity ward on the immunization coverage rate against pertussis among parents, and to assess variables that may influence vaccine acceptability.

Methods:

Phase 1: A standardized questionnaire (socioeconomic and demographic data, education, immunization status, pertussis knowledge) was addressed to mothers. **Afterwards**, information on pertussis disease and prevention was provided to families. Parents' vaccination in community was strongly recommended and assessed six months later.

Phase 2: Information was provided **before** fulfilling the standardized questionnaire. On site vaccination was proposed to interested parents.

Results:

Table 1. Recruited Mothers.	FIRST Phase n = 101	SECOND Phase n = 244	
Pertussis Immunization coverage rate before intervention % (n)	6.5 (5/101)	7.0 (17/242)	p = 0.475
Vaccinated mothers after intervention : n (% of accepting mothers)	4 (7.3)	106 (89.8)	p < 0.001
Pertussis Immunization coverage rate after intervention % (n)	11.4 (9/79)	50.6 (123/243)	p < 0.001

[Table 1. Recruited Mothers.]

Mothers' acceptability of dTap vaccine was not influenced by socio-economic status, level of education and disease knowledge. Fathers' immunization rate was significantly higher when offered in the maternity ward (58.5%) than in the community (6.5%) p < 0.0001.

Conclusion: Pertussis immunization coverage rate was low among new parents. Vaccine acceptability was independent of disease knowledge or information provided. Unlike the community setting, a cocoon strategy implemented in a maternity ward significantly increased immunization coverage rate.

RISK OF CONVULSION FOLLOWING COMBINED MEASLES-MUMPS-RUBELLA -VARICELLA (MMRV) VACCINE IN CHILDREN AGED 12-23 MONTHS OLD IN QUEBEC, CANADA

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Background: Quebec, Canada, introduced a universal varicella immunization program using a monovalent varicella vaccine administered at 12 months in January 2006 and a combined MMRV (Priorix-Tetra®) vaccine as of June 2008. Given reports of increased risk of convulsion following the MMRV vaccine (Pro-Quad®), we aimed to estimate the risk of convulsions and fever following the administration of MMRV (Priorix-Tetra®) vs MMR+V given at the same visit, at 12-23 months of age.

Methods: Convulsions - febrile and afebrile - were retrieved from the Adverse Effect Following Immunization (AEFI) passive surveillance database. We compared two periods: January 2006 to May 2008 (MMR+V) and August 2008 to February 2011 (MMRV). Incidence rates were estimated per 100 000 vaccinees (birth cohort * vaccination coverage for each period). Rate ratios and risk differences were calculated for 0-43, 5-12 and 0-4 days post immunization.

Results: A total of 13 (8.6/100 000) and 24 (13/100 000) convulsions were reported in the MMR+V and MMRV cohorts respectively. For the 0-43, 5-12 and 0-4 days period, rate ratios for convulsions were 1.5 (CI95%:0.8-3.0) 1.3 (0.4-4.2) and 1.7 (0.6-5.6) after MMRV vs MMR+V, with a risk difference of 4.2 (-2.8;11.2), 0.9 (-3.3;5.1), and 2.5 (-2.0;7.0) per 100 000 vaccinees respectively.

Conclusions: This study showed a non significant increased risk of convulsions after MMRV vaccine. Given the study's low statistical power, ongoing surveillance is required. We need to weigh the advantage of needing less injections and the positive impact on vaccination coverage with the risk of convulsion following MMRV.

ASSESSMENT OF KNOWLEDGE ABOUT HPV AND HPV VACCINE TO PARTICIPANTS FOR VACCINATION CAMPAIGN HELD IN COMPANY, RIO DE JANEIRO

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Objective: To assess knowledge about HPV and HPV vaccine on employees and families of private company (BNDES) during implementation of HPV vaccination campaign.

Method: We interviewed 493 participants in vaccination campaign conducted in October 2011 through a questionnaire applied by trained professionals. Data were analysed qualitatively and quantitatively.

Results: From 493 respondents, 51.3% were male. 70.3% were between 16 and 25 years, 83.3% had heard of HPV before the campaign. 53.3% reported that this knowledge was acquired through news vehicles information. 66.9% believe that HPV can be prevented by the use of condoms. 85.5% do not associate HPV infection by the relationship with many partners. 97.1% believe that vaccination does not release regular consultations to the gynecologist. 58.6% refer not knowing which diseases HPV causes, and the most commonly cited disease, associated with HPV, was cancer. 72.2% claimed that the stimulating factor in recommending them to the vaccination was the lecture held in the vaccination campaign carried out by BNDES-FAPES. Only 6.6% reported that their doctor recommended the vaccine.

Conclusion: The information on the ways of infection and the diseases caused by HPV vaccination need to be continuously broadcasted to get adherence in the vaccination campaign and to increase the improvement of immunization coverage. The vehicles of massive communication should always be associated with the dissemination of health education for its high penetration in society, as well as medical societies should take an active role in the dissemination of knowledge for both the medical professionals and the general population.

COMMUNITY SUPPORT FOR ADOLESCENT IMMUNISATION THROUGH SCHOOL BASED IMMUNISATION PROGRAMS

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Background and aims: Adolescent immunisations such as HPV have been implemented in several countries including Australia through school based immunisation programs (SBIP). We assessed community attitudes to this immunisation delivery mode.

Methods: A population survey was conducted (Oct-Dec 2011) using computer assisted telephone interviews. Adults from randomly selected metropolitan and rural households in South Australia were interviewed.

Results: Participation rate was 57.9% (n=1926/3326). Overall, 73.3% (n=1412) of respondents regarded school as the best place to offer adolescent immunisations, with 15.8% (n=304) preferring the family physician. SBIP was preferred by younger adults with 85.4% (n=204/239) of 18-24 year olds and 74.5% (n=254/341) of 35-44 year olds preferring a SBIP (p< 0.001); and by males (78%) compared with 69% of females (p< 0.001). Rural respondents preferred family physician practice (21.7%, n=110/507) compared to 13.7% (n=194/1419) of metropolitan households (p< 0.001). In 11.2% (n=215/1926) of households at least one adolescent was currently attending high school and 87.9% (n=189/215) had participated in the SBIP. Reasons for participation in the SBIP included public funding for the service (31.5%, n=59/189) ease/convenience (27.5%, n=52/189), and compliance with immunising their child (15.9%, n=30/189). Of the 19 respondents whose child did not use the SBIP, eight were uncertain of the reason, four preferred the family physician and three the council clinic. Two reported child anxiety or embarrassment, one a previous adverse reaction, and one previous immunisation.

Conclusions: Public support for the SBIP is high, with greater support in metropolitan than rural communities and among males and younger adults.

INFLUENZA VACCINE COVERAGE AMONG CHILDREN AND ADOLESCENTS AGED 0-18 YEARS IN 2004-2010 IN WARSAW

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Background and aims: Influenza is responsible for 10-405 acute respiratory tract infections with fever annually. Results of scientific research indicate that influenza is a serious clinical, epidemiological and economical problem of childhood.

The aim of the study was to establish the influenza vaccine coverage among children and teenagers aged 0-18 years in out patient clinics in Warsaw in 2004-2010.

Material and methods: The analysis of medical documentation (vaccination cards and vaccination reports) of 21.280 patients was conducted.

Results: Number of pediatric patients vaccinated against influenza ranged from 166 to 472, and the proportion of vaccinated patients was from 0,8% (in 2008) to 3% (in 2005). 878 children required two doses of vaccination against influenza, but this recommendation was not realized by 73,2% of patients. In 44,1% of patients the vaccination against influenza was coadministered with another vaccine, mainly against hepatitis A and Streptococcus pneumonia (polysaccharide vaccine).

Conclusion: The influenza vaccine coverage among healthy children and teenagers aged 0-18 years was extremely low (< 3%). More effective educational activities are required to increase the influenza vaccine coverage in a pediatric population.

STUDY OF FACTORS AFFECTING THE POSITIONS OF PARENTS ON VACCINES IN GREECE

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Background and aims: Vaccines and the National Immunization Program (NIP) is an effective public health intervention. The purpose of this study was to record the knowledge of parents about vaccinations and factors that influence it.

Methods: The study was conducted in kindergartens in Athens. 2995 questionnaires were distributed (one per child) and 1044 finally used.

Results: At a rate of 86.1% parents aware of the NIP, 94.3% agree with the administration of vaccines, 99.2% follow NIP. The majority of parents (89.5%) agree with vaccines because they protect their children from infectious diseases. The main reason of disagreement was the fear of possible side effects (81%). The relationship of the demographic data of parents and the source of their information with the knowledge of parents about vaccinations studied by logistic regression (Table 1).

	B	e ^B (OR)	95% C.I. for e ^B		p-value
Age of mother	0,035	1,035	1,001	1,071	0,045
School attendance of father					0,043
Some classes of high school	-1,359	0,257	0,082	0,804	0,020
Nationality of mother (Greek)	1,479	4,390	2,793	6,901	0,000
Mother's profession					0,002
household	-0,980	0,375	0,157	0,899	0,028
unemployed	-1,583	0,205	0,064	0,659	0,008
Pediatrician	0,953	2,594	1,076	6,256	0,034
Media and internet	0,509	1,664	1,204	2,300	0,002

[table 1]

Conclusions: The knowledge and valid information are key factors that positively influence the views of parents about vaccination.

IMPACT OF VARICELLA VACCINATION FOR CONTROL CLUSTERS IN DAY-CARE CENTERS IN SÃO PAULO STATE, BRAZIL

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Background and aims: Varicella can cause complications and deaths even in healthy children, particularly in those attending day care centers (DCC). Since 2003, varicella vaccine (VV) is offered free of charge to control varicella clusters in DCC in São Paulo state. The aim of this study is to describe the trends of deaths caused by varicella after the implementation of this vaccination policy.

Methods: We describe the number of varicella deaths registered in SINAN in SP state, from 2002 until 2011, by age group, and year of notification, and analyzed difficulties to implement this policy and its impact in the target age group (1-5 years) for vaccination.

Results: In the last 10 years, 267 deaths caused by varicella were registered in SP state: 14.2% in children < 1 year; 56.4% in children aged 1-4 y; 15% in children 5-9 y and 14.2% in people > 10 years. The minimum number of varicella deaths in the target age group for vaccination was registered in 2006 (16), but there were 34 and 19 varicella deaths, and 4,303 and 2,351 clusters in DCC, respectively, in 2010 and 2011. The majority of deaths (60%) were confirmed in children aged 12 to 60 months.

Conclusions: The introduction of varicella vaccine to control cluster in DCC is difficult to implement and demonstrated lower impact in reducing the number of deaths, in comparison with the impact observed after VV introduction in routine schedule at 12 months. Children should receive VV before admission at DCC.

MENVEO® ELICITS PROTECTIVE IMMUNE RESPONSES DESPITE HIGH LEVELS OF ANTIBODIES AGAINST MENINGOCOCCAL SEROGROUP W-135 IN HEALTHY KOREAN ADOLESCENTS

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Background: As part of a registration trial the immunogenicity and reactogenicity of one dose of quadrivalent meningococcal CRM-conjugate vaccine (MenACWY-CRM) was studied in Korean 11-17 year-old adolescents.

Methods: In this phase 3, multi-center, observer-blind, placebo-controlled study, 269 healthy adolescents, randomized 2:1, received one dose of MenACWY-CRM (Menveo, Novartis Vaccines) or placebo. Immunogenicity was assessed before (Day 1) and one month after vaccination (Day 29) as serum bactericidal activity with human complement (hSBA). Subjects reported local and systemic reactions for 7 days, and any adverse events throughout the study period.

Results: On Day 1, 91% of adolescents were already seropositive (hSBA titres ≥ 4) against serogroup W-135; rates were 13%, 56% and 55% against serogroups A, C and Y, respectively. Levels did not change in the placebo group at Day 29, but MenACWY-CRM induced 21-, 41-, 2.3-, and 10-fold increases in geometric mean titres for serogroups A, C, W-135 and Y, respectively. Associated seroprotection rates (hSBA titres ≥ 8) were 83%, 100%, 98% and 95% in MenACWY-CRM vaccinees and 9%, 32%, 91% and 43% in placebo recipients. There were no serious adverse events, and MenACWY-CRM was generally well tolerated, although there were more reports of mild/moderate injection site reactions (pain, erythema, induration) than with placebo.

Conclusions: Despite unexpectedly high baseline antibody levels against serogroup W-135 in Korean adolescents, one dose of MenACWY-CRM elicited responses such that 83-100% had seroprotective titres against the four serogroups. MenACWY-CRM was well tolerated, only rates of transient mild/moderate local reactions being higher than placebo.

IMMUNOGENICITY AND SAFETY OF ENHANCED INACTIVATED POLIO VACCINE IN KOREAN CHILDREN

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Background and aims: The enhanced inactivated polio vaccine first introduced in 2002 and other inactivated polio vaccines licensed in Korea. Reliable data by a prospective study on the immunogenicity and safety of the inactivated vaccines is required.

Methods: Normal healthy infants aging 6 to 12 weeks-old were enrolled in this study. Initial immune status of the subjects were checked before vaccination and basic polio vaccination constituting of 3 inoculations were carried out in intervals of 2 months. Neutralizing antibody (NTAb) values were checked 4-6 weeks after vaccination. Immunogenicity was evaluated by seroconversion rates and geometric mean titers obtained by analyzing NTA values. Localized and systemic reactions were recorded on diary cards by parents until the 7th day after each inoculation.

Results: NTA tests were performed among 150 infants (IPVAX®: 40, IMOVAX®: 52, POLIORIX®: 58) who were vaccinated with polio vaccines. The seroconversion rates for the group vaccinated with IPVAX were 100% in all 1, 2, 3 types, with IMOVAX® were 98.1%, 96.2%, 96.2% and with POLIORIX® were 98.3%, 100%, 100%, respectively. For the IPVAX® group, localized adverse reactions were 40%, 45%, 40%, respectively. For the IMOVAX® group, localized adverse reactions were 46.2%, 32.7%, 42.3%, respectively. For the POLIORIX® group, localized adverse reactions were 43.1%, 31.0%, 29.3%, respectively. No cases of 2nd degree adverse reactions were reported.

Conclusion: The currently used inactivated polio vaccines are suitable for achieving appropriate seroconversion rates and mean titers of neutralizing antibodies. There were also no severe adverse reactions.

A TWO-DOSE REGIMEN OF THE 2009 MONOVALENT H1N1 INFLUENZA A VACCINE INCREASES SEROCONVERSION AMONG CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background and aims: Children with haematological malignancies are more susceptible to complications from influenza infection. Previous studies have documented an impaired immunological response to influenza vaccine among paediatric patients with malignancies. The aim of this study was to document the safety and immunogenicity of the 2009 pandemic H1N1 influenza monovalent vaccine in a population of children with a diagnosis of acute lymphoblastic leukemia (ALL) receiving chemotherapy.

Methods: The enrolled children were vaccinated with a two-dose regimen. Haemagglutination-inhibition (HAI) antibody titres were tested before each dose and three months after the second dose. The main study end point was the seroconversion rate, which was defined as the proportion of subjects with a four-fold increase in HAI titre (seroresponse) and/or a postvaccination HAI titer $\geq 1:40$ (seroprotective level).

Results: Fifty-seven children being treated for ALL had their immunological response measured after vaccination. Fifteen percent (7/47) of the children tested seroresponded after one dose of vaccine. Seven further patients seroresponded after the second dose bringing the overall documented seroconversion rate to 25% (14/57). Seroprotective levels were still present among all of those who seroconverted three months after the second dose of the vaccine. No significant adverse effects to the vaccine were documented among the cohort.

Conclusion: The monovalent vaccine for the 2009 pandemic H1N1 influenza A was immunogenic in only a proportion of children with ALL (25%). A two-dose regimen is justified to increase the seroconversion rate, and produces a sustained immunological response.

DPT VACCINATION AND PAIN MANAGEMENT BY BREAST FEEDING: A RANDOMIZED CONTROL TRIAL STUDY

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Diphtheria, Pertussis, and Tetanus (DPT) vaccination is one of usual course of childhood immunization, started from 2 months, and is more painful procedure in comparison of childhood and adults. Its management is one of important aspect in health and cure.

Objective: To examine the pain relieving effect of breast feeding during DPT vaacination in healthy neonates.

Materials and methods: 76 healthy 2- 4 months years old term infants, which had been brought to the health centers of West of Tehran for DPT vaccination by their mothers after their parents signed informed consent was involved in this randomized controlled trial study. (Year 2008-2009) By randomized collection one group were breast-fed, 2 minutes before, during, and 15 seconds after the DPT immunization injection, and second group according to routine of clinic lied on the examining table during Vaccination. Objective changes in appearance of Neonates were assessed by Modified Behavioral Pain Scale (MBPS) during 5 second before immunization till 15 second after it.

Results: There were no statistically significant difference between 2 groups according to age, gender and the time of feeding prior to vaccination. There were significant differences in Behavioral Pain Scores of two groups in all parts include: facial expression (4 items), cry (5 items), and movements (6 items). ($P < 0.0001$).

Conclusion: Regarding to significant difference in behavioral of Pain responds in two groups, it is suggested that, with simple and safe intervention of straight breast feeding, health care workers, and physicians reduce pain during immunization and muscular injections too.

PROTECTIVE STATUS OF END STAGE RENAL DISEASE CHILDREN AGAINST TETANUS AND DIPHTHERIA VACCINATION

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Objective: Vaccination against fatal viral and bacterial diseases is still the best protective way to lower morbidity and mortality rate in end stage renal disease (ESRD) patients. It has been reported that there is high incidence of low protective levels of IgG after vaccination in ESRD adult patients. The aim of this study was to evaluate the protective status of vaccination against diphtheria and tetanus in ESRD children in Iran after completing routine vaccination.

Methods and material: This cross sectional study was carried on 83 participants less than 18 years including 27 patients on hemodialysis- or peritoneal dialysis and 56 normal populations from February 2008 until December 2008 at St. Alzahra hospital, Isfahan, Iran.

To determine anti tetanus and anti-diphtheria antibodies level, Tetanus IgG ELISA kit (IBL International, Germany, RE56901) and Diphtheria IgG ELISA kit (IBL International, Germany, RE56191) were used. The participants must not received immunoglobulin, blood products or immunosuppressive medication in the current 6 months.

Results: The mean age of case and control group were 12.5 ± 2.7 years and 11.7 ± 3.3 years respectively, $p > 0.05$. According to IgG levels, 93% of hemodialysis patients and approximately 87% of peritoneal dialysis children needed booster doses of diphtheria vaccination. The results for IgG titer against tetanus revealed that in 91% of hemodialysis patients and 83% of peritoneal dialysis children booster doses of tetanus were recommended.

Conclusion: Booster doses of vaccines may be required in ESRD children. Measuring serum IgG levels against vaccines to define protective levels are recommended.

VACCINOLOGY CAPACITY BUILDING FOR DEVELOPING COUNTRIES THROUGH EDUCATIONAL PROGRAMS: A UNIQUE ACADEMIA AND INDUSTRY JOINT-VENTURE

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Background and aims: Successful immunisation programs are based on cost-effective vaccines, high coverage, sustainable financing, technological innovation, and well-trained local public health officials for implementation. To support immunisation capacity building in developing countries, in 2009 we introduced a postgraduate “Master Programme in Vaccinology”.

Methods: Medical graduates from developing countries, with 2 years postgraduate experience in clinical medicine, follow a one year learning curriculum by external and internal experts covering public health, infectious disease epidemiology, immunology and vaccinology, Health Systems and Health Economics, pharmacovigilance and benefit-risk assessment, regulatory affairs, and clinical vaccine development including statistics and GCP. After a 6 month internship in Development at NVGH or NVD, students have to write and defend a scientific thesis at the UNISI Medical School. Successful students receive a “Postgraduate diploma in Vaccinology” from UNISI.

Results and conclusions: 24 students from 18 developing Asian and African countries have been admitted so far in two “Masters”. Eleven of 12 participants who started in 2009 graduated successfully, with 4 achieving the highest academic rate (“cum laude”) from UNISI. Most students used their thesis as basis for their first scientific publication. Most of the graduates have already found positions in the vaccine sector in their home countries. The annual operational costs of the course and the financial support of the students totalled 1 million Euros, supported by a sustained grant from NVD and a training grant from the EU Commission. The third course of this unique private-public partnership to build vaccinology capacity will start in late 2012.

PERSISTENCE OF PERTUSSIS ANTIBODIES AMONG CHILDREN OF DIFFERENT AGE GROUPS**G. Kuli-Lito**¹, S. Lito², Z. Ylli³, G. Sulcebe³

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Background: Pertussis vaccine is a component of DTP which is a part of mandatory immunization schedule in our country. Basal immunization includes 3 doses at 2, 4, 6 months and a booster at 18 months. Nevertheless, the incidence of the infection is increasing in our country.

Methods: The study was performed in three different districts of Albania. Antibody titers to B. pertussis among children of two age groups were analyzed by the ELISA method. The children of two age groups 2.5-3 and 7-8 years were examined.

Results: We examined 140 children of first age group and 247 of second. A decline of geometric means is associated with growing age ($p < 0.05$). A protective titer was found in slightly more than 50% of the children, while 11% of them displayed titers of an unstable protection. The respective positive values for the studied areas were 56%, 67% and 48%. The percentage of negative titers of antibodies was 25.3 in younger age group compared with 42.6 found at the others.

Pertussis is an infection which has never been eliminated so far and since 2004 its incidence tends to increase worldwide. The problem of waning immunity with growing age remains regardless the type of vaccine, antigenic content or age.

Conclusions: Our data confirms once more the fact that the immunity wanes remarkably after a time lag of more than 5 year since the basal vaccination and enforces the necessity of application of "booster" doses at elder age.

IMPROVING COUNSELING SKILLS TO INCREASE THE COMPLIANCE TO ANTI-ROTAVIRUS VACCINATION

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Background and aims: In Italy Rotavirus vaccination (RVV) coverage is low and it's not usually recommended. We evaluated if a one-day residential course on counseling skills on RVV could affect the opinion about this vaccine of some Italian primary care paediatricians, physicians and nurses of vaccinations centres.

Method: Twelve residential courses were carried out in different Italian towns. Participants were interviewed about their opinion and troubles with RVV. A seminar on RVV was offered together with an interactive session on counseling abilities and patient and family centred care (PFCC). A post-course survey was carried out.

Results: 209 health professionals were enrolled with 125 primary care paediatricians (60%). 28%(65/209) of participants recommended RVV, 17%(35/209) recommended it seldom and 52%(109/209) didn't at all. The main trouble with RVV was the costs, communication with families about the vaccine and some perplexities on the cost/effectiveness ratio of RVV. In the post-course survey, on a rating scale from 1 to 5 where 5 was the maximum, 57% answered "≥4" and 22% answered "=3" to the question "did you increase your preference for RVV?"; 80% answered "≥4" when asked "do you think that counselling and communication skills are useful for RVV?"; 82% answered "≥4" when asked if they were interested to other courses of vaccination counseling.

Conclusions: A brief residential course about counseling and PFCC for RVV increased the awareness about the importance of RVV. Paediatricians and vaccinating physicians perceived counseling and PFCC as useful for RVV and their daily clinical practice.

RESULTS FROM 2 YEARS OF SURVEILLANCE OF HOSPITALISED CHILDREN WITH ACUTE GASTROENTERITIS FOLLOWING INTRODUCTION OF ROUTINE ROTAVIRUS VACCINATION IN FINLAND

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Background and aims: Finland introduced universal rotavirus (RV) vaccination into the national immunization programme (NIP) in September 2009, with exclusive use of human-bovine reassortant vaccine RotaTeq (SP-MSD) following a schedule 2, 3 and 5 months. The coverage quickly rose to 95-97 %, similar to other vaccines in NIP. This study was set to monitor the impact of RV vaccination on hospitalizations due to RV acute gastroenteritis (AGE).

Methods: Since December 2009 a prospective observational surveillance study is being conducted in the University Hospitals of Tampere and Oulu on all children \leq 15 years of age hospitalized because of AGE. RV is detected in stools by ELISA and confirmed and typed by RT-PCR.

Results: As of August 2011, 301 cases of AGE with adequate stool specimens were investigated and 100 tested positive for RV. Among these RV cases there were only two children who received RotaTeq vaccine in NIP; one was fully vaccinated and the other had received 2 doses. The vaccine effectiveness was not calculable among NIP eligible children due to very high vaccine coverage and effectiveness; which was estimated to be 95% in a larger population of children born after December 2007. The most prevalent RV types were G4P[8] in the 1st season and G1P[8] in the 2nd season.

Conclusion: Universal immunization programme with RotaTeq had a dramatic impact on hospitalizations and RV associated AGE in vaccine eligible children. The surveillance will be continued to study the duration of impact, annual variations and possible indirect benefits on unvaccinated children.

VARICELLA-RELATED HOSPITALIZATIONS DURING INFANCY PERIOD (< 1 YEAR OF AGE) IN TURKEY (VARICOMP STUDY 2008-2011): NEED STRATEGIES FOR PREVENTION

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Background: The incidence of many infectious diseases is higher in infancy period and are incompletely protected by existing vaccine strategies. Current studies showed that the mean duration of passive immunity is shorter and young infants are susceptible to varicella infection. The aim of this study was to evaluate varicella-related hospitalizations under 1 year of age.

Method: VARICOMP study is an ongoing trial (27 centers in 14 cities, representing ~50% of population), which aim to provide epidemiological and economic data on pediatric varicella hospitalization in Turkey.

Results: 372 children under 1 year of age (86.6% previously healthy, boys to girls ratio was 1.65) were hospitalized for varicella over the 3-year period (2008-2011). The estimated incidence of hospitalization was 20.5-28.7 per 100.000 children < 1 year of age. Among 372 hospitalized patients, 98 infants are < 3 months, 150 infants (40%) are aged between 9-12 months of age. 13.4% out of hospitalized infants have an underlying condition such as malignancies, prematurity, neurological disorders. 109 children (29.3%) were hospitalized because of primary varicella. The most common complications requiring hospitalization during infancy are respiratory (n=78, %21), followed by secondary bacterial infection 20% (including skin and skin structure infections), neurological complication 12.4% (including meningitis/encephalitis in 6.1%) and feeding difficulties 7.7%. Median length of hospital stay was 5 days (1-42 days). 61% of patients have been received acyclovir, median duration was 5 days. Four infants requires intensive care unit stay and mechanical ventilation. Median cost hospitalization per patient was 468 Euros.

Conclusion: This study confirms that varicella-related hospitalizations -especially respiratory- are common during infancy. There are different immunization strategies for early life infections including maternal immunization, neonatal immunization, to maximize herd immunity by reducing the incidence of disease / transmission of the pathogen and to use existing vaccines more effectively. First and important prevention strategy for children < 1 year of age is the varicella vaccination of all children and high-risk adult to maximize herd immunity. Second strategy could be earlier administration of varicella vaccines, possibly at the 9th month of age.

EFFECT OF ACTIVE INTERVENTION TO INCREASE INFLUENZA IMMUNIZATION RATES IN A PEDIATRIC PRIMARY CARE CLINIC

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Background and aims: Influenza vaccines have been proven to be effective and safe, yet their delivery remains problematic. In Israel, immunization of high risk patients is recommended by the Health Ministry with the Health Funds being responsible for vaccination delivery. Current national pediatric vaccination rates are very low (2-9%). The study aim was to determine if active intervention has increased rates in a pediatric primary care clinic (PPCC).

Methods:

Setting: PPCC which serves approximately 10,000 children.

Intervention:

- 1) Immunization recommendation to all children < 5 years of age.
- 2) Vaccination by both physicians and nurses. 3) Phone contact of high-risk patients.

Data collection: Retrieval from Health Fund computerized database.

Analysis: Comparison of annual vaccination rates between study clinic and other clinics from 2004-2011 with the use of the z-test.

Results: The immunization rates in the study PPCC increased from 3.6 to 21% from 2004-2011 ($p < .001$). Vaccination rate was higher in PPCC every study year ($p < .001$).

Conclusions: Promotion efforts seem to increase vaccination rates. However, even 21% is not enough for production of a herd effect. We believe that vaccination in PPCCs is insufficient and should be supplemented by mass immunization in day care facilities and schools.

PERSISTENCE OF BACTERICIDAL ANTIBODIES FOLLOWING EARLY INFANT IMMUNISATION WITH SEROGROUP B MENINGOCOCCAL VACCINES AND IMMUNOGENICITY OF PRE-SCHOOL BOOSTER DOSES

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Background and aims: At least 93% of infants given 4 doses of an investigational serogroup B meningococcal vaccine containing recombinant-proteins and an outer-membrane vesicle (4CMenB) had serum bactericidal antibody (SBA) titres $\geq 1:4$ against 3 reference strains (44/76-SL, NZ98/254, 5/99). We evaluated persistence of these antibodies.

Methods: In this extension study participants given 4CMenB or recombinant-proteins alone (rMenB) at 2,4,6,12 months received a fifth dose of the respective vaccines at 40 months (groups 4D-4CMenB and 4D-rMenB). Infants given a single dose at 12 months were immunised at 40 & 42 months (groups 1D-4CMenB & 1D-rMenB). MenB vaccine naïve participants received 4CMenB at 40 & 42 months (control group).

Results: At 40 months proportions of 4D-4CMenB participants with SBA titres $\geq 1:4$ were 65% (95% CI 38-86%) for strain 44/76, 76% (50-93%) for 5/99, 41% (18-67%) for NZ98/254 & 67% (38-88%) for M10713 (N=15-17). For 4D-rMenB recipients these proportions were 45-68% for all strains except NZ98/254 (3%, 95% CI 0.09-18%) (N=28-29). Pre-booster 0-38% 1D-4CMenB recipients had SBA titres $\geq 1:4$ for all strains (N=8), compared with 7-57% in 1D-rMenB recipients (N=13-14). For controls (N=40) proportions were 0-3% for strains 5/99 and NZ98/254, 63% (46-77%) for strain 44/76-SL and 68% (51-81%) for strain M10713. A booster dose in the 4D-4CMenB group increased proportions to 88-100% for all strains.

Conclusion: SBA titres wane following infant immunization with rMenB or 4CMenB but there is an anamnestic response to a booster dose.

NON-SPECIFIC EFFECT OF BACILLE CALMETTE-GUÉRIN VACCINE ON THE ANTIBODY RESPONSE TO ROUTINE IMMUNISATIONS IN INFANCY

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Background: Bacille Calmette-Guérin (BCG) is one of the most commonly administered vaccines worldwide. In addition to protection against tuberculosis (TB), BCG immunisation has non-specific effects and is associated with a significant reduction in child mortality attributable to causes other than TB. BCG immunisation has also been shown to increase antibody levels against poliomyelitis and hepatitis B after routine immunisation. This study compared the antibody response to routine immunisations in BCG-immunised and non BCG-immunised infants.

Methods: Healthy BCG-immunised and BCG-non-immunised infants were recruited in Melbourne. Immunisations were given at 2, 4 and 6 months of age according to the Australian National Immunisation Program. Four weeks after the 6-month immunisations, antibodies against tetanus toxoid (anti-TT) and hepatitis B surface antigen (anti-HBs) were measured using commercially-available kits. Antibodies against pneumococcal capsular polysaccharide antigen (anti-PnPs) for serotypes 4, 6B, 9V, 11A, 14, 18C, 19F, 23F and *Haemophilus influenzae* type b PRP-antigen (anti-Hib-PRP) were measured using an in-house ELISA.

Results: 106 infants were recruited (56 BCG-immunised and 50 BCG-non-immunised). The geometric mean concentration (GMC) of anti-PnPs IgG for serotypes 9V and 18C were higher in the BCG-immunised than the BCG-non-immunised group ($p=0.01$ and $p=0.04$). The GMC of anti-HBs IgG was lower in the BCG-immunised group ($p=0.02$). The GMCs of anti-Hib-PRP and anti-TT IgG were higher in the BCG-immunised group but were not statistically significant.

Conclusions: BCG immunisation at birth influenced the antibody response to routine immunisations. These findings support the contention that BCG has non-specific effects on the immune response in early infancy.

AUDIT OF THE COMPLETENESS OF ROUTINE IMMUNISATIONS OF CHILDREN IN A&E OR ADMITTED TO PAEDIATRIC WARDS IN A LONDON HOSPITAL

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Background: Children in the UK are routinely vaccinated against a number of infectious diseases as a public health measure to prevent spread and reduce associated morbidity and mortality. High immunisation rates ensure same protection to non-immunised population through herd immunity. There are concerns that immunisation rates are not as high as expected to achieve this.

Our audit aimed to determine the upto date status of routine immunisations of children presenting to A&E and those admitted to the paediatric wards at St George's Hospital.

Method: Between 12th to 23rd September and 5th to 16th December 2011, parents of children attending the A&E department or admitted to the paediatric wards were approached. With their consent the child's immunisation record was extracted from the parents held child's health records. If this was not available their consent was obtained to get this information from their GP. An audit proforma was then completed. Parents were also asked about their views on opportunistic vaccination.

Results: The parents of 216 children were approached, 201 (93%) agreed to participate and complete immunisation record was available for 141 (70%) children. The mean age (SD) was 4.3 years (4.4) range 2 months- 17 years and 72 (51%) were male. 100 children (71%) were up to date with their immunisation for age.

Conclusion: Most children seen in our hospital during the audit period are upto date with their immunisation. There remain a proportion of children not fully immunised. There might be a case to improve vaccine coverage through opportunistic immunisation.

PROTECTIVE EFFICACY AND IMMUNOGENICITY OF HELPER-DEPENDENT ADENOVIRUS VECTOR ENCODING CODON-OPTIMIZED F PROTEIN OF HUMAN RESPIRATORY SYNCYTIAL VIRUS

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Human respiratory syncytial virus (RSV) is a serious pediatric pathogen of the lower respiratory tract worldwide. There is currently no clinically approved vaccine against RSV infection. Helper-dependent Ad (HDAd) vectors have all Ad coding regions deleted, and are able to stimulate immune responses against transgene better than the replication deficient first generation adenovirus (FGAd) vectors and are one of the important solutions to avoid disadvantage related with FGAd vectors. Therefore, HDAd vectors may represent potential and safe vaccine vectors. Currently, no virus challenge has been investigated following mucosal vaccination with HDAd vector vaccines. To evaluate such immunization efficacy of HDAd as an RSV vaccine vector administered intranasally, we constructed HDAd vector encoding codon-optimized fusion glycoprotein (Fsyn) of RSV, designated HDAd-Fsyn, and reported humoral and cellular immune responses as well as protective immunity against RSV infection induced by intranasal (i.n.) vaccination of HDAd-Fsyn in BALB/c mice. The RSV specific humoral and cellular immune responses were generated in BALB/c mice, and the serum IgG with neutralizing activity was significantly elevated after homologous boost with HDAd-Fsyn intranasally. The humoral and cellular immunities could be observed even 10 weeks after single immunization. Upon challenge, i.n. immunization with HDAd-Fsyn displayed an effective protection against RSV infection. These results indicate that HDAd-Fsyn has the ability to induce powerful and long-lasting systemic immunity against subsequent i.n. RSV challenge in a mouse model of infection and is a promising candidate vaccine against RSV infection.

REDUCTION IN THE INCIDENCE RATES OF ROTAVIRUS-RELATED HOSPITALIZATION IN CHILDREN UNDER 5 YEARS OF AGE AFTER ROTAVIRUS VACCINE

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Background and aims: Rotavirus is the leading cause of rotavirus-related hospitalization in children. To determine the effectiveness of rotavirus vaccines and if it could reduce rotavirus-related hospitalization in children under 5 years of age. The RotaTeq vaccine was launched in 2007 and the Rotarix vaccine was launched in 2008 in Korea.

Methods: We evaluated the hospitalization rate of rotavirus gastroenteritis before and after. Total 2,557 gastroenteritis children were hospitalized in Hallym University Sacred Heart Hospital, in Korea from 2006 to 2011. Also the seasonal distribution was evaluated.

Results: Total 2,557 gastroenteritis children were hospitalized during the 6 years.

The numbers of gastroenteritis related hospitalization were 516 in 2006, 537 in 2007, 430 in 2008, 407 in 2009, 337 in 2010 and 330 in 2011. Among them, the numbers of rotavirus related hospitalization were 139 in 2006, 148 in 2007, 128 in 2008, 151 in 2009, 73 in 2010 and 70 in 2011. The rotavirus related hospitalization rate was 33% from 2006 to 2009 (before the vaccine effect), but the rate was reduced to 24% from 2010 to 2011 (after rotavaccine effect) among the gastroenteritis related hospitalization children.

Conclusions: The effective rotavirus vaccines could substantially reduce the rotavirus-related hospitalization in children under 5 years of age. The seasonal peak rotavirus gastroenteritis developed from January to March. April and May also have a high incidence rate in Korea.

EARLY IMPACT OF MENINGOCOCCAL C CONJUGATE VACCINATION PROGRAM ON DISEASE TRENDS IN SAO PAULO, BRAZIL

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Background and aims: Meningococcal disease (MD) is endemic in Brazil, with 80% of the identified cases associated to serogroup C and the highest age-specific incidence observed in infants, motivating the introduction of the meningococcal C conjugate vaccine (MCC) into the Brazilian Immunization Program, in late 2010, in a 2 + 1 schedule for all children younger than 2 years. The aim of this study was to evaluate the early impact of immunization on the incidence of MD in the State of São Paulo.

Methods: We analyzed population-based data from the Notifiable Diseases Surveillance System to evaluate trends in the burden of MD before and after the introduction of a publicly funded vaccination program. Changes in the incidence of MD in 2011 were assessed against baseline values from 2005-2010.

Results: We identified 2,054 cases of MD in children aged < 2 years during the study period. The rates of MD in children aged < 2 years declined from an average of 25.4/100,000 persons in the pre-vaccination baseline period (2005-2010) to 18.0/100,000 in 2011. This represents a 29.1% ($p < 0.01$) reduction in the incidence rate after the introduction of the vaccine. In the other age groups no reductions were observed.

Conclusions: The introduction of MCC into the routine vaccination program provided a rapid and significant reduction in incidence rates of MD in children aged < 2 years, the age group targeted for vaccination. In countries like Brazil, where the immunization program did not incorporate catch-up campaigns, herd immunity effects are not likely to be observed.

EFFICIENCY OF MENINGOCOCCAL SEROGROUP C CONJUGATE VACCINES: SYSTEMATIC REVIEW**J. Ruiz-Aragón**¹, S. Marquez-Pelaez²

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Background and aims: Meningococcal serogroup C conjugate (MCC) vaccines have been introduced in routine infant immunization schedule in some countries, but many other countries are considering its introduction. The efficacy and safety of these vaccines are well documented, but nowadays, because the budget restrictions, is very important to assess the efficiency of the interventions.

Methods: A systematic review of literature (1995-2011) of economic evaluation studies was carried out. The main databases used were Medline, Embase, Cochrane Library, CEA Registry, and CRD. A combination of MESH terms as "meningococcal disease", "meningococcal vaccine", "conjugate vaccine", "costs and cost analysis", and "quality-adjusted life year" was used. Inclusion criteria were studies with MCC vaccines in children, type of study: cost-effectiveness analysis (CEA), cost-utility analysis (CUA), cost-benefit analysis (CBA). Outcomes measured were costs, costs per life year gained (LYG), and cost per quality adjusted life year (QALY). Quality of studies has been measured according to the checklist of economic studies proposed by CASP.

Results: 479 references were identified, after selection process, 4 CUAs and 3 CEAs were included in the review. The incremental cost-effectiveness ratios were under the usual threshold of 30,000-50,000€ per QALY.

Conclusions: According to the included studies, vaccination with MMC vaccines is a cost-effectiveness intervention if we consider usual thresholds of willingness to pay.

HEALTH BENEFIT FOR CHILD AND PROMOTION OF COMMON GOOD ARE THE TWO MOST IMPORTANT REASONS FOR PARTICIPATION IN VACCINE TRIAL

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Background and aims: Finnish Invasive Pneumococcal disease (FinIP) trial is a nation-wide cluster-randomized, double-blind vaccine trial designed to demonstrate PHiD-CV (GlaxoSmithKline) effectiveness against *S.pneumoniae* and *H.influenzae* diseases in vaccinated children and indirect effects in unvaccinated populations. Together with parallel carriage/AOM trial, over 47000 children were enrolled, which was 52% of the target. We conducted a questionnaire study to assess perceptions and attitudes of parents of children invited to the trial.

Methods: A questionnaire was designed to evaluate parents' attitudes to vaccine trials in general and especially to FinIP. It was mailed to parents of 2969 children invited to participate in the trial (half participants, half non-participants) after the enrolment period.

Results: Altogether 1323 (45%) parents answered the questionnaire: 897 (68%) were participating FinIP trial, 298 (22%) had refused to participate, and 128 (10%) had exclusion criteria or other reasons for not participating.

The most important reasons for participation were,

- 1) the potential benefit of immunization against pneumococcal diseases 75% (675/897) and
- 2) the promotion of common good 11% (98/897).

The main reasons for refusal were suspicions of vaccine safety (36%, 106/298) and double-blind trial setting (12%, 35/298).

Conclusions: The expected health benefit for child was the most important reason for participation. However, also promotion of common good was seen among the most important reasons. Vaccine safety concern was the main reason for refusal; this may have been inflated due to special media attention of the relationship of pandemic flu vaccine and narcolepsy at the time of the questionnaire study.

COMPLIANCE WITH NATIONAL CHILDHOOD VACCINATION RECOMMENDATIONS OF CHILDREN BORN 2006/07/08 IN GERMANY

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Background: In Germany, primary childhood immunization should be complete at 24 months of age. Because continuous, nationwide surveillance of vaccination coverage (VC) of this age-group is nonexistent, health services data for birth cohorts 2006/07/08 were analyzed instead.

Methods: Anonymized billing data from Associations of Statutory Health Insurance Physicians (ASHIP) were analyzed, covering 85% of the population in 12 out of 16 federal states. Patients can be followed over time within their associated ASHIP and were included if physician contacts both at 0-4 months and at 24-26 months within the same ASHIP were documented. Vaccination histories were construed for these individuals. Follow-up over longer time periods allowed to validate the method with available VC data from kindergarten and school children.

Results: Nationwide VC of 4 doses of diphtheria, tetanus, pertussis, polio and Hib vaccines was 80% (no difference between birth cohorts). VC for 4 doses of HepB and pneumococcal conjugate vaccine (PCV) increased from 71% to 73% and from 42% to 70%, respectively. VC of MMR was high for dose 1 (94%) compared to dose 2 (66%) (no difference between cohorts). VC increased across 2006/07/08-cohorts for 1-dose MenC (75/77/79%) and first (77/81/85%) and second varicella dose (39/53/60%). Validation showed good agreement with all other data sources.

Conclusions: VC of established vaccines is at moderate levels at 24 months, first dose MMR even high. VC of recently introduced vaccines PCV, MenC, and varicella is increasing. ASHIP data analysis can serve as continuous, nationwide surveillance system to monitor compliance with childhood immunization recommendations.

THE SOCIAL PERCEPTION OF VACCINATION

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For the first time in Poland on such a great scale was made a study of social perception of vaccination. The concept of the study was prepared by pediatrics (members of the board of Polish Vaccination Society) working on Medical University in Poznan and sociologist, specialized on sociology of health from Warsaw University. The study was conducted in randomly selected children's clinics. The all study involved almost 500 respondents and questionnaire had 32 almost 60 closed questions.

The main aim of the study was to determine the attitudes of polish parents on vaccines. Researches wanted to know, what Poles think about vaccines, what are their opinions, attitudes and which kind of vaccine's myths are still alive in people's mind. Do they trust doctors? What is their self-knowledge about vaccines? Where their find information about vaccines? Do they believe vaccines help?

Two-thirds respondents declare that they are in favor in vaccination. Most respondents assess their knowledge about vaccination well, but in the same time they agreed about popular vaccine's myths. Every third respondent believes that the doctor has the same responsibility for the vaccine and its effects as parents. Every third person has met heard the doctor advised immunize a child. Despite the trust to pediatricians (83%) most parents (74%) looking for information about vaccines in the internet and 40% of them always verified doctor's vaccination recommendations in the internet.

HPV VACCINE ACCEPTANCE IN ADOLESCENTS IN VALENCIA, SPAIN

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Background and objectives: HPV vaccination in 14 year old girls is recommended in Valencia since 2007. Vaccine coverage decreased from 85% to 66% due to safety concerns and contradictory information in the media.

The objective was to study vaccine acceptance among adolescents and to assess risk factors for non-vaccination.

Methods: 1279 questionnaires to both mothers and girls (that should have been vaccinated) were distributed in 35 schools selected at random, and representative of the Valencia population. Questionnaires collected socio-sanitary data, knowledge about HPV diseases and vaccines, risk perception and information received by their doctors and/or nurses in relation to the vaccine. Vaccination status was obtained from questionnaires and the Valencian vaccine registry (RVN)

Results: 833 questionnaires from mothers, and 833 from girls, were collected (65%). 74,5% of the girls had been vaccinated.

After adjusting for confounding factors, variables associated with not being vaccinated were:

Mother not being Spanish in origin (aOR: 0.49; 95%CI: 0.24-0.98). Parents not living together (aOR: 0.33; 95%CI: 0.13-0.81), and not feeling at risk of having the disease (aOR: 0.01; 95% CI: 0.002-0.05),

And with being vaccinated: their primary care paediatrician or nurse strongly recommended vaccination (aOR: 6.57; 95%CI: 3.19-13.56)

Conclusions: The major driver for vaccination was the positive recommendation given by their paediatricians or nurses, and also the girl's feeling that they were at risk of contracting the disease. Therefore, in order to increase the vaccine coverage, health personnel should advocate for vaccination and focus on the young girls' health education.

ANTIBODY PERSISTENCE UP TO 36 MONTHS FOLLOWING VACCINATION WITH MENACWY-TT IN TODDLERS AGED 1-< 2 YEARS

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Background and aims: Rates of meningococcal disease burden are highest in children < 2 years. Long-term protection after vaccination against meningococcal disease relies on circulating antibodies; we report the persistence of antibodies 36 months after vaccination of toddlers with an investigational meningococcal serogroups A, C, W-135, Y tetanus-toxoid conjugate vaccine (MenACWY-TT) or MenC-CRM₁₉₇.

Methods: This phase IIb, open, controlled persistence study included toddlers aged 1-< 2 years (Year 3 cohort, N=223) who received one dose of MenACWY-TT or MenC-CRM₁₉₇ (NCT00427908). Persistence of functional antibodies was measured using rabbit and human complement serum bactericidal activity assays (rSBA; hSBA) with cut-offs of 1:8 and 1:4, respectively, at 1, 12, 24 and 36 months post-vaccination. Vaccine-related serious adverse events (SAEs) were recorded retrospectively up to 36 months post-vaccination.

Results: At 36 months post-vaccination, ≥90.8% subjects receiving MenACWY-TT retained rSBA titres ≥1:8 against each serogroup and ≥73.6% retained hSBA titres ≥1:4 for serogroups C, W-135, and Y (hSBA-MenA was lower, consistent with other reports [Gill *et al. Hum Vaccin.* 2010;6:881-7]). Exploratory analyses revealed no significant differences between vaccine groups for subjects with rSBA-MenC titres ≥1:8 and hSBA-MenC titres ≥1:4, or MenC GMTs. No vaccine-related SAEs were reported.

Percentage of subjects with rSBA titres ≥1:8, hSBA titres ≥1:4 and GMTs (ATP cohort for persistence Year 3)

Antibody	Group	Time point	rSBA			hSBA		
			N	% ≥1:8 [95% CI]	GMT [95% CI]	N	% ≥1:4 [95% CI]	GMT [95% CI]
MenA	MenACWY-TT	M1	177	100 [97.9-100]	3787.4 [3351.2-4277.8]	172	92.4 [87.4-95.9]	56.9 [46.4-69.9]
		M24	165	99.4 [96.7-100]	575.2 [494.0-669.9]	157	39.5 [31.8-47.6]	4.9 [4.0-6.0]
		M36	170	98.8 [95.8-99.9]	518.6 [447.6-600.8]	170	21.8 [15.8-28.7]	3.3 [2.8-3.8]
	MenC-CRM ₁₉₇	M1	32	31.3 [16.1-50.0]	14.4 [7.0-29.4]	36	8.3 [1.8-22.5]	2.4 [1.9-3.0]
		M24	30	70.0 [50.6-85.3]	56.5 [28.5-112.2]	35	34.3 [4.8-30.3]	2.3 [2.0-2.7]
		M36	32	84.4 [67.2-94.7]	117.1 [65.0-211.2]	36	5.6 [0.7-18.7]	2.2 [1.9-2.6]
MenC	MenACWY-TT	M1	175	100 [97.9-100]	887.0 [770.4-1021.2]	176	98.9 [96.0-99.9]	182.7 [154.0-215.8]
		M24	171	100 [97.9-100]	141.2 [120.3-165.6]	165	95.8 [91.5-98.3]	62.9 [50.9-77.8]
		M36	174	90.8 [85.5-94.7]	125.1 [96.7-162.0]	166	88.6 [82.7-93.0]	65.1 [49.6-85.5]
	MenC-CRM ₁₉₇	M1	36	100 [90.3-100]	727.6 [478.7-1105.8]	36	86.1 [70.5-95.3]	44.1 [25.2-77.3]
		M24	36	100 [90.3-100]	158.6 [103.8-242.2]	36	65.7 [47.8-80.9]	18.8 [9.2-38.4]
		M36	37	97.3 [85.8-99.9]	185.7 [118.3-291.5]	33	75.8 [57.7-88.9]	32.5 [16.0-65.9]
MenW-135	MenACWY-TT	M1	177	100 [97.9-100]	5563.5 [4976.9-6219.4]	138	81.2 [73.6-87.3]	39.1 [28.8-53.1]
		M24	173	99.4 [96.8-100]	439.3 [379.0-509.4]	153	96.1 [91.7-98.5]	112.8 [90.6-140.4]
		M36	174	98.9 [95.9-99.9]	439.8 [370.5-522.0]	164	79.9 [72.9-85.7]	40.8 [31.1-53.6]
	MenC-CRM ₁₉₇	M1	36	38.9 [23.1-56.5]	17.5 [9.2-33.6]	33	3.0 [0.1-15.8]	2.1 [1.9-2.3]
		M24	30	50.0 [31.3-68.7]	22.9 [11.6-45.1]	35	11.4 [3.2-28.7]	3.1 [2.0-4.8]
		M36	33	72.7 [54.5-86.7]	64.5 [33.5-124.3]	35	8.0 [1.8-23.1]	3.0 [1.9-4.7]
MenY	MenACWY-TT	M1	177	100 [97.9-100]	2875.6 [2540.0-3255.6]	161	68.3 [60.5-75.4]	24.8 [18.3-33.5]
		M24	171	98.2 [95.0-99.6]	512.8 [439.7-645.6]	149	89.3 [83.3-93.7]	70.4 [51.9-91.8]
		M36	177	98.3 [95.1-99.6]	583.2 [479.0-709.9]	159	73.6 [66.0-80.3]	37.3 [27.2-51.2]
	MenC-CRM ₁₉₇	M1	36	80.6 [64.0-91.8]	101.5 [54.3-189.7]	34	8.8 [1.9-23.7]	2.8 [1.8-4.4]
		M24	35	77.1 [58.9-89.6]	100.6 [50.6-200.0]	31	38.7 [23.8-57.8]	6.7 [3.7-12.3]
		M36	36	91.7 [77.5-98.2]	176.0 [97.6-317.3]	33	27.3 [13.3-45.5]	6.0 [3.0-11.9]

GMT, geometric mean titre; ATP, according-to-protocol; CI, confidence interval; N, number of subjects with available results; M1, post-vaccination at Month 1; M24, post-vaccination at Month 24; M36, post-vaccination at Month 36

[Table]

Conclusions: Overall ≥90.8% of subjects receiving MenACWY-TT retained rSBA titres ≥1:8 for each serogroup, indicating that seroprotection extends up to 3 years following primary vaccination in toddlers.

HIGH INCIDENCE OF MEASLES IN THE REGION OF MADRID (SPAIN) FROM 2011 DESPITE HIGH IMMUNISATION COVERAGE

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A national measles elimination plan was launched in Spain in 2001 with the aim of interrupting endemic measles transmission. Strategies of the plan included strengthening surveillance and increasing vaccination coverage with two doses of MMR vaccine to a minimum of 95%, as recommended by the World Health Organization. We describe the increase in measles incidence observed from February 2011 in the child population of the region of Madrid and the control measures adopted.

The study is based on information including demographic, clinical, epidemiological and microbiological data, collected by the Epidemiological Surveillance Network of the Region of Madrid from 7 February 2011 to date.

From 7 February 2011, 620 measles cases were notified in the region of Madrid. In 2010 only 28 cases were reported. Of the 620 cases 323 were children younger than fifteen years (52.0%). Among them, only 13 were vaccinated (4.0%). 165 of child cases were of gypsy origin (51.0%). Among gypsy cases, 129 were older than 15 months (78.1%), whereas among non-gypsy cases 120 were 15 months or younger (75.9%). 137 gypsy cases (83.0%) and 62 non-gypsy cases (39.5%) were targeted to receive MMR vaccine. Four genotypes were identified, D4 being the most frequent. In June 2011 the first dose of MMR was brought forward by 12 months of age. Additionally, specific measures to improve vaccination coverage in gypsy population were taken.

This report underlines once more the need for additional measures targeting susceptible populations to achieve high vaccination coverage with two doses of MMR vaccine

ANTIBODY PERSISTENCE UP TO 36 MONTHS FOLLOWING VACCINATION WITH MENACWY-TT IN CHILDREN AGED 2-10 YEARS

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Background and aims: Invasive meningococcal disease is a serious infection that is vaccine-preventable. Long-term protection relies on the persistence of antibodies. Here we report long-term antibody persistence up to 36 months following one dose of an investigational MenACWY-TT conjugate vaccine as compared with a licensed polysaccharide vaccine (MenACWY-PS) in children aged 2-10 years.

Methods: This phase IIb, open, controlled persistence study (NCT00427908) included subjects who received one dose of MenACWY-TT or MenACWY-PS vaccine as children aged 2-10 years (N=239 at month 36). Functional antibodies, detected by serum bactericidal activity assay (rabbit complement [rSBA] cut-off 1:8), were measured at 1, 12, 24 and 36 months post-vaccination. Vaccine-related serious adverse events (SAEs) were recorded retrospectively up to 36 months post-vaccination.

Results: Three years post-vaccination, >98% of MenACWY-TT recipients retained rSBA antibody titres $\geq 1:8$. Exploratory analyses showed that a statistically significantly higher proportion of subjects had rSBA antibody titres $\geq 1:8$ for all four serogroups in the MenACWY-TT group compared with the MenACWY-PS group. GMT titres against all four serogroups remained higher than pre-vaccination levels. No vaccine-related SAEs were reported.

Percentage of subjects with rSBA titres equal to or above the cut-off values of 1:8 and GMTs (ATP cohort for persistence Year 3)

Antibody	Group	Time point	N	% $\geq 1:8$ [95% CI]	GMT [95% CI]
MenA	MenACWY-TT	M1	196	100 [98.1-100]	7513.7 [6740.4-8375.7]
		M24	193	100 [98.1-100]	1352.7 [1191.4-1535.7]
		M36	192	100 [98.1-100]	1184.2 [1054.2-1330.0]
	MenACWY-PS	M1	37	100 [90.5-100]	2244.3 [1737.7-2898.6]
		M24	35	94.3 [80.8-99.3]	240.1 [149.5-385.7]
		M36	34	91.2 [76.3-98.1]	218.8 [128.9-371.5]
MenC	MenACWY-TT	M1	196	100 [98.1-100]	2524.9 [2162.1-2948.5]
		M24	195	100 [98.1-100]	273.1 [229.3-325.1]
		M36	192	98.4 [95.5-99.7]	244.3 [200.8-297.3]
	MenACWY-PS	M1	37	100 [90.5-100]	2433.7 [939.0-2188.0]
		M24	37	100 [90.5-100]	237.9 [144.0-393.0]
		M36	37	83.8 [68.0-93.8]	163.5 [83.8-319.2]
MenW-135	MenACWY-TT	M1	196	100 [98.1-100]	12158.8 [10949.9-13501.1]
		M24	195	99.5 [97.2-100]	1324.4 [1154.4-1519.4]
		M36	196	100 [98.1-100]	1737.1 [1503.8-2006.7]
	MenACWY-PS	M1	37	100 [90.5-100]	2602.6 [1795.6-3772.4]
		M24	34	88.2 [72.5-96.7]	182.8 [104.0-321.2]
		M36	35	82.9 [66.4-93.4]	112.9 [59.9-212.6]
MenY	MenACWY-TT	M1	196	100 [98.1-100]	6655.7 [6009.1-7372.0]
		M24	195	100 [98.1-100]	1556.4 [1355.9-1786.6]
		M36	195	100 [98.1-100]	1551.6 [1381.2-1743.1]
	MenACWY-PS	M1	37	100 [90.5-100]	1823.8 [1235.6-2662.5]
		M24	37	81.1 [64.8-92.0]	116.2 [59.3-227.7]
		M36	37	81.1 [64.8-92.0]	103.8 [54.3-198.3]

GMT, geometric mean titre; ATP, according to protocol; CI, confidence interval;

N, number of subjects with available results; M1, post-vaccination at Month 1;

M24, post-vaccination at Month 24; M36, post-vaccination at Month 36

[Table]

Conclusions: Overall >98% of subjects receiving MenACWY-TT retained rSBA titres $\geq 1:8$ for all serogroups, indicating that seroprotection extends up to 3 years following primary vaccination in children.

ROTAVIRUS VACCINE EFFECTIVENESS TO PREVENT ROTAVIRUS GASTROENTERITIS HOSPITALIZATION IN CHILDREN LESS THAN THREE YEARS OLD. RETROSPECTIVE COHORT STUDY. VALENCIA, SPAIN

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Background and aims: Rotavirus vaccines are not included in the Valencia Vaccination Schedule, but are bought by parents and recommended by pediatricians. It is estimated that 30% of children received at least one vaccine dose between 2007 and 2010.

Our objective was to assess rotavirus vaccine effectiveness to prevent hospitalizations for rotavirus acute gastroenteritis (RVAG) in children less than three years old.

Methods: Retrospective cohort study on children 7 months-3 years of age living in Valencia, born between January 2007 and August 2010. The information was obtained from the databases of Valencia's Health System, 95% population covered .

Cases of acute gastroenteritis (AG) hospitalizations were ascertained by the discharge codes ICD-9-CM 001-009 or 558.9; and RVAG those with the 008.61 discharge code.

Children were considered immunized two weeks after receiving all recommended doses.

Vaccine effectiveness was computed as $(1-RR)*100$.

Results: The total cohort consisted of 206,439 children with 42,424 (20.6%) completely immunized (216,785 non-immunized person-years and 66,307 immunized children-years).

We ascertained 1,163 AG and 712 RVAG hospitalizations: 210 AG and 20 RVAG in immunized children, 884 AG and 681 RVAG in non-immunized, 7 RVAG cases in partially vaccinated children and 3 cases in children with unknown vaccine status.

Vaccine effectiveness to prevent RVAG was 90.4% (95%CI: 85.-93.8) and for AG 22.3% (95%CI: 9.7-33.2).

Conclusions: Rotavirus vaccine is very effective even in non universal vaccination programs. Protection against non RVAG suggests that a number of undiagnosed gastroenteritis could be due to rotavirus.

VACCINATION STATUS OF SCHOOL AGED CHILDREN IN A GREEK ISLAND**S. Gkouliavoudi**¹, C. Maragou², D. Cassimos³*¹PPI Alonnisou, Alonnisos, ²General Hospital of Corfu, Corfu, ³Dimokritio Panepistimio of Thrace, Alexandroupolis, Greece*

Background and aims: Alonnisos is an isolated Greek island where there was no paediatrician till recently. There are 251 children aged 4 to 18 years old living in the island who attend school. The aim of this study was to assess the vaccination status of children who attend school at all grades.

Methods: The “health books” of all children attending school in Alonnisos were collected and their vaccinations were evaluated by the Pediatric Physician of the island, from September till December 2010.

Results: The sample consisted from 200 children, aged 4-10 years of age who lived permanently in the island and attended school. Out of 200 children, that their “health books” have been evaluated, only 41 were fully immunized. In accordance to the Greek vaccination schedule there were missing 671 doses, more specifically 72 DTP (10,73%), 72 IPV (10,73%), 1 Haemophilus influenza (0,15%), 39 HBV (5,8%), 2 PCV (0,3%), 28 MCV (4,17%), 49 MMR (7,3%), 169 varicella (25,18%), 113 HAV (16,84%), 6 BCG (0,89%) and 120 HPV (17,88%) vaccines. Most doses (60,35%) were missing among the high-school/lyceum students, that fully immunized were only 4/77 (5,19%). The most compliant with the National Vaccination Schedule, were primary school students 30/81 (37%) followed by nursery attending children 7/42(16,6%).

Conclusions: School aged children are susceptible to vaccine preventable diseases. In order to apply the vaccination program throughout childhood, it is fundamental that the schedule is functioning “automatically” and the medical personnel are appropriately trained.

FUNCTIONAL SNPS WITHIN TLR3 INFLUENCE IMMUNE RESPONSES TO SEROGROUP C MENINGOCOCCAL CONJUGATE VACCINE

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Background: Serogroup C meningococcal (MenC) conjugate vaccination has successfully controlled the burden of disease associated with this serogroup in many countries. However, considerable variation in the immune response to MenC vaccine has been observed. Little is currently known about the determinants of inter-individual variation in vaccine responses, although genetic factors have been implicated. Recently we showed intronic SNPs within the *TLR3* gene to be associated with persistence of MenC-specific antibody, following vaccination. We report here exonic variants, of functional relevance, within the *TLR3* gene to be associated with responses to MenC conjugate vaccine in infancy.

Methods: Three hundred and eighteen infants were given a primary course of MenC vaccination, and specific-IgG concentrations and serum bactericidal assay titres measured one month later. We sequenced the exonic regions of the *TLR3* gene to assess the influence of exonic SNPs on responses to MenC vaccination. These SNPs were also tested for functionality *in vitro* following stimulation with Poly I:C (an artificial TLR3 agonist).

Results: A total of five exonic SNPs were identified, two of which rs3775291 ($P = 0.024$) and rs3775290 ($P = 0.056$), were associated with MenC-specific antibody concentrations following vaccination. Furthermore, a two allele exonic haplotype (rs3775291-rs3775290) was shown to be associated with lower specific-IgG responses ($P = 0.009$), there was also a trend for peripheral blood mononuclear cells from individuals with this haplotype to be less responsive to TLR3 stimulation in cell culture.

Conclusion: This report implies a role for functional SNPs within *TLR3* in immune responses to serogroup C meningococcal conjugate vaccines.

PRACTICAL CONDUCT OF A NATIONWIDE VACCINE FIELD TRIAL IN COOPERATION WITH PUBLIC WELL-BABY CLINICS - THE FINIP EXPERIENCE

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Background and aims: Finnish Invasive Pneumococcal disease (FinIP) trial is a cluster-randomized, double-blind trial designed to demonstrate PHiD-CV (GlaxoSmithKline) effectiveness against *S.pneumoniae* and *H.influenzae* diseases. Huge sample size necessitated a nation-wide field trial to be conducted in municipal well-baby clinics (WBC) in which community health nurses and physicians regularly follow all children free of charge including implementation of national immunization programme.

Methods: THL signed contracts with municipal health care centers (HCC) managing the WBCs. THL field personnel (13 study nurses and 3 physicians) conducted education rounds at regional, HCC and WBC levels prior to trial start. THL sent individual invitation letters to families with new-born children. WBC nurses gave oral information, took the informed consent, administered study vaccinations and followed children for safety during regular check-up visits. THL surveillance and support tools included follow-up visits to WBCs, telephone and email support, secure website and monthly newsletters to WBC nurses. Outcome data is collected using national health registers.

Results: Altogether 77% (N=139) of the municipal HCCs managing the local WBCs (N=650) with >2000 WBC nurses cooperated and enrolled >41000 children during 16 months. In a random subset of 2000 children, >96% received all the age-specific vaccine doses.

Conclusions: Nation-wide trial network of collaborating WBCs was successfully established. Enrolment target was not achieved due to lower than expected participation of families. However, the vaccination compliance seems excellent. The blinded follow-up was extended to ensure adequate statistical power. Furthermore, the cluster-randomized design will allow indirect effect evaluation.

INFLUENZA REVACCINATION IN CHILDREN PRIMED WITH MF59[®]-ADJUVANTED OR NON-ADJUVANTED SEASONAL INFLUENZA VACCINE

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Background and aims: Having previously demonstrated higher efficacy of MF59[®]-adjuvanted trivalent influenza vaccine (ATIV: Fludax[®], Novartis Vaccines) over non-adjuvanted vaccine (TIV: Influsplit SSW[®], GSK) in 6 to < 72 months-old children in 2008-2009, we evaluated immunogenicity and safety of their revaccination with ATIV versus TIV (TIV: Agrippal[®], Novartis Vaccines) in 2010-2011.

Methods: Children primed with two doses of ATIV or TIV were re-randomized to receive either ATIV or TIV for revaccination. Control subjects immunized for the first time received ATIV. Vaccine dose was 0.5 ml for children ≥36 m and 0.25 for < 36 m. Immune responses were assessed 21 days post-vaccination.

Results: ATIV administered two years later to ATIV or TIV-primed children elicited higher GMTs to all 3 viral types than TIV, but also TIV administered to ATIV primed children resulted in high responses (**Table 1**). TIV-primed children, revaccinated with ATIV/TIV, or controls receiving ATIV showed good responses to A/H1N1 and A/H3N2, but responses to B remained low following TIV+TIV vaccination. ATIV but not TIV provided cross B-lineage priming. Both ATIV and TIV were well-tolerated on revaccination.

Conclusions: ATIV administered two years later to ATIV or TIV primed children produced higher antibody responses than TIV, with the added benefit of cross B-lineage response. However, TIV boosting of ATIV primed children resulted in adequate immune responses to all strains.

Table 1. HI GMTs in children primed with ATIV and TIV containing A/Brisbane/59/2007 (H1N1), A/Brisbane/10/2007 (H3N2), and B/Florida/4/2006) and subsequent revaccination in 2010*

		2010 vaccination					
		A/California/7/2009 (H1N1)		A/Perth/16/2009 (H3N2)		B/Brisbane/60/2008	
		ATIV	TIV	ATIV	TIV	ATIV	TIV
ATIV- Priming	GMT Day 1	N=42 57 (39-84)	N=25 55 (34-90)	N=42 123 (77-195)	N=25 109 (59-198)	N=42 7 (5-9)	N=25 11 (7-15)
	GMT Day 22	1228 (825-1825)	520 (311-869)	1871 (1481-2364)	735 (543-995)	127 (91-177)	115 (75-177)
TIV- Priming	GMT Day 1	N=52 56 (38-82)	N=26 48 (28-81)	N=52 55 (33-93)	N=26 29 (14-62)	N=52 6.89 (6-8)	N=26 5 (4-6)
	GMT Day 22	1396 (1051-1854)	666 (446-995)	830 (597-1155)	284 (178-453)	45 (31-64)	20 (12-33)
Non- influenza control-priming	GMT Day 1	N=25 63 (37-107)	N=0 -	N=25 130 (64-266)	N=0 -	N=25 5.9 (5-7)	N=0 -
	GMT Day 22	1810 (1229-2667)	-	1810 (1208-2713)	-	45 (22-85)	-

*none of the subjects shown were vaccinated with pandemic or seasonal vaccine in 2009

[Pic_1]

BORDETELLA PERTUSSIS REVIEW

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Background and aims: Despite vaccination, the disease caused by *Bordetella pertussis* increased in industrialized countries. Children under 12 months are at increased risk of contracting disease and the majority of hospitalizations and deaths occur in children younger two months. Our goal is to do a literature review to find strategies to prevent disease in this age group.

Methods: Literature review of period 2003-2012 using the keywords “pertussis vaccination” in databases: CINAHL, CUIDEN, DOCUMED, EMBASE, ERIC, IBECs, IME, LILACS, MEDLINE, OvidMD, PubMed, SciELO.

Results: We found a large number of published articles, although few clinical trials. The degree of evidence for most recommendations is based on expert opinion.

Conclusions:

The GPI (Global Pertussis Initiative)¹ recommended a 3-dose primary vaccination, a booster dose in the second year of life, a dose at preschool age. The epidemiology of the disease indicates that vaccination in adolescents would be beneficial. There is evidence to support the recommendation to vaccinate health care workers, but their implementation requires prior training. Improve surveillance and diagnosis of disease will allow a better assessment of the epidemiology and adjust better the vaccination after infancy.

The ACIP (Advisory Committee on Immunization Practices)², about cocoon strategy, it's difficult to implement.

The CDC (Centers for Disease Control and Prevention)³ recommends vaccination with dTpa pregnant women after 20 weeks of gestation. It's expects that maternal antibodies pass to the fetus and, at birth, it has protection against *B. pertussis* until it can be vaccinated at 2 months of age.

DECREASE OF INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN YOUNGER THAN 2 YEARS IN THE REGION OF MADRID (SPAIN), 2008-2010

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Background and aims: In the Region of Madrid pneumococcal conjugate vaccine (PCV) was included into the routine childhood schedule in 2006, changing heptavalent (PCV7) to 13-valent (PCV13) in June 2010. The aims of this study are to describe the incidence and the epidemiological characteristics of invasive pneumococcal disease (IPD) in children younger than 2 years in the period 2008-2010.

Methods: IPD is a notifiable disease in the Region of Madrid. The case definition of the disease includes the identification of pneumococcus in a normally sterile site. Incidence and mortality annual rates per 100,000 inhabitants were calculated. We compared the rates in 2010 to 2008 by risk ratio (RR).

Results: In the period 2008-2010, 208 cases of IPD were registered. 59.6% were younger than 1 year and 59.6% were males. Bacteraemia (31.3%), pneumonia (28.4%), and meningitis (20.2%) were the most frequent diagnoses. The case-fatality rate was 2.4%. Underlying risk factors for pneumococcal was observed in 7.7% of patients. The most frequent serotypes identified were 19A (46.1%), 7F (10.0%), 5 (6.1%) and 1 (5.0%); all of them included in PCV13. No vaccine failure of PCV7 was detected but one of PCV13. IPD incidence rate was 63.86 in 2008 and 33.66 in 2010 (RR=0.53 p=0.00) and mortality was 1.47 in 2008 and 1.32 in 2010 (RR=0.90 p=0.64). Incidence by serotypes included in PCV13 but not in PCV7 was 38.17 in 2008 and 22.44 in 2010 (RR=0.59 p=0.01).

Conclusions: The incidence and mortality decreased in this period. An early effect of PCV13 was observed.

SPONTANEOUS ABORTIONS AND PERINATAL HEALTH AFTER PANDEMRIX VACCINATION IN FINLAND 2009-2010

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Background: Immunisations during pregnancy, especially during the 1st trimester, have led to questions on their safety. Countries with nationwide health-care registers, high immunisation coverage and unique personal identifiers provide an optimal platform to study the safety of such immunisations.

Aim: To study whether the adjuvanted (AH1N1v) vaccine Pandemrix® given during pregnancy affected the course of pregnancy or perinatal health between October 2009 and December 2010.

Methods: Immunisation records of women in reproductive age were linked to Medical Birth Register data and Hospital Discharge Register data on spontaneous abortions (ICD 10 codes O00-O03) treated in specialised health-care.

Results: There were 193 spontaneous abortions treated within one week after the vaccination. The numbers were similar in the second week (189), the third week (190) and fourth week (196) after vaccination.

Of the 76 043 newborns, 55.2% were exposed to Pandemrix® during pregnancy. 16.7% of mothers were vaccinated in 1st trimester, 18.4% in 2nd and 20.1% in 3rd trimester. The frequency of the following outcomes were compared between vaccinated and unvaccinated: perinatal death including stillbirths (from 22 weeks of gestation), early neonatal deaths (0-6 days), very preterm births (below 28 weeks), preterm births (below 37 weeks), very low birth weight (below 1500 grams), and low birth weight (below 2500 grams). Immunisation was associated with protection from all compared outcomes. (statistically significant adjusted ORs between 0.45 and 0.71).

Discussion: Pandemrix vaccination during pregnancy did not affect the course of pregnancy. Further, immunization had protective effect on all the major perinatal outcomes studied.

THE INCIDENCE RATE OF LYMPHADENITIS AFTER BCG VACCINATION

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Background and aims: BCG lymphadenitis is a relatively frequent local adverse reactions after BCG vaccination. Its incidence rate is usually < 1%. However, this rate may be different according to BCG strain, vaccination method or skill, etc. In Republic of Korea, two BCG strains are immunizing: intradermal Dannish-1331 or percutaneous Tokyo-172. We surveyed these incidence rates of BCG lymphadenitis.

Methods: This survey was performed in total 25 centers (4 general hospitals, 21 private pediatric clinics). Immunized type of BCG strain in study subjects was verified by directly observing (a) scar(s). The occurrence of BCG lymphadenitis was asked to their parent. In cases of BCG lymphadenitis, their onset age, location, size, progression of suppuration, and treatment method were investigated, as well.

Results: The total number of study subjects was 3,379 (men, 1,750; women: 1,629). Among these, Tokyo strain was 2,631, Danish strain was 739, and unknown was 9 subjects. BCG lymphadenitis developed in each five of subjects per strains, therefore, its incidence rate was 0.19% in Tokyo and 0.68% in Dannish strain, respectively ($P=0.077$). Among 10 cases with BCG lymphadenitis, it developed at axilla in 9 and at supra-clavicular area in 1 case. The diameter 1.5 cm or more lymphadenitis developed in 5 cases: 2 in Tokyo and 3 in Danish strain. Four cases progressed to suppuration. Four cases were surgically treated.

Conclusions: The incidence rate of lymphadenitis in two BCG types, percutaneous Tokyo and intradermal Dannish strain BCG, is 0.19% and 0.68%, respectively. Both rates are acceptable.

NEUTRALIZATION ANTIBODY TITER CORRELATE OF INFLUENZA VACCINE EFFICACY IN 6 MONTH TO < 72 MONTH OLD CHILDREN

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Background and aims: Correlates of influenza vaccine efficacy have relied on hemagglutination inhibition (HI) antibody titers but the assay has limitations. A neutralization test (NT) correlate may more accurately reflect vaccine efficacy (VE) and clinical protection.

Methods: Post second-dose sera from 771 6 to < 72 month old subjects in a randomized trial that demonstrated efficacies of trivalent inactivated influenza vaccine (TIV), MF59[®]-adjuvanted TIV against H3N2 influenza were previously tested by HI and were retested by NT^{1,2}. H3N2 virus and serum dilution mixtures were incubated with Madin Darbin Canine Kidney (MDCK) cells for 7 days and viral neutralization assayed by measuring supernatant hemagglutinating activity.

A population-based correlate based on the Dunning model (used in previous determinations of HI correlates of protection and VE) fulfilled Prentice criteria.

Results: NT titers of 145 and 485 were associated with VE of 50% and 80%, respectively (Table 1).

Table 1. Comparison of neutralizing antibody and hemagglutination inhibition antibody titers correlating with protection against laboratory-confirmed H3N2 influenza virus infection in previously unimmunized 6 to <72 month old children

Probability of Protection Against Laboratory-Confirmed H3N2 Influenza Virus Infection	H3N2 Neutralizing Antibody Titer <small>(Helme H, et al. Immunogenicity of a monovalent, aluminum-adjuvanted influenza whole virus vaccine for pandemic use. <i>Virus Res.</i> 2004; 103:163-71.)¹</small>	H3N2 Hemagglutination Inhibition Antibody Titer <small>(Black S et al. <i>PLoS</i> 2011; 30: 1081-6)²</small>
50%	145	110
60%	206	151
70%	303	215
80%	485	330
90%	983	629

[Plc_1]

Conclusions: While an HI titer of ≥ 40 is correlated with 50% clinical protection against influenza in adults, no NT correlate is established. In the more sensitive NT, a titer of 145 was associated with 50% protection in < 72 month old previously unimmunized children. The more robust NT can now replace HI in evaluating pediatric inactivated influenza vaccines¹.

IMPACT OF ROUTINE VARICELLA IMMUNIZATION ON VARICELLA INFECTION AND HERPES ZOSTER INCIDENCE RATES AMONG CHILDREN AND ADOLESCENTS IN GREECE

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Background and aims: The impact of routine varicella immunization upon the occurrence of varicella infection and herpes zoster (HZ) among children in Greece has not been evaluated. The study compared the incidence rates of varicella infection and HZ following the introduction of routine varicella immunization.

Materials: A retrospective cohort study was conducted among all emergency department attendees at the "P. & A. Kyriakou" Children's Hospital between 1.1.1998-31.12.2010. Incidence rates (per 10,000 children) of varicella infection and HZ during the prelicensure (1998-2003) and postlicensure (2007-2010) periods of routine varicella immunization were calculated with survey statistical procedures and compared with the Rao-Scott Chi-Square test.

Results: Among the study sample (n=4316), 98.1% (n=4234) had varicella infection and 1.9% (n=82) HZ. Varicella infection rates (per 10,000 children) diminished from 9.1(95% CI:8.0-10.3) to 2.4(95% CI:1.7-3.0) in the postlicensure period ($p < 0.0001$). Mean(\pm SD) patient age (years) did not differ between the prelicensure and postlicensure periods (5.95 \pm 3.26 vs. 5.91 \pm 3.67; $p=0.804$). However, the proportion of infected cases belonging to minority groups was higher during the postlicensure period (33.0%(n=984) vs. 52.5%(n=248); $p < 0.0001$). Therefore, the incidence rate decreased solely among Greek children ($p < 0.0001$). Similarly, the incidence rate (per 10,000 children) of HZ diminished from 0.1(95% CI:0.1-0.2) to 0.0(95% CI:0.1-0.2) in the postlicensure period ($p < 0.0001$). Among children aged >4 years, HZ incidence rate diminished by four-fold during the postlicensure period ($p < 0.0001$).

Conclusions: Following the introduction of routine varicella immunization, the incidence rates of both varicella infection and HZ have decreased notably in Greek children. However, these remain elevated among underserved minority groups.

THE SHORT-TERM ECONOMIC IMPACT OF TWO CHILDHOOD PREVENTIVE HEALTH PROGRAMS IN SAUDI ARABIA

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Background: Childhood immunizations underpin public health programs worldwide, but their value for money is often uncertain. This study estimated the budget impact of pediatric immunization against pneumococcal disease and prophylaxis against severe respiratory syncytial virus (RSV) infection, in Saudi Arabia.

Methods: Incidence-based models compared the annual budget impact, from the perspective of the Saudi Arabian healthcare system, of the two programs, based on current guidelines. Model inputs were from published literature. Outputs included total program cost, disease costs and disease cost offsets (2011 USD).

Results: A heptavalent pneumococcal conjugate vaccine (PCV7) vaccination program, covering 554,872 infants, prevented an estimated 142 cases of invasive disease, 543 cases of pneumococcal pneumonia and 757 cases of pneumococcal otitis media. An RSV prophylaxis program in a target population of 3,009 high-risk Saudi infants was expected to prevent 166 hospitalizations for severe RSV disease. Total disease costs in the first year of the model, without the programs, were \$2,777,140 (pneumococcal disease) and \$6,110,211 (RSV disease). Total disease costs, with the programs, but excluding the cost of prophylaxis were \$1,461,732 (pneumococcal disease) and \$5,647,078 (RSV disease), for annual savings of \$1,315,408 and \$463,133 respectively. The prophylaxis costs were: \$162,022,479 (pneumococcal disease) and \$14,311,189 (RSV disease). Both were associated with net cost savings, when excluding administration costs.

Conclusion: Both programs had substantial acquisition costs, but annual net savings, when the costs of the program were excluded. Even programs considered expensive are well-positioned financially within the context of other preventive health strategies, when targeted to appropriate populations.

IMMUNE MEMORY 2-3 YEARS AFTER VACCINATION WITH PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN-D CONJUGATE VACCINE (PHID-CV), WITH OR WITHOUT PROPHYLACTIC PARACETAMOL

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Background and aims: Prophylactic paracetamol (PP) administered concomitantly with vaccination decreases immunogenicity of paediatric vaccines.¹ This follow-up study (NCT00950833) evaluated immune memory 2-3 years after PHiD-CV primary and booster vaccination, and allowed assessment of the effect of previous PP.

Methods: To assess immune memory, anamnestic responses were evaluated in children previously vaccinated with PHiD-CV (primed aged 3,4,5 months, boosted aged 12-15 months) with/without concomitant PP (PP/Non-PP groups) who received an additional PHiD-CV dose aged 40-49 months. Immunogenicity was assessed before and 7-10 days post-vaccination and compared with a Control group (no previous pneumococcal vaccine, age-matched having received MenACWY-TT aged 12-15 months) receiving a first PHiD-CV dose aged 36-50 months.

Results: For each vaccine pneumococcal serotype, regardless of prior PP, robust increases in antibody GMCs (9.8-72.1-fold [PP]; 8.2-59.9-fold [Non-PP]) and OPA GMTs (16.7-2029.6-fold [PP]; 19.4-1097.5-fold [Non-PP]) were observed from pre- to 7-10 days post-vaccination. Antibody GMCs and OPA GMTs tended to be lower in the PP *versus* Non-PP group (trends less pronounced for OPA than ELISA), but were markedly higher than Control group for most serotypes (Table).

Conclusions: Strong boostability of response indicated PHiD-CV induced long-term immune memory irrespective of PP administration at primary and booster vaccination, although the PP group tended to have lower responses to the additional PHiD-CV dose than the Non-PP group, especially for antibody GMCs.

¹Prymula. *Lancet* 2009;**374**;1339-50.

Table. Anti-pneumococcal antibody GMCs ($\mu\text{g}/\text{mL}$) and OPA GMTs 7-10 days following a PHiD-CV dose (ATP cohort for immunogenicity)

Vaccine serotype	Antibody GMCs ($\mu\text{g}/\text{mL}$) (95% CI)			OPA GMTs (95% CI)		
	PP (N=109)	Non-PP (N=106)	Control (N=204)	PP (N=99)	Non-PP (N=99)	Control (N=190)
1	5.85 (4.81, 7.13)	10.01 (8.07, 12.42)	1.24 (1.07, 1.42)	2677.1 (2146.0, 3339.7)	3593.9 (2922.1, 4420.2)	632.0 (524.4, 761.7)
4	10.82 (8.92, 13.13)	15.57 (13.14, 18.46)	4.52 (3.96, 5.17)	23340.6 (17599.4, 30954.8)	31718.5 (24963.8, 40300.8)	13109.9 (11080.6, 15510.7)
5	8.16 (6.69, 9.94)	11.74 (9.50, 14.50)	0.72 (0.63, 0.84)	852.5 (695.5, 1045.0)	1220.3 (969.3, 1536.2)	145.8 (111.7, 190.3)
6B	7.04 (5.80, 8.54)	8.38 (6.92, 10.14)	0.27 (0.22, 0.33)	6386.7 (4585.5, 8895.3)	5237.2 (3882.8, 7064.2)	1472.2 (1053.2, 2057.8)
7F	5.25 (4.34, 6.35)	8.13 (6.74, 9.79)	1.37 (1.19, 1.58)	19386.3 (15148.8, 24809.1)	20616.8 (16163.4, 26297.2)	13647.4 (11801.9, 15781.3)
9V	7.77 (6.31, 9.57)	12.32 (10.23, 14.83)	0.69 (0.58, 0.83)	18806.1 (14406.6, 24549.3)	17169.8 (12704.8, 23204.0)	14668.8 (12476.1, 17247.0)
14	20.05 (16.34, 24.62)	26.68 (21.97, 32.39)	1.01 (0.80, 1.27)	14642.4 (11235.8, 19082.0)	18068.7 (14101.7, 23151.6)	4454.3 (3921.1, 5059.9)
18C	26.99 (21.69, 33.60)	39.51 (32.84, 47.53)	3.25 (2.71, 3.90)	7693.4 (5575.6, 10615.6)	7155.4 (5596.6, 9148.4)	9092.2 (7381.2, 11199.9)
19F	34.90 (29.40, 41.44)	45.59 (35.17, 59.10)	4.31 (3.59, 5.17)	5811.9 (4023.0, 8396.1)	6766.7 (4601.7, 9950.2)	902.5 (659.2, 1235.6)
23F	8.43 (6.73, 10.56)	10.15 (8.02, 12.85)	0.25 (0.20, 0.32)	13847.2 (9499.4, 20184.9)	17626.8 (13421.5, 23149.7)	5776.5 (4686.8, 7119.5)

GMCs, geometric mean concentrations; OPA, opsonophagocytic activity; GMTs, geometric mean titres; N, maximum number of available results (actual number of children included in the analysis varied according to serotype, depending on serum availability); PP, prophylactic paracetamol

[table1]

SURVEILLANCE OF VACCINES ADVERSE EFFECTS IN ISTANBUL**A. Kılıç**¹, E. Unuvar¹, M. Sidal², G. Gökçay²¹*Istanbul University, Istanbul Medical Faculty,* ²*Istanbul University, Institute of Child Health, Istanbul, Turkey*

Background and aims: In vaccination practices among society, it is of up most importance to differentiate between vaccine side effects and other irrelevant events occurring incidentally following vaccination. The documenting were adverse effects of measles, MMR, DPT-OPV, Hepatitis B, BCG, DT vaccines in İstanbul.

Methods: From September 2003 until August 2008, vaccine side effects were documented among children younger than 14 years living in Istanbul using active and passive surveillance methods. In study period, 1 485 489 children were vaccinated yielding a total dose of 9 575 936. Side effects were given account of per 100.000 doses.

Results: 151 children (76 girls, 75 boys) accounting for per 100 000 doses of 1.5 of total, experienced one of the following side effects; 49 neurologic, 28 acute allergic reactions, 23 syncope, 3 anaphylaxis, 21 maculopapular rash, 14 serious local reaction, 8 fever, and 5 lymphadenitis. Based on vaccine types, 55 were due to measles, 44 DTP, 22 MMR, 16 Hepatitis B, 7 DT, 5 BCG and 1 case was documented for each DTIPVHIB. Active surveillance revealed 20 cases while passive surveillance revealed 131. 106 of cases were classified as vaccine side effect due to improper administration.

Conclusions: As we revealed much more vaccine side effects using passive surveillance method, active surveillance method was proven beneficial in documenting rare complications such as encephalitis, anaphylaxis. Actual vaccine side effects are less compared to those found by either active or passive methods.

EFFECTIVENESS OF ONE DOSE OF VARICELLA VACCINE AFTER INTRODUCTION OF ROUTINE VARICELLA VACCINATION IN GERMANY

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Background and aims: Germany introduced routine varicella vaccination in 2004, with one dose in children aged 11-14 months. We assessed effectiveness of one dose of varicella vaccine, including *Varilrix*TM (GSK Biologicals) and other marketed varicella vaccines, under conditions of routine use.

Methods: Matched case-control study across 35 paediatric practices (Munich, Germany) conducted from February 2008 to October 2010. The primary outcome was effectiveness of one dose of *Varilrix*TM against PCR-confirmed varicella (any severity), adjusted for possible confounders.

Results: The final analysis included 432 children with varicella and 432 matched controls aged 1-6 years. In total, 57 (13.2%) varicella cases and 196 (45.4%) controls had received any varicella vaccination. Mean time to disease onset for vaccinated cases was 28.2 months. Vaccinated cases (n=57) experienced milder ($p < 0.0001$) and shorter-duration (8 vs 9 days, $p = 0.004$) disease compared with unvaccinated cases (n=375). Adjusted vaccine effectiveness of one dose of *Varilrix*TM against PCR-confirmed varicella of any severity was 71.5% [95% confidence interval: 49.1-84.0], and 94.7% [77.8-98.7] against moderate and severe varicella. Effectiveness of any varicella vaccine against any varicella disease was 86.4% [77.3-91.8] and 97.7% [90.5-99.4] against moderate and severe varicella. Vaccine effectiveness appeared to decline over time.

Conclusions: In a population with vaccine coverage below 50%, one dose of *Varilrix*TM showed high effectiveness against moderate and severe varicella; effectiveness against varicella of any severity was lower in comparison to other varicella vaccines. Two-dose varicella vaccination (recommended in Germany since 2009) and long-term effectiveness warrant further investigation.

PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS INFECTION WITH PALIVIZUMAB: 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 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 92 patients (43 gestational age < 32 weeks, 30 gestational age 33-35 weeks, 16 with a congenital cardiac disease and three affected by Kartagener's syndrome); the second group was composed by 87 patients (35 gestation age < 32 weeks, 40 gestational age 33-35 weeks, 12 with a congenital cardiac disease).

Results: In the first group 4/92 patients (4.3%) were hospitalized for severe pulmonary infection by RSV during the first year of life, while in the second group 33/87 (37.9%) 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, particularly in special group of newborns with high risk. This data is very important in relation to frequent respiratory sequels correlated to this infection.

TIMELINESS OF PNEUMOCOCCAL CONJUGATE VACCINATION IN GREECE

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Background and aims: Since January 2006, the Hellenic National Immunization Program recommends pneumococcal conjugate vaccine (PCV) for routine administration as a 4-dose series for infants at 2, 4, 6, and 12-18 months of age. The present study investigated the timeliness of pneumococcal vaccination in Greece.

Methods: Between December 2010 and June 2011, the immunization history of 233 children attending day-care centers (DCCs) was recorded. The DCCs were located in an urban (Athens, n=4, 113 children) and a rural/semi-urban area (prefecture of Viotia, n=6, 120 children). The interviewing pediatrician recorded the exact dates of immunization with PCV from each child's health booklet.

Results: The median age of the 233 attendees was 42 months (range 24-59 months). Of a total of 756 PCV doses, 731 (96.7%) were of the 7-valent (PCV7), 21 (2.8%) of the 13-valent (PCV13), and 4 (0.5%) of the 10-valent vaccine (PCV10). The percentage of children that had been already immunized with the respective number of PCV doses at specific ages appear in the following table:

Dose administered	4 mos	8 mos	12 mos	16 mos	20 mos	24 mos	28 mos	32 mos
First	51.1	68.6	85.3	88.7	90.5	91.8	94	96.1
Second	3	49.8	73.1	82.1	85.5	86.3	88	89.3
Third	0	28.8	46.8	55	58.5	67.9	74.7	76
Fourth	0	0	0.4	4.3	15.9	37.4	50.3	52.5
Fifth	0	0	0	0	0	0	0.8	1.2

[Table 1]

Conclusions: Our data indicate that a high proportion of infants in Greece may receive pneumococcal vaccination at delayed terms.

ATTITUDE AND KNOWLEDGE OF HEALTHCARE PRACTITIONERS (HCP) TOWARDS HPV VACCINATION FOR BOYS 12-17 YEARS; A EUROPEAN SURVEY**J. Cortes¹, P. Le Calve², A. Darras³***¹Spanish Society of Obstetrics and Gynaecology, Palma de Mallorca, Spain, ²Ifop Healthcare, Paris, ³Sanofi Pasteur MSD, Lyon, France*

HPV diseases and cancers are known to account for a high human and economic burden in females and males. In addition to boys, Gardasil was recently approved in Europe for use in young men up to 26 years for prevention of genital warts and, in United States, also for prevention of intraepithelial anal neoplasia and anal cancer causally related to HPV. A market survey was performed in November 2011, in 4 European countries (Norway, Denmark, Portugal, Spain) among 558 general practitioners and paediatricians to assess knowledge and attitude towards HPV vaccination prescription for boys and young men. Spontaneously, almost all physicians (97%) are aware of HPV burden in males. 86% physicians think relevant and 42% very relevant to prevent these diseases. While 84% know that boys can benefit from HPV vaccination, only 16% spontaneously think of offering it to boys aged 12-17 years. Of note, 45% Danish HCP respondents have prescribed HPV vaccine, at least once, to boys. Following a brief presentation on HPV diseases and cancers in both genders, relevance to vaccinate boys rose from 42% to 67% (very relevant, $p=0.01$) thus showing the importance of education about burden of disease. According to physicians, vaccinate boys would have a positive impact on HPV vaccination acceptance among parents (92%), and could even increase coverage rate in girls (81%). HPV vaccination is no longer perceived as a female-only benefit. Boys' vaccination is gaining acceptance and this survey subsequently stresses the importance of disease education and primary prevention through vaccination.

FACTORS ASSOCIATED WITH COMPLIANCE WITH PALIVIZUMAB PROPHYLAXIS IN THE CANADIAN RSV EVALUATION STUDY FOR SYNAGIS (CARESS) REGISTRY (2005-2011)**B.A. Paes**¹, A. Li², I. Mitchell³, K. Lanctot²¹*Pediatrics, McMaster University, Hamilton,* ²*MORE Research Group, Sunnybrook Health Sciences Center, Toronto, ON,* ³*Pediatrics, University of Calgary, Calgary, AB, Canada***Background:** CARESS assesses utilization, compliance and outcomes of infants receiving palivizumab during the respiratory syncytial virus (RSV) season.**Objective:** Determine factors affecting compliance.**Methods:** Prospective registry of infants who received ≥ 1 dose of palivizumab during 6 RSV seasons across 30 sites. Neonatal and demographic data were collected from the parent/caregiver at enrolment. Palivizumab utilization, compliance, and outcomes data related to respiratory illness (RI) and RSV hospitalization were collected monthly. Compliance was defined by: interval between doses, and percentage of expected injections received.**Results:** Of 10,452 infants enrolled, 7492 (71.7%) complied with timing of doses. Overall, 91.9% \pm 27.1% of expected injections was received. A greater proportion of non-compliant infants were hospitalized for an RI (7.5% versus 6.0%, $p=0.005$), but compliance did not affect RSV-positive hospitalizations (1.79% versus 1.53%, $p=0.177$). Compliant infants (all $p < 0.05$): were younger at enrolment (5.4 \pm 5.9 versus 5.9 \pm 6.1 months), had siblings (61.3% versus 58.5%), were a multiple (29.7% versus 27.2%), and had >5 household individuals (23.9% versus 21.7). More non-compliant infants had smoke exposure (30.5% versus 28.4%, $p=0.033$). Bronchopulmonary dysplasia and premature infants were more compliant than those prophylaxed for CHD or "other" reasons. Six factors influenced compliance in regression analysis: age (HR=0.989, 95%CI: 0.982-0.996, $p=0.002$), siblings (HR=1.104, 95%CI: 1.007-1.211, $p=0.034$), >5 household individuals (HR=1.114, 95%CI: 1.001-1.241, $p=0.047$), smoke exposure (HR=0.891, 95%CI: 0.811-0.980, $p=0.018$) CHD (HR=0.805, 95%CI: 0.700-0.927, $p=0.002$), and RI-related hospitalization (HR=0.837, 95%CI: 0.705-0.903, $p=0.041$).**Conclusions:** Siblings and >5 household individuals is associated with increased treatment compliance; being older, smoke exposure, having CHD and RI hospitalization decreased compliance.

INFECTIOUS MARKERS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASES**I. Zakharova**¹, I. Berezhnaya²¹*Russian Medical Academy of Postgraduate Education*, ²*Tushinskaya Children's Hospital, Moscow, Russia***Objective:** To check for infectious markers in children with inflammatory bowel diseases (IBD).**Materials and methods:** 101 children with IBD aged from 18 months to 15 years were recruited into the study. 22 patients were diagnosed to have ulcerative colitis, 5 - Chron's disease, 42 - eosinophilic colitis, 32 - undifferentiated colitis. The control group included 101 children with chronic constipation and gut microflora disorders. Serum antibodies to Salmonella, Shigella and Yersinia were measured by reaction of indirect hemagglutination, antibodies to Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) were tested with ELISA.**Results:** Children from IBD group were found to have positive antibodies titers to Salmonella and Yersinia significantly more often than patients from control group: in IBD group positive titers to Salmonella were found in 46,5% children, to Yersinia - in 81,1% patients, while in control group - in 24,7% and 60,4%, respectively ($p < .05$). IgG class antibodies to CMV were found in 89,1% patients from IBD group and just in 63,3% cases from control. Antibodies to EBV nuclear antigen were elevated in all children with inflammatory bowel disease and just in 25% children from control group ($p < .005$). The level of antibodies to EBV nuclear antigen in IBD patients was found to be 3 times higher than in control group, while the level of antibodies to capsid antigens - 1,5 times lower, demonstrating incomplete immune response to EBV in patients with IBD.

CHANGING POPULATION CHARACTERISTICS OF INFANTS RECEIVING RSV PROPHYLAXIS IN THE CANADIAN RSV EVALUATION STUDY FOR SYNAGIS (CARESS) REGISTRY (2005-2011)

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Background: CARESS assesses utilization, compliance and outcomes of infants receiving palivizumab during the respiratory syncytial virus (RSV) season.

Objective: Examine the changing profile of infants who received RSV prophylaxis from 2005-2011.

Methods: A prospective, observational, registry of infants who received ≥ 1 dose of palivizumab across 30 Canadian sites. Neonatal and demographic data were collected from the parent/caregiver at enrollment. Data related to respiratory infection (RI) and RSV hospitalization (RSVH) were collected monthly.

Results: 10,452 infants were enrolled; average age 5.5 ± 5.9 months. Participants were typically male (56.2%), Caucasian (71.3%), average gestational age (GA) 32.3 \pm 5.6 completed weeks. 7007 (67.1%) infants were premature (< 35 weeks GA) only, 836 (8.0%) had bronchopulmonary dysplasia (BPD), 1048 (10.0%) had congenital heart disease (CHD) and 1561 (14.9%) were prophylaxed for other conditions such as Down syndrome, neuromuscular disorders, airway anomalies and cystic fibrosis. Patients received $91.9\% \pm 27.1\%$ of their expected injections. The hospitalization rates for RI and RSVH were 6.4% and 1.6% respectively. Between 2005-2011, the change in proportion prophylaxed for prematurity (55.3% to 50.3%), 33-35 weeks GA infants (20.6% to 14.0%), BPD (14.2% to 6.9%), CHD (5.6% to 10.2%) and others (4.4% to 18.6%) were -1.1, -1.5, -2.1, 1.8 and 4.2-fold respectively.

Conclusions: Overall there is a changing trend with a steady increase in the percentage of infants with CHD receiving palivizumab, and the largest proportional increase was in infants with underlying medical disorders. Healthcare providers are strongly advocating for RSV prophylaxis in special populations with pre-existing illnesses, despite universal restrictive guidelines.

RADIOISOTOPIC CHOLESCINTIGRAPHY CHALLENGES THE DIAGNOSIS OF ACALCULOUS CHOLECYSTITIS FOR EBV GALLBLADDER INVOLVEMENT

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Background: Involvement of the extrahepatic biliary outflow tract in patients with EBV infection is already known in the literature as EBV induced acalculous cholecystitis.

Case report: A 11-year-old girl with EBV infection was initially diagnosed on clinical grounds and the diagnosis was confirmed by positive IgM antibodies to EBV viral capsid antigen (VCA) and a positive Monospot test. The patient also complained about abdominal pain during the illness course, mainly at the palpation of the right upper quadrant of the abdomen with a positive Murphy sign. Gallbladder involvement was disclosed by using ultrasound imaging (thickened oedematous gallbladder wall of 7,3 mm without dilation of the biliary tract). A radioisotopic cholangiography was also performed which showed that the emptying of gallbladder was not accomplished even after the administration of a fatty meal and ejection fraction was negligible at 45 min. A repeated ultrasonographic examination, ten days later, revealed normal thickness of the gallbladder wall. A repeated cholescintigraphic examination of the gallbladder, one month later, showed that the motility of the gallbladder has been considerably improved since the initial examination with an ejection fraction calculated to > 70%, although emptying was not fully accomplished at the end of the study at 60 minutes.

Conclusion: Based on the scintigraphic data of our patient we consider that impaired gallbladder contractility in EBV infection cases actually represents biliary dyskinesia and by no means acalculous cholecystitis, a term that may misinterpret the data.

ALLITRIDIN INHIBITS TREG AMPLIFICATION IN CYTOMEGALOVIRUS INFECTION IN VIVO AND IN VITRO

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Objective: To explore the effects of allitridin on murine cytomegalovirus -induced CD4⁺CD25⁺Foxp3⁺ regulatory T cell amplification in vivo and in vitro.

Methods: MCMV-infected mice were randomly allocated into two groups for treatment with allitridin or placebo. Mock-infected mice were randomly allocated as controls for the allitridin treatment and placebo treatment groups. The mice were sacrificed at various time points after infection (out to 120 days) to evaluate the effects of treatment on Treg presence and function, as well as MCMV infective load. A mouse embryo fibroblasts and MCMV co-culture system was established to perform evaluations of the allitridin-mediated Treg and anti-CMV effects. Changes in Foxp3 mRNA and protein levels were measured by real-time PCR and Western blot, respectively. Percentages of T cell subsets were analyzed by flow cytometry. Levels of Treg-related cytokines, IL-10 and TGF- β , were detected by double-antibody sandwich ELISA.

Results: Allitridin treatment did not influence Foxp3 expression and Treg proportion in uninfected mice, but did down-regulate each in infected mice during the chronic infection period. Additionally, allitridin treatment reduced the MCMV load in salivary glands. Allitridin in vitro treatment partially blocked MCMV induction of Foxp3 mRNA and protein expression, significantly increased the percentages of Tc1, Tc2, and Th1, reduced the secreted levels of IL-10 and TGF- β 1, and significantly suppressed viral loads.

Conclusions: Allitridin can promote MCMV-induced Treg expansion and Treg-mediated anti-MCMV immunosuppression. Therefore, allitridin may be useful as a therapeutic agent to enhance the specific cellular immune responses against CMV.

SEROLOGIC PROFILE OF EPSTEIN-BARR VIRUS INFECTION IN PATIENTS WITH INFECTIOUS MONONUCLEOSIS SYNDROME

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Primary Epstein-Barr virus (EBV) infection occurs during childhood and is asymptomatic, or is associated with the clinical syndrome of infectious mononucleosis (IM). Detection of heterophile antibodies, being positive in up to 85% of cases, is widely used for diagnosis of IM. However, there are antibodies to several antigen complexes that more precisely detect EBV: viral capsid antigen (VCA), early- (EA), and nuclear antigen (EBNA). The aim of our study was to determine the classes of antibodies to different EBV antigens in patients with infective mononucleosis syndrome. The investigation included 60 sera from juvenile patients (age 4-22 years) with IM syndrome admitted in our laboratory during a period of six months (June-December 2011). Full blood count and IM serology testing were performed with: MNI test (Fumouse, France) and Virapid Mono M&G (Viracell, Spain) for specific EBV antibodies according to the manufacturer's recommendations. Out of the total of 60 patients, 45 had both clinical symptoms and full blood parameters suggestive for IM. The two serological tests for IM performed on those sera revealed the following results: out of 35 sera (78%) positive to MNI test, 30 were IgM positive for VCA only and 5 were IgM positive both for EA and VCA. However, out of the 15 MNI negative sera, 7 had IgM VCA, 3 had IgG VCA and 5 were negative for all EBV markers. The presence of IgM antibodies to VCA and EA, is indicative for acute infection, which was confirmed with specific EBV test, since MNI test lacks the sensitivity needed for this infection.

SIGNIFICANCE OF TREG, NK CELLS AND NKT CELLS IN PERIPHERAL BLOOD OF CHILDREN WITH CHRONIC HEPATITIS B VIRUS INFECTION

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Background and aims: The cellular immune mechanism of chronic hepatitis B (CHB) is not fully understood. The roles of the CD4⁺CD25⁺Foxp3⁺regulatory T cells (Treg), CD3⁺CD16⁺CD56⁺NK cells and CD3⁺CD16⁺CD56⁺NKT cells, and the potential relationship in pediatric subjects of Asymptomatic HBV carriers (AsC) and CHB should be clarified.

Methods: Fresh peripheral venous blood samples were obtained from 36 cases of AsC, 21 cases of CHB and 33 healthy counterparts. The number and distribution of CD4⁺CD25⁺Foxp3⁺Treg cells, CD3⁺CD16⁺CD56⁺NK cells and CD3⁺CD16⁺CD56⁺NKT cells were analyzed by flow cytometry. Liver function and HBV DNA level were determined for each patient.

Results: Compared with normal control, CD4⁺CD25⁺Foxp3⁺Treg cells were risen significantly ($P < 0.05$) in peripheral venous blood in children with CHB, and the frequency was positively correlated with total serum bilirubin (Tbil) ($r=0.223$, $P=0.015$). While, CD3⁺CD16⁺CD56⁺NK cells and CD3⁺CD16⁺CD56⁺NKT cells were significantly lower than that of normal control ($P < 0.05$). The frequency of CD3⁺CD16⁺CD56⁺NK cells was negatively correlated with serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ($r=-0.605$ and -0.540 , $P=0.013$ and 0.031 , respectively), and CD3⁺CD16⁺CD56⁺NKT cells was negatively correlated with Tbil ($r=-0.616$, $P=0.011$).

Conclusions: Treg cells, NK cells and NKT cells are related to liver cell damage and they are obviously associated with the process of the disease. Treg cells are potentially involved in the immune tolerance in HBV infected-children and chronicity of the hepatitis B through suppression of NK cells and NKT cells.

MORNING AND EVENING SALIVARY CORTISOL IN A PROSPECTIVE COHORT OF ADOLESCENTS WITH CHRONIC FATIGUE SYNDROME AND CONTROLS FOLLOWING INFECTIOUS MONONUCLEOSIS

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Background and aims: Chronic fatigue syndrome (CFS) is a complex condition involving severe fatigue and disabling musculoskeletal and cognitive symptoms. Whether endocrinologic dysfunction accompanies CFS is unclear. Previous studies have reported mixed results regarding CFS and salivary cortisol levels. We examined morning and nighttime salivary cortisol levels 6, 12 and 24 months following infectious mononucleosis (IM) both in adolescents who met the criteria for CFS at those time points and recovered controls matched for age, sex and Tanner stage.

Methods: Nine adolescents with CFS following IM and 9 matched, recovered controls had morning and nighttime salivary cortisol levels measured blindly using standard methodology, 6, 12 and 24 months following IM. The time the sample was obtained was recorded. Levels were judged to be normal, depressed or elevated by a pediatric endocrinologist blinded to the patient's clinical diagnosis.

Results: There were 27 evaluable salivary cortisol levels in the patients with CFS and 38 in the recovered controls. There was only a single depressed morning salivary cortisol among the patients with CFS (and that same patient had an elevated nighttime salivary cortisol). Among the recovered controls, there was also a single depressed morning cortisol, 1 depressed nighttime cortisol and 4 elevated nighttime cortisols (one of whom had the single depressed morning value).

Conclusions: We found no evidence of depressed salivary cortisol levels in adolescents with CFS following IM. These data are consistent with previous clinical trials demonstrating little if any benefit of cortisol replacement therapy in CFS.

CYTOMEGALOVIRUS - EBSTEIN BARR VIRUS SUPERINFECTION: AN ACUTE HEPATITIS UNCOMMON CASE

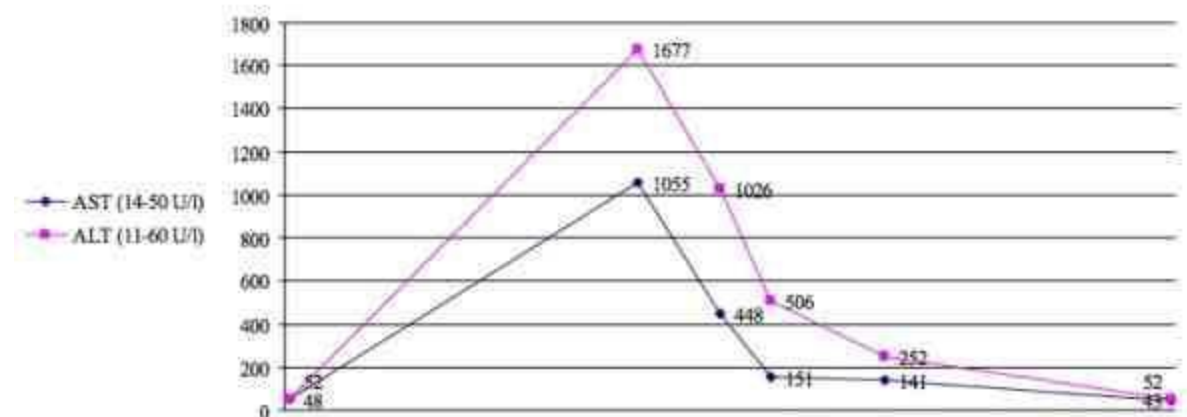
G. Nicolini, G. Longo, E. Bressan, M. Micera, P. Peverelli, L. Memo

Ospedale San Martino, Belluno, Italy

Background: When CMV and EBV involve liver, they are responsible for acute hepatitis with transaminases mild increase. No one case of superinfection is described.

Case report: A 5 year old boy came for fatigue, fever, abdominal pain; biochemistry showed mild transaminases level increase, positive EBV serology, negative CMV serology. After 34 days he presented lymphadenopathy and hepatosplenomegaly. The blood tests showed a high increase of transaminases, positive serology both for EBV and for CMV. Blood EBV-DNA, blood and urine CMV-DNA tests were positive. We saw resolution of symptoms and hepatosplenomegaly, normalization of transaminases in 60 days.

Conclusion: Our patient presented a mononucleosis with a mild hepatic impairment; after one month the significant increase of transaminases suggested the involvement of a further injurious agent, identified in CMV. The degree of liver injury was similar to those produced by major hepatotropic viruses. CMV superinfection on a liver damaged by recent EBV infection, increased the level of cytolysis that would cause EBV or CMV alone.



[Hepatic values]

Date	14/01	17/02	25/02	2/03	13/03	10/4
Ac. Anti-CMV IgM (pos > 30 UA/ml)	8		240		194	86,6
Ac. Anti-CMV IgG (pos > 0.6 UI/ml)	<0,2		2,5		3,2	11,3
Blood CMV-DNA (copies/ml)				12968		
Urine CMV-DNA				POSITIVE		
Ac. Anti EBV IgM	POSITIVE	POSITIVE	POSITIVE		POSITIVE	POSITIVE
Ac. Anti EBV IgG	POSITIVE	POSITIVE	POSITIVE		POSITIVE	POSITIVE
Blood EBV-DNA (copies/100.000 lymphomonocytes)				POSITIVE < 300		

[Biochemistry]

A RARE CAUSE OF MULTIPLE ORGAN DYSFUNCTION SYNDROME: HUMAN HERPES VIRUS 6 INFECTION**H. Tekguc**^{1,2}, C. Dalkan¹¹*Paediatrics, Near East University, Nicosia, Cyprus,* ²*Paediatric Intensive Care Unit, Akdeniz University, Antalya, Turkey*

Human herpes virus 6 (HHV-6) is a member of the β -herpes virus subfamily which targets mainly CD4 T cells and is a well-known cause of roseola infantum. Fever without roseola, encephalitis and hepatitis however are not uncommon. More severe clinical cases are commonly observed in immune compromised patients.

Case: An 11-month old girl, with a 24-hour fever and poor appetite, was treated with Amoxicillin/clavulanic acid at a clinic on arrival. The following day, the patient continued to experience high fever, hematemesis and a tendency to sleep and therefore was hospitalized. Lab results showed thrombocytopenia, and alanine aminotransferase was over 3000U/L, INR was 2.5 and urea and creatinine were elevated at 75mg/dl and 1.1mg/dl, respectively. Serum electrolytes, blood glucose and calcium levels were normal. Ceftriaxone and teikoplanin were started. Due to persistent high fever and somnolence, a lumbar puncture was performed. The cerebrospinal fluid was clear of any cells; protein and glucose were within normal range. Acyclovir was added to the treatment. With four organ dysfunctions, the central nervous, hematologic, renal and hepatic systems, the girl was transferred to the PICU. Organ functions were normalized in a week with supportive treatment. Test results were positive for HHV-6 DNA at CSF; serum, lymphocytes, other viral markers, and bacterial cultures were negative.

HHV-6 is a benign virus that very rarely causes severe infection and hardly ever leads to a fatal infection. However in the current literature there is no previous report of MODS due to the HHV-6 virus in a healthy child.

NEUROLOGICAL MANIFESTATIONS IN ACUTE ONSET OF VIRAL (ROTA & ADENO) GASTROENTERITIS**S. Noorbakhsh**, F. Ehsanipour, H.R. Monavari, A. Eizadi, A. Tabatabaei*Research Center of Pediatric Infectious Diseases, Tehran University of Medical Sciences, Tehran, Iran***Objective:** to evaluate the prevalence of neurological manifestations in acute onset of viral gastrointestinal.**Methods:** A cross sectional /descriptive study performed upon 50 children admitted due to acute viral gastrointestinal infections in Department of pediatric Infectious Disease, Rasul Hospital, Tehran, Iran, 2010-2011. Initially, a questionnaire was completed by an authorized physician for each case (eg age, gender, clinical signs, vomiting, diarrhea (type, time of onset, frequency) , attending time from onset ,type of neurologic symptoms ,analysis of lab test (stool direct exams, biochemical parameters, stool culture, direct viral test in stool). All cases with bacterial or other known causes (except viral causes) for gastroenteritis ,chronic diarrhea excluded from study. The studied cases were evaluated for existence of neurologic signs .Stool samples were searched for viral antigens (Rota & Adeno virus) by Rapid immunochromatographic test. P-values less than 0.05 were considered statistically significant.**Results:** neurological manifestations reported in 16% of cases included seizure=12%; aseptic meningitis= 4%. **20% of adenoviral, 13.5% of rota virus and 33.3% of biinfection had neurologic signs, with no differences.** (P=0.619) Mean age of cases had not significant difference between cases with and without neurologic manifestation. There was no significant association between neurological symptoms with age (P=0.755), sex, virus type, and attending time (P > 0.05).**Conclusions:** We concluded that one out of six children with acute onset of acute viral GE would develop neurological symptoms that is usually as seizure and is not related to age, sex, virus type, and attending time.

DETECTION OF REACTIVATED EPSTEIN BARR VIRUS VIREMIA BY PLASMA EBV-DNA REAL TIME POLYMERASE CHAIN REACTION FROM IMMUNOCOMPETENT KOREAN CHILDREN

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Purpose: Latent Epstein Barr Virus (EBV) infection can be reactivated by various conditions, such as concomitant infections, or transient immunosuppression. The diagnosis of EBV reactivation has been dependent on the results of serologic tests. However, the detection rate is usually low. We used cell-free plasma EBV-DNA real time quantitative polymerase chain reaction (RT-qPCR) in this study.

Methods: A total of 8 samples of patients, whose anti-EBV Ab profiles showed past EBV infection by positive EBNA, was confirmed as having EBV viremia by RT-qPCR with EBV BALF5 gene sequence. We examined the clinical characteristics of EBV reactivation by medical record review.

Results: All cases showed elevated liver enzymes. Five of 8 cases revealed hepatitis A(HAV) co-infection by positive HAV IgM. One case was Mycoplasma co-infection, diagnosed by positive Mycoplasma IgM. One case was diagnosed as Mycoplasma and Rotavirus co-infection diagnosed by positive Mycoplasma IgM and direct detection of rota viral antigen. One case was hemophagocytic lymphohistiocytosis due to EBV reactivation caused by scrub typhus. Both EBV VCA IgM and IgG were positive in 4 cases. Only EBV VCA IgG was positive in 2 cases. Neither EBV VCA IgM nor IgG was positive in 2 cases.

Conclusion: Our data suggest that the plasma EBV PCR may be useful in the detection of reactivated EBV viremia regardless of EBV Ab profile. Potent immunogenic infections such as HAV, mycoplasma and scrub typhus can reactivate the latent EBV infection even in immunocompetent children. Detecting EBV viremia could help clinicians to avoid unnecessary work up.

PICU VERSUS NON-PICU RSV MORBIDITY: SEASONALITY AND IMPLICATIONS FOR PROPHYLAXIS**K.L.E. Hon**, T.F. Leung, P.K.S. Chan*The Chinese University of Hong Kong, Hong Kong, Hong Kong S.A.R.***Objectives:** We investigated factors associated with morbidity and pediatric ICU (PICU) admission in children with RSV infection, and explored seasonality and implication of prophylaxis.**Methods:** Retrospective study between 2006 and 2008 of every child with a laboratory-confirmed RSV infection.**Results:** 670 RSV admissions were identified. 10 (1.5%) required PICU admissions. Children admitted to PICU were younger than non-PICU admissions (Median [IQR] age = 0.3[0.11-0.48] versus 1.18[0.46-2.49] years, $p=0.001$). Odds associated with PICU admissions included history of chronic lung disease (OR [95% CI]: 18.08 (2.29-114.95), $p=0.010$), history of acyanotic heart disease (7.61[1.04-42.59], $p=0.043$), and neurodevelopmental conditions (mental retardation, cerebral palsy or neuromuscular disease; 8.41[1.63-38.57], $p=0.012$). Odds of bacterial co-infections was 13.50[1.77-81.29], $p=0.017$. There appeared no significant PICU predilection in terms of gender, history of prematurity, cyanotic heart disease, seizure disorders, chromosomal disorders or malignancy. RSV infections accounted for 2.4% of PICU annual admissions. Median length of hospital stay was significantly longer in the PICU category (8.5 versus 3 days, $p<0.001$). There was no death in the study period. 3% admissions involved neonates < 30 days of age. Incidence was lowest between October and January.**Conclusions:** Majority of infants has mild disease and do not require PICU support. Young infants with history of chronic lung disease, congenital heart disease and neurodevelopmental conditions appear to be at significantly increased risk for PICU support. There is no winter seasonality for RSV disease in Hong Kong. Therefore, any prophylaxis for at-risk population should provide adequate coverage for the warmer months in subtropical regions.

PATTERN RECOGNITION RECEPTOR RESPONSES IN CHILDREN WITH CHRONIC HEPATITIS B VIRUS INFECTION

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Background: Several studies have demonstrated that Hepatitis B virus (HBV) affects the expression and function of Toll like receptors (TLRs), but data on TLR function in HBV infection are mainly from adult patients. The natural history of chronic hepatitis B (CHB) infection is distinctly different in children, since 90% of children become chronic carriers compared to 5% of adults when infected with HBV. We have studied the function of TLRs and cytosolic DNA receptors in children with CHB infection compared to healthy children.

Methods: PBMCs from 19 children with CHB and 19 healthy children were stimulated with ligands for TLR 2,3,4,7 and 9 for 24 hours. For activation of cytosolic DNA receptors, cells were transfected with a double-stranded DNA using Lipofectamine 2000. Supernatants were analyzed for levels of IFN- α , TNF- α , IL-6, CXCL10 and CCL3 by Luminex.

Results: Stimulation with ligands for TLR2, TLR3 and TLR9 induced IL-6, CCL3 and CXCL10 to a significantly higher level in children with CHB compared to healthy children. CHB patients displayed significantly lower IFN- α production compared to healthy children after stimulation with ligands for TLR2, TLR3 and TLR4. Stimulation of intracellular DNA sensors with synthetic double-stranded DNA elicited significantly higher induction of the inflammatory cytokines and chemokines IL-6, TNF- α and CCL3 in the CHB patients as compared to the healthy children.

Conclusion: Our results indicate a TLR-mediated inflammatory response in children with CHB infection. Furthermore, our study is the first to show that the responses of intracellular DNA receptors are affected in CHB.

MYOCARDITIS AFTER HHV6 INFECTION?**A. Beyersdorff**¹, S. Armbrust¹, K. Schulz², R. Bruns¹¹*Department of Paediatrics University Hospital, ²Institute of Medical Microbiology University Hospital, Greifswald, Germany***Introduction:** HHV6 (human herpesvirus 6) causes roseola infantum and other febrile childhood diseases. Here HHV6 was found at serious myocarditis.

1: Boy, 19 month, no history. Since 1d cough, peripheral hospital - echocardiography: global heart insufficiency, PICU admission.

Sudden rise of oxygen need (100%), intubation, mechanical ventilation, relaxation, positive inotrope therapy and afterload reduction. Drainage of pleural effusion bilateral. Reduced urine output even under high support, development of lung oedema. Worsening ventilation and circulation parameters under maximum support. Transferral under this conditions not possible. Reanimation and maximum support, death 9h after arrival.

Autopsy: Fulminant lung failure with membrane damage, oedema, bleeding, pneumonia, otitis. Main cause massive myocarditis with heavy load of Parvovirus B19 and HHV6 in the myocardium.

2: Boy, 3 month, ASD II. Rhinitis since 2d. Sudden cyanosis, insufficient breathing on arrive of rescue service, somnolent, stridor with inspiration - inhalation, oxygen application, saturation 100%. On arrive of emergency physician stable, sufficient breathing, admission to PICU. There self breathing, good saturation. X-ray mild central infiltrations. After 30 min sudden decompensation and respiratory failure, intubation, mechanical ventilation. Antibiotic therapy with ampicillin/ sulbactam. Echocardiography - large dilatation of left ventricle, massive pump dysfunction. Positive inotrope therapy and reduction of afterload, some stabilisation but no improvement. Transport to heart centre. Detection of HHV6 in myocard biopsy.

Conclusion: Both cases show massive myocarditis with sudden onset in previous healthy children. HHV6 could be found in both which seemed to be the leading cause in addition with Parvovirus B19 in the first case.

SAFETY AND PHARMACOKINETICS OF OSELTAMIVIR FOR PROPHYLAXIS OF NEONATES EXPOSED TO INFLUENZA H1N1**H. Maltezos**¹, N. Drakoulis², T. Siahaidou², V. Karalis², E. Zervaki², Y. Dotsikas², Y. Loukas², M. Theodoridou²¹*Hellenic Center for Disease Control and Prevention*, ²*University of Athens, Athens, Greece*

Neonates are at increased risk for serious illness and complications following influenza, however pharmacokinetic studies on oseltamivir prophylaxis in this age group are missing. The aim of this study is to investigate the pharmacokinetics of oseltamivir prophylaxis at 1.0 mg/kg b.i.d, for 10 days to neonates exposed to influenza A H1N1. A total of 13 neonates with a median chronological age of 15 days and a median weight of 3565g were prospectively studied. Plasma samples were analyzed with an improved LC-MS/MS protocol. A population pharmacokinetic model was developed and pharmacokinetic parameters were estimated. No neonate developed influenza. Four neonates developed gastrointestinal symptoms during the follow-up period. No neurologic, hematologic, renal, or hepatic adverse effects or rash occurred among them. The mean C_{max} values for oseltamivir and oseltamivir carboxylate were found to be lower than those reported for children 1-5 years old, while T_{max} values were in accordance. Age and gender were found to affect significantly oseltamivir clearance. The volume of distribution of the carboxylate metabolite was equal to the extracellular fluids. In conclusion, our data demonstrate that neonates can metabolize oseltamivir. In this age group, oseltamivir at 1.0 mg/kg b.i.d. for 10 days appears to be safe for prophylaxis against influenza. First estimates for the pharmacokinetic parameters are derived. Further prospective studies with large number of patients are needed.

PREVALENCE OF VIRAL HEPATITIS B IN CHILDREN UNDER 5 YEARS IN COTE D'IVOIRE

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Background and aims: Viral hepatitis B is a public health problem in our country. The fight goes through vaccination and administration of Immunoglobulins against hepatitis in newborns of AgHBs positive mothers. However, Côte d'Ivoire, as in other African countries, where since 2003, the hepatitis B vaccine was introduced from 6 weeks into the Expanded Program Immunization, the Immunoglobulins against hepatitis are not available. This study aims to improve the prevention of viral hepatitis B in children under 5 years. The specific objectives are:

- Determine the seroprevalence of viral hepatitis B in children under 5 years
- Determine the immunization coverage against Hepatitis B
- Identify the elements of hepatitis B vaccine efficacy
- Identify risk factors associated with viral hepatitis B

Methods: This cross-sectional study began since October 2011 and will end in March 2012. It concerns 250 children aged from 9 months to 5 years who came in Paediatric Consultation at Cocody University Hospital or at General Hospital of Jacqueline. The sera obtained from venous blood samples are sent to the Pasteur Institute of Côte d'Ivoire for the detection of viral markers of hepatitis B (HBsAg, antiHBc total Ac, Ac antiHBs, HBeAg) by ELISA and markers of HIV by rapid tests like in national algorithm.

Results: Preliminary results are about 86 children with 45.3% (39) of male. The average age is 23.6 months. The seroprevalence of HBsAg was 8.1% (7 / 86) with female predominance.

Conclusions: Seroprevalence of viral hepatitis B among children remains high in our country.

HERPESVIRUS INFECTIONS IN PAEDIATRIC ONCOLOGY PATIENTS WITH EPISODES OF FEVER UNKNOWN ORIGIN (FUO)**D.T. Catalan¹, S.D. Passos², S.C.B. Costa¹, S.H.A. Bonon¹***¹Internal Medicine, University of Campinas, Campinas, ²Paediatric Infectious Diseases, GRENDACC, University of Jundiaí, Jundiaí, Brazil*

Patients with malignancies have periods of severe neutropenia and are particularly vulnerable to infectious complications. The treatment with chemotherapy and the underlying disease promote greater depletion of immune system. Most episodes with febrile neutropenia are treated with empiric broad-spectrum antibacterial therapy without identifying the site of infection or agent, such as fever unknown origin (FUO). Through the conventional diagnostic methods a small number of aetiologic agents are identified, blood cultures are usually negative and time-consuming to identify the source of infection. Given the urgency of care to cancer patients and fever necessitates rapid diagnosis of infections in these particular cases. In order to promote higher accuracy in the identification of pathogens in these patients, the search for news laboratory tests is important. The aim of this study is to identify active infections caused by herpesvirus (EBV, CMV, HHV-6 and HHV-7) in paediatric oncology patients experiencing episodes of fever. 160 samples of whole blood and serum collected from patients with episodes of fever were analyzed using nested-PCR methods and cytomegalovirus was analyzed by antigenemia and N-PCR. Active infection caused by Epstein-Barr virus occurred in 4/160 (2,5%); Cytomegalovirus 11/160 (6,9%); HHV-6 17/160 (10,6%) and HHV-7 32/160 (20,0%). This results shows that active infections caused by EBV, CMV, HHV-6 and HHV-7 are frequent in children receiving cancer treatment, representing high prevalence this cases of fever, with or without neutropenia. Further studies with news methods how the introduction quantitative PCR are needed to identify other virus, bacterial and fungal pathogens.

Financial Support: FAPESP.

DETECTION OF EMERGING VIRUSES IN CHILDREN WITH ACUTE GASTROENTERITIS IN PATRAS, GREECE

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Background and aims: A one-year study (2009-2010) of paediatric diarrhoea was performed on hospitalised children admitted with symptoms of acute diarrhoea to the University Hospital of Patras, Greece.

Methods: Faecal samples were investigated for rotaviruses (RV), adenoviruses (hAdV), and enteroviruses (EV), in an attempt to characterize the enteric viruses, implicated in diarrhoea.

Results: A 44.8% (13/29) incidence of viral infection was reported for the viral targets on these cases. Sequencing of positive samples allowed identification of adenovirus types 1 (hAdV1), 2 (hAdV2) and 6 (hAdV6), at 4/29, 1/29 and 1/29, respectively. Regarding the EVs, Enterovirus 71 (2/29), Coxsackievirus A4 (1/29), Echovirus 11 (1/29), and Enterovirus 96 (1/29) were identified. Rotaviruses G4 (2/29), G9 (1/29) and G12 (2/29) were also characterized.

Conclusions: The results of the present study and specifically the detection of RV G12 and EV71 strains, address the need for continuous epidemiological surveys of circulating virus strains to investigate if uncommon strains or newly strains are emerging, and to provide epidemiological pictures of pediatric infections circulating in the community.

FIRST EXPERIENCES WITH CMX001 IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) RECIPIENTS WITH REFRACTORY DOUBLE- STRANDED DNA VIRUS INFECTIONS

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Background and aims: CMX001, hexadecyloxypropyl-cidofovir, is a new oral antiviral active against double-stranded DNA viruses. So far it is available for compassionate use only. We describe our experience in 3 female pediatric allogeneic hematopoietic stem cell transplantation (alloHSCT) recipients.

Methods: Retrospective review of medical records.

Results:

Patient 1 (8 months) has hereditary Hemophagocytic Lymphohistiocytosis (HLH) syndrome and prolonged CMV infection as possible trigger of HLH. Intermittent CMV PCR negativity was achieved by long term pre-emptive CMV- therapy (ganciclovir, CMV- Hyperimmunoglobulin, foscarnet) and successfully maintained by CMX001 during alloHSCT course. After CMX001 cessation CMV levels promptly rose to $2,1 \times 10^2$ copies/ μ l.

Patient 2 (8-years) and patient 3 (23-years) underwent alloHSCT for severe aplastic anemia.

Patient 2 developed BKV associated painful hemorrhagic cystitis leading to prolonged hospitalization, impaired kidney and bladder function. Initial BK-viruria was above 10^7 copies/ μ l dropping gradually to zero within 2 weeks of CMX001 treatment.

Patient 3 developed graft vs. host reaction, graft failure and atypical hemolytic uremic syndrome paralleling HHV-6 reactivation. After start of CMX001 treatment HHV6 load decreased from $4,1 \times 10^4$ copies/ μ l to $5,3 \times 10^2$. The patient denied further treatment after one month and HHV6 levels rose to $3,5 \times 10^5$ immediately.

CMX001 dosage in all three patients was 4mg/kg twice weekly administered orally. No specific side effects were registered.

Conclusion: Although our observations are difficult to interpret due to co-treatment, different viral agents and lack of controls, CMX001 seems to be a promising treatment option for infections with different DNA viruses in severely immunocompromised pediatric patients.

POLYOMAVIRUS INFECTION IN CHILDREN WITH RENAL TRANSPLANTATION, EXPERIENCE IN 450 CASES

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Introduction: BK Virus (BKV) belongs to the polyomavirus family of double stranded non-enveloped DNA viruses.

BK virus nephropathy (BKN) is a cause of renal transplant dysfunction, especially in patients with high dose immunosuppression. Herein we present our experience in BK Virus infection and nephropathy in renal transplant children in Labbafinejad Hospital.

Material and method: Between January 1985 and November 2011, 450 kidney transplantations were performed in children under 15 years in Labbafinejad Hospital Tehran. Immunosuppressive medications consist of prednisolone, Cyclosporin A and Mycophenolate Mofetil (Cellcept). Eleven patients received Basiliximab (Simulect) as adjunct induction therapy.

BK Virus was tested in 104 urine samples from 74 transplant patients who were in regular follow-up by Polymerase Chain Reaction (PCR) and in blood if patient was symptomatic. Decoy cells were also tested in symptomatic patients.

Results: BK Virus particles were detected in 21 transplant children (28%) (20 in urine and one only in Blood) of whom 3 patients had Decoy cells in urine and a dramatic rise in plasma creatinine (BKN: 4%). PCR examination of blood for BK Virus was tested in 38 patients and was positive in only 4 of these patients.

Immunosuppressive medications were reduced as first step of treatment for 4 patients with BKN, it was effective in 3 patients presenting with reduction of plasma creatinine. Cidofovir was used for third patient which was partially effective leaving a plasma creatinine of 1.9 mg/dl.

Conclusion: BK Virus Nephropathy should be considered as a cause of each allograft dysfunction in transplant children.

THE EVALUATION OF HOSPITALIZED CHILDREN WITH VARICELLA AND ITS COMPLICATIONS IN A TRAINING HOSPITAL

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Zeynep Kamil Maternity and Children Research and Training Hospital, Istanbul, Turkey

Aim: Varicella is a common childhood disease in non-vaccinated populations. The aim of this study was to evaluate retrospectively the data of children with varicella and its complications.

Material and method: The hospital records of 63 children with varicella and its complications between January 2006 -December 2010 were reviewed. Age, gender, time of hospitalization, type of complication, duration and cost of hospital stay, treatment options were assessed.

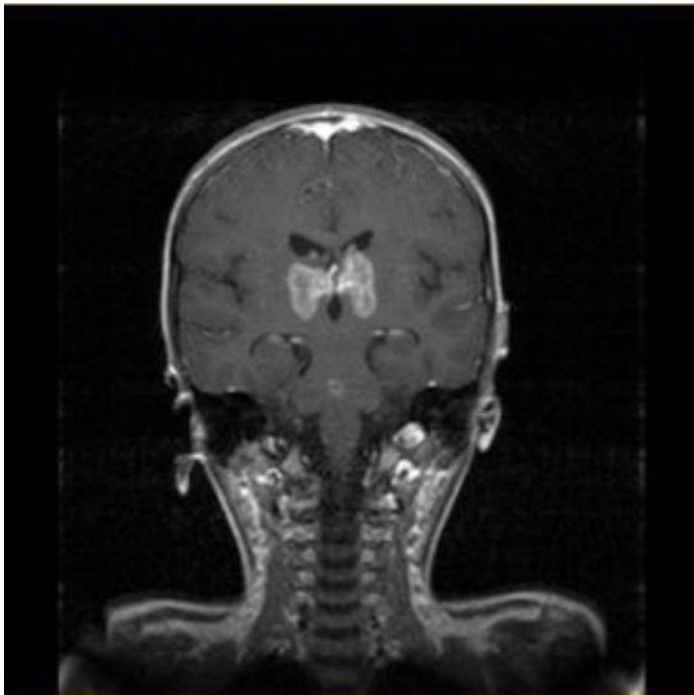
Results: Out of 63 children, without varicella vaccination, 60.3 % were boys. The mean age was 37.8±41.6 months, mean hospital stay was 8.4±6 days. The peak hospitalization rate was in 2007 (38.1%) and during spring (38.1%). The most common complication was due to respiratory system involvement(41.3%) followed by secondary skin infections(17.4%) and neurologic complications(15.9%). Patients ≥6 years stayed longer in hospital than other age groups ($p < 0.001$). The mean duration of acyclovir treatment and antibiotherapy were 5.1±3.9 days and 6.7 ±4.1 days, respectively. According to complication groups significant differences were observed in acyclovir treatment, antibiotherapy and duration of hospital stay ($p=0.018$, $p=0.01$, $p=0.01$, respectively) but no difference in the cost ($p=0.19$). The cost of a patient's day was calculated as 75,32 TL(48.59 \$- 58.38 \$). The mean cost per patient was 444,68±447,34\$ in 2006, 467,92±414,38\$ in 2007, 428,60±325,73\$ in 2008, 613,29±603,09\$ in 2009, 400,33±395\$ in 2010.

Conclusion: Varicella and its complications cause significant morbidity with high hospitalization rates and costs. We think a varicella vaccination program in Türkiye will be beneficial in order to reduce the hospitalization rates and costs.

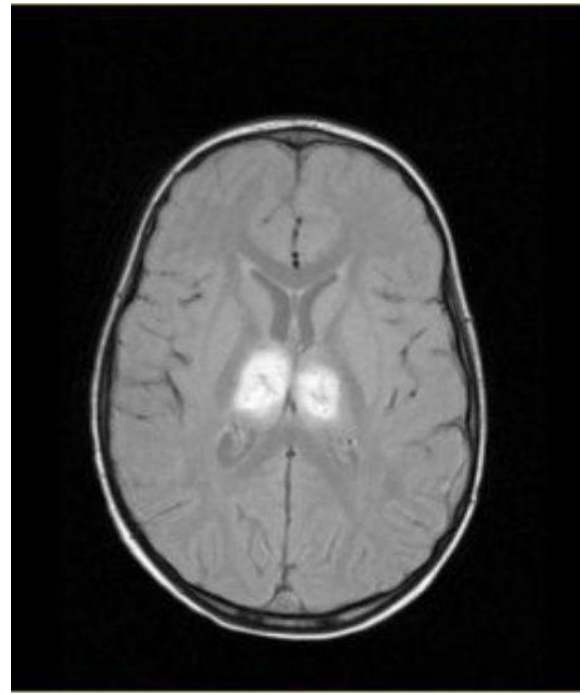
ACUTE NECROTIZING ENCEPHALOPATHY ASSOCIATED WITH H1N1 INFLUENZA INFECTION IN A CHILD**F. Khodapanahandeh***Pediatrics, Tehran University of Medical Sciences, Hazrat-e Rasul-e Akram Hospital, Tehran, Iran***Aims:** To report unusual neurological manifestation of influenza A H1N1 virus infection in a child.**Methods:** Case report

Case: A 4-year-old boy admitted to the hospital because of fever and focal seizures. The patient had been well until approximately 2 days earlier, when he developed a febrile illness with malaise, cough and abdominal complaints. His temperature measured up to 39.5°C. He was given acetaminophen. The following day he experienced persistent high fevers, focal seizures and decreased level of consciousness. He was referred to our hospital. Emergent Ct-scan on admission showed abnormal bilaterally symmetric heterogeneous attenuation in the thalami.

Lumbar puncture that had been performed in the first hospital was normal. The patient was intubated, supportive care, treatment with anticonvulsive, acyclovir and oseltamivir started but no acute improvement was noticed. Contrast-enhanced MR imaging demonstrated bilateral hyperintense lesions and focal necrosis in both thalami (Fig 1). Treatment with high dose corticosteroid and IVIG was not effective. Plasmapheresis improved patient's situation and level of consciousness gradually returned to normal. Real-time PCR of the nasopharyngeal swab for influenza A H1N1 virus was positive. Patient discharged from the hospital with moderate neurologic deficit.



[fig1 a]



[Fig1 b]

Conclusion: Although influenza is a relatively benign illness in the majority of healthy children, physicians should be aware of ANE and should maintain a high degree of clinical suspicion in any child presenting with acute mental status changes in the setting of influenza infection.

VARICELLA ZOSTER VIRUS INFECTION OCCURS AT YOUNG AGE IN THE NETHERLANDS

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Background: For varicella zoster virus (VZV) vaccination strategies the age of infection is very relevant since the risk on varicella complications rises with age. A cross-sectional serosurveillance study in 1995/1996 (Pienter-1) showed that the Dutch population is infected at relatively young age. A second study provided the opportunity to investigate this notable finding further.

Methods: In February 2006-July 2007, a second cross-sectional serosurveillance study (Pienter-2) was conducted among Dutch inhabitants aged 0-79 years within 40 municipalities throughout the country; 6386 blood samples were collected. Serological testing was performed with a bead-based multiplex immunoassay (Luminex technique). In Pienter-1 a VZV IgG ELISA kit was used.

Results: In Pienter-2, the total seroprevalence of VZV antibodies among persons aged 0-79 years was 94.6% (95%CI 93.2-96.0). In Pienter-1 the total seroprevalence was 95.6% (95%CI 94.9-96.3). The seroprevalence increased sharply with age in the Pienter-2 study: 1 year 27.9%, 2 year 52.3%, 3 year 69.8%, 4 year 77.8% and 5 year olds 84.7% which was comparable to Pienter-1: 18.4%, 48.7%, 59.0%, 75.7% and 93.0%. Furthermore, after the age of 20 years the geometric mean concentration of VZV antibodies was significantly lower for women than for men.

Conclusions: The Pienter-2 study confirmed the young age of VZV infection in the Netherlands which could be a plausible explanation for the lower reported disease burden due to varicella compared to other European countries. The lower geometric mean concentration for women above 20 years of age might be an explanation for the higher incidence of herpes zoster among women.

UTILITY OF RESPIRATORY VIRAL PCR IN LIMITING THE USE OF ANTIBIOTICS IN CHILDREN

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Background and aims: We examined the utility of respiratory viral PCR in limiting the use of antibiotics in confirmed viral respiratory infections in children.

Methods: The survey was done during the peak winter period in the UK. Our hospital sends respiratory samples for polymerase chain reaction (PCR) to a neighbouring Virology reference laboratory whose turnaround time is 56hours (excluding transportation times).Patients' clinical details were obtained retrospectively from case notes. Viral PCR results were matched by dates with antibiotic and other laboratory information.

Results: 19 inpatients (10 males and 7 females), aged 5 days to 17 months, had positive viral PCR of their nasopharyngeal aspirates. Case notes of two patients were missing and therefore only 17 patients were analysed. Viruses detected were respiratory syncytial virus, rhinovirus, adenovirus and coronavirus, some of which were mixed. Eight patients received antibiotics as monotherapy, in combination or as added on therapy, duration ranging from 3-10 days (mean of 6.5 days).

Conclusion: It can be argued that most, if not all, of our patients who received antibiotics would not have had more than 3 days of antibiotics if the viral PCR results were promptly available. There is a case therefore for viral PCR to be made more widely available as a tool for antibiotic stewardship as clinical features for viral respiratory infections cannot be entirely relied on. Obviously, this would significantly cut down on the turnaround times, which would render the tests more clinically useful in limiting the use of antibiotics at district general hospitals.

SUCCESSFUL TREATMENTS OF TWO CHINESE CHILDREN INFECTED HIGHLY PATHOGENIC AVIAN INFLUENZA A (H5N1) VIRUS AND FOLLOW-UP

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Objective: A large-scale avian influenza had been transmitted in several provinces of Mainland China between October 2005 and February 2006. During the period, two boys infected highly pathogenic avian influenza A (H5N1) virus confirmed by serologic analysis were successfully treated in our hospital. To summarize their clinical features, diagnostic and therapeutic strategies, and provide effective experiences for physicians in prevention and cure of human avian influenza in future.

Methods: To analyze on their clinical and following up data, and summarize the therapeutic strategies.

Results: One 9-year-old boy with fever and dry cough, on day 7 after onset, his body temperature reached 40°C, accompanying large-areas lung consolidation, decreased peripheral blood leukocyte counts and most neutrophilic granulocytes. After therapies with amantadine and glucocorticoid, his body temperature returned to normal on day 3 after admission, the inflammatory on lung began to change and lung fibrosis was obviously absorbed on day 5, leukocyte counts became normal on day 6 and no complication, he discharged on 25 days. Another 6-year-old boy with high fever, cough, polypnea, left lung consolidation, less hemogram, after therapies with short-term symmetrel and ribavirin, low-dosage glucocorticoid for 4 weeks and CPAP assistant ventilations, his hemogram raised, lung pathological changes began to appear gradually, left lung fibrosis started to be absorbed on day 7 after admission, obviously appeared at day 16, his breath function and internal organs functions became better, patient discharged on day 46.

Conclusions: Children's successful treatments attributed to timely discovery, promptly diagnosis and effectively treatments of antiviral drugs.

ASSOCIATION OF ACUTE HEPATITIS E INFECTION AND AMINOTRANSFERASE LEVEL IN MAJOR B-THALASSEMIA CHILDREN. JAHROM, IRAN

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Background and aims: The hepatitis E virus (HEV) has a global distribution and is known to have caused large waterborne epidemics of icteric hepatitis. Transmission is generally via the fecal-oral route. Some reports have suggested parenteral transmission of HEV. There are not prevalence data of HEV among β -thalassemic patients in IRAN. The aim of this study was to determine the prevalence of anti-HEV antibodies in β -thalassemic patients in west-southern of Iran.

Methods: This descriptive and cross-sectional study was conducted in March of 2008. We tested 110 β -thalassemic patients attending the thalassemic unit in the city of Jahrom, west-southern part of Iran, for anti-HEV IgM using enzyme-linked immunosorbent assay (ELISA). Aspartate aminotransferase (AST) and Alanin aminotransferase (ALT) levels were determined by Spectrophotometric methods.

Results: The overall seroprevalence of hepatitis E was 1.8%. Significant association was found between anti-HEV IgM positivity and ALT and AST levels.

Conclusions: Observed high anti-HEV antibody prevalence was lower than its prevalence in other countries. There was no association between HEV and blood borne infections (HBV, HCV, and HIV) in our β -thalassemic patients.

PEDIATRIC PATIENTS HOSPITALIZED WITH PANDEMIC INFLUENZA A/H1N1 INFECTION: A 2 YEAR RETROSPECTIVE STUDY

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Background and aims: The pandemic influenza A/H1N1 infection was first identified in the spring of 2009 worldwide. It caused severe illness and death in patients. As a result, it strongly problematized clinicians and researchers. This study aims to report incidence, clinical features and outcomes of the disease among hospitalized pediatric patients of Hellenic population.

Material and method: We conducted a two year, monocentered, retrospective study. We searched medical records, laboratory and radiologic findings of all the children that were admitted to our pediatric clinic of a general 3rd level hospital since 2009-outbreak of the disease- till 2011, because of clinical features of H1N1 influenza. Examination of naso-pharyngeal specimen, chest radiographs and blood tests were performed to all hospitalized children, suspected of H1N1 infection.

Results: A total of 136 children were admitted to hospital on suspicion of influenza A/H1N1 infection from 2009-2011, with ages from 6 months old up to 13 years. In 22 children, radiographic evidence of pneumonia was indicated. Moreover, 1 child developed haemolytic uraemic syndrome, in 2 diarrhoea syndrome was occurred, 2 were identified with seizures and in one patient there was a very low white blood count. One child had to be transferred to an intensive care unit for further treatment. No deaths were occurred.

Conclusion: No significant differences in age or sex were identified among infected children as far as severity was concerned. However, it is worth-noticing that there was a high incidence of children that were affected by A/H1N1 influenza pneumonia, in a per cent of 16.18%.

TOXIC EPIDERMAL NECROLYSIS SYNDROME IN A CHILD ASSOCIATED WITH VARICELLA ZOSTER VIRUS INFECTION

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Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening drug reactions considered to be part of the spectrum of a single pathological process. The SJS/TEN complex is a true dermatological critical condition that also affects children. Any drug can be the causative agent, more frequently anticonvulsants and antibiotics. Varicella-zoster infections were rarely reported to be associated with SJS/TEN on the contrary to his close relatives, herpes-zoster viruses.

Patients: We describe a 13 month-old-male; who had developed TEN after having varicella infection. The TEN diagnosis based on the confluence of cutaneous lesions leading to detachment from 30% of the body surface area; mucosal membrane involvement; histopathological examination of lesional skin showing full-thickness epidermal necrosis. The patient was diagnosed as varicella zoster infection due to the seropositivity of IgM antibody and the tzanck smear. The patient had full recovery with intravenous immunoglobulin treatment.

Conclusion: Within this case report, we suggest that the association VZV infection with TEN is more probably than reported before; and in case of possibility of TEN; skin biopsy should be performed in varicella infections.

NON-PULMONARY MANIFESTATIONS OF THE NOVEL H1N1 INFLUENZA IN CHILDREN

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Introduction: A novel reassortant strain of influenza A (H1N1) virus containing swine, avian, and human elements emerged in Mexico in March 2009. Influenza-related neurological complications (INC) are diverse and of variable severity and outcome. Febrile seizures, aseptic meningitis, acute and post-infectious encephalopathy/encephalitis, Reye syndrome, Guillain-Barré syndrome, stroke or decompensation of an underlying neurological disorder have been previously reported.

Aim: To review three cases of non-pulmonary novel influenza H1N1 in children. **Case reports:** We reviewed three cases of novel H1N1 influenza in children, without severe pulmonary complications. First patient was admitted to the Pediatric Intensive Care Unit having epileptic status without fever. Second child was admitted with epileptic status and high fever. The third patient was admitted with clinical signs of fulminant encephalopathy. All cases were verified as novel H1N1 influenza.

Conclusion: Although the majority of symptoms linked to H1N1 influenza are related to the respiratory system, a large amount of children had experienced non-pulmonary complications. Out of these, the most severe are neurological complications, because of the severity of the clinical presentation, and also because if not recognised as H1N1 related symptoms can easily lead to unwanted resolution of the disease, even death.

ACUTE EPSTEIN BARR VIRUS INFECTION IN CHILDREN COMPLICATED WITH ACUTE LIVER FAILURE - CASE PRESENTATION

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Background and aims: Acute infection with Epstein Barr virus (EBV) is a self-limited illness specific for children and adolescents, sometimes accompanied by complications. Acute hepatitis is one of the most frequent complications of infectious mononucleosis. There are extremely rare cases where infectious mononucleosis is complicated with cholestasis and acute liver failure.

Methods: In this article we present the clinical case of a 9 years old boy admitted in our unit for fever, loss of appetite, odynophagia, dysphagia, abdominal pain, jaundice, dark urine, pale stools. In clinical examination we discovered that the patient presented malaise, fever, intense jaundice, poliadenopathy, purpuric rash, tonsillitis, hepatosplenomegaly, sensitive abdomen.

Results: Laboratory investigations confirmed acute infection with EBV complicated with severe cholestasis and liver failure. Blood count showed leukocytosis with lymphomonocytosis, thrombocytopenia and anemia. The patient receives treatment with dexamethasone, fresh frozen plasma, infusion for rebalancing, liver trophic. After 3 weeks of evolution the general status improves, and the child leaves the hospital without fever and subjective complaints, cardio-respiratory balanced, without digestive symptoms but with moderate jaundice. The laboratory investigation tests at discharge showed slightly elevated ALT, direct bilirubin, γ -GT and serum cholesterol. The evaluations after one month and then after 6 months from discharge showed that the patient was fully recovered and laboratory tests were within normal limits.

Conclusions: Infectious mononucleosis is a self-limited disease in most cases, but in the presented case, we have showed that complications may appear, like acute liver failure, which is in itself severe and needs appropriate treatment.

CLINICAL COURSE OF H1N1 VIRAL INFECTION IN CHILDREN AND ADOLESCENTS WITH HAEMOGLUBINOPATHY

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Background: Some population groups are considered of high risk when affected by H1N1 influenza A virus and early vaccination against the virus was recommended. Patients with haemoglobin diseases are considered one of them.

Aim: Recording of the patients with haemoglobinopathy that were infected by H1N1 and were hospitalized, their manifestations and the severity of the disease.

Methods and results: 40 children with haemoglobin disorders are being treated regularly in our hospital. 6 of them (4 boys and 2 girls) were infected by H1N1 virus as confirmed with PCR examination. Three children, 2.5-18 years old, with hemoglobinopathy H, one (10 years old) with heterozygous β thalassemia intermedia and two (12.5, 16 years old) with homozygous β thalassemia major are treated with blood transfusions on tactical basis. All of the children had high grade fever lasting from 2-5 days and upper respiratory tract symptoms with unremarkable findings in lung auscultation or in chest x-ray. In a thalassemia and heterozygous β thalassemia intermedia patients, the hemoglobin level decreased by 1-2 units and were not transfused. In major homozygous anemia patients, blood transfusion was performed on day three and seven. One developed a positive indirect Coombs test which lasted two months, with no need for further transfusions. None experienced complications from other systems. The patients received prophylactic antibiotics but no anti-viral agents were administered.

Conclusions: haemoglobin patients yield a favorable clinical course similar to that of the non hemoglobinopathy counterpart without remarkable complications.

HOSPITALIZATION OF CHILDREN WITH INFLUENZA A (H1N1) VIRUS IN CORFU DURING THE 2009 OUTBREAK IN GREECE

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Background: The disease burden of seasonal influenza in the pediatric population is generally attributed to a combination of immunologic naivety, prolonged virus shedding, and enhanced transmission opportunity in child-care and educational institutions.

Aim: To describe the clinical characteristics of children hospitalized with 2009 influenza A H1N1 infection in General Hospital of Corfu.

Methods: We reviewed the medical reports of 14 children with pandemic H1N1 Influenza A hospitalized to the pediatric clinic of General Hospital of Corfu between July to December 2009.

Material: All patients were laboratory-confirmed with 2009 influenza A (H1N1). The most frequent clinical presentations were influenza-like illness and wheezing exacerbation. Predisposing underlying illnesses were detected in 3 of the patients who have viral-induced asthma. Pneumonia diagnosed in 3 of all patients of whom 2 had a history of viral-induced asthma and the third was infant. More than two_ thirds received combination of antiviral and antibacterial treatment. The median length of stay in hospital was 2,6 days. None of the children died or need admission in intensive care unit.

Conclusions: Despite the fact that 2009 outbreak of Influenza A H1NI did not cause serious disease or complications in pediatric population of Corfu island, the clinicians should maintain a high suspicion in children with febrile respiratory illness and promptly treat those with underlying risk factors.

HERPESVIRUSES REACTIVATION IN IMMUNOCOMPETENT CHILDREN ADMITTED IN INTENSIVE CARE UNIT

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Background: Human herpes viruses (HHV) establish lifelong latency after primary infection and may reactivate in immunocompromised patients causing significant morbidity. Recent studies indicate that approximately 30% of CMV seropositive immunocompetent ICU adult patients present CMV reactivation associated with poor outcome.

Aims: Primary aim is to investigate whether CMV reactivation occurs among critically ill immunocompetent children. Secondary aim is to assess the reactivation of other herpesviruses (EBV, HHV6, HHV7). Finally, data collected may identify risk factors associated with reactivation and assess its clinical impact.

Methods: Herpesviruses reactivation is evaluated weekly by detecting DNA in peripheral blood with real-time PCR (Entherpex, GENOMICA, Spain). Clinical progress, laboratory findings, management, and complications are recorded during the 28 days following ICU admission.

Results: Preliminary data from this ongoing observational prospective study among 18 CMV seropositive pediatric ICU patients (median age 7 years, 8boys), indicated that 14 children (77%) had detectable HHV-DNA in blood. . Most were admitted for trauma or surgery (10/18). Median ICU hospitalization was 5,7 days. Five children (27.8%) had detectable CMV-DNA, nine children (50%) HHV6-DNA, three (16,6%) EBV-DNA, and two (11%) HHV7-DNA. HHV-DNA was detected between day 7 and 21 post ICU admission. Six children (33,3%) had multiple herpesviruses reactivations.

Conclusions: These preliminary data confirm similar rates of reactivation in children as reported in adult population. Risk factors associated with herpesviruses' reactivation (underlying disease, stress markers, severity of disease) will be accumulated. The clinical significance of these observations remains to be determined.

CLINICAL PROFILE OF CHILDREN ADMITTED FOR MEASLES IN A TERTIARY HOSPITAL IN QUEZON CITY: A REVIEW FROM 1999-2009

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Background and aims: Measles remains a leading cause of death among young children despite the availability of safe and effective vaccine for the past 40 years. This study is done to document the clinical profile of children presenting with measles with or without prior measles vaccination in a pediatric tertiary hospital in Quezon City from 1999 - 2009.

Method: 145 children with measles (diagnosed clinically) admitted in a pediatric tertiary hospital from 1999-2009 were included. The age, gender, residence, signs/symptoms, seasonability, complications, outcome and immunization status were gathered for each patient.

Results: 82% of the cases were 0-5 years old. 30% were < 1 year old, 21%- 1-2 years old, 31%- 3-5 years, and almost equally distributed among males and females (54% and 46% respectively). Patients are almost equally distributed among residents of Quezon City and outside Quezon City. Initial signs/symptoms showed 84% initially presented with fever, 63% cough, 54% rash, 50% colds, 22% diarrhea. Bronchopneumonia (60%) and diarrhea (23%) were the two leading complications. Majority occurred during the dry season, most of which cases were seen during the months of February and March. Among these patients who developed measles, 70% have no vaccination and 30% had vaccination but still developed measles. There were two mortalities and the rest improved and had an average hospital stay of 6 days.

Conclusion: There is persistence of a high disease-specific burden of measles due to non-immunization status and in both immunized children and those less than 9 months old.

CLINICAL PROFILE OF INFANTS WITH DENGUE VIRUS INFECTION ADMITTED IN A TERTIARY HOSPITAL IN QUEZON CITY, PHILIPPINES, 2001- 2010

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Background and aims: Infants remain a vulnerable and unique population at risk for dengue in endemic areas. This study aims to determine the clinical profile of infants < 12 months old admitted in a Tertiary pediatric hospital in Quezon City with Dengue Virus infection, 2001-2010.

Methods: Charts of patients < 12 months old with final diagnosis of Dengue Fever Syndrome, Dengue Hemorrhagic Fever and Dengue Shock Syndrome by clinical manifestations and Serologic Analysis admitted at a Tertiary Medical Center in Quezon City between January 2001- December 2010 were reviewed. Age, gender, signs/symptoms, management and outcome were gathered and shown in frequency.

Results: Out of the 28 cases of dengue infection in infancy. 71% were >7 months old and 29% were < 7 months old. 46% were males and 54% were females. 39% of cases were DFS, 21.5% DHF I, 32.5% DHF II and 7% DHF IV. The most common symptoms were fever (100%), refusal of feeds (100%), vomiting (29%) and diarrhea (25%). Petechiae were seen in 46% and significant hepatomegaly in 21%. All cases of DHF IV required the need of Fluid bolus and 50% of DHF IV required the need of inotropes. All cases improved and no mortality was present among the subjects.

Conclusion: This study shows that there is an increasing incidence of Dengue Virus Infection among infants aged < 12 months. Dengue infection can have potentially fatal consequences, and to date, vector control methods to prevent the spread of the virus might have been unsuccessful.

ACUTE SUPPURATIVE ARTHRITIS: A RARE MANIFESTATION OF ENDEMIC TYPHUS (MURINE TYPHUS) IN A CHILD

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Background and aim: Endemic typhus is a zoonotic disease caused by *Rickettsia typhi*. Rats are natural reservoirs of the pathogen. Clinical presentation usually includes fever, headache, rash and arthralgias. Murine typhus is endemic in subtropical and temperate coastal regions, such as Greece. We describe the case of a 6-year old girl with *R. typhi* infection and acute suppurative arthritis.

Methods: A six-year old girl presented with limping and pain on the right knee and hip. The finding of 50.000 WBC/ μ L (88% neutrophils, 12% lymphocytes) in synovial fluid supported the diagnosis of septic arthritis. Treatment with antibiotics (cefotaxime and clindamycin) resulted in remission of pain. The following days the patient complained of pain on the left hip accompanied by fever and maculopapular rash, which lasted for one week. After blood and synovial fluid cultures proved negative, malignancy and connective tissue disease were excluded by the appropriate investigations. On further investigations for other causes of infection, IgG antibodies to *R. typhi* (Indirect immunofluorescence assay-IFA) were detected with a 4-fold raise in the antibody titers after 4 weeks.

Results: The diagnosis of endemic typhus was made. Given that rickettsial infections in children are usually benign and self-limited, and the complete remission of the symptoms, no additional treatment was offered. No recurrence was noted.

Conclusions: Clinical manifestations of endemic typhus are not always typical. To our knowledge, this is the first case of acute suppurative arthritis as a manifestation of endemic typhus in children.

CLINICAL ASPECTS OF BOUTONNEUSE FEVER IN CHILDREN AND ADOLESCENTS FROM CONSTANTA**S.C. Cambrea**¹, S. Halichidis¹, M.M. Ilie², D.E. Tanase², S. Diaconu², E. Dumea¹, S.D. Carp³¹*Infectious Diseases Clinic, Faculty of Medicine, 'Ovidius' University,* ²*Children Infectious Diseases Department,*³*Clinical Laboratory, Clinical Infectious Diseases Hospital Constanta, Constanta, Romania*

Background: The disease caused by *Rickettsia conorii* is known by various geographically recognized names, including Mediterranean spotted fever, boutonneuse fever, Kenya tick typhus, Indian tick typhus, Israeli spotted fever, and Astrakhan fever. It is a moderately severe vasculotropic rickettsiosis that is often initially associated with an eschar at the site of the tick bite.

Objective: Retrospective analysis of 73 children and 39 adolescents hospitalized with boutonneuse fever in Children Infectious Diseases Clinic of Clinical Infectious Diseases Hospital of Constanta.

Material and method: Retrospective analysis of boutonneuse fever hospitalized in Children Infectious Diseases Department during a period of 9 years (2003 - 2011). We evaluate demographic, clinic, serologic and therapeutic data.

Results: During a period of 9 years in our department we followed 112 cases of boutonneuse fever. From the total of cases 34.89% were from rural area, 45.53% were male. The majority of cases were registered in warm season. The eschar (tache noir) was present in 72 patients. Fever had a 6 days mean duration. Maculopapular rash with nodular boutonneuse lesions was detected in 71 cases, 4 having petechial lesions. Serological diagnosis was accomplished in 75 patients. Etiologic treatment was done for 5-7 days with Chloramphenicol in 61 patients, Azithromycine in 19 cases, Clarithromycine in 16 cases, Ciprofloxacin in 10 cases, and Tetracycline in 6 cases.

Conclusions: From the total of cases with boutonneuse fever childrens represents 14.12%. The epidemiological and clinical diagnosis, confirmed by ELISA for *R. conorii* requires beginning of etiologic treatment.

FOUR YEARS PNEUMOCOCCAL CONJUGATE INFANT VACCINATION IN GERMANY: IMPACT ON INCIDENCE OF INVASIVE INFECTIONS AND SEROTYPE DISTRIBUTION IN CHILDREN

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Background: Vaccination of infants with pneumococcal conjugate vaccine (PCV7) was recommended in Germany in July 2006. Additionally, PCV10 was available from April 2009 and PCV7 was replaced by PCV13 in December 2009.

Objective: To compare the incidence and serotype distribution of invasive pneumococcal disease (IPD) in children from 2007 to 2010 with reference to the pre-vaccination period (1997-2002).

Methods: Nationwide surveillance of IPD for children < 16 years in Germany was based on two independent reporting sources: active surveillance in paediatric hospitals and passive web-based sentinel surveillance through microbiological laboratories. Serotyping was performed using the Neufeld Quellung reaction. Case definition: isolation of *Streptococcus pneumoniae* from a normally sterile body site. IPD incidence was estimated by capture-recapture analysis. Rate ratios comparing post- to pre-vaccination incidence were calculated.

Results:

Table: IPD incidence rate ratios post- vs. pre-vaccine introduction

age	2007	2008	2009	2010 (95% CI)
0-1y	0.58	0.58	0.63	0.64 (0.35-1.06)
0-4y	0.77	0.66	0.89	0.75 (0.45-1.15)
5-15y	1.22	1.23	1.72	1.77 (0.50-4.28)
0-16y	0.87	0.78	1.06	0.94 (0.59-1.39)

[Table]

The incidence of PCV7 serotypes decreased from pre-vaccination years to 2010 (< 2y: -91% from 13.25 to 1.16 per 100.000), < 16y: -88% from 2.41 to 0.29), while the incidence of non-PCV7 serotypes increased (< 2y: +72% from 6.84 to 11.74 per 100.000), < 16y: +123% from 0.78 to 1.74).

Conclusion: Infant PCV7 vaccination in Germany prompted a decrease in the incidence of IPD in infancy, but no significant overall IPD reduction in children < 16.

POPULATION IMMUNITY TO POLIOVIRUSES IN THE CONTEXT OF A LARGE-SCALE OUTBREAK OF POLIOMYELITIS - TAJIKISTAN, 2010

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Background: A nationwide serosurvey was conducted in Tajikistan to better understand population immunity to polioviruses (PV) before and after the poliomyelitis outbreak in 2010 caused by imported wild PV type 1 (PV1) (460 confirmed cases among children and young adults). The serosurvey was conducted after mOPV1 and before tOPV immunization rounds implemented to control the outbreak.

Methods: Serum specimens from a nationwide sample of persons aged 1-24 years selected through stratified cluster sampling (n=2447) were tested for neutralizing antibodies to all three PV types. Samples with titers < 1:8 were considered seronegative.

Results: Proportion of seronegatives was 1.1% (95% CI, 0.7-1.8) to PV1, 1.2% (95% CI, 0.9-1.7) to PV2, and 13.1% (95% CI, 11.5-14.9) to PV3. Seronegativity to PV3 exceeded 10% in all age groups except 15-19 years (8.3%), and was highest (17.3%) among 1-4 year-olds. Seronegativity to PV3 was $\geq 10.0\%$ in all regions, and was highest (20.0%-23.7%) among 1-4 year-olds in the two regions where the outbreak began among young children in early 2010.

Conclusions: Based on a high seronegativity to PV3 across wide age range (used, in the absence of pre-outbreak specimens, as a proxy for pre-outbreak PV1 immunity), the outbreak in Tajikistan resulted from accumulation of susceptibles due to historic weaknesses in immunization program, particularly where early cases occurred. Low current PV1 seronegativity indicates that mOPV1 rounds with expanded target age (≤ 15 years) succeeded in closing the immunity gap. To accelerate control of outbreaks in areas polio-free for >10 years, expanding SIA target age groups should be considered.

COST-EFFECTIVENESS OF 13-VALENT RELATIVE TO 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN THE UNITED KINGDOM

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Background and aims: Seven-valent pneumococcal conjugate vaccine (PCV7) has had a profound public health impact by preventing disease caused by seven *Streptococcus pneumoniae* serotypes. PCV13 covers six additional serotypes while PCV10 covers an additional three. The study objective was to assess the cost-effectiveness of PCV13 versus PCV10 paediatric vaccination in the United Kingdom (UK).

Methods: A static steady state model was developed to estimate the impact of PCV13 and PCV10 on invasive pneumococcal disease (IPD), pneumonia, and acute otitis media (AOM). Pneumococcal disease cases were estimated based on 2009/10 UK incidence and serotype coverage, vaccine effectiveness, and indirect effects. Direct effects for PCV13- and PCV10-covered serotypes were assumed to be similar to PCV7. IPD serotype distribution was used for pneumonia and AOM. Indirect "herd" effects were assumed only for PCV13 as PCV10 has not demonstrated significant reduction in nasopharyngeal carriage in vaccinated individuals. Assumptions were tested in sensitivity analyses.

Results: It is estimated that PCV13 will have a greater impact than PCV10 on all forms of pneumococcal disease under base-case assumptions due to higher serotype coverage. Compared with PCV10, PCV13 is expected to further reduce direct medical costs by over £60 million and add 30,000 QALYs annually. For all scenarios tested, PCV13 was either cost-saving or cost-effective with an ICER < £1,000 per QALY gained when indirect effects were included.

Conclusions: Continuing national PCV13 paediatric vaccination in the UK is expected to be cost-saving or cost-effective by providing a substantial further reduction in pneumococcal disease cases when compared to PCV10.

VACCINE DERIVED BOVINE ROTAVIRUS G1P[8] REASSORTANT IN INFANTS WITH ACUTE GASTROENTERITIS**M. Hemming**¹, T. Vesikari^{1,2}¹*Vaccine Research Center, University of Tampere School of Medicine,* ²*Department of Pediatrics, Tampere University Hospital, Tampere, Finland*

Background: RotaTeq® (Merck) is a live human-bovine reassortant rotavirus vaccine containing five reassortant strains G1P[5], G2P[5], G3P[5], G4P[5] and G6P[8]. RotaTeq® is generally considered to be a very safe vaccine, but a low rate of diarrheal symptoms after dose 1 was described in the safety and efficacy trials prior to licensure. Recently cases of diarrhea associated with a new vaccine derived double reassortant G1P[8] have been reported in the USA and Australia. We describe three such cases from Finland. Finland has had universal rotavirus vaccination program with RotaTeq® since 2009.

Materials and methods: Stool specimens were collected from 316 children with acute gastroenteritis seen in 2009-2011 at the Tampere University Hospital outpatient clinic or ward and examined for gastroenteritis viruses by RT-PCR. Specimens from exclusively rotavirus positive children (N=79) who had received RotaTeq® vaccine were analyzed to determine the VP7, VP4 and VP6 types by RT-PCR and sequencing.

Results: Three immunocompetent infants with gastroenteritis symptoms after their first or second immunization with RotaTeq® were found to shed a G1P[8] human-bovine double reassortant virus. The VP7, VP4 and VP6 gene segments were 100% identical to cognate gene segments from the corresponding vaccine viruses G1P[5] and G6P[8] in RotaTeq®.

Conclusion: Formation of G1P[8] double reassortants may explain diarrheal symptoms in a small percentage of RotaTeq® recipients. The reassortment between two vaccine strains may occur during intestinal replication even in immunocompetent infants. Such a double reassortant virus might also be transmitted to contacts in the environment.

ESTIMATED REDUCTION IN MENINGOCOCCAL DISEASE BY 4CMENB VACCINATION

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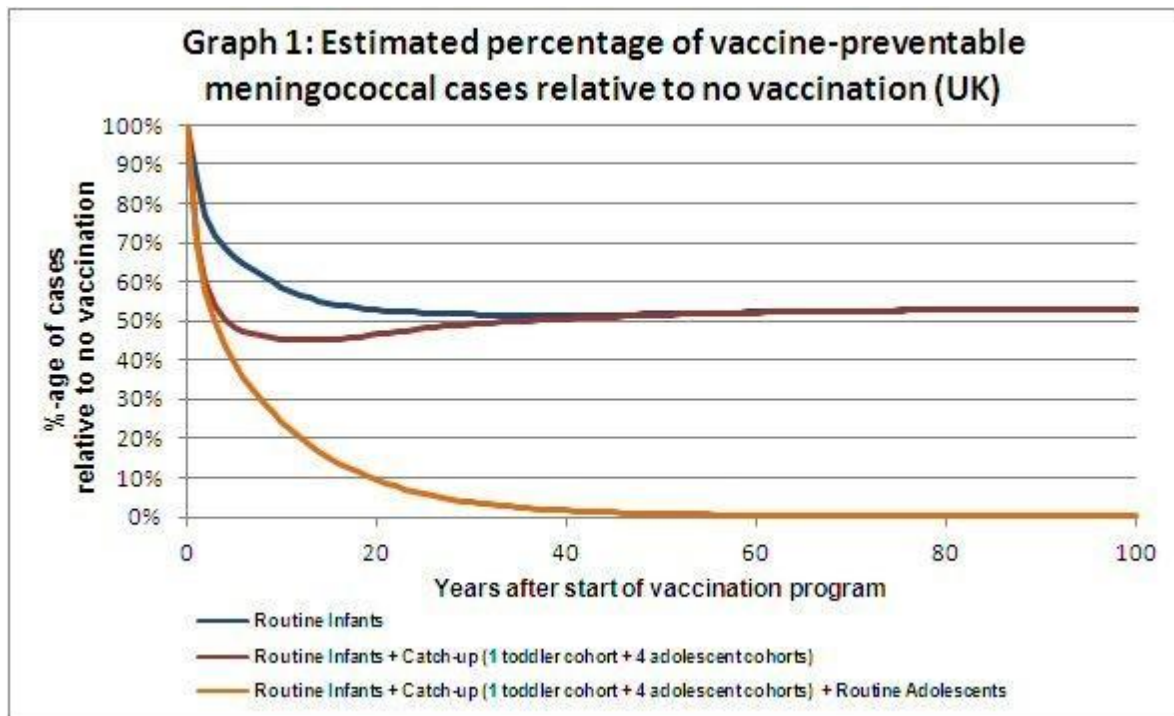
¹Life Sciences, OptumInsight, Medford, MA, USA, ²Novartis Vaccines and Diagnostics AG, Basel, Switzerland,

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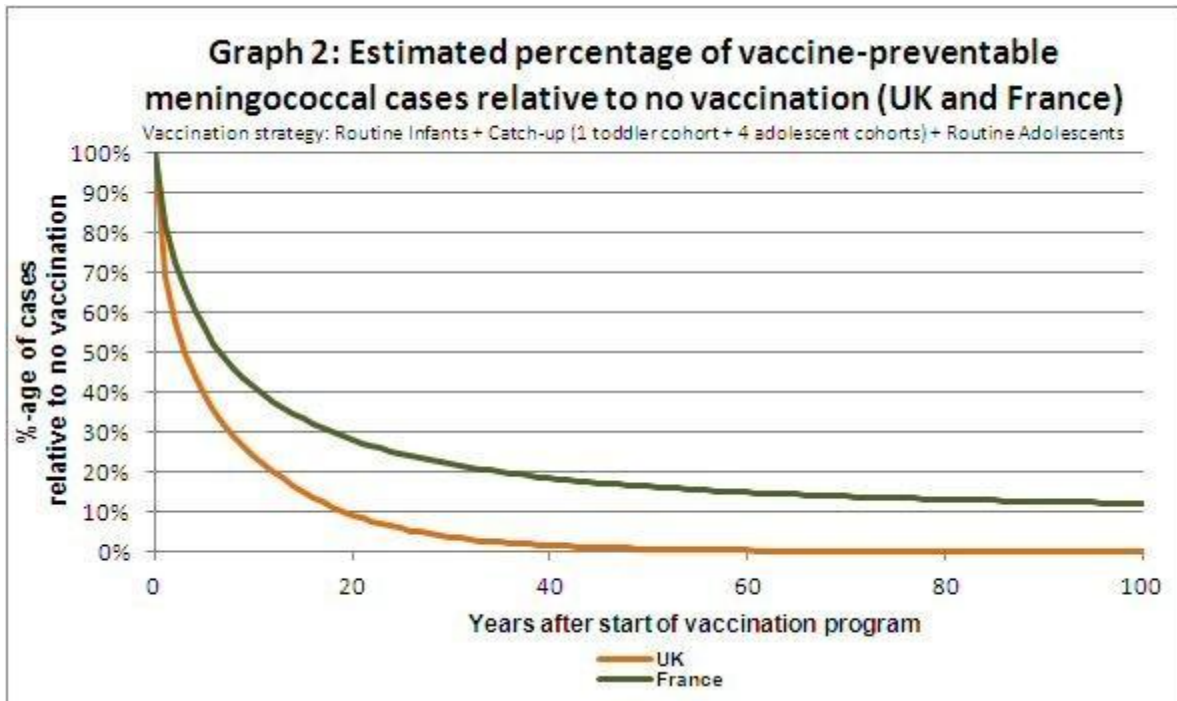
Background and aims: >70% of invasive meningococcal cases in the EU27 (2009) and nearly all infant cases are attributable to serogroup B. Adolescents are the main carriers; 72% and 80% of all tested circulating disease-causing strains (all serogroups) were estimated to be vaccine-preventable with 4CMenB vaccine in the UK and France, respectively. We evaluated the reduction potential in meningococcal disease after 4CMenB introduction.

Methods: A published transmission model was adapted, applying a model horizon of 100 years. Three vaccination strategies were evaluated, realistically assuming lower vaccination rates for France than the UK. All model inputs were derived from published literature or governmental databases.

Results:



[Figure 1]



[Figure 2]

Conclusion: Routine infant vaccination ensures direct protection against meningococcal disease in infants. Catch-up programs support a faster reduction of cases. Elimination of vaccine-preventable disease requires high vaccination rates in both, infants and adolescents. A vaccination program targeting fast onset of protection and long-term elimination of vaccine-preventable cases should comprise a routine vaccination of infants and adolescents, combined with a reasonably sized catch-up program. Examples from France and the UK show a potential for long-term reduction of vaccine-preventable cases from 88% to nearly 100%.

ROTAVIRUS VACCINATION: A RISK FACTOR FOR INTUSSUSCEPTION?**D.F. Oberle**¹, A.C. Jenke², R. von Kries³, D. Mentzer¹, B. Keller-Stanislawski¹

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Background and aims: Studies conducted in Mexico and Australia associate the currently authorized Rotavirus (RV) vaccines with intussusception (IS). Aim of this study was to investigate whether, in Germany, there is evidence for excess IS cases in RV vaccinees compared to the background incidence before market authorization in 2006.

Methods: Individual case safety reports (ICSR) of IS following receipt of RV vaccines submitted to the German Federal Institute for Vaccines and Biomedicines from 2006 to 2010 were reviewed and validated according to the criteria of the Brighton Collaboration's definition for IS. An observed versus expected analysis was conducted based on confirmed IS cases using standardized morbidity ratio (SMR) methods.

Results: A total of 27 ICSR of suspected IS in RV vaccinees were obtained. A significantly increased SMR for IS was found in a time window of 1-7 days after the 1st dose of Rotarix (4.6; 95% CI: 1.5-10.7) in infants aged 4-6 months of life. With respect to RotaTeq, there was also a significantly elevated SMR within 1-7 days following the 1st dose in children aged 4-6 months (5.8, 95% CI: 1.2-17.1). However, when combining all doses administered in the 1st year of life there was no evidence for excess IS cases 1-7 days after receipt of either RV vaccine.

Conclusions: Subgroup analyses revealed that infants aged 4-6 months are at increased risk to develop IS 1-7 days after the 1st dose of either RV vaccine. It might therefore be advisable to avoid starting RV immunization at this vulnerable age.

SPONTANEOUS ABORTIONS AND PERINATAL HEALTH AFTER PANDEMRIX VACCINATION IN FINLAND 2009-2010

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Background: Immunisations during pregnancy, especially during the 1st trimester, have led to questions on their safety. Countries with nationwide health-care registers, high immunisation coverage and unique personal identifiers provide an optimal platform to study the safety of such immunisations.

Aim: To study whether the adjuvanted (AH1N1v) vaccine Pandemrix® given during pregnancy affected the course of pregnancy or perinatal health between October 2009 and December 2010.

Methods: Immunisation records of women in reproductive age were linked to Medical Birth Register data and Hospital Discharge Register data on spontaneous abortions (ICD 10 codes O00-O03) treated in specialised health-care.

Results: There were 193 spontaneous abortions treated within one week after the vaccination. The numbers were similar in the second week (189), the third week (190) and fourth week (196) after vaccination.

Of the 76 043 newborns, 55.2% were exposed to Pandemrix® during pregnancy. 16.7% of mothers were vaccinated in 1st trimester, 18.4% in 2nd and 20.1% in 3rd trimester. The frequency of the following outcomes were compared between vaccinated and unvaccinated: perinatal death including stillbirths (from 22 weeks of gestation), early neonatal deaths (0-6 days), very preterm births (below 28 weeks), preterm births (below 37 weeks), very low birth weight (below 1500 grams), and low birth weight (below 2500 grams). Immunisation was associated with protection from all compared outcomes. (statistically significant adjusted ORs between 0.45 and 0.71).

Discussion: Pandemrix vaccination during pregnancy did not affect the course of pregnancy. Further, immunization had protective effect on all the major perinatal outcomes studied.

GENOTYPIC AND PHENOTYPIC CHARACTERIZATION OF AMPICILLIN-RESISTANT *HAEMOPHILUS INFLUENZAE* STRAINS ISOLATED FROM CHILDREN IN BULGARIA

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Background and aims: To investigate the mechanisms of ampicillin resistance of clinical strains *H. influenzae* from children with meningitis, acute otitis media and respiratory tract infections.

Methods: A total of 186 *H. influenzae* clinical strains were collected from children, aged 0 to 14 years: 53 cerebrospinal fluid (CSF), 5 blood, 24 sputum, 36 middle ear fluid and 68 upper respiratory tract samples. Serotyping was done by a coagglutination test and by PCR capsular genotyping. Beta-lactamase production was determined by the chromogenic cephalosporin test with nitrocephin. The antimicrobial susceptibility was done by microbroth dilution method. According to the ampicillin minimal inhibitory concentrations (MIC), all ampicillin non-susceptible strains were investigated for point mutations in their *ftsI* gene, indicating amino acid substitutions in PBP3.

Results: Overall, 58 strains *H. influenzae* belonged to serotype b (31.2%), 1 strain was type e, and 127 isolates (68.3%) were non-typeable. The total ampicillin non-susceptibility rate by MIC was 22.6%. Of all the 186 isolates, beta-lactamase positive ampicillin-resistant (BLPAR) strains were 14.3%, 5.6% were beta-lactamase negative ampicillin-resistant isolates (BLNAR). Another 2.7% were beta-lactamase positive amoxicillin/clavulanate-resistant (BLPACR) strains, implying the presence of both enzymatic and non-enzymatic mechanisms. The most frequent (80%) amino acid substitution was Asn-526 -> Lys which places the isolates in group II and the rest in group I due to Arg-517 -> His substitution.

Conclusions: The only mechanism of ampicillin resistance within the meningitis isolates was due to beta-lactamase production. BLNAR strains were found only among *H. influenzae* from respiratory tract infections and acute otitis media.

MULTIPLE ANTIMICROBIAL RESISTANCE IN ESCHERICHIA COLI URINARY TRACT INFECTION IN HOSPITALIZED CHILDREN IN HONG KONG: 2006 TO 2011J.Y.C. Chan¹, M. Hui², S. Griffiths¹¹*School of Public Health and Primary Care,* ²*Department of Microbiology, The Chinese University of Hong Kong, Hong Kong, Hong Kong S.A.R.*

Background: Antibiotic resistance has become an increasingly pressing threat to public health worldwide. Being the most common pathogen for urinary tract infection (UTI) in children, *Escherichia coli* (*E. coli*) is also the most common antibiotic-resistant bacterial urinary pathogen. Furthermore, *E.coli* has been observed to develop resistance to multiple groups of antibiotics and therefore be highly challenging to clinicians when managing children with UTI. We aimed to describe the evolving trend of multiple antimicrobial resistance in urinary *E.coli* in hospitalized children in Hong Kong.

Methods: Hospital microbiology laboratory database of Prince of Wales Hospital, a University hospital in Hong Kong, from 1 January 2006 through 31 December 2011 were queried for culture-confirmed *E.coli* urinary tract infection in paediatric patients hospitalized during the 6-year study period. The patients from one month of age to less than 18th birthday were included in the analysis.

Results: There were 568 cases of *E.coli* urinary tract infection included in the analysis. A high prevalence of resistance for *E.coli* was observed against ampicillin and 1st generation cephalosporin (71% and 49% respectively). Other antibiotic resistance rates were: cotrimoxazole (46%), gentamicin (32%), ciprofloxacin (23%), amoxicillin/clavulanate (22%), 3rd generation cephalosporins (23%) and nitrofurantoin (19%). Extended-spectrum beta-lactamase (ESBL) producing *E.coli* was found in 24% of cases. Furthermore, we detected that 48% of *E.coli* cases were resistant to 3 or more groups of antibiotics.

Conclusions: Our results documented the emergence of multiple antimicrobial resistance among urinary *E. coli* in children and highlighted the need to explore strategies for their containment.

DETECTION OF ESBL TYPES BLA-CTXM, BLA-SHV, BLA-TEM AMONG CLINICAL ISOLATES OF ACINETOBACTER BAUMANNII IN PATIENTS FROM TABRIZ, IRAN

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Acinetobacter spp. has been recognized over the last two decades as important opportunistic pathogens. Extensive use of antimicrobial chemotherapy in clinical environments has contributed to the emergence and dissemination of multidrug resistant nosocomial *Acinetobacter (A.) baumannii* infections. These bacteria are resistant to all known antibiotics. The most common mechanism of- β lactam resistance is enzymatic degradation by β -lactamase enzymes. The aim of this study was to determined the genotype of ESBL (TEM, CTX-M, SHV) produced by *A. baumannii* clinical isolates in patients from Tabriz north-west of Iran.

A total of 100 *A. baumannii* strains isolated from different clinical specimens were identified by standard microbiological methods. Production of ESBL was determined by testing resistance of the isolates against ceftazidime, cefotaxime, ceftriaxone and verified by Double Disk Synergy Test. Prevalence of *bla*TEM, *bla*SHV and *bla*CTX-M was determined among ESBL positive isolates by PCR technique.

Antimicrobial susceptibility testing showed that the lowest resistance rate was against polymixin B (16%) and colistin (19%) whereas the highest resistance rate was observed against Ticarcillin (100%), Cefixim (100%) and Ceftizoxim (100%). PCR results showed that among 60 ESBL positive *A. baumannii*, 31.6% of isolates were positive for *bla*SHV, followed by *bla*CTX-M (13.3%) and *bla*TEM (12%).

A high frequency of ESBL production was observed among studied *A. baumannii* isolates. The prevalence of SHV gene in this isolates was more than TEM and CTX-M genes.

VARIATION IN ANTIBIOTIC SENSITIVITY TESTING: POTENTIAL RELEVANCE FOR THE INTERPRETATION OF CHILDHOOD BACTERAEMIA RESISTANCE PATTERNS FROM ROUTINE CLINICAL DATA

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Background and aims: Laboratory methods can introduce bias in surveillance of antimicrobial resistance based on routine data. We aimed to establish the degree of variation in antibiotic sensitivity testing (AST) in a sample of European children's hospitals processing neonatal and paediatric blood cultures.

Methods: Thirteen partner laboratories in a large European project were asked to indicate their AST practices for six key EARS-Net pathogens (*S.aureus*, *S.pneumoniae*, *E.faecalis/faecium*, *E.coli*, *K.pneumoniae* and *P.aeruginosa*). A survey was conducted to establish whether a total of 68 pre-defined bug/drug combinations formed part of local routine AST.

Results: Individual laboratories indicated that 29.6-81.8% of the 68 possible bug/drug combinations across all 6 pathogens formed part of their routine first line panels. Up to 49.1% of bug/drug combinations were never used in AST by specific laboratories.

Second line AST was specifically assessed and pre-defined based on resistance detected towards any of the antibiotics tested in the first line panel. Three centres used less than 40% of the specified bug/drug combinations in first line AST, but additionally reported including up to 28.3% of the bug/drug combinations in second line panels. Conversely, 3/4 centres testing more than 60% of bug/drug combinations as first line did not use any further combinations in second line AST.

Conclusions: Variation exists in testing panels for neonatal and paediatric bacteraemia, with laboratories significantly differing in the breadth of routine AST and use of second line AST. When not formally considered, this could potentially bias observed antimicrobial resistance patterns based on surveillance using routine laboratory data.

INFECTIONS DUE TO CARBAPENEM-RESISTANT GRAM-NEGATIVE PATHOGENS (CRPs) IN CHILDREN: PRELIMINARY RESULTS FROM THE NATIONAL SURVEILLANCE SYSTEM IN HOSPITALS IN GREECE

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Aim: CRPs are emerging as a major cause of nosocomial infections with an increased impact on morbidity, mortality, and health-care costs. Our knowledge about infections due to CRPs in children is very limited. We present the characteristics and outcome of children with infections due to CRPs notified through the National Surveillance System in Greece.

Methods: Data were collected prospectively from Greek hospitals.

Results: During January-October 2011, 47 children (19 boys; 40.4%) with a median age of 2 years (1 month-14 years) were notified. Underlying conditions existed in 72% of patients. Infections were: pneumonia (16 cases; 34%, including 13 (81.3%) ventilator-associated), bacteremia (13; 27.7%), urinary tract infection (12; 25.5%), and surgical site infection (6; 12.8%). Isolates were: *Acinetobacter baumannii* (20; 40.8%), *Pseudomonas aeruginosa* (19; 38.8%), and *Klebsiella pneumoniae* (10; 20.4%). 66.7% of *Klebsiella* isolates were KPC-producing; the remaining were VIM. The first positive culture occurred a median of 22 days (0-256) after admission. At the onset of infection, 31 (65.9%) were hospitalized in an Intensive Care Unit. Regarding risk factors for colonization, 15 (31.9%) had a history of hospitalization in the previous 6 months; 30 (63.8%) and 25 (53.2%) had received broad-spectrum antibiotics or carbapenems in the previous 6 months, respectively; 34 (72.3%) were on mechanical ventilation; 29 (61.7%) had a central vascular catheter and 26 (55.3%) a urine catheter. Eleven (23.4%) children died a median of 7 days (0-47) after the first positive culture.

Conclusions: Infections due to CRPs are associated with an increased morbidity and mortality among hospitalized children.

CARBAPENEM RESISTANCE IN ACINETOBACTER BAUMANNII ISOLATES CAUSING INFECTIONS IN CHILDREN AT UNIVERSITY HOSPITAL CENTER ZAGREB

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Carbapenems have potent activity against Acinetobacters and are often used as last resort for the treatment of infections due to multiresistant *Acinetobacter baumannii*. However, Acinetobacters may develop resistance to carbapenems through various combined mechanisms including decreased permeability and overexpression of efflux pumps.

Nine *Acinetobacter baumannii* strains were isolated from children's specimens at intensive care units during last three months of 2009 at Clinical Hospital Center Zagreb. The aim of the study was to characterize carbapenem-resistance mechanisms in these isolates. The antimicrobial susceptibility to a wide range of antibiotics was determined by broth microdilution method. Modified Hodge Test was used to screen for production of carbapenemases. E-test was used to screen for production of metallo- β -lactamases. Genes encoding oxacillinases and metallo-beta-lactamases were detected by multiplex PCR. Genotyping of the strains was performed by pulsed-field gel electrophoresis (PFGE) and determination of sequence groups by multiplex PCR.

Three of nine strains were resistant to imipenem and meropenem. They were found to produce OXA-24 β -lactamase, belonged to sequence group 1 (EU clone II) and were clonally related by PFGE. Other six strains were susceptible or intermediate susceptible to carbapenems but showed resistance to gentamicin, expanded-spectrum cephalosporins, piperacillin/tazobactam and ciprofloxacin. Multiplex PCR revealed only the intrinsic, naturally occurring OXA-51 β -lactamase of species *A. baumannii*. These strains showed distinct PFGE profiles and were not clonally related.

The study demonstrated occurrence of carbapenem resistant OXA-24 producing *A. baumannii* at paediatric units of University hospital center Zagreb. Infections with such multiresistant isolates are associated with increased mortality and morbidity.

DETERMINATION OF EXTENDED-SPECTRUM B-LACTAMASES (ESBLs) IN ENTEROPATHOGENIC ESCHERICHIA COLI (EPEC) STRAINS ISOLATED FROM CHILDREN WITH DIARRHEA

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Background and aims: Enteropathogenic Escherichia Coli is a major cause of diarrhea in children in developing countries. The aim of this study is to determine the antibiotic resistance pattern and considering the prevalence of ESBLs coding genes including TEM, SHV, CTX-M and OXA gene and insertion sequence of ISE-CP1 in EPEC strains isolated from children with diarrhea.

Methods: Totally, 192 strains of EPEC isolated from children with diarrhea were included. The susceptibility of isolates to 14 antimicrobial agents was determined by the disc diffusion method and interpreted according to the CLSI recommendations. Production of ESBL in the isolates was determined by combined disk test and the presence of CTX-M, SHV, TEM, OXA and ISE-CP1 genes was detected by PCR.

Results: The results showed that these strains had the most resistance to cefpodoxime (97%), trimethoprom (60.7%), tetracycline (58.4%) and ampicillin (45.8%). Multidrug resistance was 68.7 percent. These strains showed the most sensitivity to imipenem, ceftriaxone, and ciprofloxacin antibiotics. The percentage of ESBLs prevalence in EPEC strains was estimated 79.7 %. PCR approach showed that different ESBL gene prevalence, including, TEM, SHV, CTX-M, OXA and ISE-CP1, respectively are 13.5, 11.9, 10.9, 7.3, and 61.7 percent.

Conclusion: This study highlighted the needs to establish antimicrobial resistance surveillance networks for *EPEC strains* to determine the appropriate empirical treatment regimens. The high prevalence of multidrug resistance and production of ESBLs in *EPEC* isolates confirms the necessity of protocols considering these issues and the exact application of antibiogram test before antibiotic prescription for complete treatment.

COLONIZATION OF NEONATES WITH CARBAPENEMASE-PRODUCING ENTEROBACTERIACEAE (CPE)

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Background: Carbapenemase-producing Enterobacteriaceae (CPE) have emerged as a major public health threat worldwide with particularly high rates in adult ICUs in Greece. There is a lack of data about the epidemiology of CPE in children. We aimed to determine the prevalence of CPE in neonatal intensive care units (NICU).

Method: A point prevalence study was conducted between November, 2011 and January, 2012 in 8 NICUs in 5 public hospitals in Athens, including the 2 largest children's hospitals. We collected rectal and umbilical swabs from infants in 8 NICUs. All the specimens were inoculated on McConkey agar plates containing meropenem and incubated for 48 hours. Enterobacteriaceae were identified to the species level by the API 20E method. All isolates were examined for production of carbapenemases by combined disk synergy test utilizing disks containing meropenem, EDTA and boronic acid. The bla_{VIM} and bla_{KPC} genes were detected by PCR using specific primers. Demographic and clinical data were extracted from the patients' medical records.

Results: 157 neonates were included in our study, 79 were males (50%). The mean age was 40 days and 67% were born prematurely. Out of 314 samples, only one CPE strain (VIM) was isolated in both rectal and umbilical cultures from the same neonate.

Conclusions: *We found a low prevalence of colonization with CPE in NICU patients. Our finding contrasts significantly with colonization rates in adults. Factors associated with this phenomenon need to be further determined in order to design interventions to prevent the emergence of CPE in children.*

EPIDEMIOLOGY OF THE HOSPITALIZATIONS DUE TO ROTAVIRUS INFECTION IN SPAIN (2005-2009)

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Background: This epidemiological survey was undertaken to estimate the burden of hospital admissions for rotavirus in children under 5 in Spain during a five year period (2005-2009). Rotavirus vaccines were introduced in Spain between late 2006 and early 2007. The vaccination coverage was 17% in 2007, 35% in 2008 and 38% in 2009.

Methods: Retrospective survey reviewing data of the National Spanish Surveillance System for Hospital Data. Codes for infectious gastroenteritis due to rotavirus were selected by using the 9th International Classification of Diseases. The annual rate of hospital admissions was calculated by using census-derived population estimates. Results were gathered by age.

Results: A total of 26,500 hospital discharges for acute gastroenteritis due to rotavirus were reported during the study period. The overall annual rate of hospitalization was 235 cases per 100,000. The higher hospitalization rate was observed among children < 12 months (692.3 per 100,000) and it decreased with increasing age to 17.5 per 100,000 in 4-year-old children. Among the study period the hospitalization rate decreased from 300.3 to 174.1 per 100,000. This decrease was more marked in children < 2 years of age. For children up to 12 months the hospitalization rate reduced from 906.1 to 477.1 per 100,000 and in the second year of life from 416.5 to 251.3 per 100,000.

Conclusions: Hospital burden of rotavirus infections has decreased in young children during the last years in Spain. These data can contribute to evaluate the impact in hospitalization rates of non-systematic use of rotavirus vaccine in Spain.

PERTUSSIS SURVEILLANCE IN THE FRENCH HOSPITALS: RESULTS FROM 1996 TO 2010

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¹InVS, Saint-Maurice, ²Centre National de Référence de la Coqueluche et autres Bordetelloses, Institut Pasteur, Paris, France

This study presents the 15 years results of the French paediatrician hospital-based network surveillance (Renacoq) set up in 1996 to monitor the trend of pertussis (whooping cough) in infants and the impact of vaccination strategies.

Microbiologists from 42 hospitals participating on a voluntary basis notify pertussis diagnosis and paediatricians fill in a questionnaire for infants less than 6 months of age that fulfil the microbiological, clinical or epidemiological case definition. The network covers about 30% of pertussis paediatric cases seen in French hospitals.

Since March 1996, the network has described 2070 cases of pertussis less than 6 months of age which represent around 150 cases annually. Four peaks occurred. The male-female ratio was 1.0. The estimated national average incidence rate for the 0-2 months-old children is 244/100 000, among which 16% were admitted in intensive care units. The average case fatality ratio was 1%. Vaccination status was confirmed through medical records for 87% of infants and 99% were not yet fully vaccinated. The source of contamination was identified for 54% of cases and was in majority the parents.

Renacoq data confirmed the risk for young children and the need of a timely pertussis vaccination. The proportion of parents as contaminators increased over the study period despite a vaccination recommendation for adults since 2004 whereas the proportion of siblings as contaminators decreased, probably as a consequence of the adolescent booster recommendations since 1998. Improving vaccination coverage in adults in contact with infants too young to be protected is needed.

BURDEN OF ROTAVIRUS GASTROENTERITIS AMONG CHILDREN AGED < 5 YEARS IN SAUDI ARABIA: A HOSPITAL-BASED PROSPECTIVE SURVEILLANCE (2007-2008)

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Background and aims: Globally, rotavirus (RV) is the leading cause of severe gastroenteritis (GE) in children aged < 5years. Recently published epidemiological data for RVGE in Saudi Arabia is limited. This active hospital-based prospective study aimed to estimate the disease burden of RVGE and dominant RV-serotypes in children aged < 5years in Saudi Arabia during a 12-month period.

Methods: 1007 children hospitalized due to GE were enrolled from four study centers in Saudi Arabia (February 2007-March 2008) using WHO's generic protocol for RVGE-based surveillance. Stool samples were tested for RV using ELISA and RV-positive samples were serotyped by PCR. Vesikari scale (severe RVGE=Vesikari score \geq 11) was used to assess the severity of RVGE.

Results: 970 children were included in the according-to-protocol analyses; 395 were RV-positive, 568 were RV-negative and 7 had an unknown RV status. The proportion of RVGE among GE hospitalizations was 40.7% (95%CI:37.6, 43.9). The percentage of RVGE hospitalizations seen in children aged < 2years was 83.0%. While RVGE occurred year-round, peak in RV cases was seen in June 2007 (57.1%). The most common RV types detected were G1P[8] (33.7%), G2P[4] (3.3%) and G9P[8] (0.5%). Severe RVGE episodes were reported in 88.1% of RV-positive and 79.6% of RV-negative children before hospitalization.

Conclusion: These results show that RV was responsible for a high proportion of GE hospitalizations in children aged < 5years. Routine RV vaccination in children may reduce RVGE-associated morbidity, mortality and disease burden in Saudi Arabia.

HOSPITAL ADMISSIONS FOR INFECTION IN INFANCY AND EARLY CHILDHOOD: A PROSPECTIVE STUDY

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Background: Infectious diseases are a leading cause of morbidity during childhood worldwide.

Aim: To prospectively investigate the incidence of hospital admissions for infections in infancy and early childhood and to define possible risk factors in Crete, Greece.

Methods: In a representative sample of 1,049 infants, 926 (88.3%) of infants were followed-up all during infancy and 590 (56.2%) during the first six years of life. Hospital admissions for infections, including acute otitis media (AOM), acute respiratory infection, gastroenteritis and urinary tract infection were recorded at 1, 3, 6, 9 and 12 months as well as 6 years of life.

Results: Hospital admission for infection was required for 14.5% of infants and 17.6% of children aged 1-6 years. Duration of exclusive breastfeeding (r_s -0.06), birth in winter (RR 0.33, 95% CI 0.20 to 0.55) and parental education years (r_s -0.14) were demonstrated to affect admissions for infections during infancy. Admissions for infection at the age of 1-6 years were related to non-Greek ethnicity (RR 2.25, 95% CI 1.13 to 4.49) and maternal perceived ill-health during pregnancy (RR 1.48, 95% CI 0.89-2.45). For admissions due to AOM in particular, parental smoking was found to be a significant risk factor ($r_s=0.086$).

Conclusions: This prospective study in a well-defined child population of adequate healthcare standards suggests that infections remain a leading cause for hospitalization in childhood. Factors associated with hospitalization for infection seem to differ between infants and toddlers.

AGE AND TEMPERATURE SPECIFIC RESPIRATORY CENTILES CAN PREDICT LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN

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Aim: We aimed to validate the ability of age-specific and temperature dependent centile charts of respiratory rate to predict lower respiratory tract infections (LRTIs).

Methods: Respiratory rate centile charts were derived using data from 1,555 children with fever attending the paediatric emergency department (PED) of the Erasmus MC - Sophia children's university hospital, the Netherlands, in 2006 and 2008. The predictive ability of the centile charts was validated in 671 febrile children at risk of LRTI who were recruited at the PED of the Erasmus MC - Sophia (n=311, 2003 - 2005) and at the paediatric assessment unit of the University Hospitals of Coventry and Warwickshire (n=360, 2005 - 2006). We calculated diagnostic performance measures of children with 'definite bacterial LRTI', 'probable viral LRTI' and 'other infections'. We compared the diagnostic performance of the centile charts with the APLS threshold values and the continuous reference values as described by Fleming et al.

Results: The age and temperature dependent 97th centile cut-offs were more useful to rule in LRTI (specificity 0.94 (95% confidence interval (CI): 0.92-0.96), positive likelihood ratio (LR+) 3.66 (2.34-5.73)) than APLS thresholds (specificity 0.53 (0.48-0.57), LR+ 1.59 (1.41-1.80)) and the 99th centile of the reference values of Fleming et al. (specificity 0.78 (0.75-0.82), LR+ 2.13 (1.69-2.68)). None were able to differentiate between definite bacterial and probable viral LRTI.

Conclusion: The 97th centile cut-offs of the age-specific and temperature dependent centile charts outperformed existing respiratory rate thresholds to rule in presence of LRTI.

EPIDEMIOLOGY OF LOWER RESPIRATORY TRACT (LRT) ISOLATES OBTAINED FROM INTUBATED CHILDREN IN A PEDIATRIC INTENSIVE CARE UNIT (PICU)

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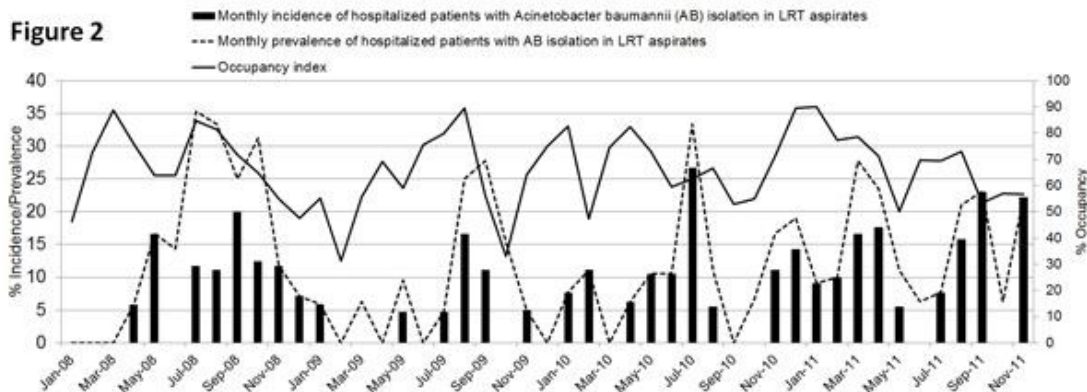
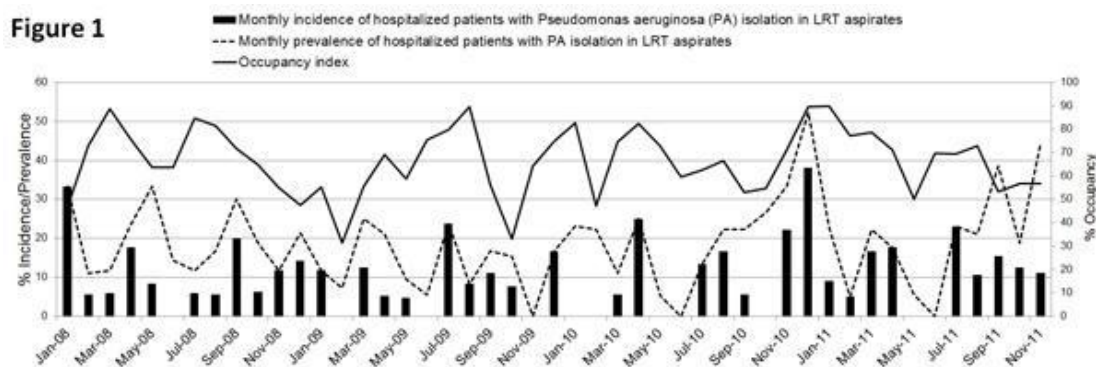
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Background and aims: LRT infections are common in PICU. We studied the epidemiology of LRT pathogens isolated from patients hospitalized in a PICU.

Methods: A retrospective analysis of LRT specimens was conducted in an 8-bed polyvalent PICU of a general university hospital from 2008 to 2011. LRT specimens were collected from intubated children on admission and thereafter routinely twice weekly or on suspicion of LRT infection.

Results: Among 424 intubated children, 144 (34%) had a positive LRT culture at least once. Of 2246 LRT specimens collected, 624 (28%) were positive for *Pseudomonas aeruginosa* (PA, 59%), *Acinetobacter baumannii* (AB, 28%), *Stenotrophomonas maltophilia* (5%), *Staphylococcus aureus* (3%) and other bacteria (5%). Isolation of PA and AB from LRT on a monthly base is shown in figures 1 and 2, respectively. Monthly incidences of PA and BA correlated to monthly prevalences of PA ($r=0.6$, $p<0.0001$) and BA ($r=0.83$, $p<0.0001$), respectively. Table 1 depicts antimicrobial resistance rates of PA and BA.

Conclusion: High incidence of LRT colonization/infection was found. Non-fermenters predominate, and high level of antimicrobial resistance is of concern.



Antimicrobial	Resistance rates (%) of <i>Pseudomonas aeruginosa</i>				Resistance rates (%) of <i>Acinetobacter baumannii</i>			
	2008	2009	2010	2011	2008	2009	2010	2011
Imipenem	54	34	49	42	96	95	97	77
Ceftazidime	54	50	34	13	100	100	93	94
Piperacillin/tazobactam	11	56	23	13	100	100	93	94

[Table

1]

SEROPREVALENCE AND RISK FACTORS OF CYTOMEGALOVIRUS INFECTION IN THE NETHERLANDS

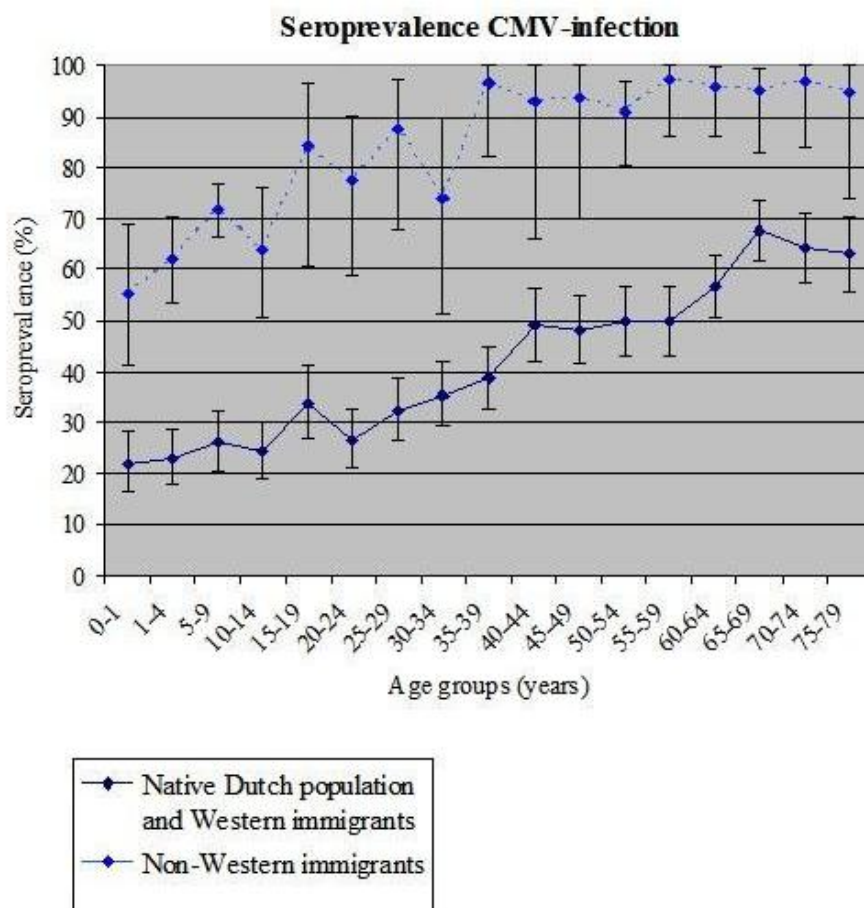
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Background and aims: Cytomegalovirus (CMV) is an endemic virus which seldom causes clinical symptoms in healthy individuals. However, in congenital CMV infection symptoms occur at birth in about 12% and long term sequelae is seen in approximately 20%. The risk of congenital CMV infection is related to the seroprevalence in future mothers. The aim of this study was to determine the seroprevalence and risk factors of CMV infection in the Netherlands.

Methods: A total of 4774 sera from individuals, participating in a population-based serum bank (PIENTER-2, 2006-2007), were tested for CMV-specific IgG antibodies using ELISA (ETI-CYTOK-G PLUS DiaSorin, Saluggia, Italy). CMV seroprevalence rates for the overall population and several subgroups were assessed using SAS.

Results: The overall seroprevalence of CMV in the general population (0-79 year) was 49%. Among native Dutch women of childbearing age (19-44 years) the seroprevalence increased from 30% to 50%. Groups with low income, low education level and non-western immigrants had higher seroprevalence.



[Seroprevalence of CMV-infection]

Conclusions: Almost half of the population showed serological evidence of prior CMV infection. In accordance with the literature CMV infection is more prevalent among non-Western immigrants and groups with lower socio-economic status. The increase of seroprevalence in women of childbearing age showed that primary infections occur frequently during this period with a risk of vertical transmission and associated sequelae for the unborn child.

ELUCIDATING THE PERFECT STORM: MULTIPLE PNEUMOCOCCAL SEROTYPES & BACTERIAL SPECIES, AT HIGH DENSITY & WITH NEAR-UNIVERSAL RHINITIS IN YOUNG CHILDREN

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Background and aims: Nasal ecology changes with age & evolves under vaccine selection pressure. Colonisation in young children is exuberant & complex. Its dynamics underlie disease pathogenesis & epidemiology.

Methods: In February-March 2010 we swabbed the nasopharynges of 586 children, aged 6m-6y, attending 6 nurseries in Coimbra, Portugal. Swabs, stored in STGG broth at -80°C were cultured for pneumococcus (Sp), *M.catarrhalis* (Mc), *H.influenzae* (Hi) & *S.aureus* (Sa). Colonies were counted & scored: 0=none, 1=1-5; 2=>5-20; 3=>20-50; 4=>50-100; 5=>100/50µL broth. Rhinitis symptom scores were recorded (n=566): 0=asymptomatic, 1=mild, 2=moderate, 3=severe nasal discharge. Sp serotyping was by multiplex PCR & microarray.

Results: 56% of children (96% 0-1y, 86% 1-2y) had symptoms. Rates of colonisation were: Sp(45.7%), Mc(68.8%), Hi(51.7%) & Sa(15.5%), colonisation was associated with age (all $p < 0.05$) and highest in youngest for all except Sa. Sp density was associated with symptom score, independently of age ($p < 0.001$). 62.8% had multiple bacterial species & 90% colonised with Sp, also carried another species. ≥ 2 species was commoner in younger children ($p < 0.001$) an association not affected by recent antibiotics or Sp vaccination. Among 267 Sp+ samples, 29 serotypes were detected, including vaccine types 3, 7F, 18C*, 19A & 19F (*previously undetected). 29.1% of Sp carriers had multiple serotypes- 2: 21.4%, 3: 4.5%, >5: 0.8% with higher density than single (OR=1.74; $p < 0.001$))

Conclusions: Traditional culture & serotyping misses serotypes commonly present alongside others. Drivers of pneumococcal transmission (colonisation density & rhinitis symptoms) are mutually associated and, critically, may be important determinants of disease.

SEROTYPE DISTRIBUTION OF STREPTOCOCCUS PNEUMONIAE IN HEALTHY TURKISH CHILDREN AFTER THE INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE

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Background and aims: The 7-valent pneumococcal conjugate vaccine (PCV7) was added to Turkish national vaccine schedule in November 2008 for children born in May 2008. The aim of this study was determining serotype distribution and related risk factors of *Streptococcus pneumoniae* in healthy Turkish children in the era of community-wide PCV7 use.

Methods: The study was conducted on 1101 healthy children less than 18 years of age. Specimens were collected with nasopharyngeal swabs between April 2011 and June 2011. Serotypes of the isolates were determined by Quellung reaction.

Results: The pneumococcal carriage rate was 21.9% (241/1101). Of the pneumococci isolated from children, 184 (76.3%) could be serotyped. Half of all pneumococcal isolates were serotyped as 19F (15.2%), 6A (15.2%), 23F (10.3%) and 6B (9.3%). Serotype coverage rates of the PCV7 and non-PCV7 were 46.2% and 53.8%, respectively. However, a recently introduced 13-valent pneumococcal conjugate vaccine (PCV13) covered 62% of isolates. The most common penicillin and ceftriaxone resistant serotypes were 6A, 6B, 14, 19F and 23F. Also, resistant isolates to the penicillin and ceftriaxone were more in serotypes covered by PCV7 and PCV13 than the non-PCV7 and non-PCV13 serotypes.

Conclusions: After the community-wide PCV7 vaccination an increasing trend of the rates in non-PCV7 serotypes was seen especially in serotype 6A in healthy children in Turkey.

SLOWER REDUCTION OF MENINGITIS VS. NON-MENINGITIS INVASIVE PNEUMOCOCCAL DISEASE (IPD) RATES, POST PCV7 INTRODUCTION - HOW TO EXPLAIN THE PARADOX?

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Background: PCV7 was introduced to the Israel National Immunization Program in July 2009 (2, 4, 12 months schedule; catch-up 2 doses, 2nd year). Nationwide active IPD surveillance has been conducted since 1989.

Methods: All 27 centers performing blood/CSF cultures reported monthly all IPD (positive blood/CSF cultures). Capture-recapture was used for completeness.

Results: During 1989-2010, 6,022 IPD cases were reported; 572 (9%) were meningitis. Children < 6 months constituted 31% of the meningitis vs. 12% of the non-meningitis group. PCV7 serotypes+6A (VST) were only 30% of meningitis < 6 months (incidence rates of ~2.6/100,000 for VST and ~4.6/100,000 for serotypes 1, 3, 5, 7F and 19A).

In contrast, in children 6-59 months, non-VST meningitis rates were low (~1/100,000) and stable throughout the study period.

Compared to 2003-7, by 2010, overall and VST meningitis incidences < 5 years decreased by 21% and 50%, respectively, vs. 44% and 83% in non-meningitis IPD, with no replacement so far. (**Table 1**)

Conclusions: We speculate that the main reasons for the slower reduction in pneumococcal meningitis compared with non-meningitis rates were: 1) Most children < 6 months (age group with highest meningitis rates) were too young to be fully vaccinated; 2) The short period (18 months) post PCV7 did not allow sufficient herd immunity needed to protect infants < 6 months; 3) VST were found only in a minority of meningitis cases < 6 months.

Table 1. Incidences of pneumococcal meningitis, non-meningitis and overall IPD in children <5 years in Israel, 2003-2007 vs. 2010

	Mean ± SD incidence/100,000 population				% reduction overall	% reduction VST	P-value*
	2003-2007		2010				
	Overall	VST	Overall	VST			
Meningitis (N=572)	3.85±0.43	2.02±0.31	3.06	1.02	21% ^a	50% ^c	<0.01
Non-meningitis (N=5,450)	46.82±3.16	29.28±1.84	26.18	4.98	44% ^b	83% ^d	
Overall IPD (N=6,022)	50.68±3.40	31.30±1.87	29.24	6.0	42% ^e	81% ^f	

*P-value <0.01 for a vs. b, a vs. c, b vs. d, c vs. d, e vs. f

[Table]

IDENTIFICATION OF IMMUNODOMINANT B-CELL EPITOPES WITHIN SURFACE PNEUMOCOCCAL PROTEINS (PNPS)

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Background: Previous screening of a whole-genome- λ -display *Streptococcus pneumoniae* library with patients' sera revealed epitope-containing fragments within 6 virulent surface PnPs (CbpB, PhtD, PhtE, ZmpB, PspA and spr0075), consisting of about 2000 amino-acids. This study aimed to unveil the fine specificity of host antibody response against these antigenic fragments and identify the immunodominant epitopes in amino-acid resolution level.

Methods: To map the immunodominant epitopes, 150 synthetic 20-mer overlapping peptides (OLPs #1-#150), covering the sequence of antigenic fragments, covalently attached in polystyrene rods, were screened using 12 sera from children aged 2-16 years convalescing from invasive pneumococcal disease (IPD). Healthy children with no history of IPD, aged 1-4 years, were used as controls.

Results: Controls' sera exhibited no specific immunoreactivity with any of the 150 OLPs. However, 10 peptides were consistently recognized by patients' sera: OLP#4 (p 0.06) within CbpB, OLP#11 (p 0.002), OLP#18 (p 0.01) within PhtD, OLP#40 (p 0.002) within PhtE, OLP#125 (p 0.01), OLP#138 (p 0.06) within ZmpB OLP#76 (p 0.002), OLP#79 (p 0.002), OLP#90 (p 0.002), OLP#100 (p 0.08) within spr0075. Uniprot searches revealed that these epitopes are conserved in most pneumococcal strains, whereas they show a 80-90% amino-acid sequence similarity to other streptococcal species (e. g. oralis, mitis). Interestingly, 4/10 epitopes exist in up to 6 repeats within their parent protein, a finding suggesting stronger antibody binding.

Conclusions: Antigenic fragments of known virulent surface PnPs include specific immunodominant B-cell epitopes, consistently recognized by sera from patients with IPD, encouraging further investigation of their role in host-pathogen interaction.

MACROLIDE RESISTANCE DETERMINANTS AMONG *STREPTOCOCCUS PNEUMONIAE* ISOLATED FROM CARRIERS IN CENTRAL GREECE

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Background: We sought to characterize the temporal trends in nasopharyngeal carriage of macrolide-resistant pneumococci during a period with increased heptavalent pneumococcal conjugate vaccine (PCV7) coverage in Central Greece.

Methods: *Streptococcus pneumoniae* nasopharyngeal isolates were recovered from 2649 day-care center attendees in Central Greece during 2005-2009. A phenotypic and genotypic analysis of the isolates was performed, including the identification of macrolide resistance genes *mef(A)*, subclasses *mef(A)* and *mef(E)*, as well as *erm(B)*.

Results: Of the 1105 typeable *S. pneumoniae* isolates, 265 (24%) were macrolide-resistant; 22.2% in 2005, 33.3% in 2006, 23.7% in 2007, and 20.5% in 2009 ($P=0.398$). Among these macrolide-resistant isolates, 28.5% possessed the *erm(B)* gene, 24.3% the *erm(B)+mef(E)* genes, 41.8% the *mef(E)*, and 5.3% the *mef(A)*. A *mef* gene as the sole resistance determinant was carried by 30.8% of macrolide-resistant PCV7 isolates and 70.2% of the non-PCV7 ones. Across the 4 annual surveillances, pneumococci carrying the *mef(A)* gene were gradually disappeared, whereas serotype 19F isolates carrying both *erm(B)* and *mef(E)* genes persisted without significant yearly fluctuations. Non-PCV7 serotypes exhibiting macrolide resistance were 6A, 19A, 10A, 15A, 15B/C, 35F, 35A, and 24F. In 2009, 59% of the macrolide-resistant pneumococci belonged to non-PCV7 serotypes.

Conclusions: Across the study period, the annual frequency of macrolide-resistant isolates did not change significantly, but in 2009 a marked shift to non-PCV7 serotypes occurred. Overall, more than half of the macrolide-resistant isolates possessed the *erm(B)* gene either alone or in combination with *mef(E)* gene. *erm(B)* gene dominated among PCV7 isolates, but not among the non-PCV7 ones.

MOLECULAR EPIDEMIOLOGY OF PNEUMOCOCCI RECOVERED FROM THE NASOPHARYNX OF YOUNG CHILDREN IN NEPAL

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Background and aims: Although rates of pneumococcal carriage and disease are highest in developing countries, the pneumococcal molecular epidemiology within these regions is poorly understood. Nasopharyngeal isolates from urban (Kathmandu) and rural (Okhaldhunga) sites were genotyped by multilocus sequence typing (MLST). The main aims were to characterise the overall population structure and identify major genotypic differences between locations.

Methods: 599 pneumococcal isolates, 299 from Kathmandu and 300 from Okhaldhunga, were recovered from healthy children < 2 yrs of age and genotyped. Alleles and sequence types (STs) were assigned; 576 isolates with complete STs were analysed. goeBURST was used to define clonal complexes (CCs).

Results: 302 unique STs were detected; 187 STs were found in Kathmandu and 160 in Okhaldhunga. 229 STs were newly recognised and described 330 isolates (57% of the collection). There were 11 major CCs with ≥ 10 isolates (n; predominant serogroup/type(s)): CC63 (28; 14, 15BC); CC4209 (27; 15BC); CC193 (22; 21, 17F); CC6025 (22; 11A); CC5613 (20; 6, 15A); CC7695 (17; 35B, 18); CC4217 (12; 6); CC5080 (12; 23A); CC1439 (12; 34); CC4881 (10, 9V); and CC176 (10; 23F, 19F). Some CCs predominated in Kathmandu (CC193, 5080, 1439) and others in Okhaldhunga (CC6025, 7695, 4881); the rest were roughly equally distributed between locations.

Conclusions: The majority of genotypes in this study were novel and thus provide important information about the molecular epidemiology of carriage pneumococci in Nepal. These data also provide a baseline from which to measure genetic changes after a pneumococcal conjugate vaccine is implemented.

FULMINANT ABDOMINAL ANGIOSTRONGILIASIS (AA) PRESENTING AS AN ACUTE ABDOMEN IN A 14-MONTH-OLD COSTA RICAN (CR) GIRL

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Background: AA is caused by *Angiostrongylus costarricensis*, a nematode first described in CR. The clinical triad for suspicion is abdominal pain, leukocytosis and moderate to severe eosinophilia. Antihelminthics are contraindicated as erratic disease and mesenteric vascular occlusion can occur once treatment is given.

Case: A 14-month-old girl was admitted to our hospital with 7 days of fever, hyporexia, irritability and abdominal pain. Three weeks before, her mother noticed a slug in her mouth. On admission, she was irritable and had a diffuse abdominal pain predominantly in the right hypochondrium. CBC revealed hemoglobin 10.5 g/dL, leukocytes 22,050/mm³ (23% eosinophils), and stool smears were negative for parasites. A latex agglutination test for *A. costarricensis* was positive. An abdominal CT scan showed thickening of the ileocecal intestinal wall. The child improved slowly and went home asymptomatic 3 weeks after, without eosinophilia. She was readmitted 9 days after because of fever, pallor, irritability, abdominal distention and pain. In addition, decreased bowel sounds, melena, and fecaloid drainage from a nasogastric tube prompted surgery. WBC on admission was 35,480 leukocytes/mm³ (0% eosinophils). She required two laparotomies with resection of distal ileum and ileo-ileal anastomosis due to massive thrombosis of the superior mesenteric artery and massive intestinal necrosis, among other findings. She deteriorated clinically, and died 2 days after admission. Histopathology of different tissues demonstrated the presence of the parasite.

Conclusions: Life threatening complications such as mesenteric artery thrombosis and secondary intestinal necrosis can occur in children with AA even in the absence of eosinophilia.

PLASMODIUM FALCIPARUM MALARIA CAUSES PROLONGED IMPAIRMENT OF NEUTROPHIL OXIDATIVE BURST ACTIVITY

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Background and aims: Malaria causes susceptibility to non-typhoid Salmonella (NTS) bacteremia. We have shown that in mice malarial hemolysis impairs killing of NTS by reducing the ability of circulating neutrophils to mount an effective oxidative burst. Suppression of the neutrophil oxidative burst is a consequence of induction of the cytoprotective heme degrading enzyme heme-oxygenase-1 (HO-1) in neutrophil progenitors in bone marrow. In this study we looked for evidence of impaired neutrophil function in *Plasmodium falciparum* malaria, and for associations with hemolysis and HO-1 induction.

Methods: We quantified neutrophil oxidative burst and degranulation using flow cytometric assays in acute and convalescent samples from 58 Gambian children with *P. falciparum* malaria. We assessed HO-1 expression by intracellular flow cytometry, qRT-PCR and ELISA, and we assessed the role of hemolysis in HO-1 induction by measuring parasite biomass, erythrocyte count, and plasma heme, as well as haptoglobin and hemopexin and expression of their respective receptors.

Results: In acute malaria there were two distinct populations of neutrophils, the major population having reduced oxidative burst activity. Over 8 weeks of follow-up neutrophil function progressively normalized towards a single population of neutrophils with normal oxidative burst activity. The degree of oxidative burst impairment correlated significantly with markers of hemolysis. HO-1 expression was increased in blood during acute malaria, although at a cellular level its expression was modulated by changes in expression of the haptoglobin receptor (surface CD163).

Conclusions: Neutrophil dysfunction occurs in children with *P. falciparum* malaria and may explain the associated susceptibility to NTS infection.

SUCCESSFUL TREATMENT OF HYPERSPLENISM DUE TO VISCERAL LEISHMANIASIS BY PARTIAL SPLENIC EMBOLIZATION

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Introduction: Splenectomy had been the treatment of choice for severe hypersplenism. We think that partial splenic embolization (PSE) is another effective alternative modality for splenectomy because it is a safe, less invasive, more simple procedure that is easily performed under local anesthesia and it allows preservation of adequate splenic tissue. PSE usually performed via percutaneous femoral artery approach for embolization of approximate 60-70% of spleen parenchyma

Case report: A two and half year old girl presented with history of prolonged fever, abdominal distension, pallor for 3 weeks with huge splenomegaly and mild hepatomegaly, otherwise she was normal. Her WBC count was 1,700/mm³, platelets count was below 100,000/mm³ and Hgb of 6 gm/dL. Other investigations including Leishmania serology were negative. Normal bone marrow biopsy with No evidence for malignancy or Leishmaniasis

Splenic biopsy sample was heavily loaded by L. Donovani bodies. The patient received a full course of amphotericin B, there was no improvement of blood cell counts but the fever subsided. Few days after the Amphotericin B and because of high fever splenic biopsy was repeated and the sample turned to be normal. PSE successfully performed to our patient with no complications apart from mild fever and abdominal pains which lasted only for couple of days. Her cell count return to the normal within 2 days after PSE

Conclusion: PSE is an effective and less invasive modality for treatment of hypersplenism in children compared to splenectomy.

PSE allows preservation of splenic tissue to safeguard against overwhelming infections especially in young children.

INTESTINAL PARASITE PREVALENCE AND RELATED FACTORS IN SCHOOL CHILDREN OF GANDERBAL DISTRICT, KASHMIR VALLEY, INDIA**S.A. Wani**^{1,2}, D.F. Ahmad², S.A. Zaragr³, D.A. Amin⁴¹*Zoology, Govt. Degree College Beerwah*, ²*Zoology, Kashmir University*, ³*Gastroenterology, SK Institute of Medical Sciences*, ⁴*Zoology, University of Kashmir, Srinagar, India*

Intestinal parasitic infections are amongst the most common infections worldwide. Epidemiological research carried out in different countries has shown that the social and economical situation of the individuals is an important cause in the prevalence of intestinal parasites. Previous studies in Kashmir revealed a high prevalence of intestinal parasitic infection. The objectives of the current study were to determine the prevalence of intestinal parasitic infections in Ganderbal district among 3—15 years old children, to identify associated socio-demographic and environmental factors, behavioral habits and also related complaints. Multistage sampling was used in the selection of the study sample. A questionnaire, cellulose adhesive and a stool specimen examination were done. A total of 309 stool specimens were collected. 221 students (71.5%) were infected with one or more intestinal parasites. The most common infecting parasites were *Ascaris lumbricoides*, *Trichuris trichiura*, *Enterobius vermicularis*, *Taenia saginata*, *Giardia lamblia* and *Entamoeba* spp. Intestinal parasite prevalence was higher in the middle age group than upper and lower age groups, in children with less educated mother, in children who source river or well water, in children who who drank unboiled drinking water, in children who defecated in open latrines and in children with unhygienic conditions. Most of the complaints of the study population were not significantly related with the intestinal parasitic infection. Intestinal parasitic infection is an important public health problem in Ganderbal district. Interventions like mass chemotherapy with anthelmintics and health education on personal hygiene to the students and to the parents, especially to mothers are required.

HUMAN BOCAVIRUS TYPES 1, 2 AND 3 IN ACUTE GASTROENTERITIS OF CHILDHOOD

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Background and aims: Recently identified human bocavirus (HBoV) types 2 and 3 have been implicated as causative agents of acute gastroenteritis (AGE) in children. We studied stool specimens from children with AGE for human bocaviruses 1, 2, 3 and 4; the same specimens were also examined for known gastroenteritis viruses.

Methods: Stool specimens of 878 children with AGE and of 112 age-matched controls seen in hospital were collected in a two-year prospective study. A two step PCR method was used to detect HBoVs. Positive amplicons were sequenced to identify HBoV1, HBoV2, HBoV3 and HBoV4, respectively.

Results: HBoV of any type was found in 85 (9.7%) cases of AGE and in 6 (5.4%) controls. HBoV1 was detected in 49 (5.6%) cases and 2 (1.8%) controls, HBoV2 in 29 (3.3%) cases and 2 (1.8%) controls and HBoV3 in 8 (0.9%) cases and 2 (1.8%) controls. No HBoV4 was found. In one of the AGE cases both HBoV1 and HBoV2 were detected. In 69 (81.2%) of the HBoV positive AGE cases a known gastroenteritis virus was also found, and conversely, HBoV alone with no gastroenteritis viruses was found in 16 (1.8%) cases and in 6 (5.4%) controls. In the "pure" HBoV positive cases of AGE HBoV2 was found in 8, HBoV1 in 7 and HBoV3 in 1 patient.

Conclusions: HBoVs are rarely found alone in children with AGE, and their etiological role in gastroenteritis appears small. Further studies are warranted to confirm if HBoV2 has a minor causative role in childhood gastroenteritis.

PATTERN RECOGNITION RECEPTOR RESPONSES IN CHILDREN WITH CHRONIC HEPATITIS B VIRUS INFECTION

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Background: Several studies have demonstrated that Hepatitis B virus (HBV) affects the expression and function of Toll like receptors (TLRs), but data on TLR function in HBV infection are mainly from adult patients. The natural history of chronic hepatitis B (CHB) infection is distinctly different in children, since 90% of children become chronic carriers compared to 5% of adults when infected with HBV. We have studied the function of TLRs and cytosolic DNA receptors in children with CHB infection compared to healthy children.

Methods: PBMCs from 19 children with CHB and 19 healthy children were stimulated with ligands for TLR 2,3,4,7 and 9 for 24 hours. For activation of cytosolic DNA receptors, cells were transfected with a double-stranded DNA using Lipofectamine 2000. Supernatants were analyzed for levels of IFN- α , TNF- α , IL-6, CXCL10 and CCL3 by Luminex.

Results: Stimulation with ligands for TLR2, TLR3 and TLR9 induced IL-6, CCL3 and CXCL10 to a significantly higher level in children with CHB compared to healthy children. CHB patients displayed significantly lower IFN- α production compared to healthy children after stimulation with ligands for TLR2, TLR3 and TLR4. Stimulation of intracellular DNA sensors with synthetic double-stranded DNA elicited significantly higher induction of the inflammatory cytokines and chemokines IL-6, TNF- α and CCL3 in the CHB patients as compared to the healthy children.

Conclusion: Our results indicate a TLR-mediated inflammatory response in children with CHB infection. Furthermore, our study is the first to show that the responses of intracellular DNA receptors are affected in CHB.

THE PRETERM GUT MICROBIOTA: CHANGES ASSOCIATED WITH NECROTISING ENTEROCOLITIS AND SEPSIS

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Background and aims: The preterm gut microbiota influences important morbidity and mortality. 16S rRNA based methodologies may offer insights into microbiomic influences on infection or necrotising enterocolitis (NEC). We aimed to describe gut colonisation in infants (< 32 weeks) using both standard culture (SC) and 16S rRNA (16S) methods, exploring differences in healthy infants and those with NEC/infection.

Methods: Weekly stool collected from birth to 8 weeks was analysed by SC and 16S using PCR-DGGE. Analyses assessed the effects on gut community of gestation, sex, mode of delivery and NEC or infection. 99 stools from 38 infants, median gestation 27wks (23-32wks), and birth weight 895g (520g-1850g) were analysed by SC, 44 from 27 infants by 16S.

Results: SC identified a median of 2 organisms (0-7), DGGE median 12 (3-18). By SC commonest organisms were *Enterococcus faecalis* and coagulase negative *staphylococcus* (CONS) (40% and 39% of stools). More infants with NEC were colonised with CONS (45% vs 30%) and less with *Enterococcus faecalis* (31% vs 57%). Meconium samples were not sterile. No fungus was cultured.

By either method community structures in NEC and sepsis differed from healthy infants. SC identified *Enterococcus faecalis* associated with a reduced risk of NEC/sepsis. 16S indicated the presence of *Enterobacter*, *Flavobacterium*, *Staphylococcus* and *Propionibacterium* was associated with NEC/sepsis.

Conclusions: Important differences exist in gut community structure in preterm infants developing NEC and sepsis. The relationship of these changes to current practices in modern neonatal intensive care requires further exploration.

MOLECULAR AND CLINICAL CHARACTERIZATION OF ROTAVIRUS ACUTE GASTROENTERITIS IN FRENCH INFANTS OVER 5 EPIDEMIC SEASONS, 2006-2011

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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). Prospective surveillance is required to monitor and characterize rotavirus infections, including viral and clinical data, and to detect the emergence of potentially epidemic strains.

Methods: Between 2006 and 2011, stool samples and clinical records were collected from 3843 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 P (VP4) and G (PV7) types.

Results: The genotyping of 3670 rotaviruses showed that G1 strains (59.5% [52.9-75.9]) were predominant, G9 (16.8% [7.6-25.9]) were decreasing, G2 (8.7% [1.8-18.5]) were very changing, and G3 (3.4% [2.4-4.5]) and G4 (2.5% [0.3-5.6]) circulated locally. Most strains were associated with P[8] (87.5% [76.3-94.1]). Overall, 89 uncommon strains or possible zoonotic reassortants (2.4% [1.3-4.7]) were detected including G12, G8 and P[6] strains, some being closely related to bovine strains. No difference in clinical presentation and severity was found among genotypes.

Conclusions: The relative stability of rotavirus genotypes may ensure vaccine effectiveness in the short and medium terms in France. Moreover, the likely emergence uncommon strains, especially G12 and G8 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.

SPECTRUM AND INOCULUM SIZE EFFECT OF A RAPID ANTIGEN DETECTION TEST FOR STREPTOCOCCAL PHARYNGITIS IN CHILDREN

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Objectives: We aimed to assess whether the performance of a rapid antigen detection test (RADT) for group A streptococcus (GAS) is affected by the clinical spectrum and/or bacterial inoculum size.

Methods: Double throat swabs were collected from 785 children with pharyngitis in an office-based, prospective, multicenter study (2009-2010). We analyzed the effect of clinical spectrum (i.e., Mclsaac score and its components) and inoculum size (light or heavy GAS growth) on the diagnostic accuracy of a RADT, with laboratory throat culture as the reference test.

Results: GAS prevalence was 36% (95CI: 33%-40%). The inoculum was heavy for 85% of GAS-positive cases (81%-89%). We found a significant spectrum effect on sensitivity, specificity, likelihood ratios and positive predictive value ($p < 0.05$) but not negative predictive value, which was stable at about 93%. RADT sensitivity was greater for children with heavy than light inoculum (95% vs. 40%, $p < 0.001$). After stratification by inoculum size, the effect of clinical spectrum on RADT sensitivity was significant only in patients with light inocula ($p < 0.05$), on univariate as well as multivariate analysis.

Spectrum effect analysis: diagnostic accuracy by clinical spectrum

Clinical variable (N)	GAS (%)	Se (%)	Sp (%)	LR+	LR-	PPV (%)	NPV (%)
Mclsaac score							
≤2 (115)	24***	75*	98*	33	0.3	91	92
3 (262)	34	84	96	21	0.2	91	92
≥4 (408)	41	90	92	12	0.1	89	93
Age, y							
3-8 (663)	38**	89***	94	15	0.1***	90	93
9-14 (122)	25	67	97	20	0.3	87	90
Lack of cough							
Yes (428)	44***	90*	94	15	0.1*	92	92
No (357)	27	80	95	16	0.2	85	93
Anterior cervical adenopathy							
No (407)	35	83	98***	37**	0.2	95*	91
Yes (378)	38	90	91	10	0.1	86	94
Tonsillar swelling or exudate							
No (157)	42	83	96	19	0.2	93	89
Yes (628)	35	88	94	16	0.1	89	93
Fever							
No (246)	31*	88	93	14	0.1	86	95
Yes (539)	39	86	95	18	0.1	92	92
Total (785)	36	87	95	16	0.1	90	93

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

[Spectrum effect analysis]

Conclusions: Significant variations in RADT sensitivity are only observed in patients with light bacterial inocula who are more likely to be GAS carriers rather than true GAS infections. Because the spectrum effect does not affect the negative predictive value of the test, clinicians who want to rule out GAS can rely on negative RADT results, regardless of clinical features.

CHANGES IN THE MOLECULAR EPIDEMIOLOGY OF PNEUMOCOCCAL MENINGITIS FOLLOWING THE INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINATION IN ENGLAND AND WALES

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Background and aims: The introduction of 7-valent pneumococcal conjugate vaccine (PCV7) in September 2006 markedly reduced the burden of invasive pneumococcal disease (including meningitis). This study aimed to assess changes in the molecular epidemiology of pneumococcal isolates causing meningitis in England and Wales 2 years before and 3 years after the introduction PCV7 vaccination.

Methods: Pneumococcal isolates from blood or cerebrospinal fluid causing meningitis between July 2004 and June 2009 and sent to the Health Protection Agency Reference Laboratory for serotyping were genotyped by multi-locus sequence typing (MLST).

Results: 1,030 pneumococci from meningitis cases were serotyped and genotyped. Fifty two serotypes, 238 sequence types (ST) and 87 clonal complexes were identified. STs associated with PCV7 serotypes all declined after PCV7 introduction, with a proportionally greater decline in ST 124 (usually associated with serotype 14) which caused meningitis predominantly in children < 5y. There was no evidence of capsular switching. Replacement disease after PCV7 introduction was mainly due to serotypes 1, 3,7F, 19A, 22F and 33F through clonal expansion, suggesting a limited number of genotypes are replacing PCV7 genotypes. There was no association between case fatality and any serotype or ST.

Conclusion: Following PCV7 introduction in England and Wales, serotype replacement has changed the genetic composition of the pneumococcal population causing meningitis. The replacement of PCV7 with the 13-valent pneumococcal conjugate vaccine (PCV13) will lead to a further decline in IPD, including meningitis. Continued epidemiological and molecular surveillance is therefore essential to monitor the impact of the higher valency vaccines.

EVALUATION OF SEROTYPE SPECIFIC ANTIPNEUMOCOCCAL ANTIBODY CONCENTRATIONS IN 22 PRIMARY HUMORAL IMMUNODEFICIENCY PAEDIATRICS PATIENTS TREATED WITH INTRAVENOUS IMMUNOGLOBULIN (MULTIGAM®)

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Background and aim: The main goal of intravenous immunoglobulin (IVIg) replacement for patients with primary humoral immunodeficiency (PID) is to reduce the frequency and severity of infection, mainly related to *Streptococcus pneumoniae*. For the evaluation of pneumococcal vaccines, an anti-pneumococcal antibody (APAb) level of 0.2 µg/ml is considered a correlate of protection for invasive pneumococcal infection (WHO 14, 22F preabsorption). The protective plasma APAb level in IVIg-treated children with PID has never been established.

Methods: We measured levels of APAbs against 16 serotypes (ST) (1,3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 12F, 14, 18C, 19A, 19F, 23F) in IVIg lots (Multigam®) and in the plasma (trough and peak levels) of 22 PID patients over a period comprising 6 consecutive IVIg infusions in the context of a GCP prospective multicentre open label clinical study. APAbs were determined by an ICH-Q2(R1) validated automated high-throughput quantifying process using the calibrator 89-SF (FDA) and including 22F preabsorption. The trough and peak geometric mean concentrations (GMCs) were determined for all patients and for each serotype.

Results: The trough GMC ranged from 0.13 µg/ml for serotype 12F to 2.76 µg/ml for serotype 14. The median percentage of measurements reaching trough level > 0.2 µg/ml was 100% for all serotypes except serotypes 12F (14%), 4 (71%), and 9V (92%). A good correlation was seen between serum concentrations of APAbs against each serotype in patients and levels in Multigam®, produced from plasma collected in Belgium.

Conclusions: PID patients treated with Multigam® have protective trough levels of APAbs against the most prevalent pneumococcal serotypes.

GENOTYPE CONSTELLATIONS OF HUMAN P[6] ROTAVIRUSES FROM SUB-SAHARAN AFRICA AND ASIA ARE CLOSELY RELATED TO HUMAN P[4] AND P[8] ROTAVIRUSES

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Background and aims: P[6] rotaviruses in combination with a variety of G-genotypes have been circulating with a prevalence up to 31.85% in African and Asian countries, but only a few strains have been completely characterized. In Phase 3 clinical trials of RotaTeq™, conducted between March 2007 and March 2009 in Ghana, Kenya, Mali, Vietnam and Bangladesh, 24.3% of the 790 RV-positive gastroenteritis samples contained P[6] strains.

Methods: To investigate the genomic relationship between these human P[6] rotaviruses and common human rotaviruses circulating worldwide, we sequenced 39 P[6] strains collected in Ghana (n=14), Mali (n=18), Kenya (n=2), and Bangladesh (n=5) using 454™ pyrosequencing.

Results: Genetic analysis revealed that P[6] strains were associated with a wide range of G-genotypes: G2 (n=17), G3 (n=7), G8 (n=6), G12 (n=5), G1 (n=2), G9 (n=1), and Gx (n=1). Most rotaviruses possessed a complete Wa-like or DS-1-like backbone, with only a few exceptions containing both Wa- and DS-1-like genes. Several P[6] rotaviruses (in combination with G1, G2 or G9) potentially possessed 1 or 2 gene segments of bovine-like origin. However, potential bovine-like gene segments have also been encountered in co-circulating human rotaviruses carrying the P[4] and P[8] genotypes, indicating that the genetic backbone of the subset of analyzed human P[6] strains are similar to those of P[4] or P[8] strains.

Conclusions: These data confirm that P[6] strains constitute an important cause of rotavirus gastroenteritis in sub-Saharan Africa and Asia, and need to be closely monitored, especially because vaccine efficacy is lower in these countries.

WHY DID EARLY FLUID RESUSCITATION INCREASE MORTALITY IN AFRICAN CHILDREN WITH SEVERE FEBRILE ILLNESS AND SHOCK IN THE FEAST TRIAL?

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Background: Early fluid boluses in African children with severe febrile illnesses increased absolute 48-hour mortality by 3.3% compared to controls. We explored the effect of boluses by clinical presentation at enrolment, by change in bedside observations over the first hour following randomization, and on different modes of death according to terminal clinical events (TCE).

Methods: 3141 children (median(IQR) age 24(13-38) months), presenting to African hospitals with febrile illness plus impaired consciousness or respiratory distress and signs of impaired perfusion were randomized to boluses: 20-40ml/kg 5%albumin or 0.9%saline(n=2047) or control(n=1044). Three presentation syndromes (severe acidosis/shock, respiratory, neurological) and 3 predominant TCEs (cardiovascular collapse, respiratory, neurological) were pre-defined, and adjudicated blind to randomised arm.

Results: Among 2396/3141(76%) classifiable participants, 1647(69%) had severe acidosis/shock, 625(26%) respiratory and 976(41%) neurological presentation syndromes, alone/combined. Excess mortality in bolus versus control was apparent for all syndromes and for all their component features. By one hour, shock resolved more frequently in bolus vs control (43% vs 32%, $p < 0.001$), but excess mortality in bolus arms occurred irrespective of shock resolution. 9% bolus versus 7% control children developed hypoxia de novo by one hour ($p=0.06$), but this did not explain excess mortality with boluses. Excess terminal clinical events with boluses were mainly cardiovascular collapse (123 TCEs: 4.6%bolus vs 2.6%control, $p=0.008$), then respiratory ($n=61$; 2.2%vs1.3%, $p=0.09$) and least, neurological ($n=63$, 2.1%vs1.8%, $p=0.6$).

Conclusions: Excess mortality from boluses occurred in all subgroups. Cardiovascular collapse rather than fluid overload appeared to contribute most to excess deaths with bolus fluid resuscitation.

HOW MUCH DO YOU NEED FOR INITIAL VANCOMYCIN DOSAGE IN CHILDREN UNDERGOING ECMO AND CHDF?

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Background and aims: Critically ill patients with extracorporeal membrane oxygenation (ECMO) and continuous hemodiafiltration (CHDF) demonstrate different pharmacokinetics of vancomycin in adult study. Little is known regarding to infant and young children. Critically ill children need to achieve therapeutic level immediately. We evaluated vancomycin dosage and initial trough level to determine an optimal regimen.

Methods: We prospectively registered pediatric patients undergoing ECMO and CHDF who received vancomycin therapy from March 2010 to December 2011 at Tokyo Metropolitan Children's Medical Center in Japan. We evaluated vancomycin trough level before 4th dose and vancomycin dosage per body weight and draw the approximate line. We analyzed serum vancomycin level by enzyme immunoassay (SRL, Japan). Polymethyl methacrylate dialysis membrane (HEMOFEEL CH-0.3N®, Toray Medical Co., Japan) was used for CHDF in these patients. We measured vancomycin level at pre- and post-membrane.

Results: Eight patients were enrolled for this study. Mean age and mean body weight were 9 month-old (range, 1-33 month-old) and 4.9 kg (range, 2.5-7.8 kg), respectively. There was significant correlation between vancomycin dosage and trough level. Estimated vancomycin dosage per day to achieve 15 and 20 mcg/dl was 58.6 and 71.4 mg/kg/day, respectively. Polymethyl methacrylate dialysis membrane eliminated vancomycin by 13.9% (mean, n=5).

Conclusion: In our study, pediatric patients with ECMO and CHDF required higher dosage than conventional dosage of 40 mg/kg/day to achieve trough level between 15 and 20 mcg/dl. Although these patients need frequent therapeutic drug monitoring, initial vancomycin dosage may be loaded with 60 mg/kg/day.

CURRENT MANAGEMENT OF LATE ONSET NEONATAL SEPSIS (LOS) IN SELECTED EUROPEAN COUNTRIES AND PERFORMANCE OF NEW DIAGNOSTIC CRITERIA

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Background and aims: Clinical trials of treatment of LOS are urgently required but few validated definitions of sepsis are available. We evaluated appropriateness of new expert panel-derived criteria defining LOS and described the current management of LOS.

Methods: Prospective observational study performed between July 2010 and September 2011 recruited infants < 3 months with suspected LOS, based on clinical and laboratory criteria of sepsis (Lutsar et al. 2011 or Goldstein et al. 2005) depending on age.

Results: Of 166 screened patients from 15 centres in 5 countries 113 fulfilled enrolment criteria. Median age at onset of LOS was 14 days, median birth weight 1190g, and 62% were male. 61% had culture proven sepsis (41% CoNS, 35% Enterobacteriaceae, 16% other Gram positive and 9% non-fermentative Gram negative organisms). In infants \leq 44 weeks of corrected age of 21 clinical criteria, mottled skin, impaired peripheral perfusion and increased oxygen requirement were the most commonly observed (approximately 40% each). Of laboratory markers, CRP > 15 mg/L and platelet count < 100×10^9 cells/L were the most frequent, occurring in 85% and 42% of subjects respectively. Overall 18 antibiotics in 49 treatment regimens were used for empiric therapy. Meropenem +/- vancomycin or vancomycin + amikacin were the most frequent, used in 9% of patients each. All-cause mortality was 8%.

Conclusions: The expert panel - derived diagnostic criteria performed well in this study identifying a high rate of culture proven sepsis. Future studies should address the significant variability of empiric treatment regimens for LOS in Europe.

A PROTEIN PATTERN IN SERUM AS A BIOMARKER TO DIAGNOSE ACTIVE TUBERCULOSIS IRRESPECTIVE OF HIV STATUS

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Background and aims: A major impediment in controlling TB is the lack of a fast and reliable diagnostic test which would improve case detection. In the presence of HIV, the clinical and radiological features of TB do not discriminate TB from a range of other HIV associated opportunistic infections. Thus, an effective diagnostic test is urgently needed.

The aim of this study is to examine the serum protein profiles of systematically collected patients with (1) active TB, (2) latent TB and (3) other infections with clinical features resembling TB and to identify a protein pattern that uniquely characterizes active disease from any other condition, irrespective of HIV infection.

Methods: Serum samples were collected from children (n=600) and adults (n=600) with active TB (culture confirmed), latent TB (IGRA+ and TST+) and other infections, all equally including HIV+/- cases. Patients were recruited from two sub-Saharan Africa regions with differing patterns of HIV and TB prevalence. SELDI-TOF MS technology was used to define the proteomic profiles. An advanced bioinformatics analysis pipeline was designed to identify the most-predictive protein set to characterize active TB.

Results: SELDI analysis generated over 10,000 protein profiles. Approximately 700 proteins were differentially expressed between patients with active TB from those with latent and other infections regardless of HIV status. The minimal set of proteins that achieves prediction with very high accuracy (>85%) is selected using advanced statistical approaches.

Conclusions: SELDI proteomic profiling has identified serum biomarkers of active TB, which will be used as a diagnostic signature of disease.

ASSOCIATION BETWEEN HPV VACCINE UPTAKE AND CERVICAL CANCER SCREENING IN THE NETHERLANDS; IMPLICATIONS FOR FUTURE IMPACT OF PREVENTION

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An increasing number of countries has introduced HPV vaccination additionally to cervical cancer screening. Information on the association between participation in either programme and on potential risk groups for non-participation, is essential for estimating the future impact of cervical cancer prevention. We studied the association between participation in screening (mothers) and in vaccination (girls) and studied the impact of this association on the effectiveness of cervical cancer prevention. Furthermore, we investigated risk groups for non-participation and calculated population attributable fractions.

Girl's vaccination status (from the vaccination registry) was matched by houseaddress with her mother's screening participation (from the cervical cancer screening database). We performed multivariable multilevel logistic regression.

Our results, based on 89% of all girls invited for HPV vaccination (n=337,368), show that vaccination status was significantly associated with mother's screening participation (OR: 1.54 (95%CI 1.51-1.57)). If mother's screening participation is taken as proxy of a girl's future screening behaviour, only 13% of the girls will not participate in any prevention programme compared to 23% non-participation if only screening is available. The positive association between vaccination and screening participation resulted in slightly lower model estimates of the impact of vaccination on cervical cancer incidence compared to estimates based on random participation.

Girls with non-western ethnicities, with young mothers, who live in urban areas with low SES are at risk for non-participation. A significant part of potential non-screener may be reached through vaccination.

The association between vaccination and screening participation has almost no bearing on the effectiveness of the vaccination programme.

POSTMARKETING SURVEILLANCE OF INTUSSUSCEPTION FOLLOWING MASS INTRODUCTION OF THE ATTENUATED HUMAN ROTAVIRUS VACCINE IN MEXICO

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Background and aims: Mexico initiated mass vaccination with the attenuated human rotavirus vaccine (Rotarix™; GlaxoSmithKline Biologicals) in 2006. This postlicensure study aimed to assess any potential temporal association between vaccination and intussusception in Mexican infants.

Methods: Prospective, active surveillance for intussusception among infants aged < 1 year was conducted in 221 hospitals across Mexico from the Mexican Institute of Social Security from January 2008-October 2010. The temporal association between vaccination and intussusception was assessed by self-controlled case-series analysis.

Results: Of the 753 episodes of intussusception reported in 750 infants, 701 were in vaccinated infants (34.5% post-dose 1, 65.5% post-dose 2). The relative incidence of intussusception within 31 days of vaccination was 1.75 (95.5% CI: 1.24-2.48; P=0.001) post-dose 1 and 1.06 (95.5% CI: 0.75-1.48; P=0.75) post-dose 2. The relative incidence of intussusception within 7 days of vaccination was 6.49 post-dose 1 (95.5% CI: 4.17-10.09; P< 0.001) and 1.29 post-dose 2 (95.5% CI: 0.80-2.11; P=0.29). Clustering of intussusception within 7 days of vaccination was observed post-dose 1. An attributable risk of 3-4 additional cases of intussusception per 100000 vaccinated infants was estimated.

Conclusions: This is the largest surveillance study for intussusception following rotavirus vaccination to date. A small temporal increase in risk for intussusception was seen within 7 days of administration of the first vaccine dose. This finding should be put in perspective with the well-documented substantial benefits of rotavirus vaccination. It is still uncertain whether rotavirus vaccination has any impact on the overall incidence of intussusception.

IMMUNIZATION COVERAGE AND PREDICTIVE FACTORS FOR COMPLETE AND AGE- APPROPRIATE VACCINATION AMONG PRESCHOOLERS IN ATHENS, GREECE

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Background and aims: To assess immunization coverage and identify factors influencing complete and age-appropriate vaccination among children attending public nurseries in the municipal Athens area, following a full reimbursement policy (since 2008 for MenC, PCV7, varicella and hepatitis A vaccines).

Methods: A cross-sectional study, using stratified sampling was performed during 2010-2011. Immunization history was obtained from vaccination booklets while demographic and socioeconomic characteristics along with parental attitudes towards immunization by telephone interviews. Percentages of vaccination were estimated by sample weighted proportions while associations between complete and age-appropriate vaccination and possible determinants by logistic regression analysis.

Results: A total of 731 children (mean age: 46, median: 48, range: 10-65 months) were included (participation rate: 90%). Complete vaccination coverage was satisfactory overall, exceeding 90% for traditional antigens (DTP, polio, Hib, hepatitis B, 1st dose of MMR) but ranging between 61-92% for newly reimbursed vaccines. However, immunization was significantly delayed for new vaccines, as well as for hepatitis B (only 28% were vaccinated at 12 months of age), and 2nd dose of MMR (65% at 60 months of age). Child's increasing age as well as belonging to immigrant group were significantly associated with under- or delayed immunization status while use of multivalent vaccines had a positive impact on complete and age-appropriate immunization with most vaccines.

Conclusions: Our results highlight the need to monitor uptake of new vaccines and reinforce appropriate administration of booster doses and hepatitis B vaccine. Immigration was identified as risk factor for suboptimal immunization that may warrant targeted intervention.

CELLULAR RESPONSES AND ANTIBODY KINETICS INDUCED BY PCV7 IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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Aim: Memory B cells (MBCs) have been associated with establishment of immunological memory and antibody (Ab) persistence. We evaluated the kinetics of PCV7-induced pneumococcal serotype (PS)-specific MBCs and Abs in children with idiopathic nephrotic syndrome (INS) in remission compared to controls.

Methods: 32(17 male) children with INS [median age(range): 9(4-17)yrs] and 16(10 male) controls [14(7-20)yrs] (no history of pneumococcal vaccination/infection) received PCV7. PS-specific IgM MBCs (d0, d6-8, d28) and IgG Abs (d0, d28, m12) were analysed by ELISPOT (peripheral blood mononuclear cells (PBMCs) stimulation with SAC, PKW and CpG2006) and ELISA, respectively.

Results: At d6-8, MBC frequencies increased significantly over baseline for all PS in patients and controls ($p < 0.05$) and remained elevated ($p < 0.05$) at d28 after PCV7. MBCs were similar between groups for all PS at detected time points (median spot counts/ 10^5 PBMCs at d0vsd6-8vsd28: 58vs64vs58, 46vs57vs58, 35vs63vs48 in patients and 30vs65vs53, 35vs57vs49, 33vs61vs68 in controls for PS 6B, 14, 23F, respectively). Despite lower GMCs in INS subjects for PS 6B and 23F before PCV7 ($p=0.02$), both groups achieved significant increase in Abs at d28 for all PS, which persisted at 12 months after vaccination (GMCs at d0vsm1vsm12: 0.04vs3.62vs1.23, 0.12vs6.68vs3.15, 0.19vs7.33vs3.20 $\mu\text{g/ml}$ in patients and 0.42vs9.22vs3.74, 0.51vs11.64vs4.93, 0.44vs10.09vs4.20 $\mu\text{g/ml}$ in controls for PS 6B, 14, 23F, respectively, $p < 0.01$, comparisons with baseline). No significant differences in GMCs were observed between patients and controls after vaccination.

Conclusions: Similar cellular responses in patients and controls and Ab persistence up to 1 year after PCV7 suggest successful induction of immunological memory in INS children.

EFFICACY OF 13-VALENT VERSUS 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13; PCV7) IN PREVENTING NASOPHARYNGEAL COLONIZATION: A RANDOMIZED DOUBLE-BLIND TRIAL IN ISRAEL

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Background and aims: This double-blind study assessed the efficacy of PCV13 versus PCV7 in preventing nasopharyngeal (NP) colonization in infants; serotype 6C, a serotype with similar structure to 6A, was also assessed.

Methods: Healthy infants were randomly assigned to receive PCV13 (n=932) or PCV7 (n=934) at ages 2, 4, 6 and 12 months (m). Eight NP-swabs were collected between ages 2-24m. New NP-acquisitions (rate ratio; RR) within ages 7-24m, and prevalence (odds ratio; OR) at 5 age points were evaluated.

Results: For the 7 common serotypes, NP-acquisition and prevalence with 19F was lower in PCV13 recipients and did not differ for the other 6 serotypes (Table 1). For the 6 additional PCV13-serotypes grouped, 6A/6C grouped, and single serotypes 1, 6A, 6C, 7F and 19A NP-acquisition were reduced in PCV13 recipients (Table 2); there was a similar impact on the prevalence of colonization.

Conclusions: PCV13 should be more effective than PCV7 in preventing vaccine-type pneumococcal disease, in particular for the 6 additional serotypes, and non-vaccine serotype 6C, and perhaps 19F.

Serotypes Grouped or Single Serotype	PCV13	PCV7	PCV13:PCV7 Rate Ratio	95% CI
	N=833-881	N=831-873		
PCV7/PCV13 serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F	23.6	27.4	0.86	0.73, 1.01
19F	7.9	12.2	0.65	0.48, 0.87

[New Acquisitions Age 7-24 Months: PCV7-serotypes]

Single Serotype	PCV13	PCV7	PCV13:PCV7 Rate Ratio	95% CI
	N=832-880	N=806-872		
1	0.0	0.9	0.00	NE, 0.44
3	1.8	1.9	0.99	0.48, 2.06
5	0.1	0.2	0.50	0.02, 5.54
6A	7.7	13.2	0.58	0.43, 0.78
6C	2.7	6.0	0.44	0.27, 0.71
7F	0.3	1.3	0.27	0.04, 0.90
19A	12.6	22.9	0.55	0.44, 0.68

[New Acquisitions Age 7-24 Months: PCV13-unique, 6C]

BACTERICIDAL ANTIBODY PERSISTENCE TWO YEARS FOLLOWING MENINGOCOCCAL B VACCINATION AT 6, 8 AND 12 MONTHS IN 40 MONTH OLD CHILDREN

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Background and aims: In a previous study 60 infants receiving a serogroup B meningococcal vaccine containing recombinant-proteins alone (rMenB) or the proteins with an outer-membrane vesicle (4CMen B) at 6, 8 and 12 months of age produced serum bactericidal antibody (SBA) responses against multiple meningococcal strains. We studied persistence of the response.

Methods: In this extension study, rMenB and 4CMenB recipients had SBA titres evaluated before and after booster doses of their respective vaccines at age 40 months. Men B naïve age-matched children served as a control group.

Results: Prior to the booster, the proportions of 4CMenB recipients with SBA titres $\geq 1:4$ were 36% (n=14, 95% C.I. 13-65%) for strain 44/76-SL, 100% (77-100%) for 5/99, 14% (2-43%) for NZ98/254 and 79% (49-95%) for M10713. These percentages were 14 to 29% for rMenB recipients (n=14), except for strain 5/99 (93%, C.I. 66-100%). For controls (n= 40) these proportions were $\leq 3\%$ for all strains except M10713 (53%, C.I. 36-68%).

One month after the booster, $\geq 93\%$ of 4CMenB recipients had SBA titres $\geq 1:4$ for all 4 strains.

For controls receiving their first dose of 4CMenB, 23% (11-39%) had SBA titres $\geq 1:4$ for NZ98/254, compared with 62% to 87% for the remaining strains.

Conclusion: These data suggest waning of bactericidal antibodies following infant immunisation with rMenB or 4CMenB, but an anamnestic response to a booster-dose. Booster doses of 4CMenB may be required to maintain immune protection through childhood and adolescence.

PERSISTENCE OF BACTERICIDAL ANTIBODIES FOLLOWING EARLY INFANT IMMUNISATION WITH SEROGROUP B MENINGOCOCCAL VACCINES AND IMMUNOGENICITY OF PRE-SCHOOL BOOSTER DOSES

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Background and aims: At least 93% of infants given 4 doses of an investigational serogroup B meningococcal vaccine containing recombinant-proteins and an outer-membrane vesicle (4CMenB) had serum bactericidal antibody (SBA) titres $\geq 1:4$ against 3 reference strains (44/76-SL, NZ98/254, 5/99). We evaluated persistence of these antibodies.

Methods: In this extension study participants given 4CMenB or recombinant-proteins alone (rMenB) at 2,4,6,12 months received a fifth dose of the respective vaccines at 40 months (groups 4D-4CMenB and 4D-rMenB). Infants given a single dose at 12 months were immunised at 40 & 42 months (groups 1D-4CMenB & 1D-rMenB). MenB vaccine naïve participants received 4CMenB at 40 & 42 months (control group).

Results: At 40 months proportions of 4D-4CMenB participants with SBA titres $\geq 1:4$ were 65% (95% CI 38-86%) for strain 44/76, 76% (50-93%) for 5/99, 41% (18-67%) for NZ98/254 & 67% (38-88%) for M10713 (N=15-17). For 4D-rMenB recipients these proportions were 45-68% for all strains except NZ98/254 (3%, 95% CI 0.09-18%) (N=28-29). Pre-booster 0-38% 1D-4CMenB recipients had SBA titres $\geq 1:4$ for all strains (N=8), compared with 7-57% in 1D-rMenB recipients (N=13-14). For controls (N=40) proportions were 0-3% for strains 5/99 and NZ98/254, 63% (46-77%) for strain 44/76-SL and 68% (51-81%) for strain M10713. A booster dose in the 4D-4CMenB group increased proportions to 88-100% for all strains.

Conclusion: SBA titres wane following infant immunization with rMenB or 4CMenB but there is an anamnestic response to a booster dose.

NEUTRALIZATION ANTIBODY TITER CORRELATE OF INFLUENZA VACCINE EFFICACY IN 6 MONTH TO < 72 MONTH OLD CHILDREN

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Background and aims: Correlates of influenza vaccine efficacy have relied on hemagglutination inhibition (HI) antibody titers but the assay has limitations. A neutralization test (NT) correlate may more accurately reflect vaccine efficacy (VE) and clinical protection.

Methods: Post second-dose sera from 771 6 to < 72 month old subjects in a randomized trial that demonstrated efficacies of trivalent inactivated influenza vaccine (TIV), MF59[®]-adjuvanted TIV against H3N2 influenza were previously tested by HI and were retested by NT^{1,2}. H3N2 virus and serum dilution mixtures were incubated with Madin Darbin Canine Kidney (MDCK) cells for 7 days and viral neutralization assayed by measuring supernatant hemagglutinating activity.

A population-based correlate based on the Dunning model (used in previous determinations of HI correlates of protection and VE) fulfilled Prentice criteria.

Results: NT titers of 145 and 485 were associated with VE of 50% and 80%, respectively (Table 1).

Table 1. Comparison of neutralizing antibody and hemagglutination inhibition antibody titers correlating with protection against laboratory-confirmed H3N2 influenza virus infection in previously unimmunized 6 to <72 month old children.

Probability of Protection Against Laboratory-Confirmed H3N2 Influenza Virus Infection	H3N2 Neutralizing Antibody Titer (Helme fi, et al. Immunogenicity of a monovalent, aluminum-adjuvanted influenza whole virus vaccine for pandemic use. <i>Virus Res.</i> 2004; 103:163-71.) ¹	H3N2 Hemagglutination Inhibition Antibody Titer (Black S et al. <i>PLoS</i> 2011; 30: 1081-6) ²
50%	145	110
60%	206	151
70%	303	215
80%	485	330
90%	983	629

[Pic_1]

Conclusions: While an HI titer of ≥ 40 is correlated with 50% clinical protection against influenza in adults, no NT correlate is established. In the more sensitive NT, a titer of 145 was associated with 50% protection in < 72 month old previously unimmunized children. The more robust NT can now replace HI in evaluating pediatric inactivated influenza vaccines¹.

LATE ONSET SEPSIS AND 5-YEAR NEURODEVELOPMENTAL OUTCOMES OF VERY PRETERM INFANTS: THE EPIPAGE STUDY

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Background and aim: Neonatal infections are frequent complications of very preterm infants receiving intensive care. To determine if late onset sepsis are associated with increased risks of adverse neurodevelopment at 5 years of age in a population-based cohort of very preterm children.

Methods: We included all live births between 22 and 32 weeks of gestation from 9 regions in France in 1997 (EPIPAGE study). Of the 2665 live-births, 2193 were eligible for follow-up evaluation at 5 years of age, 1769 had a medical examination and 1495 a cognitive assessment. Cerebral palsy and cognitive impairment were studied according to number of episode of late onset sepsis (LOS) and pathogen type after adjustment for potential confounding variables using multivariate logistic regression models.

Results: In total, 591 (22%) of the 2665 live births included had one episode of LOS and 225 (8%) two episodes of LOS. At 5 years, the rate of cerebral palsy was 9% (157/1769) and cognitive impairment 12% (177/1495). Compared with uninfected infants, cerebral palsy was increased in the group of one episode of LOS (OR = 1.42, 95% CI: 0.91-2.23), in the group of two episodes of LOS (OR = 1.54, 95% CI: 0.85-2.77), and in the group of coagulase-negative staphylococci (OR = 1.32, 95% CI: 0.72-2.39). There was no association between late onset sepsis and cognitive impairment.

Conclusion: Late onset sepsis among very preterm infants are associated with an increased risk of cerebral palsy at 5 years of age.

PREVENTION OF PERINATAL GROUP B STREPTOCOCCUS (GBS) DISEASE: EFFECTIVENESS AND COST OF GBS INTRAPARTUM PCR SCREENING STRATEGY

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Background: GBS intrapartum PCR screening has been implemented routinely 24/7 for term deliveries in a Paris hospital. Our objective was to estimate the effectiveness and cost of intrapartum PCR screening on early-onset GBS disease compared with the antenatal lower-vagina culture screening recommended in France.

Methods: This was a single-institution study, comparing the intrapartum PCR screening strategy implemented in 2010 with antenatal culture strategy in place in 2009. Early-onset GBS disease in newborns was exhaustively monitored. We estimated direct costs, including screening test costs and hospital costs, for deliveries of healthy versus GBS-infected newborns. Costs in 2009 and 2010 were compared on an intention-to-treat basis.

Results: Term deliveries were 2,761 and 2,814 in 2009 and 2010, respectively. Among the screened mothers, the vaginal GBS colonization rate was 11.7% based upon antenatal GBS culture screening in 2009 vs. 16.7% in 2010 using the intrapartum PCR testing. The overall probabilities of neonatal GBS disease were 0.9% vs. 0.5%, and the average total cost per delivery €1,390+/-955 in 2009 vs €1,386+/-665 in 2010 (p=0.9) in antenatal and intrapartum screening strategies, respectively. The number and severity of early-onset GBS disease and the resulting hospital costs were higher in 2009.

Conclusions: In our hospital, PCR intrapartum screening strategy used 24/7 in routine clinical situations for term deliveries in 2010, was cost-neutral when compared to the 2009 antenatal lower-vagina culture screening, with a significant decrease in early-onset GBS disease.

GENETIC RELATEDNESS OF COAGULASE-NEGATIVE STAPHYLOCOCCI (CONS) FROM GASTROINTESTINAL TRACT (GIT) AND BLOOD OF NEONATES WITH LATE-ONSET SEPSIS (LOS)

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Background and aims: In neonates CONS are the first colonizers of GIT and the most common causative agents of LOS. Skin is considered the primary source; translocation from gut has been suggested but not unequivocally proven. We aimed to assess genetic relatedness of CONS isolated from blood and GIT in neonates with LOS.

Methods: From August 2006 to November 2007 22 neonates with CONS LOS with available blood isolates were included. Rectal swabs were collected twice weekly from birth. CONS were identified to species level by *tuf* gene sequencing. For genetic relatedness, *Staphylococcus epidermidis* (SE) was typed by multilocus variable number of tandem repeats analysis and multilocus sequence typing, *Staphylococcus haemolyticus* (SH) by pulsed field gel electrophoresis.

Results: In 22 neonates (median gestational age 26.5w) LOS (median age at onset 10d) was caused by SH in 13, SE in 7 and *Staphylococcus hominis* in 2. Prior GIT colonization with CONS was present in 21 but three did not harbour CONS of same species. Typing of CONS was performed thus in the remaining 18 patients. Blood isolate and ≥ 1 antecedent colonizing isolates were genotypically similar in 3/7 and 10/11 patients with SE and SH infection, respectively. Concordant GIT strain was present 0-7 days prior to positive blood culture.

Conclusions: Genetic relatedness between bloodstream and GIT isolates supports the hypothesis of the gut origin of CONS sepsis, at least in some cases of LOS. Considering the ubiquity of CONS our results should be interpreted with caution with regard to translocation.

CORRELATION BETWEEN UREAPLASMA BIOVARS DETECTED BY REAL-TIME PCR FROM A SINGLE VAGINAL SMEAR AND PRETERM DELIVERY: PRELIMINARY RESULTS

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Background and aims: Although numerous studies have associated *Ureaplasma* spp with preterm delivery and adverse outcome for preterm infants, the proof of a causal relation between vaginal isolation of *Ureaplasma* species and adverse pregnancy outcome is missing. We hypothesize that it is important to differentiate between *Ureaplasma* biovars with potentially high and low pathogenicity and that pregnant women with isolation of vaginal *Ureaplasma parvum* (Biovar 1) are at increased risk for preterm delivery compared to women with isolation of *Ureaplasma urealyticum* (Biovar 2) or negative results. We report on preliminary results of our ongoing multicenter study.

Methods: Vaginal swabs are obtained during routine nuchal translucency screening and are analyzed for *Ureaplasma* biovars by real-time PCR. PCR results are correlated with pregnancy outcome. It is planned to include 4000 pregnant women in the study.

Results: Until January 2012, PCR results were available from 1840 women. 1003 swabs revealed negative PCR results. *Ureaplasma parvum* was found in 742 (40,33%) whereas *Ureaplasma urealyticum* was found in 140 (7,61%) women. 45 women had a concurrent infection with *Ureaplasma parvum* and *Ureaplasma urealyticum*. Pregnancy outcome is available for 886 women. Preterm delivery occurred in 66 (13,7%) pregnancies with negative culture results, in 55 (15,10%) pregnancies with isolation of *Ureaplasma parvum* and in 10 (14,7%) pregnancies with isolation of *Ureaplasma urealyticum* ($p>0,05$).

Conclusions: These preliminary data show no statistically significant correlation between rates of preterm delivery and isolation of *Ureaplasma* biovars in vaginal swabs during first-trimester pregnancy.

HUMAN BETA DEFENSIN 2 (HBD2) SERUM LEVELS MAY PREDICT SUSCEPTIBILITY TO INFECTIONS IN PRETERM NEONATES

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Background: Preterm neonates (gestation age (GA) < 37 weeks) are particularly susceptible to infections in the first month of life. Antimicrobial peptides (AMPs) such as HBD2 being part of the innate immunity are known to have activity against a variety of microorganisms and may play an important role in the above setting. No data exist regarding HBD2 levels in cord blood.

Objective: Observational study to determine HBD2 levels in cord blood and to relate HBD2 levels to infections in neonates.

Methods: Determination of HBD2 serum levels in cord blood of 31 preterm neonates using ELISA-Kit (PhoenixPharmaceuticals). Clinical and laboratory data were collected and analyzed retrospectively.

Results: 31 preterm neonates with a median GA of 30 weeks (IQR 29-31) and a birth weight (BW) of 1328g (IQR 1049-1580) were enrolled. 11 out of 31 preterm neonates suffered from late-onset sepsis. Organisms were isolated in 7/11 patients: *S.epidermidis* (4); *K.pneumonia* (2); *E.faecalis* (1). HBD2 serum levels were significantly lower in patients suffering from late-onset sepsis (median 556 pg/ml, IQR 391-880) compared to those neonates who did not suffer from the above (median 1552 pg/ml, IQR 633-2775; p=0.01). This observation was not related to birth weight, gestational age, chorioamnionitis or the use of corticosteroids before birth. Two patients with very low HBD2 levels (98 and 54pg/ml respectively) suffered from *K.pneumonia* sepsis, the latter being fatal.

Conclusion: Low HBD2 levels at birth might be a predictor of increased susceptibility to neonatal infections in preterm neonates. Prospective studies are needed to confirm our observations.

NOSOCOMIAL INFECTIONS IN NEONATAL INTENSIVE CARE UNIT: EPIDEMIOLOGY AND PATHOGENS

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This paper presents an epidemiological profile of nosocomial infections (NIs) diagnosed in a neonatal intensive care unit (NICU) from a Brazilian hospital.

Methods: Prospective surveillance of NI according to National Healthcare Safety Network (NHSN) protocols for events occurred between oct/2008 and sep/2011.

Results: 337 infections were diagnosed in three years; 83% refer only to three major sites: 169 (50%) primary bloodstream infections (BSI); 80 (24%) ear, eyes, nose, and throat infections and 30 (9%) pneumonia. BSI are the major infections in all weight categories, but we observed significant differences in other types of infections according to birth weight (p-value = 0.011). We collected data from 1,603 patients (PTs) of 5 birth weight categories: 92 PTs ≤750g, 213 PTs 751-1,000g, 357 PTs 1,001-1,500g, 586 PTs 1,501-2,500g, and 355 PTs >2,500g. The risk of infection decreases significantly with increasing birth weight (p-value < 0.001): ≤750g = 34%, 751-1,000g = 35%, 1,001-1,500g = 22%, 1,501-2,500g = 18%, and >2,500g = 13%. Incidence of ventilator-associated pneumonia (VAP), calculated by #VAPs/1,000 ventilator-days, stratified by weight categories: ≤750g = 8.1, 751-1,000g = 4.2, 1,001-1,500g = 2.3, 1,501-2,500g = 4.4, and >2,500g = 6.1. Central line-associated primary bloodstream infections (CLABSIs), calculated by # CLABSIs/1,000 central line-days: ≤750g = 16.2, 751-1,000g = 12.3, 1,001-1,500g = 11.6, 1,501-2,500g = 10.6, and >2,500g = 6.4. Only 4 microorganisms caused 50% of NIs: MRSE, *K. pneumoniae*, *A. baumannii* and *P. aeruginosa*.

Conclusion: In this NICU, BSI was the most common NI. Types of infection and pathogens differed with birth weight.

LONG TERM IMPACT OF TREATED CONGENITAL TOXOPLASMOSIS: VISUAL PERFORMANCE AND QUALITY OF LIFE IN FRENCH YOUNG ADULTS FOLLOWED-UP SINCE BIRTH

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Background and aims: Little is known concerning the long-term impact of congenital toxoplasmosis on the life-quality and visual function of patients treated ante- and postnatally. The benefit of systematic postnatal follow-up is also debated. We present data based on a cohort of young adults who were regularly monitored since birth at a French centre.

Methods: A questionnaire study was conducted on 126 adults with congenital toxoplasmosis (mean age: 22 years; range: 18-31). The main outcomes were measured using a quality of life (Psychological General Well-Being Index: PGWBI) and a visual function (VF14) questionnaires and correlated with disease-specific factors.

Results: Of the 102 patients (81%) who responded, 12 (12%) suffered from neurological effects and 60 (59%) manifested ocular lesions leading to reduced visual function in 13 (13%). The overall global quality of life score (75 ± 14) lay close to the expected normal range for the general population (74 ± 15) and was not influenced by the clinical characteristics of congenital toxoplasmosis. Overall, visual function was only slightly impaired ($M = 97$ on a 0-100 scale [95% confidence interval, 96-99]). Neurological pathologies, reduced visual acuity, the foveal location of the retinal lesion and squinting contributed to decreased visual function. Follow-up was perceived as useful by 98% and reassuring by 92%.

Conclusions: Congenital toxoplasmosis has very little impact on the quality of life and visual function of individuals treated pre- and postnatally. Follow up is however perceived as useful by patients. These findings may help paediatricians to inform parents and to manage children with congenital toxoplasmosis.

BACTERIAL MENINGITIS IN BABIES 0-90 DAYS OF AGE: A UK AND REPUBLIC OF IRELAND PROSPECTIVE STUDY

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Background and aims: Meningitis in the first 3 months of life is associated with significant mortality and morbidity. Previous UK studies were conducted in the 1980s and 1990s. It is important to define the current burden of disease in order to prioritise treatment and prevention strategies.

Methods: Cases were identified prospectively by active surveillance through the British Paediatric Surveillance Unit, routine microbiological surveillance through the Health Protection Agency and via parents of cases through meningitis and Group B streptococcus (GBS) support charities. The surveillance period was July 2010 - July 2011.

Results: From all sources, 863 reports were received and 300 met the case definition. 261 (87 %, preliminary incidence 0.36/1000 livebirths) were from England, 14 (4.7%) from Wales and 11 (3.7%), 7 (2.3%) and 7 (2.3%) were from Scotland, Northern Ireland and the Republic of Ireland respectively. 170 (57%) were male and the median age of disease was 13.5 days (range 0-88). 238 bacterial isolates were obtained from cerebrospinal fluid and / or blood cultures: GBS (119, 50%) was the most common isolate followed by *Escherichia coli* (30, 13%) *Streptococcus pneumoniae* (21, 9%), *Neisseria meningitidis B* (16, 7%), *Listeria monocytogenes* (9, 4%) and other Gram negative bacteria (21, 9%). The case fatality ratio was 7.4%.

Conclusion: There remains a significant burden of bacterial meningitis in the first 3 months of life but the mortality appears to have declined over the last 2 decades. GBS is the most common causative bacteria. New strategies for prevention are required.

CATHETER ASSOCIATED CENTRAL LINE INFECTIONS IN PAEDIATRIC ONCOLOGY - IMPACT OF A CENTRAL VENOUS CATHETER MAINTENANCE BUNDLE OF CARE

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Background and aims: Paediatric oncology patients require prolonged intravenous access with central venous lines. This combined with persistent immunosuppression puts these children at high risk for Central Line Associated Blood Stream Infections (CLABSI), yet little data exists in this patient population. **Methods:** We retrospectively assessed the impact of the implementation of a central venous care bundle (including aseptic non-touch technique) on CLABSI rates in a tertiary paediatric oncology unit. Pre-intervention data was collected May 2008-April 2010, Post-intervention data May 2010-October 2011. **Results:** We identified 295 oncology patients with a central access devices totalling 103,404 catheter days. There were 142 CLABSI (153 pathogens) representing an average rate of 1.4 CLABSI per 1000 catheter days (CI 1.19-1.61). One year after the introduction of the care bundle there was a reduction to 0.68 CLABSI per 1000 catheter days; this was not sustained with a CLABSI rate of 1.38 per 1000 catheter days in the last quarter of the study. Fifty % (76/153) of CLABSIs were due to Gram positive organisms; Viridans Group *Streptococcus*(21) and Coagulase negative *Staphylococcus*(21) being most commonly isolated, 39% Gram negative organisms and 11% fungi.

Conclusion: This study describes a stable rate of 1.4 CLABSI per 1000 catheter days in paediatric oncology patients, despite the introduction of a high impact intervention for the care of central venous lines. This may reflect need for long term surveillance, further auditing of the maintenance bundle of care and the possible role of gut translocation in the pathogenesis of CLABSI in immunosuppressed patients.

AN OUTBREAK OF INFLUENZA A (H1N1) 2009 IN A NEONATAL INTENSIVE CARE UNIT

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Background and aims: Outbreaks of influenza A (H1N1) 2009 have rarely been reported in NICUs. Annual immunization of all health care workers (HCW) against seasonal influenza is recommended but compliance rate to vaccination is low and exposure to infected staff as the source of nosocomial outbreaks has been described. We report an outbreak of H1N12009 in a tertiary level NICU that resulted in considerable morbidity.

Methods: A total of 22 neonates were hospitalized at that time in the unit, of which 11 (50%) were born preterm. H1N1 2009 was detected in nasopharyngeal aspirates by indirect immunofluorescence assay (IFA) and PCR. Oseltamivir was administered for prophylaxis and treatment. All infants were closely monitored for the manifestation of symptoms compatible with influenza and for potential clinical and laboratory adverse effects of antiviral treatment.

Results: Two infected infants who were immature by gestational age and birth weight developed pneumonitis requiring respiratory support, while a third full term neonate had a mild uncomplicated illness. No significant adverse effects were noted during antiviral treatment or prophylaxis. The survey conducted identified infected HCWs as the source of the outbreak as well as a very low immunization rate of 15% among nursing staff. Strict infection control measures were applied in the unit successfully.

Conclusion: Nosocomial influenza can cause considerable morbidity especially in the high risk neonatal population and is readily transmissible in the NICU setting by unvaccinated staff members who contract influenza. Therefore, in addition to infection control measures, the implementation of HCW immunization is of utmost importance.

DEVELOPING A STANDARDIZED EUROPEAN METHOD OF MONITORING HEALTHCARE-ASSOCIATED BLOOD STREAM INFECTION RATES IN NICUS

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Background and aims: Newborns admitted to NICUs are at high risk for developing healthcare-associated bloodstream infections (HABSIs), in particular central line-associated BSIs (CLABSIs). Infection rates reported in literature are often difficult to compare. We aimed to determine whether it may still be possible to use published data for defining standard rates for benchmarking and inter-hospital comparisons.

Methods: A systematic literature review was conducted of studies published after 2000 up to October 2011 carried out in individual NICUs reporting both the rate and cumulative incidence of HABSI or CLABSI and total patient-days in the evaluation period.

Results: 18 studies fulfilled the inclusion criteria. Cohort size ranged from 150 to 5,102 neonates with 2,195 to 64,607 patient-days of observation. Study periods were between 9 and 84 months. Several characteristics differed strongly among NICUs. Although NICUs mostly provided level II or III neonatal care, mean length of stay and proportion of high-risk babies (VLBW ranging from 7.3% to 50.6%) were widely different and therefore difficult to compare. Moreover, few groups provided information about the percentage of surgical neonates. 15 studies reported an overall HABSI rate of 6.6 /1000 pt days (range 2.0-14.9) and 9 studies an overall CLABSI rate of 12/1000 CVC days (range 3.2-21.8), with around a seven fold variation in reported rates.

Conclusion: Reported rates for both HABSI and CLABSI in this group of studies were high. There is a need to develop a standardised method of monitoring HABSI in NICUs taking into account population characteristics such as gestational age and case-mix.

PRIMARY BLOODSTREAM INFECTIONS IN NEONATAL INTENSIVE CARE UNIT: THREE YEARS OF SURVEILLANCE

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Central line catheters are important resources in neonatal intensive care units (NICUs). However, they are also risk factors for nosocomial infections in critical ill patients.

Objective: To evaluate the incidence, microbiology and outcomes of bloodstream infections (BSIs) in a NICU from a Brazilian hospital.

Methods: Prospective surveillance of NI according to the device-associated module from National Healthcare Safety Network (NHSN) protocols for events occurred between oct/2008 and sep/2011.

Results: 166 BSIs were diagnosed in three years, 50% of all infections in the NICU. The majority of BSIs (85%) refer to the late-onset sepsis, i.e., diagnosed after 48 hours of birth. Laboratory-confirmed bloodstream infection represents 70% of all BSIs (119 cases). BSIs are the major infections in all weight categories. Incidence of central line-associated primary bloodstream infections (CLABSIs), considering the whole period, all weight categories and all central lines types, was equal 11.9 CLABSIs/1,000 central line-days. The BSI risk associated with umbilical catheter is significantly higher than in other line types (p-value < 0.05): 20.9 CLABSIs/1,000 central line-days (umbilical catheter) versus 8.5 CLABSIs/1,000 central line-days (epicutaneous catheter). The BSI risk decreases with birth weight. CLABSI incidence by birth weight (#CLABSIs/1,000 central line-days): ≤750g = 16.2, 751-1,000g = 12.3, 1,001-1,500g = 11.6, 1,501-2,500g = 10.6, and >2,500g = 6.4. CLABSI was caused mainly by multiresistant *Staphylococcus epidermidis* (29%) and *Klebsiella pneumoniae* (13%).

Conclusion: CLABSI rates in all birth categories are high outliers, i.e., above the 90th NHSN percentile. The BSI risk associated with umbilical catheter is significantly higher than epicutaneous catheter.

CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS IN 6 POLISH NEONATOLOGY INTENSIVE CARE UNITS IN 2009

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Background: Central Line Associated Bloodstream Infections (CLABSI) are the most common form of nosocomial infections among Neonatal Intensive Care Unit (NICU) patients. Understanding the epidemiology of CLABSI in very low birth weight (VLBW) neonates is a key step in development of targeted prevention strategies and reduce antibiotic consumption.

Aims: The aims of study were to analyze epidemiology and microbiology of CLABSI in 6 Polish NICUs.

Materials and methods: Data collection on CLABSI in LBW newborns was made retrospectively from January to December 2009. Study covered 910 neonates of birth weight < 1500 g in 6 Polish NICUs, among which 95 cases of CLABSI (using Gastmeier definition) were detected. Device-associated infection rates are calculated and stratified according to birth weight groups:

(I) ≤499 g;

(II) 500-999 g;

(III) >1000 g.

Results: The CLABSI incidence per 1000 CVC/pds were 0 in group I, 10.6 in group II and 9.2 in group III. The etiological agents were dominated by *Staphylococcus* genus (77%) with a majority of methicillin resistant coagulase-negative staphylococci (64% of all cases) and *Staphylococcus aureus* MRSA (13%). Gram rods were detected in 15% with a majority of *E.coli* (6%); ESBL strains were detected in 25%. Fungemia caused by yeast-like fungi was detected in 4.7% cases.

Conclusions: Between studied units situation with CLABSI epidemiology was statistically different. The key to any successful program to lower the CLABSI rates is an intensive educational program that promotes best practices. Use of a prevention strategy and education of staff is essential. Study financed by N N401 615 340.

A 10-YEAR STUDY OF PATHOGENS ISOLATED FROM BLOOD CULTURES IN A PAEDIATRIC ONCOLOGY UNIT

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Aim: To investigate the long-term trends in prevalence and antimicrobial resistance of pathogens isolated from blood cultures in paediatric oncology patients.

Methods: All positive blood cultures from a single paediatric oncology unit during 2002-2011 were retrospectively included and analyzed.

Results: Overall, 317 bacteraemias and 2 candidaemias occurred in 175 patients (median age 5yrs, 61% boys) suffering from haematologic malignancies (67%) and solid tumors (33%). The leading pathogens were coagulase-negative staphylococci (CNS, 52.7%), *Klebsiella* spp. (9.5%), *Pseudomonas* spp. (8.8%), *Escherichia coli* (7.6%), *Streptococcus* spp. (4.1%), *Enterobacter cloacae* (3.8%), *Staphylococcus aureus* (3.5%) and *Acinetobacter* spp. (2.2%). Since the beginning of the study Gram-negative episodes increased (from 5.2 to 19.9/1000 patients, chi-square for trend $p < 0.01$) and Gram-positive episodes decreased (from 25.2 to 14.9/1000 patients, $p = 0.004$). Among *Klebsiella* spp. and *E. coli* isolates, there were 46% and 50% extended-beta-lactamase-producers (ESBL), respectively. All but one ESBL-producing *E. coli* isolates were susceptible to piperacillin-tazobactam. Resistance to imipenem was noted in 8% of *K. pneumoniae* isolates and in no *E. coli*. 20% of *Pseudomonas aeruginosa* isolates were ceftazidime-resistant. 80% and 9% of CNS and *S. aureus*, respectively, were methicillin-resistant. Vancomycin resistance was noted in 16.7% of *Enterococcus faecium* isolates. An outbreak of ESBL-producing *E. coli* was observed in 2011. The all-cause mortality was 22.8%.

Conclusions: Gram-negative bacteria have recently predominated in our unit bearing considerable resistance to frequently used antibiotics. These results suggest the importance of continuous surveillance for antimicrobial drug susceptibility and of antibiotic stewardship in order to confront the emerging challenge of antibiotic resistance.

INVESTIGATION AND MANAGEMENT OF AN IMIPENEM-RESISTANT ACINETOBACTER BAUMANNII (IRAB) OUTBREAK IN A NEONATAL INTENSIVE CARE UNIT

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Background and aims: IRAB frequently causes nosocomial infection outbreaks difficult to eradicate. We describe investigation and management of IRAB outbreak in a NICU in a general university-affiliated hospital.

Methods: In a 44-bed NICU, a bundle of actions were taken after identification of 7 cases of IRAB infections (including 4 cases of bloodstream infections). The bundle included enhanced infection control measures (patients cohorting, contact precautions, hand hygiene, environmental hygiene), active surveillance screening (ASS), case control study, staff education, daily audits and closure of the unit for 12 days. For ASS, perianal/stool samples were collected weekly from all neonates. IRAB were isolated on McConkey agar supplemented with imipenem (2mg/l) and tested for susceptibility using Vitek2. PCR and PFGE were used for molecular analysis.

Results: A total of 216 samples were obtained from 96 neonates (43% of neonates had at least 2 samples). During the 1st, 5th and 6th week of ASS, 5, 2 and 2 new IRAB acquisitions were detected, respectively. Prevalence of IRAB decreased from 19% (1st ASS week) to 4% (7th week) and finally to 0% (8th and 9th week). One colonised neonate developed IRAB bloodstream infection and died. PCR revealed that all isolates were positive for the OXA-58 gene and the intrinsic chromosomal OXA-51 gene. PFGE revealed that all IRAB isolates belonged to the same clone. No significant risk factors were found between case and controls.

Conclusion: Intense active surveillance and enhanced infection control measures were important to rapidly combat high incidence of IRAB monoclonal colonization/infection in the NICU.

EVALUATION OF RESPIRATORY VIRAL INFECTIONS IN CHILDREN WITH CANCER WHO DEVELOPED FEVER AND NEUTROPENIA

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Background: Respiratory viral infections may cause significant morbidity and mortality in children with cancer. We present a cohort of children with cancer with fever and neutropenia (FN) evaluated for respiratory viral infection.

Methods: All children with cancer with FN admitted to the hospital from October 2010 to December 2011 were prospectively enrolled. Children were evaluated for respiratory infections by performing viral PCR in nasal/nasopharyngeal wash on admission. We also determined cytokine levels in blood. Children with a viral respiratory isolate (group 1) were compared with children without viral isolate (group 2) by analyzing demographics, symptoms, laboratory parameters and outcome.

Results: Twenty four children were enrolled in this study with 10 (41.7%) having a respiratory viral isolate; 80% of them diagnosed by PCR. Two children had a severe infection, both in group 2. There was a significant difference in the percentage of children with any positive cytokine level (14% for group 1 vs 90% for group 2; $p=0.004$) and a trend in the time since cancer diagnosis (144 vs 77 days; $p=0.09$) at presentation. Group 1 had lower CRP at 48 hours (5 vs 10; $p=0.05$) with fewer children with CRP > 10 mg/dl (0% vs 50%; $p=0.019$). There were several significant correlations between cytokines and CRP/procalcitonin, especially with interleukin (IL)-12 and TNF.

Conclusions: In our cohort a high proportion of children with FN had a respiratory viral isolate. This group of children may have less risk for developing a severe infection, especially if IL-12 and TNF are not detected.

HYPERTONIC SALINE NEBULIZATION IN ACUTE BRONCHIOLITIS: HIGHER CONCENTRATION OR HIGHER FREQUENCY?**B.S. Sharma**¹, M.K. Gupta², S.P. Rafik³¹*Pediatrics, SPMCHI, SMS Medical College,* ²*Pediatrics, Mahatma Gandhi Medical College,* ³*Pediatrics, SMS Medical College, Jaipur, India***Objective:** To compare the improvement in clinical severity scores and length of hospital stay among children with bronchiolitis nebulized with 3% hypertonic saline (HS) and 0.9% saline (NS).**Design, material and methods:** Randomized, double-blind, controlled trial. 250 hospitalized infants & children aged 1 to 24 months with acute bronchiolitis were assigned to receive either 4 ml of nebulized HS or NS every 4 hourly, six treatments daily along with nebulized salbutamol 2.5 mg in each group till the patient was ready for discharge.**Results:** Two study groups were similar in baseline characteristics. Mean age was 4.93 ± 4.31 months in HS group and 4.18 ± 4.24 months in NS group, male (76.2%) outnumbered females and majority (79%) of patients were below 6 months of age. Mean duration of symptoms at enrollment was 3.6 ± 1.87 days in HS group and 3.8 ± 1.34 days in NS group. Baseline O₂ saturation % was 93.43 ± 2.77 in HS group and 94.23 ± 2.45 in NS group. Base line median clinical severity score was 6 in both groups. Clinical severity scores monitored 12 hourly till discharge (132 hours) did not show statistically significant differences in NS group and HS group. Mean length of hospital stay was 63.93 ± 22.43 hours in HS group and 63.51 ± 21.27 hours in NS group (P=0.879). No adverse events were reported by the parents, caregivers or treating medical attendants in both groups.**Conclusion:** Nebulized 3 % hypertonic saline is not superior to 0.9% saline in children with acute bronchiolitis.

CARRIAGE OF THE ALLELE-G AT POSITION -1082 OF THE IL-10 PROMOTER PROTECTS CHILDREN FROM POST-BRONCHIOLITIS ASTHMA

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Acute bronchiolitis is a common cause for hospitalization among infants and even up to 40% of hospitalized post-bronchiolitis patients have symptoms of asthma later in childhood. The individual variation between genetic factors and immune responses to viral infections have been suggested as potential asthma driven factors. IL-10 is an anti-inflammatory cytokine, and the IL-10 promoter polymorphism has been connected to asthma and atopic dermatitis. Previously, from this same cohort, we showed that those who were non-carriers of allele-G of IL-10 were in greater risk for rhinovirus infection, and possibly asthma, in early life. In this study we evaluated the associations between preschool asthma and polymorphism of IL-10-1082 G/A, IL-18-137 G/ C, TLR4-896 A/G and IFNG-874 T/A after bronchiolitis in early infancy.

In all, 205 infants were hospitalized for bronchiolitis at < 6 months of age. Asthma and allergy were studied from a total of 166 children at 6.4 years (mean). 135(81.3%) frozen whole blood samples were available for cytokine genotyping.

Asthma was present in 17 (12.6%), atopic eczema in 47(34.8%) and allergic rhinitis in 36(26.7%) patients. Those who were homozygous for allele-G at position-1082 of IL-10 were rarely asthmatics, only 1/32(3.1%) had asthma at 5-7 years of age ($p=0.04$). 10% of those with allele-G vs. 21% of non-G allele carriers of IL-10 had asthma at preschool age.

The results of this study suggest that carriage of the allele-G at position -1082 of the IL-10 promoter protects children from post-bronchiolitis asthma.

SORE THROAT IN CHILDREN AT THE EMERGENCY DEPARTMENT: BEST MEDICAL PRACTICE?**I. Roggen**¹, G. van Berlaer¹, F. Gordts², I. Hubloue¹¹*Emergency and Disaster Medicine, ²ENT, UZ Brussel, Vrije Universiteit Brussel, Jette, Belgium*

Background: Even though Belgian antibiotic (AB) policy guidelines clearly state the uselessness of AB in sore throat, in otherwise healthy individuals, 35% of all children in our Pediatric Emergency Department (ED) receive a prescription for AB.

Objective: We wanted to discover if there were specific factors influencing our physician's AB prescription rate.

Methods: Using a retrospective cohort study design, we analyzed all medical records of children below the age of 16, who were diagnosed in 2009 and 2010 with sore throat. Children with underlying chronic diseases and those already on AB treatment were excluded. Out of a total 33,152 PED visits, 1345 met our criteria.

Results: Children below the age of 5 received more easily an AB prescription (38 vs. 28%; $p=0.0006$), while the incidence of β Hemolytic Group A Streptococcus (GAS) is lower in this group (23 vs. 41%; $p=0.0002$). Children of Caucasian origin received less frequent AB compared to children from other origins (32 vs. 37%; $p=0.03$). More AB were prescribed during nightshifts (39 vs. 32%; $p=0.008$). Physicians with a Belgian degree prescribed less frequent AB compared to doctors who studied in The Netherlands (23% vs. 46%; $p<0.0001$).

Conclusion: Assessing at adherence to AB guidelines in children with sore throat, we find several "practical" factors, rather than clinical arguments, to have an influence on the AB prescription rate.

VITAMIN D DEFICIENCY IS ASSOCIATED WITH AN INCREASED RISK OF RECURRENT ACUTE OTITIS MEDIA WITH REPEATED TYMPANIC MEMBRANE PERFORATION

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Background: Several studies have demonstrated that VD has relevant immunomodulatory effects and that its deficiency can lead to an increased risk of respiratory infections. This study was planned to evaluate whether VD deficiency can be considered an additional risk factor for RAOM.

Methods: Children with a documented history of RAOM were enrolled. 25OHVD3 level was determined on blood sample drawn 28-30 days following the last episode of RAOM. Multiple linear regression analysis was applied to assess the association between VD level and RAOM events during all time of life. Models with event as dependent variable included terms for VD level, number of older siblings, pacifier use, day-care attendance and exposure to passive smoking.

Results: A total of 128 children (mean age, 35.7 ± 19.8 months) were enrolled. VD level was < 20 ng/mL in 39 (30.5%), 20-30 ng/mL in 34 (26.6%) and >30 ng/mL in 55 (42.9%). RAOM was non-significantly inversely associated with VD level both in the unadjusted and in the multivariate model. However, when children with RTMP were analyzed separately, it appeared that RTMP was significantly inversely associated with level of vitamin D in the multivariate model ($\beta = -0.002$, $p=0.03$). Risk of RTMP was associated with a VD level of < 30 ng/mL.

Conclusion: VD deficiency seems to be an independent and additive risk factor for the development of RAOM with RTMP. These data suggest that in children with RAOM and RTMP determination of VD level has to be performed and VD supplementation could be considered.

NASOPHARYNGEAL (NP) COLONIZATION WITH PATHOGENIC BACTERIA (PB) IS ASSOCIATED WITH INCREASED DISEASE SEVERITY IN CHILDREN WITH RSV BRONCHIOLITIS

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Background: The impact of NP bacterial colonization on RSV disease has not been characterized. We evaluated the frequency of pathogenic bacteria (PB) colonization in children with RSV bronchiolitis, and determined its association with disease severity.

Methods: Previously healthy children < 2yrs hospitalized with a first episode of RSV bronchiolitis and healthy controls were enrolled. NP bacterial swabs collected within 24h of admission were cultured for: *S. aureus*, *S. pneumoniae*, *M. catarrhalis*, *H. influenzae*, and β -hemolytic *Streptococcus*. Demographic, clinical, laboratory and disease severity parameters were compared between patients who tested positive or negative for PB.

Results: From 12/2010 to 9/2011, 136 children with RSV bronchiolitis (62% males; 2.53 [1.5-4.4] months) and 23 matched controls were enrolled. NP cultures were negative for PB in 43% (59/136) of RSV children and among those 76% had received antibiotics. Patients not treated with antibiotics (69/136; 51%) were colonized more frequently with Gram-negative bacteria (GNB, 43%; 15/35) whereas healthy controls were mostly colonized with Gram-positive bacteria (GPB, 93%; 13/14)($p=0.01$). RSV patients colonized with PB had higher WBCs in NP samples ($p=0.03$), higher blood neutrophil% ($p=0.02$) and lower basal O₂ sats ($p< 0.05$) than those not colonized with PB. Moreover, colonization with GNB, but not GPB, was associated with longer needs for O₂ ($p=0.04$).

Conclusions: Infants with RSV colonized with PB showed a clear trend for increased disease severity, especially those colonized by GNB that required O₂ for longer periods of time. Further studies are needed to elucidate the clinical significance and mechanisms of RSV-bacterial interactions.

RESPIRATORY DISTRESS SYNDROME (RDS) AT BIRTH IS A RISK FACTOR FOR LOWER RESPIRATORY TRACT INFECTION (LRTI) HOSPITALIZATION IN INFANCY

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Objective: Preterm infants are at risk of RDS at birth, and of hospitalization for LRTI (specifically, respiratory syncytial virus) in infancy. Whether RDS at birth is an independent risk factor for LRTI is unknown. We therefore estimated the risk of LRTI-related hospitalization among preterm infants with RDS at birth.

Methods: The population-based cohort was identified from Québec administrative data, and included all late preterm babies (32 to 36 weeks gestational age) from 1996-1997. RDS at birth was identified by ICD code 769, and a comparison cohort generated from all late preterms without RDS. A multivariable model estimated the risk of LRTI-related hospitalization before age 1 among late preterms with RDS at birth, adjusted for other significant risk factors.

Results: Of the 7,488 late preterms, 459 (6.2%) had RDS at birth and 525 (7.0%) were hospitalized for LRTI before age 1. The adjusted odds ratio (OR) for LRTI-related hospitalization after RDS at birth was 1.6 (95% confidence interval (CI), 1.2-2.2). Other significant risk factors included male sex (1.4 (1.1-1.7)), or diagnosis with other respiratory conditions (1.5 (1.2-1.9)), diaphragm anomalies (6.7 (1.2-37.4)), bacteremia (3.6 (1.2-10.7)), intraventricular hemorrhage (4.5 (1.5-13.4)), congenital heart disease (2.3 (1.6-3.2)), or congenital respiratory system anomalies (3.2 (1.6-6.3)) within the first year of life.

Conclusion: Late preterm infants with RDS at birth are at a 60% increased risk of LRTI-related hospitalization before age 1, compared to late preterm infants without RDS. Such infants may benefit from interventions that decrease the risk of contracting respiratory viruses causing acute LRTI.

CONFORMITY OF ANTIBIOTICS PRESCRIPTIONS WITH THE CURRENT RECOMMENDATIONS IN CHILDREN PNEUMONIA IN FRANCE

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Pneumonia is a frequent cause of antibiotic treatment in children. Non adhesion to recommendations could be responsible for a misuse of antibiotics, leading to bacterial resistance and additional cost. The objective of this study was to determine the frequency of the “out of recommendation” antibiotic prescriptions and then to identify their characteristics, determiners and consequences.

Cases of pneumonia were prospectively collected by a network of 10 paediatric emergency departments between May 2009 and 2011 and classified according to the 2005 AFSSAPS French recommendations.

Among 3034 antibiotic treatments, 1472 (48 %) were considered “out of recommendation”. The deviations concerned the nature of the molecule (69,8 %), the route of administration (37,2 %) and the use of a first line antibiotics association (13,2 %). Logistic regression analysis showed that the main factors associated with “out of recommendation” antibiotherapy were: age of less than 1 year (OR=0,32 [0,22-0,50]), severity signs (OR=0,48 [0,40-0,58]), pneumococcal infection risk factors (OR=0,41 [0,28-0,60]), emergency department centre (OR=0,22 [0,13-0,36]), winter and spring seasons (OR=0,76 [0,61-0,95]). Moreover, the incidence of adequate prescription increased in 2011 (OR= 1,46 [1,05-2,04]). The clinical outcome was not influenced by the conformity of the prescriptions antibiotics (99 % of favourable outcome, 6 deaths).

This snapshot of antibiotic use to treat pneumonia in french children shows that half of the prescriptions are not in compliance with the current recommendations. An urgent improvement is needed to generalize amoxicillin by oral route as the first line treatment, even in young children with signs of severity.

PREVENTION OF GROUP B STREPTOCOCCUS INFECTION BY PERPARTUM SCREENING IN THE DELIVERY ROOM. USE OF XPERT GBS TEST IN POC

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Introduction: In France, *Streptococcus agalactiae* (Group B *Streptococcus*: GBS) is the most common organism in severe neonatal infection, it may lead to sepsis and death of the newborn, or cause severe neurologic sequelae.

The female genital tract colonization by GBS is intermittent, the mother's prevalence during pregnancy is between 10% and 30%.

Since 2001, antenatal screening for GBS of all pregnant women is recommended by ANAES. In case of positive, an intravenous penicillin antibiotic is prescribed at the time of delivery.

Screening performed between 34 and 38 weeks has been shown to be unreliable for predicting the status of intrapartum carriage. A high proportion of women positive during antenatal screening is negative at birth and receives an excessive antibiotic treatment; conversely, negative women are carriers during childbirth.

Objectives: Our approach aimed to prevent GBS infection by intrapartum screening for an optimal management of mothers at risk and children.

Materials and methods: We used the Xpert GBS test (Cepheid, France) at the time of delivery. All required standard procedures (repeatability, reproducibility,) were performed. A vaginal swab was kept to confirm the PCR results by conventional bacteriological techniques, look for the presence of other pathogens and perform an antibiogram in case of penicillins allergy.

Conclusions: The innovative Xpert GBS test, routinely used since 2011, enabled us to identify 155 positive women (12.7%) and to treat properly the positive mothers at the time of delivery. The better efficiency of antibiotic treatment convinced the patients to accept these new screening and prevention terms.

PEDIATRIC INVASIVE HAEMOPHILUS INFLUENZAE (HI) INFECTIONS IN ISRAEL IN THE HAEMOPHILUS INFLUENZAE TYPE B VACCINE ERA: A NATIONWIDE PROSPECTIVE STUDY

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Background: Hib vaccination (since 1994) resulted in a marked decrease in Hib morbidity. Presently, pediatric Hi invasive disease (PHiID) is caused primarily by *non-capsulated Haemophilus influenzae (ncHi)*. We studied the epidemiological trends and selected clinical characteristics of PHiID in Israel in the Hib vaccine era.

Methods: This is an ongoing, nationwide, prospective study. Cases with Hi isolated from blood or cerebrospinal fluid were enrolled during 2003-2009.

Results: 278 cases of ncHi (64.5%), Hib (26.5%) and *non-b encapsulated Hi* (9%), were identified. The overall mean incidence (/100,000 children < 16 years \pm SD) was 1.8 ± 0.3 , and was stable for all serotypes. Serotype-specific mean incidence was 1.1 ± 0.2 , 0.5 ± 0.2 and 0.2 ± 0.1 , respectively. The highest incidences ($P < 0.0001$) occurred in children < 1 year: 6.3, 5.3 and 1.4 respectively. PHiID incidence decreased with increasing age, and was rare >4 years. PHiID incidence was higher in non-Jewish vs. Jewish children: 2.3 vs. 1.6, ($P < 0.006$, IRR:1.42; 95% CI:1.11-1.82), respectively. This trend was more accentuated in girls. Bacteremia without focus was the most common manifestation in non-b Hi (60%), whereas meningitis was the most common manifestation in Hib (43%). Case-fatality rate was 5.9%, (75% of deaths from ncHi). 11% of the patients had comorbidity with no differences between serotypes; the mortality among this group was 20%.

Summary: In the Hib vaccine era, PHiID and its associated mortality are primarily attributed to ncHi. The low rate of invasive Hib is sustained. Additional studies to investigate differences in population-specific disease and risk factors associated with invasive disease are warranted.

NEISSERIA MENINGITIDIS W135 INVASIVE INFECTIONS IN CHILDREN: EPIDEMIOLOGICAL, CLINICAL AND GENOTYPIC FEATURES IN A FRENCH NATIONAL SURVEY

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Background and aims: Invasive Meningococcal Disease (IMD) due to W135 serogroup has been described since 40 years, but few data are available, especially for children. The epidemiological, clinical and microbiological features of W135 IMD collected from 2001 to 2008 in two French national surveys are presented here.

Methods: The French National Reference Center for meningococci and the GPIP/ACTIV network of 252 pediatric wards prospectively collected the cases of IMD: W135 IMD was defined by a positive culture or PCR in a normally sterile site. Genotyping was performed to classify positive cultures according to clonal complex.

Results: A total of 119 cases of W135 IMD (4% of IMD) were reported in children, among which 54% were infants (peak incidence between 6 and 9 months). The M/F sex ratio was 1.2. The number of cases decreased from 24 in 2002 to 9 in 2008. The initial clinical status was meningitis (66%), arthritis (8%), purpura fulminans (5%) or meningococemia (21%). Among the 99 genotyped isolates, 53 were ST-22, 42, ST-11, 3, ST-174 and 1, ST-23. Clonal complex ST-11 prevailed in greater Paris, Reunion island and Mayotte, and ST-22 in the rest of France. Meningitis was more frequent for ST-11 (83% vs. 57% for ST-22, $p = 0.007$). Mortality was 6% (7/119) and did not differ according to clonal complex.

Conclusions: Isolates of the clonal complex ST-22 were the most prevalent in W135 IMD and were frequently associated with non-meningeal presentation. Further investigations of clinical tropism of W135 isolates are warranted.

ANTI-ADHESIVE EFFECTS OF BIOTECHNOLOGICAL SYNTHESIZED HUMAN MILK OLIGOSACCHARIDES**S. Weichert**¹, S. Jennewein², S. Schmohl¹, H. Schrotten¹, J. Putze¹¹*Pediatric Infectious Diseases, University Children's Hospital, Medical Faculty Mannheim, Heidelberg University, Mannheim*, ²*Jennewein Biotechnology GmbH, Rheinbreitbach, Germany*

Background: Beyond nutritional aspects human milk provides further health benefits by preventing adhesion of pathogens to epithelial surfaces, which is attributed to human milk oligosaccharides (HMOs). In this study, we were for the first time able to use enzymatic engineered HMOs to investigate the antiadhesive effects on pathogen attachment.

Methods: Adherence of *Pseudomonas aeruginosa* strain DSM 1707, enteropathogenic *Escherichia coli* (EPEC) strain O119 and *Salmonella typhis* on two epithelial cell lines (A549, Caco-2) in the presence of lactose, mannose, 2'-fucosylated lactose (2'-FL), 3-fucosylated lactose (3-FL) and human milk was determined by cultural enumeration.

Results: Adherence of *Pseudomonas aeruginosa* on A549 cells was highly significantly inhibited by 2'-FL and 3-FL (25% and 23% inhibition, respectively), whereas no inhibition was observed with lactose. 2'-FL and 3-FL highly significantly inhibited adhesion of *Pseudomonas aeruginosa* to Caco-2 cells by 28% and 39%, respectively, as well as did human breast milk (inhibition of 59%). Adhesion of the enteropathogenic bacteria *Salmonella typhis* and EPEC O119 to Caco-2 cells was significantly inhibited by 2'-FL and 3-FL, as well as by mannose (inhibition of 17%, 16%, 68%, and 18%, 21%, 24%, respectively), whereas with lactose no inhibitory effect was shown. Furthermore, adhesion of EPEC O119 to Caco-2 cells was significantly inhibited by human breast milk (33% inhibition).

Conclusion: We were for the first time able to proof the efficient inhibition of different pathogens by enzymatic engineered HMOs in two human cell culture models. HMOs might play an important role as supplementary infant formula ingredients in near future.

MENINGOCOCCAL MENINGITIS IN CHILDREN: FRENCH SURVEILLANCE NETWORK FROM 2001 TO 2009

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Background: Since 2001, the GPIP/ACTIV set up an active surveillance network to analyze the epidemiological, clinical and biological features of meningococcal meningitis in France.

Methods: From 2001 to 2009, 252 French pediatric wards and 166 microbiology laboratories enrolled all children (0-18 years old) with bacterial meningitis. The inclusion criteria were a clinical meningeal syndrome, cerebrospinal fluid (CSF) pleiocytosis and at least one positive microbiological test (positive culture, PCR, slide agglutination or smear detection in CSF and/or blood culture). Risk factors, signs and symptoms, vaccination status, CSF analysis, treatments and case fatality rate were recorded.

Results: During the period of the study, 1661 meningococcal meningitis were reported among 3769 (44.1%) bacterial meningitis. Serogroup distribution of the isolates was 61.3%, 27.0%, 2.4%, 0.6% and 0.3% for serogroups B, C, W135, Y and A, respectively. Mean age was 4.4-year-old (median 2.5) and 2/3 of cases occurred in children under 5-year-old. Cases peaked in < 1 year, 33.8% for the serogroup B and 23.4% for the serogroup C. 27.5% of children had received an antibiotic treatment up to 24 hours before lumbar puncture. A shock was reported in 31.0% of cases. No vaccine failure was reported with MenC conjugate vaccine. All patients had received beta-lactamin. Global case fatality rate was 6.5% but was higher (9.2%) for serogroup C than for serogroup B (5.9%) (p=0.02).

Conclusion: This is among the largest series of meningococcal meningitis to date. Effective meningococcal serogroup B vaccine and serogroup C vaccination recommendations could control the burden of meningococcal meningitis.

COMPLEMENT FACTOR H-RELATED 5 (CFHR5) PROTEIN LEVELS ASSOCIATED WITH THE CLINICAL SEPSIS PHENOTYPE IN CHILDREN WITH MENINGOCOCCAL DISEASE

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Background and aims: A genome-wide association study^[1] identified complement factor H (CFH) gene family variants in meningococcal disease (MD). The CFH family comprises CFH itself, and five genes that encode structurally similar proteins termed CFH-related proteins. Of the five CFH-related proteins, CFHR5 has been proposed to be important in the regulation of complement within the kidney^[2]. Here, we measured serum CFHR5 protein levels in a healthy paediatric cohort and in children with MD.

Methods: Serum CFHR5 was quantified by ELISA in 57 patients with MD and 40 controls. Serum CFHR5 levels were correlated with MD phenotype.

Results: The mean serum CFHR5 was significantly lower in MD patients during the acute phase (1.219 µg/ml) compared to healthy controls (2.348 µg/ml, $p < 0.0001$). However, there was no significant difference in the mean CFHR5 in convalescent MD samples when compared to controls. Mean serum CFHR5 was higher in convalescent than acute MD samples ($p < 0.0001$). Levels did not differ between males and females.

Acute CFHR5 levels were compared to sepsis severity scores, there was significant positive correlation with: ICU free days ($p=0.042$) and negative correlation with: Rotterdam score ($p=0.055$), GMSPS ($p=0.002$), PRISM ($p=0.033$). Mean acute CFHR5 ($p=0.019$) and C3 ($p=0.012$) levels were lower in the patients requiring renal support (haemodialysis) on PICU.

Conclusions: Serum CFHR5 levels in MD follow those of C3 and CFH, falling acutely and normalising during convalescence. We hypothesise that this represents sequestration of serum CFHR5 by (1) binding to the pathogen directly or (2) binding to tissue C3 during sepsis.

THE GLN27GLU POLYMORPHISM OF THE BETA-2 ADRENERGIC RECEPTOR ASSOCIATES WITH HAEMODYNAMICS AND OUTCOME IN CHILDREN WITH SYSTEMIC MENINGOCOCCAEMIA

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Background: Meningococcal disease (MD) may present as sepsis, meningitis or a combination of both. Peripheral vascular failure, as seen in meningococcal septic shock, may be facilitated by distinct single nucleotide polymorphisms in adrenergic receptor genes. The Gln27Glu polymorphism in the β_2 adrenergic receptor gene (ADRB2) leads to attenuated down-regulation of the receptor, resulting in constant receptor densities on vascular smooth muscles, despite agonist action. This prospective, multicentre study examined the relationship between MD and the ADRB2 Gln27Glu variant.

Methods: 420 previously healthy children with MD from 107 paediatric hospitals in Germany, Switzerland, Italy, and Austria were included in the CEMGS study. Another cohort of 360 confirmed paediatric cases of MD recruited through a national research network (ESIGEM - www.esigem.org) from 41 Spanish hospitals, was used for replication analysis. The Gln27Glu polymorphism was analysed using a MALDI-TOF MS (ESIGEM) and a HRM assay (CEMGS).

Results: Patients homozygous for the Gln27 variant (Gln27Gln) showed significantly higher systolic blood pressure nadirs (83.5 mmHg vs. 75.7 mmHg, P -value = 0.02) and improved outcome (2.9% vs. 9.5% fatality rate, P -value = 0.009, OR = 3.5, 95%CI = 1.2-10.3). Refractory hypotension was rare in this group (7.6% vs. 17.6%, P -value = 0.04, OR = 2.6, 95%CI = 1.1-6.7), and length of vasopressor use (2.2 days vs. 6.7 days, P -value < 0.0001) was markedly shorter than for patients with other genotypes.

Conclusion: In our study we provide first evidence that the ADRB2 Gln27Glu polymorphism directly interferes with sepsis haemodynamics and is associated with outcome in meningococcaemia.

USING DATA LINKAGE METHODOLOGY TO DETERMINE RATES OF HOSPITAL-ACQUIRED BLOODSTREAM INFECTIONS IN CHILDREN IN ENGLAND

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Objectives : To determine the epidemiology of hospital-acquired (HA) bloodstream infection (BSI) and antimicrobial resistance (AMR) in children aged 1 month-18 years in England.

Methods : Episodes of BSI and associated AMR data in children voluntarily submitted to the Health Protection Agency's microbiological database between January 1st 2009 and March 31st 2010 were extracted. Microbiological reports were probabilistically linked to England Hospital Episode Statistics (HES) in-patient data to capture admission and discharge dates. Reports of positive blood cultures from children taken ≥ 2 days after admission were defined as hospital-acquired (HA) and were analysed in terms of pathogen and AMR.

Results : A total of 8,718 episodes of paediatric BSI were reported during the study period, of which 82% were linked with HES data. A total of 1,734 (23%) episodes were HA, equating to a rate of 4.89/1,000 admissions lasting ≥ 2 days. Median age at BSI was 1 year, and 54% occurred in males. The most commonly reported organisms were coagulase-negative staphylococci (30%), *Enterococcus* spp. (13%), *Staphylococcus aureus* (11%), *Escherichia coli* (8%) and *Klebsiella* spp. (7%). AMR for Gram-negative organisms was 4% for piperacillin/tazobactam and gentamicin and 5% for meropenem. AMR in Gram-positive organisms was 3% for vancomycin therapy.

Conclusion : This study outlines the first national estimates of HA BSI rates in children in England and characterises the causative organisms. AMR to common antibiotic treatments was low. This study demonstrates the value of data linkage for conducting epidemiological investigation at a national level.

PATHOGENESIS OF TUBERCULOSIS IN CHILDREN IDENTIFIED BY GENE EXPRESSION PROFILING

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Background: Children have a high risk of developing active tuberculosis (TB) from close contact with an infectious adult. Most children remain undiagnosed since detection is more difficult in children due to unreliable standard laboratory investigations and diagnosis based mainly on clinical symptoms. However, blood transcriptional profiling has improved diagnosis and understanding of disease pathogenesis, leading to the development of serological biomarkers, but this has yet to be applied to children with TB.

Methods: Two cohorts of children (HIV positive and HIV negative) from South Africa and Malawi with active TB, latent TB infection and controls (other inflammatory diseases with similar presentation to TB) were recruited with whole blood collection into PAXgene tubes. After RNA extraction and amplification, biotinylated cRNA was hybridised to Illumina HT-12 BeadChip arrays for 334 samples (TB/HIV-, TB/HIV+, OD/HIV-, OD/HIV+, LTBI/HIV-). We assessed transcriptional biomarker signatures identified from variable selection analysis between the different disease categories for insight into the pathogenesis of the disease.

Results: We identified distinct subsets of genes differentially expressed between the disease categories in the biomarker signatures, with multiple biological pathways activated including those mainly involved with the inflammatory response, dendritic cell maturation and in cell-to-cell signaling and interaction.

Conclusions: RNA expression analysis provides a way of studying the complex inflammatory and metabolic processes in ill children. Our analysis provides an insight into the complexity of the host response to tuberculosis infection in children.

GENETIC ANALYSIS OF *MYCOBACTERIUM TUBERCULOSIS* DRUG-RESISTANCE GENES FROM SAMPLES SHIPPED IN PRIMESTORE MTM AND SEQUENCED USING THE NEXT-GENERATION ION TORRENT

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Background/aims: Mycobacterium tuberculosis (MTB) kills on average 1.7 million people worldwide each year and an increasing number of strains are multidrug-resistant (MDR) or extensively drug-resistant (XDR). Emergence of highly resistant MTB strains has made it critical to detect and track new mutations that may confer novel MTB drug resistance. In previous studies PrimeStore Molecular Transport Medium (MTM) rapidly killed MTB, preserved DNA and facilitated DNA extraction. A novel Ion Torrent drug resistance sequencing chip was evaluated by multiplexing MTB samples collected and preserved in PrimeStore at ambient temperature during prolonged shipment.

Methods: Four sets of PCR primers were designed for amplification of *rpoB*, *katG*, *GyrA*, and *rrs* genes known to confer MDR and XDR resistance in first and second line antibiotics. MTB samples preserved/stabilized in PrimeStore MTM were collected/shipped from Pretoria, South Africa to San Antonio, Texas, USA. Genetic analysis was performed using Ion Torrent sequencing.

Results: Compared to HAIN Line Probe Assay (LPA), this method correctly detected all mutations from 12 of 12 multiplexed MTB strains representing genetically diverse antibiotic resistance patterns. Furthermore, several new amino acid mutations not observed by LPA or by comparison to reference strains were discovered.

Conclusion: Collection and ambient temperature shipment of MTB samples in PrimeStore provides a safe and cost effective approach for global MTB drug resistance surveillance using Ion Torrent sequencing. The developed Ion Torrent method detects MDR and XDR strains with overall performance comparable to LPA testing, and offers potential discovery of novel resistance mutations.

TUBERCULOUS MENINGITIS IN CHILDREN STILL A DIAGNOSTIC DILEMMA IN DEVELOPING WORLD

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Background and aims: Clinical and investigational variables indicators of early diagnosis suffering from tuberculous meningitis in children.

Design: Case control prospective study.

Place and duration of study: Department of Neurology Children's Hospital, Lahore from March 1, 2010 to August 30, 2011.

Methods: Clinical data of 300 patients being treated as TBM (group A) admitted in the Neurology department, and another 300 patients with diagnosis of meningitis, encephalitis or cerebral malaria (group B) were evaluated. History, clinical examination and relevant investigations were evaluated and Kenneth Jones criteria were applied to both groups. All children were followed and their outcome was also studied.

Results: Data of 300 patients with TBM and controls was analyzed. Clinically 77% children were in TBM stage III and 22% were in TBM stage II and only one child was in TBM stage I.

Hydrocephalus was seen in 67 Children and 47 children develop basal meningial enhancement. 26 children had brain Tuberculoma. Above 50 ESR was seen in 43 children. Twenty children lost their lives during the first admission (period varies from 10 day to 38 days) while another 7 children expired subsequently.

Conclusion: Tuberculous meningitis remains a serious health threat in developing countries. The variable, natural history and accompanying clinical features of TBM had significant capacity for the early diagnosis and prognosis. There is a need to educate primary care pediatricians about early diagnosis of Primary TB and TBM.

OCULAR MANIFESTATIONS OF CANDIDEMIA IN A PEDIATRIC POPULATION

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Background: *Candida* spp. are among the most frequent causes of blood stream infections and can often disseminate resulting in ocular disease and vision loss. There is a paucity of data regarding the incidence of ocular involvement in children. The aim of this study was to determine the frequency of ophthalmologic findings in children with candidemia.

Methods: We conducted a retrospective cohort study of children with candidemia from 2000 - 2009. Ophthalmology notes were reviewed. Chorioretinitis was defined as disease of the choroid or retina; endophthalmitis as disease extending to the vitreous. The analysis was restricted to patients who survived 7 days after infection diagnosis.

Results: A total of 349 children with candidemia were included. The median age was 5.7 years (IQR 0, 18.3 years). 254 (72.8%) had an ophthalmologic exam. 8 patients (2.3%), including one neonate, had ocular involvement. 4 (1.1%) had chorioretinitis and 4 (1.1%) had endophthalmitis. Of the patients with ocular involvement, 4 had *C. albicans*, 2 *C. tropicalis*, and 1 each had *C. parapsilosis* and *C. glabrata*. 1 patient diagnosed with endophthalmitis had a vitreous biopsy and culture which showed no evidence of fungus. Of the 8 patients, ocular disease resulted in retinal detachment in 2 patients and corneal perforation in 1 patient.

Conclusions: This study found that ocular candidiasis is an uncommon but serious sight-threatening complication in pediatric patients with candidemia. Future studies need to address risk factors for ocular disease in order to identify patients who should be screened.

INDUCTION SPUTUM VERSUS GASTRIC LAVAGE FOR MICROBIOLOGICAL CONFIRMATION OF PULMONARY TUBERCULOSIS IN INFANTS AND YOUNG CHILDREN

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Background and aims: Diagnosis of pulmonary tuberculosis (PTB) is difficult in infants and young children. For microbiological confirmation of PTB children, sequential gastric lavages (GL) are recommended. Induction sputum (IS) might be an alternative or complementary tool, but the information is limited in children in developed countries.

The aim of this study is to assess the safety and diagnostic yield of IS combined with GL for PTB diagnosis in children.

Methods: The study involved 22 children with suspected PTB admitted at Getafe Hospital, from January 2007-February 2011. IS and GL were done on three consecutive days according to a standardized protocol. In all samples, BK staining, culture and PCR were done, including Genotype MTBDR plus for resistance to INF-RIF since 2008. Preliminary analysis of an ongoing prospective study is presented.

Results: Median age was 74.5 months (1 month-14 years). Seven (35%) were ≤ 5 years. Eighteen were clinically diagnosed of PTB based on positive PPD and radiological criteria. Microbiological confirmation was made in 10 (56%) by either GL or IS. *M. tuberculosis* was identified from GL in 8 (44%) children, and by IS in 7 (39%). One infant (2 IS samples) had transient oxygen desaturation recovered spontaneously.

Conclusions: IS appears to be safe and well tolerated in children for diagnosis of PTB and more convenient. It may be a complementary technique to increase the diagnostic yield of PTB in children with PTB. Further studies are necessary to define the role of IS in pediatric PTB in developed countries.

NEONATAL INVASIVE FUNGAL INFECTIONS IN ENGLAND 2004-2011

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Background and aims : Rates of invasive fungal infection are highest amongst neonates, especially those that are premature and very low birth weight (VLBW). This study aimed to describe the epidemiology, clinical presentation and current treatment of invasive neonatal fungal infections in England.

Methods : From 2004-2011 prospective multicentre surveillance was conducted by 12 neonatal intensive care units within neonIN, a neonatal infection surveillance network. Clinicians completed a standardized proforma for each positive fungal culture.

Results : From 2004 to 2011 78 cases were reported. The majority of cases (86%) occurred in babies born at < 1500g (median gestational age: 25 weeks, median birth weight: 740 g, 78% < 1000g). *C. albicans* was the most frequent pathogen isolated (69%), the median time of onset of symptoms was 13 days. 92% received at least one antibiotic course prior to the episode, 89% had ventilatory support, 95% received parenteral nutrition and 87% had a central line within 48 hours of the episode. Antifungal prophylaxis was rarely provided (22%) and although choice of treatment varied, the most commonly used was Fluconazole. The overall mortality was 31%.

Conclusions : Premature and VLBW infants are at increased risk of invasive fungal infections with a high mortality rate. The vast majority of infants in this cohort were exposed to known treatment related risk factors. Improved knowledge on the epidemiology of the disease will enable the development of better strategies to improve outcome.

TRANSCRIPTIONAL BIOMARKERS DISTINGUISH CHILDREN WITH ACTIVE TUBERCULOSIS FROM THOSE WITH LATENT TUBERCULOSIS AND TB-LIKE DISEASES

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Background and aims: Childhood tuberculosis (TB) is a major cause of death globally. Traditional diagnostic methods, such as sputum culture and chest x-rays tend to be less reliable in pediatric TB cases. Furthermore, co-infection with HIV enhances the progression to the active form of the disease, hindering TB diagnosis and increasing mortality. The aim of this study is to elucidate the host transcriptional response to childhood TB and select biomarkers to discriminate TB from other phenotypes using host gene expression profiling.

Methods: Illumina HT-12 arrays were used to examine whole blood RNA from 334 children including TB HIV+/- (111), other diseases (OD) HIV+/- (169) and latent TB infection (LTBI) HIV- (54), collected from two different sites in Africa representing urban and rural populations (South Africa/Malawi). A logistic regression model was employed to detect differences between the groups, and a variable selection method was used to identify the smallest set of "best discriminator" probes. To avoid overfitting of the signatures we used different training and testing sets.

Results: We identified distinct subsets of genes differentially expressed when comparing TB to LTBI, TB to OD, and TB to both LTBI and OD. The variable selection provided with signatures (the smallest but most informative probe set for every comparison of interest), which were used for classification of the testing cohort.

Conclusions: A minimal probe set is able to discriminate between different phenotypes and can be used as a robust signature for potential pediatric TB diagnosis, regardless HIV status and location of the population.

EXAMINATION OF CHILD TUBERCULOSIS CONTACTS WITH AN INTERFERON GAMMA ASSAY AND TUBERCULIN SKIN TEST: COMPARISON AND PREDICTORS OF POSITIVE OUTCOME

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Background and aims: Evidence of interferon gamma release assay performance for the detection of TB infection among child contacts with adult cases is limited. We compared the performance of QuantiFERON-TB Gold-In-Tube (QFT-IT) with the tuberculin skin test (TST) in detecting TB infection among children with known exposure.

Methods: A cross-sectional study was conducted among 163 children (mean age \pm SD:7.8 \pm 4.7 years) with known TB exposure evaluated with QFT-IT and TST. Comparison groups were based on patient's history of BCG immunization. Agreement between tests was evaluated with the kappa statistic. Logistic regression was used to examine the predictors of a QFT-IT(+) and TST(+) outcomes.

Results: Approximately one third of participants (n=61; 37.4%) had QFT-IT(+) outcome, while 2.4% had indeterminate results. Among BCG(-) children, concordance between QFT-IT and TST was excellent (κ =0.96) among those with household contact, good (κ =0.78) among those with non-household regular contact, and moderate (κ =0.50) in those with occasional contact. In contrast, among BCG(+) children concordance between tests was moderate among household contacts and poor in the remaining patient groups. QFT-IT(+) outcome was associated (inversely) solely with patient's origin from a low TB prevalence setting (AOR:0.36; 95%CI: 0.18-0.73), but not age, children's place of birth, or BCG immunization. In contrast, TST(+) outcome was associated with patient age (AOR:1.17; 95%CI:1.04-1.32) and prior BCG immunization (AOR:5.47; 95% CI:1.90-15.79).

Conclusions: The high concordance observed between the two tests among BCG(-) close contacts of TB index cases suggests that the QFT-IT is more specific. BCG immunization does not appear to provide protection against TB infection.

BYZANTINE SURGERY WITH SPECIAL EMPHASIS ON INFECTIONS**S. Geroulanos**

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Surgery in Byzantium with respect to the research and results achieved in many other medical fields remained more or less impenetrable, despite its major contribution in conservation, development and transfer of antique knowledge. Byzantine texts comprise surprising written sources of medical information, which apart from simple surgical procedures, such as incision and drainage of abscesses, include also descriptions of severe and very difficult operations, thus making their study a fascinating subject. At least three of the most important physicians/authors of Byzantium, like Oreibassios (325-403 A.D.), Aetios from Amida (6th c. A.D.) and Pavlos Aeginites (625-690 A.D.) describe and perform amazing operations, like craniotomies, strumectomies, aneurysmectomies, stripping of varices, transvaginal hysterectomies, a.o.

In addition to the descriptions of these, very refined, surgical techniques a huge amount of surgical instruments are mentioned or found. 1903 Schöne published for the first time the names of 54 "greco-roman" surgical instruments and in 1907 Milne attempted to attribute to the Byzantine instruments found, their Byzantine names. In 1983 Maraslis could broaden the list up to 160 instruments, while Bliquez in 1985 to 237. However, several instruments like cautery (n=18), mele (n=25), scalpels (n=24) a.o. have different forms, shapes and names, obviously made for special operations, thus increasing the number of the various byzantine instruments known to over 500. Out of these instruments 207 can be classified according to their special use to one or several surgical specialties.

In this study we will try to put our emphasis on the mentioned infections like eyelid-sty, angina, arteriitis temporalis, abscesses (incl. paratonsillar, perennial, sub hepatic & sub phrenic) necroses, gangrenes, fistulas, scrofulosis, pneumonia, empyema, pyometra, loin-gangrene or infected sequesters and their treatment.