ESPID OPENING SYMPOSIUM: ANTIBIOTIC RESISTANCE: ARE WE FACING A REAL PROBLEM IN PAEDIATRICS? PART 1: COMMUNITY SETTINGS

O01

EUROPEAN SURVEILLANCE OF ANTIMICROBIAL CONSUMPTION (ESAC): OUTPATIENT ANTIBIOTIC USE IN CHILDREN IN EUROPE

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Background and aims: ESAC (www.esac.ua.ac.be) adopted the anatomic therapeutic chemical (ATC) classification and the defined daily dose (DDD) measurement unit. The DDD has some disadvantages. An ESAC subproject aims to describe the outpatient antibiotic use by age and gender, complementing the DDD with other measurement units.

Methods: Data on outpatient use of antibacterials for systemic use (ATC J01) in 2005, 2006 and 2007, expressed in DDD (WHO version 2009), and package or prescriptions per 1000 inhabitants per day (DID, and PID or PrID, resp.) were collected by age and gender, and will be described in detail, focussing on use in children.

Results: A preliminary analysis of the 2005 data showed that use in children (0-14 years) on average represented 11.2% of the total use in DID compared to 20.5% of the total use in PID. Use in children in DID on average was lower than in other age groups (12 DID (0-14y) vs 17 (15-59y), 22 (60-79y) and 34 (80+)), whereas in PID only use in 80+ was higher (2.6 vs 1.7, 2.3 and 3.4, resp.). Only in children use was higher in boys. Nearly 80% were beta-lactam antibiotics (J01C+J01D) compared to less than 60% in other age groups.

Conclusions: Other measurement units need to complement the DDD to assess use in children and the effect of campaigns on appropriate antibiotic use (in children), e.g. the ECDC campaign for the first European Antibiotic Awareness Day. In addition, antibiotic use data should be linked to the patient's age (and gender).

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O02

EU POLICIES AND RESEARCH PROGRAMMES

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Ensuring that children have access to high-quality effective and safe medicines is crucial in order for doctors to make informed decisions about disease treatment. However, no more than about half of all medicines prescribed to children in hospitals today are either unlicensed for their age group or licensed off-label. In intensive care units, the situation is even worse with 9/10 medicines given to children not having been properly tested for paediatric use. The Paediatric Medicines Regulation aims to facilitate the development of medicinal products for use in the paediatric population and ensure that these are based on high quality and ethical research. An important new marketing incentive is the Paediatric Use Marketing Authorisation (PUMA) with aims at the development of off-patent medicinal products for exclusive use in children. The Seventh Framework Programme of the European Community for Research and Technological Development and Demonstration activities (2007-2013) offers funding for off-patent medicines for children. Research projects need to address medicinal products selected as priority by the European Medicines Agency (EMEA) and the Paediatric Committee (PDCO). Although vaccines and other preventive measures fall outside the scope of these actions, they constitute a second but equally important component in the overall European research policy to tackle paediatric infections. Currently funded research projects in both these areas will be presented.

ESPID OPENING SYMPOSIUM: ANTIBIOTIC RESISTANCE: ARE WE FACING A REAL PROBLEM IN PAEDIATRICS? PART 2: HOSPITAL SETTINGS

O03

ANTIBIOTIC RESISTANCE IN PAEDIATRIC HOSPITAL SETTINGS

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Antibiotic resistance is a growing public health crisis among hospitalized patients. Patients infected with antibiotic-resistant pathogens have increased mortality and morbidity, increased duration of hospitalization, and higher healthcare costs. Hospitalized children, including infants hospitalized in the neonatal intensive care unit, are at risk of developing infections caused by antibiotic resistant organisms (AROs). Such pathogens are frequently multidrug-resistant and include methicillin-resistant coagulase negative staphylococci, methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant enterococci (VRE), extended spectrum beta-lactamase-producing or carbapenemase-producing gram negative bacilli. Furthermore, a lack of pediatric pharmacokinetic and pharmacodynamic data and/ or an unacceptable toxicity profile for some antimicrobial agents, may limit effective therapeutic options for infections caused by multidrug-resistant pathogens.

Strategies to prevent such infections are multifaceted and require sustained implementation by an interdisciplinary team. Such strategies include:

[1] Active surveillance for infections caused by AROs and dissemination of the epidemiology of local resistance patterns to clinicians to guide empiric and targeted antimicrobial therapy.

[2] Judicious use of surveillance cultures to detect children colonized with AROs who can serve as a reservoir for potential pathogens for other hospitalized children.

[3] Accurate antimicrobial susceptibility testing to detect resistance phenotypes.

[4] Implementation of an antimicrobial stewardship program which includes administrative support, clinician education, appropriate diagnostic strategies for potential pathogens, a restricted formulary, and prescriber feedback.

[5] Compliance with hand hygiene by all staff.

[6] Implementing transmission precautions (contact, droplet, and respiratory) for children colonized or infected with multidrug-resistant pathogens.

O04

MEDICINES AND VACCINES FOR CHILDREN: NEW REGULATION IN EUROPE

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The new regulation 1901/2006 “Better medicines for the Children of Europe” has dramatically changed the way Industry has to consider their global drug development. For all new or protected compounds, a full paediatric development plan (PIP) should be submitted to the European Agency not later then the completion of the pharmaco-kinetic programme in adults. The PIP should be agreed with the PDCO and is compulsory on Industry. It can be amended and if complied to might lead to a reward (6 months of additional patent protection) even if the outcome does not allow granting the paediatric indication. The same requirement applies to any extension of indication, new route of administration and new pharmaceutical form. Compounds having no foreseeable paediatric indication or use are waived by PDCO from this obligation. Medicines no longer protected can apply on a voluntary basis for a PIP and seek for a specific marketing authorisation (PUMA) granting 10 years of specific protection if successful in their development. The importance of proposing an age appropriate formulation is key. As of January 2009, the PDCO had reviewed more than 600 indications and issued more than 160 decisions on PIPs or waivers. The legislation also foresees that the PDCO should established a list of paediatric unmet medical needs, an inventory of the drug use (on & off label) and work with the EMEA to contribute to the networking of investigators across the Union in order to facilitate the conduct of necessary clinical trials.

ESPID SCIENTIFIC SESSION 1: INFECTION CONTROL: WHAT ARE THE NEW RESPONSIBILITIES AND WHY DO WE NEED TO CHANGE?

O05

INFECTION CONTROL IN SPECIAL PAEDIATRIC SETTINGS

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Infection control for infants in the Neonatal ICU (NICU), children undergoing solid organ or bone marrow transplantation, and patients with cystic fibrosis (CF) requires an understanding of transmission of specific pathogens and effective strategies to minimize transmission. Seasonal viruses such as respiratory syncytial virus, influenza, noroviruses and rotavirus can cause sporadic infections or outbreaks among vulnerable patients. Active surveillance for healthcare-acquired viral infections, rapid diagnostic strategies and instituting presumptive transmission precautions for suspected viral illnesses prior to definitive diagnosis, appropriate vaccination of staff, and screening for ill visitors and staff can prevent transmission of seasonal viruses.Infants in the NICU and transplant recipients are at risk for catheter-related bloodstream infections (CR-BSI). Endogenous skin and intestinal flora are usually implicated in such infections although outbreaks are well described. Preventive strategies for CR-BSI include bundle strategies to implement best clinical practices for catheter insertion and maintenance, institution of transmission precautions (contact, droplet, and respiratory), when appropriate, and minimizing duration of device use.CF patients may transmit respiratory tract pathogens to others with CF. While *Burkholderia cepacia* complex are the best known example of such transmission, other pathogens including *Pseudomonas* and MRSA can be spread among CF patients. Such transmission can occur in inpatient, outpatient, and non-healthcare settings via the contact and droplet routes. Strategies to prevent transmission include: segregating patients with CF from each other, containing respiratory tract secretions, maintaining the 3 foot rule to reduce droplet transmission, and appropriately processing respiratory tract specimens to maximize detection of potential pathogens.

ESPID SCIENTIFIC SESSION 2: S. PNEUMONIAE : A PAEDIATRIC PATHOGEN

O06

STREPTOCOCCUS PNEUMONIAE COLONIZATION: THE KEY TO PNEUMOCOCCAL DISEASE

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Streptococcus pneumoniae is an important pathogen causing invasive diseases such as sepsis, meningitis, and pneumonia. The burden of disease is highest in the youngest and oldest sections of the population in both developed and developing countries. The treatment of pneumococcal infections is complicated by the worldwide emergence in pneumococci of resistance to penicillin and other antibiotics.

Pneumococcal disease is preceded by asymptomatic colonization, which is especially high in children. The current seven-valent conjugate vaccine is highly effective against invasive disease caused by the vaccine-type strains. However, vaccine coverage is limited, and replacement by non-vaccine serotypes resulting in disease is a serious threat. Therefore, the search for new vaccine candidates that elicit protection against a broader range of pneumococcal strains is important. Several surface-associated protein vaccines are currently under investigation. An important issue is whether the aim should be to prevent pneumococcal disease by eradication of nasopharyngeal colonization, or to prevent bacterial invasion leaving colonization relatively unaffected, and hence, preventing the occurrence of replacement colonization and disease.

To illustrate the importance of pneumococcal colonization in relation to pneumococcal disease and prevention of disease, the mechanism and epidemiology of colonization, the complexity of relations within and between species, and the consequences of the different preventive strategies for pneumococcal colonization will be discussed.

O07

"HANDLING PNEUMONIA"

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Pneumonia is leading cause of childhood morbidity with incidence rates ranging from 0.05 episodes per child year in developed countries to 0.29 episodes per child year in developing countries. Additionally, pneumonia is a leading cause of death in developing countries and directly proportional to under-5 mortality rates.

Reducing mortality and prevention of pneumonia is partly limited by the lack of sensitive diagnostic tools with which to make an aetiological specific diagnosis. Nevertheless, empirical antibiotic-regimens targeting *S. pneumoniae* coupled with epidemiological changes observed following the introduction of pneumococcal conjugate vaccine into developed countries confirm *S. penumonaie* to be a leading pathogen causing pneumonia.Despite respiratory viruses being frequently identified in children with pneumonia, their role in the pathogenesis of severe pneumonia appears to be related to enhancing the susceptibility of the host to superimposed pneumococcal infection.

Whilst reducing mortality by early empiric treatment with antibiotics has been highly effective in certain settings, constraints with regard to accessing curative health care for many children in developing countries has limited the success of this strategy. Evidence from The Gambia suggest that significant strides can be made in reducing under-5 mortality through pneumococcal conjugate vaccination (PCV), a more structured intervention that is more readily available to children in developing countries. However, PCV vaccination may vary geographically in preventing the total burden of pneumococcal pneumonia, because of limitations in the serotype formulation of current vaccines.

O08

MANAGEMENT OF ACUTE OTITIS MEDIA IN CHILDREN - IS IT TIME TO MOVE TO PREVENTION?

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Due to its frequency and its complications acute otitis media (AOM) constitutes a significant burden for infants, their family and the society. Since AOM also is the most frequent reason for antibiotic prescription in children, it contributes to the development of antibiotic resistance, a growing problem in daily medical practice.

Management of AOM includes diagnosis, treatment and prevention. Education is the key, which enables physicians to make the correct clinical diagnosis, thereby limiting overdiagnosis and overtreatment in children with suspected AOM. The primary focus in AOM treatment should be symptomatic pain relief and restrictive use of antibiotics. Potential antibiotic side effects as diarrhoea and post-treatment colonization with resistant bacteria have to be weighed against their rather small clinical benefit. Most guidelines agree, that AOM in children > 2 years can be usually handled without antibiotics using a “watchful waiting” approach. In children between 6 and 24 months antibiotics should be reserved for severely ill children, or children with specific clinical symptoms.

Preventive measures should be targeted early in life, including the promotion of breast feeding and avoiding of tobacco smoke exposure. The concept of vaccination against AOM has recently gained new attention by a 40% reduction of AOM visits and antibiotic prescriptions following the introduction of PCV-7 in the USA. Future vaccines will target a broader range of AOM pathogens, including more pneumococcal serotypes, non-typeable *H. influenzae* and viral pathogens. Thereby the preventive options increase against an infectious disease, where antibiotic treatment strategies have come to a limit.

ESPID SCIENTIFIC SESSION 3: EMERGING AND RE-EMERGING SERIOUS BACTERIAL INFECTIONS

O09

RESURGENCE OF TB IN WESTERN EUROPE

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Although TB in Europe makes up a small percentage of the global burden of disease, its epidemiology reflects worldwide trends. Within the WHO European Region, there are major disparities between the rates of disease between resource-poor Eastern countries and those countries in the West who have the resources to fund TB control programmes. In Western Europe, overall notification rates have declined over the last century and have remained relatively low and stable over the last decade. However there have been significant increases in some of the large metropolitan centres, such as London, which have seen fourfold increase in TB rates over the last decade. Reasons for this resurgence include increased migration/travel from high prevalence countries, poor TB control and ongoing transmission. Along with overall TB incidence, increasing rates of childhood TB in some areas, can be largely attributed to recent transmission from an infectious adult. Rates of TB in children therefore give an early indication of changes in the patterns of TB in a population and therefore represent sentinel events within those communities indicating recent transmission.

O10

GROUP A STREPTOCOCCUS - CAN HORIZONTAL GENE TRANSFERS EXPLAIN CHANGES IN STREPTOCOCCAL EPIDEMIOLOGY?

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Background: Group A streptococcus (GAS) is the most common aetiological agent for pharyngitis, impetigo, cellulitis, necrotising fasciitis, scarlet fever, toxic shock, rheumatic fever (RF) and post-infectious glomerulonephritis. However, in recent years reports of association of human group G and C streptococci (GGS) with similar spectrum of diseases have appeared frequently. In some communities, GAS isolation rates from the throat are not commensurate with the burden of RF and rheumatic heart disease in the communities. By contrast, the frequency of GGS recovery is high in the same population. In general, the GGS genome has about 50% of GAS genes for virulence or surface proteins. Horizontal genetic transfers (HGTs) between GAS and other streptococci are common.

Methods: The extent to which different mobile genetic elements (MGEs), such as phages and conjugative transposons, may contribute to differences in strain structure by genomic subtraction, screening, and *in vitro* mobilization of MGEs.

Results: HGTs between GAS and GGS are ongoing events and are not just evolutionary relics. Therefore, streptococcal strain structure in a given region is dependent of the endemicity of the region for GAS infection. Some phages move between GAS and GGS. We have also demonstrated mobilization of a conjugative transposon between GAS, GGS and group B streptococcus (GBS) *in vitro.* However, in nature movement of the transposon is more common between GGS and GBS than between GGS and GAS.

Conclusions: Emerging changes to epidemiology may be explained by HGTs among closely related streptococci. HGTs have implications to long term effectiveness of a vaccine.

O11

WHAT IS CHANGING WITH *STAPHYLOCOCCUS AUREUS* IN CA INFECTIONS

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Methicillin-resistant S. aureus isolates causing community-acquired infections (CA-MRSA) in children is major problem in several areas around the world. These isolates have a unique chromosomal cassette (SCC*mec* IV) that carries the antibiotic resistant genes and is lower in molecular weight than the cassette carried by the typical nosocomial MRSA isolates. Different CA-MRSA clones are circulating around the world. CA-MRSA generally are susceptible to clindamycin and trimethoprim-sulfamethoxazole. CA-MRSA are associated with both skin and soft tissue infections and invasive infections. Recurrent soft tissue infections and infections within the family caused by CA-MRSA isolates are common. CA-MRSA isolates containing genes encoding for pvl have been associated with serious staphylococcal pneumonia and complicated osteomyelitis, although the role of pvl in the pathogenesis of disease is not certain. Treatment of superficial skin and soft tissue infections involves surgical drainage ± an oral agent such as TMP-SMX or clindamycin. Empiric vancomycin is typically administered for more serious invasive infections such as osteomyelitis, septic arthritis or suspected Staphylococcal pneumonia. The need for targeting trough vancomycin levels of 15-20 µg/mL or adding gentamicin or rifampin in children with serious MRSA infections is uncertain. Clindamycin is efficacious in treating CA-MRSA infections caused by susceptible organisms. Linezolid is another option in selected circumstances. The role of daptomycin and other newer agents in treating children with serious CA-MRSA infections is under study.

ORAL COMMUNICATION 1: IMMUNITY AND INFECTIONS

O12

IMMUNITY AND BACTERIAL INFECTIONS

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Although medicine promotes use of antiseptic and antimicrobial agents assiduously, there are approximately ten times more bacterial cells in a human than human cells. It follows that symptomatic bacterial infection is an exception rather than a rule and that we may learn more from the study of the physiology of colonisation than of the pathophysiology of infectious diseases. From the perspective of the bacterium, inducing symptoms may be a costly mistake - while from the perspective of the human, immune responses, once induced, may sometimes do more harm than good.

Human vaccines have been developed with the primary aim of protecting the recipient from later developing symptomatic disease. Almost invariably, when the primary mode of transmission is human to human, indirect or herd immunity effects have turned out to be as or more important for effectiveness.

Despite this, immunological studies have tended to focus on the mechanisms of individual protection (and generally on serum antibody concentrations) which are the commonest surrogates and correlates.

However, the evidence that systemic and mucosal immunity are distinct and separate from eachother is beginning to look insecure - in contrast, it begins to seem hard to have one without the other.

Recognising this has profound implications for the future of vaccinology. What are the long term implications of significantly changing the ecology of the upper respiratory tract, the gut or the skin? Are there ways to elucidate - or at least accurately observe this? Are there potential strategies to compensate if this proves necessary?

O13

HOW LONG ARE NEONATES PROTECTED BY MATERNAL ANTIBODIES AGAINST MEASLES IN A LOW ENDEMIC COUNTRY?

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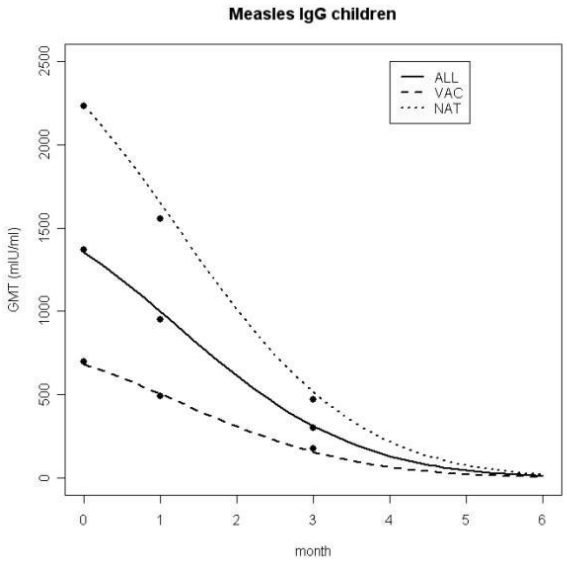
Kinetics of maternal measles, rubella and varicella antibodies in neonates was investigated in a large prospective study involving 221 women and their offspring. Differences between children of women vaccinated against measles (VAC) and naturally immune women (NAT) were studied.

IgG concentrations were measured using different ELISA tests (Dade Behring) in blood samples taken from children at 6 time-points from birth until age 1 year and from women at week 36 of pregnancy. Linear mixed models were used to model maternal antibody decay in infants with time, taking heterogeneity between, and homogeneity within infants into account.

VAC had significantly less measles antibodies (GMT 764 mIU/mL) compared to NAT (GMT 2674 mIU/mL) ($p< 0.0001$). Maternal values were highly predictive for neonatal values ($\rho=0.931$ at birth): children of VAC had significantly lower amount of antibodies at birth compared to children of NAT ($p< 0.0001$). However, the rate of decay was identical, leaving few children protected at 6 and none at 9 or 12 months of age. Likewise, for varicella and rubella, all children had lost maternal protection by 6-9 months.

The results of this unique study question protection by maternal antibodies in infants before starting immunization and confirm that vaccination should start in time.



[GMT Measles children]

Figure: GMT values until month 6, and the predicted GMT profiles for infants of ALL, VAC and NAT women.

O14

A GENOME-WIDE ASSOCIATION STUDY OF MENINGOCOCCAL DISEASE IDENTIFIES NOVEL SUSCEPTIBILITY AND SEVERITY GENES IN A PAEDIATRIC MENINGOCOCCAL PATIENT COHORT

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Background and aims: Genetic factors contribute to both susceptibility and severity of meningococcal disease (MD) and a number of genes have been associated with the disease in previous studies. However most of these case-control studies used relatively small patient cohorts and many of the associations have not been replicated in larger studies. We have established an ESPID supported European collaborative study which has collected 1, 500 MD cases from the UK, Holland and Austria. This unique cohort has been used to undertake a genome-wide association study (GWAS) to identify novel genetic determinants as well as confirm known genetic associations.

Methods: We used a staged study design with both discovery and confirmatory cohorts. In the first stage, 800 Caucasian paediatric MD cases were genotyped using the Illumina™ Infinium 550K chip. SNPs that deviated significantly from HWE, had significant Mendelian errors or failed genotyping QC were excluded. For controls, genotyping data from the UK 1958 Birth Cohort was analyzed.

Results: Genotyping and data analysis of the GWAS is currently underway and results from single SNP as well as pathway-based analysis will be presented. These genes identified will be replicated in the second confirmatory phase.

Conclusions: This is the first GWAS of MD and the largest cohort yet studied. We expect the study to identify novel variants involved in both susceptibility to and severity of MD. The study provides an example of the strengths of European collaborative research within ESPID and should make a significant contribution to understanding of the disease.

O15

INVASIVE STRAINS OF NEISSERIA MENINGITIDIS HAVE WEAKER IMMUNOSTIMULATORY EFFECTS IN COMPARISON TO COLONIZING STRAINS

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Background and aims: *Neisseria meningitidis* is an important human pathogen, which can cause severe invasive disease. Carriage state of the bacteria is common and reasons why the infection becomes invasive are not fully elucidated. The bacteria are recognized by cells of innate immunity, which detect the pathogen using different receptors including toll-like receptors (TLR). Therefore, we aimed our study at differences between expression of TLR2, TLR4, CD14 and HLA-DR as well as cytokine production after *in vitro* stimulation of monocytes by heat-killed invasive and colonizing strains of *N. meningitidis.*

Methods: In the whole blood model, we tested 23 *N. meningitidis* strains (14 invasive and 9 noninvasive) after 24-hr incubation at $37^{o}C$ in concentration of 10^{7} CFU/ml. Expression of TLR2, TLR4, CD14 and HLA-DR on monocytes was performed using flow cytometry as well as analyses of cytokines in supernatants (CBA assay, BD Biosciences USA).

Results: Invasive strains in comparison to colonizing strains caused significantly higher increase of TLR2 expression and decrease of HLA-DR expression on monocytes. Also, the changes of both parameters correlated significantly. Moreover, the colonizing strains in comparison to invasive strains of *N. meningitidis* elicited significantly more intensive cytokine production.

Conclusion: These findings indicate a weaker immunostimulatory potency of invasive strains of *N. meningitidis* contrary to colonizing strains, which could be one of the reasons why invasive strains of *N. meningitidis* gain entry into the bloodstream, whereas the colonizing strains are contained in the epithelia of the upper airways.

Ackwnoledgement: The study is supported by the grant MSM 0021620806.

O16

DEVELOPMENT OF ANTI-PSPA ANTIBODY LEVELS IN CHILDREN WITH AND WITHOUT RECURRENT ACUTE OTITIS MEDIA

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Introduction: *Streptococcus pneumoniae* (Pnc) is one of the main pathogens causing recurrent acute otitis media (rAOM). Pneumococcal surface protein A (PspA) is a conserved surface expressed protein. The aim of this study was to investigate antibody levels against PspA family 1 and family 2 in children with and without a history of rAOM and study how antibody levels develop over one year. We hypothesize that children with rAOM will initially have lower anti-PspA antibody levels and a slower increase in anti-PspA antibody levels over one year.

Methods: We recruited children with (n=75) and without (n=44) rAOM between 12 and 24 months of age. Anti-PspA antibody levels were determined in serum samples collected at the initial visit and one year later using an ELISA method developed in our laboratory.

Results: At the initial visit, children with rAOM (n=18) showed a trend of lower antibody levels compared to healthy controls (n=29) against PspA1 (38.7 vs 71.1, respectively; p=0.11) and PspA2 (39.75 vs 181.2, respectively; p=0.07).

Antibody levels in children with rAOM increased over 1 year from 38.7 to 189.3 for PspA1 (p=0.0004) and from 39.5 to 284.8 for PspA2 (p=0.005). In healthy controls anti-PspA1 antibody levels increased from 71.1 to198.7 (p=0.001). However, anti-PspA2 antibody levels did not increase due to initial high antibody titres (181.2 to 233.9; p=0.9).

Conclusions: Delayed antibody production against surface exposed protein antigens may contribute to the development or rAOM. Further studies investigating antibody levels against additional surface expressed proteins are needed.

O17

INFLUENCE OF PRIOR CARRIAGE OF *STREPTOCOCCUS PNEUMONIAE* ON ANTIBODY RESPONSE TO 11-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (11PCV) IN YOUNG FILIPINO CHILDREN

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Background: The influence of nasopharyngeal (NP) colonization by *Streptococcus pneumoniae* (Pnc) on subsequent antibody response to an investigational 11PCV in Filipino infants was analysed.

Methods: 1,111 infants were recruited into an immunogenicity and carriage study nested in a phase III trial (ARIVAC) and received 11PCV or saline placebo at scheduled 6, 10, and 14 weeks of age. Antibody concentrations to Pnc capsular polysaccharides were measured by enzyme immunoassay at 18 weeks and at 9 months of age. Antibody response was compared between groups of children among 11PCV vaccinees stratified according to their previous carriage status at 6 or 18 weeks of age; carriers (N=8-25, depending on a serotype) vs. non-carriers (N=492-522 depending on a serotype). Only the most frequently carried vaccine serotypes (6B, 19F, 23F) and vaccine-related serotypes (6A) were included in these analyses (NP swabs positive for each serotype; N≥8).

Results: Antibody response to 6B, 19F, and 23F after vaccination with 3 doses of 11PCV was significantly lower at 18 weeks and 9 months of age among children who were carriers of the specific serotype at 6 or 18 weeks of age than among non-carriers of the specific serotype. Prior carriage of 6A had no effect on antibody response to 6B. Carriers and non-carriers of these serotypes had similar antibody response to serotypes other than the one carried.

Conclusions: Nasopharyngeal colonization at young age by Pnc of serotypes 6B, 19F, and 23F results in a significantly impaired antibody response to the specific serotype after vaccination with PCV.

ORAL COMMUNICATION 2: BACTERIAL VIRULENCE IN CHILDREN: CLINICAL AND EPIDEMIOLOGICAL IMPLICATIONS

O18

STAPHYLOCOCCUS AUREUS AND TOXIN-ASSOCIATED DISEASES

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Staphylococcus aureus represents the dominant supplier of suppurative infections or diseases caused by secreted toxins.

As example, Panton-Valentine leukocidin (PVL)-positive *Staphylococcus aureus*, regardless of methicillin susceptibility, has been linked to skin and soft tissue infections but also for deep-seated infections such as necrotizing pneumonia, fasciitis or severe bone and joint infections. Skin and soft tissue infections due to PVL-positive *S. aureus* strains are mainly furuncles and primary skin abscesses. One possibility to explain the pathogenicity of PVL-positive strains on the normal skin surface, is that PVL exerts its necrotic action along the hair shaft, thus allowing *S. aureus* to invade the hair follicle. Necrotizing pneumonia mainly affects children and young adults (median age 14 years) and is fatal in one-half to three-quarters of cases. Death usually occurs rapidly, with a median survival time of only 4 days. Leukopenia below 3×10^9/L and hemoptysis appear to be predictive of fatal outcome. PVL expression can be blocked by combining a toxin-suppressing agent (clindamycin, linezolid or rifampicin) with bactericidal antibiotics acting on the cell wall. In addition, intravenous immunoglobulin (IVIg) blocks the lytic effect of PVL on polymorphonuclear cells (PMN) in vitro.

Exfoliatins are associated with bullous impetigo and staphylococcal scalded skin syndrome. Exfoliatins are serine proteases that specifically target desmoglein-1, one of the main cell-cell adhesion molecules of the epidermis.

Toxin-shock syndrome and scarlet fever are associated with the toxic shock syndrome toxin-1 (TSST-1) and with staphylococcal enterotoxins (SE), especially SEB. All of these staphylococcal toxins act as superantigens.

O19

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME TRIGGERED BY PANTON-VALENTINE-LEUKOCIDIN-ASSOCIATED STAPHYLOCOCCAL PNEUMONIA IN A CHILD

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Introduction: Anti-phospholipid antibodies are common in children with acute infection. In most cases, they are transient and have no clinical consequence. In adult, symptomatic antiphospholid syndrome associated with infections has been widely reported, especially in its severe microthrombotic form, the Catastrophic Antiphospholipid Syndrome (CAPS). In children, the association between infections and CAPS is rare. We report here a case of CAPS triggered by a Panton-Valentine-leukocidin-producing Staphylococcus aureus (PVLPSA) infection.

Case description: A 17-month-old boy was admitted in ICU for severe dyspnea, fever and hypoxemia. Investigations concluded to a pleuropneumonia. Pleural tap found a strain of meticillin-susceptible PVLPSA. The patient was treated with Cloxacillin and had good clinical response. Three days later, he developed a severe microthrombotic condition with ischemia of feet and hands with skin necrosis, associated with acute encephalopathy, renal failure, elevated liver enzymes and thrombocytopenia. Haematological investigations showed the presence of anticardiolipin IgG, without any associated haemostatic anomaly prone to induce thrombosis, leading to the diagnosis of CAPS. Low molecular weight heparin was started. The symptoms resolved completely. However, the fingers of a foot required surgical amputation. The anticardiolipin antibodies persisted 3 months after this event without any other auto-antibody, thus leading to the diagnosis of primary SAPL.

Discussion and conclusion: PVLSA has not been reported to cause microvascular skin necrosis. However, our case suggests that PVLPSA can be involved in triggering CAPS. Our report also stresses that CAPS must be remembered as a possible cause of multivisceral failure during sepsis, even in children with no underlying disease.

O20

EMM TYPES, SUPERANTIGENS AND DRUG RESISTANCE ANALYSIS OF *STREPTOCOCCUS PYOGENES* ISOLATED FROM CHINESE CHILDREN

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Background and aims: No systemic epidemiologic analysis of GAS was reported in China. We investigated the epidemiology and characteristics of 359 GAS isolates collected from Chinese pediatric patients from 1993 to 1994 and from 2005 to 2006.

Methods: Antimicrobial susceptibility test was performed using the agar dilution methods. *Emm* types and the eight superantigen genes (*speA*, *speC*, *speH*, *speI*, *speG*, *speJ*, *ssa*, and *SMEZ*) were performed by PCR and sequencing.

Results: The resistance rates of Macrolides were high for the two period´s isolates, with MIC_{50} and MIC_{90} were all 512mg/L; moreover, it found that all of strains were susceptible to penicillin, with MIC_{90} increased from 0.0625mg/L to 0.012 mg/L after 12 years. 24 *emm* types were identified, *emm1* and *emm12* were consistently the prevalent types during the two periods, while variations in the frequencies of the other types were noted. The GAS isolates carried six or more than six SAg genes increased from 46.53%to 78.39%, with the ssa, speH, and speJ genes ($P< 0.05$) increasing and the speA decreasing ($P< 0.05$) after 12 years. We analyzed nine mainly prevalent superantigen gene profiles among the prevalent emm types (*emm1*, *emm3*, and *emm12*), the SAg genes appeared to be associated with the *emm* type.

Conclusions: The resistance rates of GAS isolates to macrolides were extremely high. The *emm* type and SAg profiles of prevalent GAS exhibited significant changes over a 12-year period of observation. Moreover, the SAg was closely associated with the emm type and were independent of the disease type.

O21

PHYSIOLOGIC COLD SHOCK OF *MORAXELLA CATARRHALIS* PROMOTES ADHERENCE TO AND PROINFLAMMATORY ACTIVATION OF RESPIRATORY TRACT EPITHELIAL CELLS

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Background and aims: *Moraxella catarrhalis* (Mc), a nasopharyngeal respiratory tract pathogen, is exposed to downshifts of temperature ("cold shock") when humans breathe cold air for prolonged periods of time. We investigated the effect of cold shock on the ability of Mc strain O35E to adhere to, invade into and induce inflammatory responses in respiratory epithelial cells.

Methods: Cold shock consisted of exposing bacteria during mid-log phase to 3 hours at 26°C vs. 37°C before conducting mRNA stability assays, fibronectin and sIgA binding assays (FACS), and adherence and invasion assays, respectively.

Results: Increased expression of UspA1, a major Mc adhesin, after cold shock, resulted from greater mRNA stability (3.0 min vs. 1.8 min at 37°C, $P < 0.0001$), led to a 65% increase in binding to fibronectin, which mediates adherence through binding to a5b1 integrin and a 45% in sIgA-binding. Cold shock enhanced bacterial cell-association (adherence) to both Chang, Detroit 562 and A459 lung cells. Cellular invasion was not affected by cold shock. Cold-shocked Mc induced a significantly greater release of the proinflammatory mediator IL-8 in lung epithelial cells as compared to bacteria incubated at 37°C. Similarly, a significantly enhanced proinflammatory response was observed when epithelial cells were stimulated with outer membrane proteins isolated from strain O35E exposed to 26°C. In contrast, both a LOS-deficient mutant and purified LOS did not exhibit a cold shock response.

Conclusion: These data indicate that cold shock at physiologically relevant temperatures around 26°C may affect the nasopharyngeal host-pathogen interaction in vivo and contribute to Mc virulence.

O22

CEREULIDE-PROVEN BACILLUS CEREUS FOOD POISONING IN A FAMILY INCLUDING A FATAL CASE AND A FULMINANT ONE RECOVERED RAPIDLY AFTER HEMODIALYSIS

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Bacillus cereus food poisoning is usually self-limiting and recovery occurs within 6 to 24 hours. However, previous reports showed a few fatal cases. In October 2008, 26 year-old mother, 2 year-old sister, and 1 year-old brother ate reheated fried rice that had been prepared one day earlier. Thirty minutes after eating, they became sick and began to vomit frequently. The brother was taken to the emergency department of a local hospital 6 hours after eating, but died after intensive resuscitation for 30 minutes. Postmortem findings revealed severe brain edema which was considered as the cause of death. The others were admitted to our hospital. The mother suffered from nausea and abdominal cramping, but became well in 12 hours just by fluid infusion. The sister was lethargy and only responsive to pain. Her blood examination revealed hypoglycemia, metabolic and lactic acidosis, and hyperammonemia. Even after intravenous administration of glucose and subsequent fluid therapy, she still suffered from impaired consciousness, but rapidly became well after hemodialysis. Bacillus cereus was isolated from the stool of all three patients, whereas cereulide, the emetic toxin produced by the bacteria, was detected in the vomit and the serum only in brother and sister. Their serum concentrations of cereulide were equal. This is the first report of measuring the exact values of cereulide in food poisoning. Hemodialysis may be one of the options to remove cereulide rapidly in severely affected patients suspected of suffering Bacillus cereus food poisoning.

O23

EPIDEMIOLOGY OF INVASIVE *HAEMOPHILUS INFLUENZAE* INFECTIONS IN INFANTS YOUNGER THAN ONE YEAR IN THE ERA OF ROUTINE HIB CONJUGATE VACCINATION

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Background and aims: To describe the epidemiology of invasive Haemophilus influenzae (Hi) infections in infants in countries with routine Hib conjugate vaccination.

Methods: In 1996, an international collaboration was developed to monitor the impact of Hib vaccination on the epidemiology of invasive Hi disease. From 2000 onwards, fourteen European countries had established national Hib infant vaccination programmes and routinely serotyped all clinical Hi isolates (www.euibis.org).

Results: Between 2000 and 2006, 897 cases of invasive Hi infections were reported in infants. Of the 781 cases where the serotype was known, 391 (50.1%) were due to non-capsulated Hi (ncHi), 344 (44.0%) were due to Hib and 46 (5.9%) due to non-type b encapsulated Hi. Although the overall incidence of ncHi and Hib were similar (2.0 vs. 1.8 per 100,000), the incidence of ncHi was almost ten-fold higher in the first month of life (11.4 vs. 1.2 per 100,000) compared with 1.4 vs. 1.9 per 100,000 at 1-5 months and 1.8 vs. 1.0 per 100,000 at 6-11 months. ncHi cases were more likely to present with bacteraemia (228/391 [58.3%] vs. 74/344 [21.5%], $p< 0.0001$) while Hib cases were more likely to present with meningitis (198/344 [57.6%] vs. 43/391 [11.0%], $p< 0.0001$). The case fatality ratio for ncHi was 17.4% (68/391 cases) compared with 2.9% (10/344 cases) for Hib (age-adjusted OR 5.7, 95% CI 2.8-11.6, $p< 0.0001$).

Conclusions: In infants, invasive ncHi infections have a much higher incidence than Hib in the first month of life and have a significantly higher case fatality ratio.

For EU-IBIS

ROTAVIRUS VACCINE EXPERIENCES FROM USA, BELGIUM AND BRAZIL

O24

MONITORING UPTAKE AND IMPACT OF THE NEW US ROTAVIRUS VACCINATION PROGRAM

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Background: The implementation in 2006 and 2008 of two new vaccines for routine vaccination of US infants against rotavirus makes it imperative to assess vaccine uptake and impact of vaccination.

Methods: Vaccine uptake was assessed using data from six sentinel immunization information systems (IIS). Vaccine impact is being examined using data on reports of rotavirus detections from a national network of sentinel laboratories. Strains are being characterized from rotavirus-positive specimens obtained from a subset of laboratories.

Results: By late 2007, >10 million doses of rotavirus vaccine had been distributed in the United States and 50%-67% of infants 3 months of age at IIS sites had received at least one vaccine dose. Coverage with full 3-dose vaccine series ranged from 27%-45% at 7 months of age and 18%-32% at 13 months of age. In 2008, onset of rotavirus activity was delayed by up to 2-3 months across the country. The vast majority of sentinel laboratories reported declines in rotavirus detections of >60%-70% compared with data from the 7-8 years prior to vaccine implementation. More than 85% of rotavirus strains circulating during 1996-2007 contain antigens that are included in the licensed vaccines; data for 2007-2008 are awaited.

Conclusions: With relatively modest levels of vaccine uptake, marked delays in onset of rotavirus activity and reductions in rotavirus detections have been reported early in the 2007-2008 rotavirus season. Monitoring is ongoing to assess disease activity through the full season and to determine whether the observed changes in disease activity can be attributed to vaccination.

O25

EPIDEMIOLOGICAL IMPACT OF ROTAVIRUS VACCINES IN BELGIUM

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Background and aims: Two rotavirus vaccines were introduced in Belgium in June 2006 and 2007 respectively. Rotavirus vaccination is recommended and reimbursed for children 2-6 months since January 2007. This study analyses the impact of rotavirus vaccination after its introduction.

Methods: An active surveillance system, based on a national laboratory-network, records all positive rotavirus cases since 2005. Data from the post-vaccine period (2007-08) are compared to those from the pre-vaccine years (2005-06).

Results: In 2007, the number of rotavirus cases reported by the network decreased by 53% compared to 2005-06 (from an average of 9034 in 2005-06 to 4228 cases). A reduction was observed in all age groups, with the highest decline in children < 1 year (from 4481 to 1819 cases, -59%). The epidemiological season was delayed compared to previous seasons (peak on week 14 vs. week 6-10). Vaccine coverage was estimated at 60-80%. Preliminary 2008 data show a further decline and a lower seasonal peak. Information on hospitalization and vaccination status of cases is not available.

Conclusions: One year after rotavirus vaccine introduction, the annual number of laboratory-diagnosed rotavirus cases have halved compared to the pre-vaccine period. A decline is observed in all age-groups. The participation in the surveillance was stable in the study period. Delayed onset and diminished magnitude of the rotavirus season is also reported in the US, where rotavirus vaccination was introduced in 2006. Laboratory data provide a crude estimation of vaccine impact. In-patient data will be analyzed to assess the impact on severe cases.

O26

EXPERIENCE OF ROTAVIRUS VACCINES IN BRAZIL

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Rotavirus imposes a high burden of disease in Brazil, accounting for hospitalization rates as high as 48%. Health economic studies estimate that vaccination would prevent more than three-fourths of all rotavirus gastroenteritis, including 1,804 deaths, with total medical savings of US$19.3 million.

Brazil has participated in multi-country phase II and III trials with Rotarix™, with 778 and 3,218 infants, respectively. A major finding was the high protection against G9 strains.

Brazil was the largest single country in the world to introduce Rotarix™ into the public sector in March 2006. As factors leading to universal vaccination were political decision from the Ministry of Health; representative epidemiological data; and cold-chain storage capacity throughout most of Brazil. Approximately 12 million doses have been administered to date and, during 2008, Brazil has reached 89.9% and 76.4% vaccination coverage for first and second doses, respectively. Full-course vaccination coverage varied across the country, ranging from 53% to 83.4% in the Northern and South-Eastern regions, respectively. Although vaccination has been well accepted by the population and medical community, problems have been reported including

(a) age-restrictions,

(b) larger storage space required, and

(c) several steps for reconstitution.

Brazil has implemented a monitoring system for adverse events and a collaborative study has initiated focussing on intussusception. As from May 2008 a case-control study is underway in Belém, to assess vaccine effectiveness. This includes an extended period of strain surveillance of at least 3 years that will be essential to fully elucidate the current issue of predominance of G2P[4] strains.

ESPID SCIENTIFIC SESSION 4: BACTERIOLOGY: CLINICAL AND BASIC BACTERIOLOGY: WHAT'S IN IT?

O27

ESPID SESSION 4 - CLINICAL AND BASIC BACTERIOLOGY: WHAT'S IN IT FOR THE CLINICIAN?

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Objectives and format: This interactive session will propose a series of clinical vignettes with a special focus on pertinent diagnostic test prescribing, interpretation of test results, and their implications for medical decision in the management of bacterial infections in children. Management issues will include selecting appropriate antibiotic therapy, assessing the cause of treatment failure, identifying the need for additional infection control precautions and assessing the epidemiological significance of multi-drug resistant organisms. We will highlight the need for intensive communication between the paediatrician, microbiologist and infection control team for optimal use of laboratory resource and microbiological expertise. Insights from basic research into the clonal diversity and phenotypic adaptation of bacterial pathogens in cystic fibrosis and foreign-body infections will be discussed. Technological breakthroughs will be demonstrated to illustrate the potential for new diagnostic assays to drive changes in clinical practice, and identify unresolved issues and areas of possible future clinical research.

ESPID SCIENTIFIC SESSION 6: EPIDEMIOLOGY AND PAEDIATRIC INFECTIOUS DISEASES

O28

PREDICTIVE TOOLS IN PEDIATRIC INFECTIOUS DISEASES

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Predictive tools can be very useful in managing paediatric patients with infectious diseases. They can be used to:

(i) identify patients at high risk of severe infectious disease,

(ii) reach a diagnosis without using an invasive or distressing or very expensive gold-standard test,

(iii) distinguish as early as possible between viral and bacterial infections,

(iv) identify patients for whom a given infectious disease reveals an underlying condition, and

(v) predict the early outcome and sequels of serious infections.

Predictive tools may be a single clinical sign or laboratory test or various signs and tests combined in a score, an algorithm, or a clinical decision rule. Whatever their form, before any widespread clinical use, predictive tools must be derived and validated according to rigorous internationally accepted methodological standards such as the STARD initiative (www.stard-statement.org). Clinicians can also use these standards for a critical appraisal of the literature. Key issues for predictive tools in paediatric infectious diseases are:

(i) ensuring that predicted variable (the outcome) is independent of the predictors, and

(ii) validating the tool across various epidemiological settings (e.g., age groups, spectrum of disease severity, and causative agents).

Example of both the successes and the pitfalls of predictive tools in paediatric infectious diseases can be found in a variety of clinical settings: office-based paediatrics, emergency departments, neonatal medicine, ICU, and tropical medicine.

O29

CEREBROSPINAL FLUID PLEOCYTOSIS IN CHILDREN IN THE ERA OF BACTERIAL CONJUGATE VACCINES: DISINGUISHING THE CHILD WITH BACTERIAL AND ASEPTIC MENINGITIS

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Although bacterial meningitis remains an important cause of childhood morbidity and mortality, the incidence of bacterial meningitis has greatly decreased with the advent of polysaccharide-protein conjugate vaccines in the past two decades. The vast majority of children with CSF pleocytosis have aseptic rather than bacterial meningitis, raising the possibility that some patients may be managed as outpatients. First we will review the changing epidemiology of bacterial meningitis. Then we will discuss the available clinical decision rules that may assist the clinician in distinguishing aseptic from bacterial meningitis in patients with CSF pleocytosis. Last, we will describe the effect of antibiotic pretreatment on the CSF profiles of children with bacterial meningitis.

O30

EVIDENCE-BASED PAEDIATRIC INFECTIOUS DISEASE: HOW TO SEARCH THE LITERATURE

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In this presentation, I will decribe how even an aged technophobe can learn how to search the literature for evidence quickly and with acceptable accuracy.

Someone may already have found the best available evidence and analysed it in a high quality systematic review. The Cochrane Library contains many such systematic reviews and the rigour demanded of these ensures that almost all Cochrane systematic reviews are high quality and up to date. I recommend you always begin by searching the Cochrane Library (http://www.thecochranelibrary.com/) using various general search terms, e.g. urinary tract infection.

Even if there is no Cochrane systematic review, you may still find a non-Cochrane systematic review in Index Medicus. The easiest route is via PubMed (http://www.pubmed.gov/) which is a service provided free to all users by the NIH. After entering PubMed you should click on Clinical Queries. Clinical Queries has two different boxes which allow queries about systematic reviews and about randomised controlled trials.

Finally, I urge courage and practice. Do not be afraid to start searching the literature, be adventurous and repetition will improve your searches.

ORAL COMMUNICATION 3: INFECTIONS AND SURVIVAL IN IMMUNOCOMPROMISED CHILDREN

O31

CLINICAL EPIDEMIOLOGY OF INVASIVE *CANDIDA* INFECTIONS IN A CHILDREN'S HOSPITAL DURING A 13-YEAR PERIOD

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Background and aims: Invasive candidiasis (IC) has been well characterized in adults, but only a few studies are performed in large cohorts of children. Differences in underlying diseases between children and adults preclude extrapolation of epidemiology, management and outcome from adults to children. Our aim was to get a better insight in the clinical epidemiology of invasive *Candida* infections in pediatrics.

Methods: All children (0-18 years) with positive mycology from blood, CSF, biopsies and peritoneal-fluid in our hospital between January 1991 and December 2003 were retrospectively analyzed. Questionnaires were used to retrieve the demographic and clinical data for each patient.

Results: Of the 61 patients (mean age 2.7 yrs) included, 51% were premature newborns (55% birth weight < 1000 gram) and 23% were oncology patients. The majority (87%) were diagnosed with candidemia, 5 with peritonitis (8%) and 3 with meningitis (5%). *C. albicans* (*CA*) was the most prevalent (59%), followed by *C. parapsilosis (CP)* (20%). No shift in species distribution over time was seen. The species found was significantly related to the underlying disease ($p < 0.05$). Newborns < 1000 gram were more often infected with *CP* compared to the other neonates and older children. Treatment with (liposomal) amphotericin B or fluconazole were most commonly prescribed without differences in outcome. Having a central venous access device or catheter was significantly related to mortality ($p < 0.05$). Overall mortality was 43%, infection-related mortality was 23%.

Conclusions: Clinical epidemiology of invasive *Candida* infections in children differs considerably from those in adults.

O32

BORDETELLA HOLMESII BACTEREMIA IN 4 ASPLENIC PATIENTS

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Bordetella holmesii is a fastidious asaccharolytic oxidase-negative Gram-negative rod. It has been reported as a rare cause of bacteremia, primarily in patients with functional or anatomical asplenia. We describe 4 cases of *B. holmesii* bacteremia in unrelated children with hematologic conditions.

Patients were aged between 9 and 17-year-old. Three were suffering from sickle-cell disease, two of whom had undergone splenectomy. In the last patient, elective splenectomy was performed due to autoimmune hemolytic anemia. They all presented with fever but no other complaint, appeared well and had no remarkable findings on physical examination. Two of the patients were treated with IV ceftriaxone followed by oral ciprofloxacin for a total of 10 days. The remaining patients received only IV ceftriaxone, for 2 and 7 days respectively. The clinical outcome was uniformly favorable, without complications.

Blood cultures drawn upon presentation were detected positive for Gram-negative rods after a mean incubation time of 40h (range 30h - 47,3h). Initial identification attempt through the VITEK 2 automated system (bioMérieux Inc.) reported each time *Acinetobacter lwoffi*i (99,9% excellent identification), but some basic characteristics were discordant. *B. holmesii* was identified in all cases by 16SrDNA gene sequencing. Biochemical and antibiotic susceptibility testing showed no difference among isolates and Pulse Field Gel Electrophoresis revealed great similarity between these *B. holmesii* isolates and others previously encountered worldwide.

Our cases support the growing evidence that *B. holmesii* is a cause of bacteremia in asplenic patients. It should always be considered, particularly when the VITEK 2 system reports *Acinetobacter lwoffii*.

O33

PAEDIATRIC MORTALITY FROM HIV IN THE UK AND IRELAND: A CHIVA NETWORK SURVEY

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Aims: We aimed to explore the reasons for deaths in HIV-infected children in the United Kingdom and Ireland from 2000 to 2007.

Methods: Analysis of questionnaire based results of deaths in HIV infected children reported to the National Study of HIV in Pregnancy and Childhood (NSHPC) and followed up in the Collaborative HIV Paediatric Study (CHIPS).

Results: We received reports for 49 (98%) of the 50 deaths. 44.9% (22/49) died within 3 months of diagnosis. Cause of death was related to HIV in 87.8% (43/49), with 18.4% (9/49) caused by bacterial infection, 10.2% (5/49) Pneumocystis pneumonia, and 10.2% (5/49) HIV encephalopathy. Infants had a high risk of disease progression; 18 (36.7%) died before one year of age, with the majority (12/18) within 3 months of diagnosis and 11/18 before the advent of routine antenatal screening in 2003. 15 (30.6%) died between 5-10 years old and 9 (18.4%) after 10 years. Adverse social circumstances contributed to the child's death in 38.8% (19/49) and were noted in 50% (11/22) of those who presented late.

Conclusion: Late diagnosis is a major contributory factor to the continued mortality of children infected with HIV. The adverse social circumstances of affected families may contribute to late presentation. Paediatricians should consider the diagnosis early, and perform HIV tests as part of routine care. Missed prevention of mother to child transmission continues to occur but the number of infant deaths decreased over the audit period, which is likely to be due to improved screening during pregnancy.

O34

COGNITIVE AND MOTOR DEVELOPMENT AT THE AGE OF 7 YEARS IN HIV-UNINFECTED CHILDREN PERINATALLY EXPOSED TO ANTIRETROVIRALS

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Background and aims: Infants exposed to antiretrovirals (ARV) during pregnancy are at risk for mitochondrial toxicity. When symptomatic, mitochondrial toxicity presents with neurologic symptoms. To date, normal neurodevelopmental status up to the age of 3 years in these otherwise healthy patients has been reported; data on the long-term outcome is lacking.

Methods: A cross-sectional study in 7-year-old HIV-uninfected children perinatally exposed to ARV was performed to assess their long-term neuropsychological development; a control group of healthy children born to HCV-infected mothers was used. Upon inclusion, a comprehensive neuropsychological test battery was administered by a blinded pediatric neuropsychologist: WISC-IV, Tomal and FCR, K-BIT, Peabody and ITPA, FRC and VMI, Trail making test, FAS and CARAS test, Purdue pegboard and TALEC, and Achenbach parent and teacher rating scales.

Results were controlled for the following confounders: age and gender, caregiver education level, birth weight and prematurity, and exposition to other drugs during pregnancy.

Results: Fifty-six antiretroviral-exposed and 21 control children were assessed. No significant differences were observed between groups. When compared to age-related normative values, no cognitive or motor deficits were detected, except for Purdue Pegboard Assembly test, in the low range of normality in both groups. When the covariates were taken into account no further findings were observed.

Conclusions: Normal cognitive and motor function was observed in 7-year-old children perinatally exposed to ARV. When compared to non-exposed healthy children, no differences were neither observed. Despite low numbers, the blinded design of our study and the long-term follow-up make our results reassuring.

O35

IMPROVING SURVIVAL OF CHILDREN WITH AIDS: CONTINUING IMPROVEMENT IN BRAZIL

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Background: Brazil is well known internationally for its AIDS control programs. Brazil provides universal access to HAART, in adults and children, following national treatment guidelines, including prenatal HIV testing for all pregnant women. The first national study of survival in pediatric AIDS (1983 to 1998) showed the first evidence of the widespread impact of treatment as measured by substantially increasing survival time among AIDS cases infected through mother to child transmission. We examined more recent trends in survival by conducting a second national study among pediatric AIDS cases diagnosed in 1999 to 2002 and followed until 2007.

Methods: This retrospective cohort study was a probability sample (n=1120) of all cases reported in the 27 states of Brazil. The sampling frame was all children diagnosed with AIDS under age 13 in the national AIDS reporting data base between 1999 and 2002. Using life table analysis, the probability of survival 60 months after diagnosis was calculated. For children not known to have died, the date of censure was their most recent clinic visit.

Results: The probability of survival 60 months after AIDS diagnosis was .863 (95% c.i. .841-.885). In the first national study, this probability had been .528 (95% c.i. .419-.608.) These results thus demonstrate a substantial improvement in survival in recent years.

Conclusions: These results reinforce previous data showing increased survival among Brazilian children with AIDS on a national level. Universal access to treatment and testing can have a significant public heath impact in a developing country like Brazil.

For Brazilian Group of Survival Study in Children with AIDS, Sao Paulo, Brazil

ORAL COMMUNICATION 4: RESISTANCE IN BACTERIAL PATHOGENS

O36

INTEGRONS AND THE ANTIBIOTIC RESISTANCE GENES DISSEMINATION

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Overcoming multi-drug resistance phenomena in bacteria is a key issue in medicine for the 21st century. In most gram-negative species, the multi-drug resistance phenotype development and spread is linked to the presence of integrons. Working as natural genetic engineering platforms, these elements are able to incorporate open-reading frames and convert them to functional genes by ensuring their correct expression. They owe their success to their aptitude to assemble multi-resistance operons from a pool gathering about 130 different gene cassettes so far, which encode resistance to all class of antibiotics active against Gram-negative bacteria. These structures are also found in the genomes of numerous environmental bacterial species, specifically in most Vibrio species where they can gather hundreds of adaptive gene cassettes in structures called superintegrons. Evidence suggests that the integrons from the environmental species are a source of resistance gene cassettes for the mobile multi-resistant integrons observed within clinical isolates. We have recently shown that cassette recruitment involved a novel mode of recombination using single stranded DNA substrates, which likely accounts for the unique aptitude of this site-specific recombination system to recombine distantly related sequences. We now have data showing that the SOS response controls expression of the integrase, and as a result, the gene cassette recruitment. These elements point to single strand DNA being a central metabolite for the adaptive response of integrons and to the antibiotics, especially those inducing the SOS response, as triggers for the resistance cassette recruitment, which results in a vicious circle favoring the resistance development.

O37

SALMONELLA BLOODSTREAM INFECTION IN RURAL CENTRAL AFRICA

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Background and aims: *Salmonella* bloodstream infections represent a major health problem in sub-Saharan Africa. The incorporation of the Democratic Republic of Congo (DRC) in the WHO Global Salmonella surveillance training program allowed us to improve laboratory facilities ensuring appropriate treatment of bacteraemic children in the country. During a period of 5 years, we have evaluated clinical features, antimicrobial susceptibility patterns and molecular epidemiology of *Salmonella* isolated from blood.

Methods: Between 2002 and 2006, *Salmonella* spp. strains isolated from blood at the Lwiro Paediatric Hospital were identified and resistance to eight antimicrobials were determined. Random selections of the isolates were typed utilizing Pulsed Field Gel Electrophoresis (PFGE) to determine the genomic finger print.

Results: S. Typhimurium (60.5%) and S. Enteritidis (22.3%) were the most common serotypes found. 93.4% of them were multidrug resistant with the following proportion of strains resistant to: ampicillin (86%), chloramphenicol (92%), co-trimoxazole (95%), and tetracycline (34%). Among the 29 *S.* Typhimurium tested, 24 belonged according to dendrogramme of the PFGE to the same clonal cluster. The related strains were isolated during the first 48 hours after hospital admission as well as during a wide period after hospitalization indicating the isolates being both nosocomial and community acquired.

Conclusions: Our findings indicate the need of to use drugs rationally in order to control the spread of multi-drug resistance strains and the necessity of effective infection control practices to reduce the mortality and morbidity caused by Salmonella spp. DRC.

O38

ESBL COLONISATION AND INFECTIONS IN A PAEDIATRIC INTENSIVE CARE UNIT

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Introduction: ESBL producing gram-negative pathogens (GN) are commonly encountered in intensive care patients. Very few data are available from PICUs.

Objectives: To describe epidemiological and clinical characteristics of children colonised and/or infected with ESBL GN in our PICU.

Material and methods: PICU is a 12 beds unit in a 170-beds paediatric hospital. Annually, around 150 Algerian cardiac children are admitted for surgery. Upon admission from North Africa (NA) or PICU/NICU, patients are screened for ESBL GN. PICU patients are screened once weekly. Patients colonised and/or infected with ESBL GN are recorded. Epidemiological and clinical data were completed retrospectively for all patients for the years 2003-2006.

Results: 142 children were colonised and/or infected by an ESBL GN. Most (n=129) had stayed in cardiac ward and/or PICU. Screening was performed on admission in 82%. On admission, 31% (44/142) patients were ESBL positive, 84% of which were from NA. 75 children became ESBL positive in PICU. In 25 children rectal swab became positive within 72 hours after surgery. Among 15 infections attributed to ESBL GN, 4 were colonised on admission and 4 became positive within 72 hours. There were 9 septicaemia/bacteraemia, 4 pneumonias, 1 UTI and 1 osteomyelitis. All infected patients, but one, who died from a KP catheter related septicaemia were treated with meropenem. Median length of stay to infection was 10 days.

Conclusion: Targeted screening allowed for identification of ESBL colonised patients and appropriate antibiotic treatment in 93% of our PICU infected patients. Screening was performed as recommended in most children.

O39

USE OF INTRAVENOUS COLISTIN (COLISTIMETHATE) IN NEONATES AND CHILDREN

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Background and aims: Colistin has been increasingly used as salvage therapy of serious infections due to multi-drug resistant Gram-negative bacteria. Very little is known about its safety and efficacy in pediatric patients. We present a case series of critically ill children treated with colistin.

Methods: The records of pediatric patients who received colistin intravenously in a tertiary-care hospital (October 2007-November 2008) were reviewed.

Results: Seven children (median age 5.5 months, range 40 days to 8 years) received 8 courses of colistin. Colistin was used for the treatment of pneumonia (3 courses), CNS infection (3 courses), bacteremia (1 course) and complicated soft-tissue infection (1 course). The isolated pathogens were multidrug-resistant Acinetobacter baumannii, Enterobacter cloacae, Klebsiella pneumoniae and Stenotrophomonas maltophilia. Colistin was administered at a maximum daily dose of 3mg/kg (40,000 IU/kg) in 3 courses and 8-16mg/kg (100,000-200,000 IU/kg) in 5 courses, thrice a day. Duration of administration ranged between 12 to 70 days (>21 days in 7 courses). In 7/8 courses there was co-administration of other antimicrobial agents. In 3 courses (CNS infection) intravenous colistin was combined with intraventricular administration. In general, colistin was well tolerated. Temporary increase of serum creatinine in one patient was associated with co-administration of gentamicin. Six of 8 patients were cured. Colistin resistance developed in one patient after >6 weeks of therapy.

Conclusions: Intravenous colistin appears to be safe even at doses that are higher than those previously recommended. More data are needed to evaluate efficacy of colistin therapy in pediatric patients.

O40

ANTIMICROBIAL SUSCEPTIBILITY OF *H. PYLORI* STRAINS IN CHILDREN: RISK FACTORS FOR RESISTANCE AND EVOLUTION DURING THE LAST 5 YEARS

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Aim: The effectiveness of *Helicobacter pylori* eradication regimens is influenced by antibiotic susceptibility and compliance of patients. In this study, we evaluated risk factors associated with antibiotic resistance.

Patients and methods: January 2003-March 2007, *H. pylori* gastritis was diagnosed by endoscopy with biopsies for histology and culture in 337 children (329 before and 40 children after eradication failure).

Results: Resistance to amoxicillin was not observed. Primary resistance was 103/329 = 31,4% (16.7% for Metronidazole, 5.8% for Clarithromycine, 3.7% for Metronidazole and Clarithromycine, 1.2% for Ciproxine, 0.3% for Clarithromycine and Ciproxine, in 3.7% we found discordant value between the antrum and the fundus). Significant independent risk factors for Metronidazole resistance are ethnical background (Sub-Saharan Africa, OR 7.57, $p< 0.0001$), and country of birth (Sub-Saharan Africa, OR 7.6, $p< 0.0001$). For Clarithromycine resistance, independent risk factors are children country of birth (North Africa, OR 4.03, $p=0.008$), and chronic ENT infection (OR 6.68, $p=0.0004$). After eradication failure, 35% (14/40) of isolated *H. pylori* strains are resistant to at least one antibiotic (22.5% for Metronidazole, 7.5% for Clarithromycin, 2.5% for both Metronidazole and Clarithromycine, et 2.5% for other combinations of antibiotic resistance).

Conclusions: Clarithromycin resistance rate seems decreasing in our population (was above 20% in 2000-2002). Metronidazole resistance rate is stable. Ethnical background and country of birth as well as some clinical features such as recurrent respiratory infection appear to be independent risk factors for antimicrobial resistance, probably due to different prescription habits in different countries and in different medical fields.

O41

EMERGENCE OF VACCINE ESCAPE RECOMBINANT STREPTOCOCCUS PNEUMONIAE 7B IN CHILDREN OF BANGLADESH WITHOUT SELECTION PRESSURE OF PNEUMOCOCCAL VACCINATION?

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Background: Streptococcus pneumoniae take up exogenous DNA by natural transformation or fratricide induced by antibiotics, vaccination and other factors for phenotypic and genotypic diversification.

Aims and methods: Studied capsule switching, seroconversion and genomic similarity among pneumococci from children with invasive diseases by antibiotics resistance, serotyping and MLST analysis in Bangladesh where pneumococcal vaccines are not used routinely.

Results: Of 136 pneumococci, 11 common serogroups, representing 77% of invasive-isolates were 6, 14, 19, 5, 12, 1, 7, 45, 2, 9 and 23 (in descending order), where as 11 most common serogroups of colonized-isolates comprising 77.6% were 6, 19, 14, 23, 9, 7, 13, 15, 21, 22 and 37. 71.3% were resistant to one or more drugs, MDR in 11.7%. Six (4.4%) macrolide-resistant-isolates included four 7B, one 9V and 18C each. All four 7B had MDR, three had sequence type (ST) 1553 and one ST 1586, a single locus variant of ST 1553. 9V strain had MDR and ST 1553 indicating genomic similarity with 7B and capsule switching where prevalent MDR 9V appeared to acquire 7B capsule resulting in seroconversion. eBURST analysis of MLST 1586 and 1553, and 2681 different MLSTs of pneumococci in MLST database (www.mlst.net) showed that ST 1553 and ST 1586 were not closely related to any other clone in database.

Conclusion: Thus, newly emerged MDR pneumococcus 7B strains appeared to originate by capsule switching by non-vaccine selection pressure caused invasive disease in children. To our knowledge, this unique pneumococcal clonal complex was not described elsewhere in the world.

ESPID SCIENTIFIC SESSION 7: PERSPECTIVES FOR BACTERIAL INFECTIONS IN PAEDIATRICS

O42

SYNERGISTIC LETHALITY OF BACTERIAL AND VIRAL PNEUMONIA

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Viral upper respiratory infections may progress to bacterial pneumonia, but the extent of the contribution of bacterial pathogens to viral associated pneumonia morbidity and mortality is unknown. Pneumococcal conjugate vaccine (PCV) may be used a probe to determine the role of the pneumococcus in super - infection of viral associated pneumonias. In a double blind randomized trial of 9 - valent PCV, it was shown that PCV prevented clinical pneumonia associated with a wide range of viral respiratory pathogens, including influenza, para-influenza, RSV and HMV. The large fraction (41%) of influenza associated pneumonias prevented by PCV suggests that the majority of influenza associated pneumonias in children may be due to pneumococcal super-infection. An analysis of the contemporary literature of the 1918 influenza pandemic suggests that >80% of deaths occurred ≥ 7 days after onset of symptoms. The time to mortality of untreated pneumococcal bacteremia follows an identical time course to the 1918 influenza deaths. In autopsy studies pneumococci were isolated from lung or heart blood in up to 2/3 of victims. In studies of blood cultures taken from living soldiers with pandemic influenza associated pneumonia in 1918, pneumococci were isolated in up to 50% of patients. The data from endemic influenza hospitalization in children and from pandemic influenza mortality during 1918 suggest a significant role for pneumococci in influenza - associated morbidity and mortality. Data from both endemic influenza and past pandemics suggest that the prevention of pneumcococcal super - infection should be an essential part of pandemic influenza planning.

O43

BACTERIA, VIRUSES, AND ANTIMICROBIAL AGENTS

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The classic etiological concepts of infectious diseases, based on “one germ-one disease-one treatment” are under collapse. The acquisition of pathogenic organisms depends on and influences the entire microbial community ecology of the organic area under risk. On the other hand, the local mucosal immune-response, the anti-infective measures, from vaccination to antibiotic therapy, also shapes the microbial populations' landscape.

Direct interactions among bacteria of the respiratory tract, including allelopathic or amensalistic competitive suppression, should be considered at the time of deciding interventions. In some cases, bacterial viruses are mediating such interactions; for instance, remote-control bacteriophage induction in *Staphylococcus aureus* by *Streptococcus pneumoniae* mediates displacement of the former (lysogenic) organism. Coevolution with viruses might also driven the evolution of bacterial mutation rates, and hence of its mechanisms of genetic adaptation. *Streptococcus pneumoniae-Moraxella catarrhalis-Haemophilus influenzae* competitive interactions are also frequent and relevant in the ecology of orpharynx, as was demonstrated by biofilm-invasion procedures. The impact of respiratory viruses in enhancing bacterial colonization, sometimes mediated by neuraminidase activity, and consequently on the bacterial population size and transmission rates (favoured by symptoms associated with viral infections) is of great concern in the pediatric arena. The role of the inflammatory response mediated by viruses in the bacterial population ecology (for instance altering the total bacterial density in the pharyngeal crypts) is certainly worth to be investigated.

Finally, the effect of antimicrobial agents on microbial ecology of the respiratory tract should be considered. Available metagenomic approaches to ascertain the complexity of both the viral and the bacterial organisms in the respiratory tract should help to understand the changing ecology of the respiratory tract infections.

BACTERIAL ANTIBIOTIC RESISTANCE

P001

PATTERN OF RESISTANCE AND SEROTYPE DISTRIBUTION AMONG GROUP B STREPTOCOCCUS IN KUWAIT

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Introduction: Penicillin is the first line agent used to treat and prevent group B Streptococcus (GBS) infections. The long-term impact of widespread of intrapartum prophylaxis on penicillin susceptibility has not explored. However, resistance to second-line antimicrobials, clindamycin and erythromycin, has increased since 1996. Our goal was to assess whether there are differences in susceptibility profiles between colonizing and invasive GBS strains by capsular type. To address the issue we evaluated different antibiotics, MIC trends over 5-years period in relation to different serotypes and isolate sets.

Methods: We evaluated 534 different GBS isolates from Kuwait hospitals compromising three different sets, 59 invasive isolates (blood &CSF), 378 non-invasive isolates (urine &wound swabs) and 97 colonizing isolates (vaginal & neonatal swabs). MIC to penicillin, erythromycin, clindamycin, tetracycline and gentamicin were tested by E test, and serotyping by latex agglutination

Results: Serotype III (40.6%) was the most common isolate from invasive set while serotype V from non-invasive (42.3%) and colonizing (37.3%) isolates. Serotype VI, VII and VIII were isolated from non-invasive and colonizing sets only. All isolates were sensitive to penicillin however; invasive strains had lower MICs than others did. Isolates with high MIC (>0.064) form 11% and 35.4% of 2004 and 2007 isolates while serotype VIII, NT and Ia were less sensitive than other serotypes. Overall resistance to erythromycin, clindamycin, tetracycline, and gentamicin was 11.8%, 8.7%, 93.6% and 100% respectively.

Conclusion: GBS remains susceptible to penicillin, however MIC to penicillin is changing and continuous monitoring is necessary to identify potentially resistant isolates.

P002

SEQUENTIAL THERAPY VS. STANDARD TRIPLE THERAPIES FOR HELICOBACTER PYLORI INFECTION IN CHILDREN

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Aim: Eradication rate of *Helicobacter pylori* with a sequential treatment regimen, impact of antimicrobial susceptibility on eradication rates.

Methods: Prospective multi-center study. Children with non-ulcer dyspeptic manifestations. Infection proven by histology and culture, no anti-*H. pylori* drugs during 4 weeks. Children received randomly either a 10-days sequential treatment (omeprazole-amoxicillin (AMO) 5 days and omeprazole-clarithromycin(CLA)-metronidazole(MET) the remaining 5 days or a 7-days treatment, (omeprazole-AMO-CLA when *H. pylori* strains susceptible to CLA or MET in case of resistance to CLA. *H. pylori* eradication assessed by ^{13}C urea breath test at least 8 weeks after treatment.

Results: October 2007-September 2008, 98 children included (58 female/42 male, median age 11y range 1,5 to 17). Eradication achieved in 74 children out of 88 who returned for a follow-up test. Intention-to-treat eradication rate (ITT) 76% (sequential 41/55 = 75%, triple therapy 33/43 = 77%) and per-protocol cure rate (PP) 84% (sequential 41/49 = 84%, triple therapy 33/39 = 85%). When CLA resistance, ITT eradication rate 9/14 (sequential 7/12 = 58%, triple therapy 2/2) and PP 9/13 (sequential 7/11 = 64%, triple therapy 2/2). When MET resistance, ITT eradication rate 13/18 (sequential 9/13 = 69%, triple therapy 4/5) and PP 13/15 (sequential 9/10 = 90%, triple therapy 4/5).

Conclusion: Sequential treatment seems highly effective with similar or higher eradication rate than with triple therapy prescribed in accordance with antimicrobial susceptibility. Since cure rate is decreased in case of CLA resistance, sequential treatment may not be used as first line therapy when CLA resistance rate exceed 20%.

P003

ANTIMICROBIAL RESISTANCE OF URINARY *ESCHERICHIA COLI ISOLATES* IN COSTA RICAN (CR) CHILDREN (CH)

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Background: Urinary tract infections (UTI) are common in ch and can be associated with complications in patients (pts) with underlying genitourinary abnormalities. Knowing the local antibiotic (ATB) resistance pattern of *Escherichia coli*, the leading etiology of pediatric UTI, is crucial.

Methods: Retrospective review of all positive *E.coli* isolates in urine cultures obtained from ambulatory or hospitalized ch who were attended at the only paediatric tertiary referral hospital of CR. Information was retrieved from the database of the Bacteriology Laboratory Division. Antimicrobial susceptibility testing was performed using Vitek 2 Compact System (BioMerieux®). Study period: June 1, 2006 - April 18, 2008.

Results: 1,713 *E.coli* positive urine cultures were identified. 34 (2%) of the tested strains were ESBL (+). ATB resistance rates (%) among all tested isolates are listed below:

ATB	% resistance / # of isolates	ATB	% resistance/ # of isolates
Amikacin	1/1,695	Gatifloxacin	6/1,610
Ampicillin	65/599	Meropenem	1/1,695
Cefotaxime	9/1,558	Ertapenem	0/1,713
Ceftazidime	2/1,678	Nitrofurantoin	7/1,593
Ceftriaxone	3/1,661	Gentamicin	13/1,490
Ciprofloxacin	9/1,558	TMP-SMX	49/873
Levofloxacin	7/1,593		

Conclusions: Resistance rates of *E.coli* to ampicillin and TMP-SMX, the 2 most commonly used oral ATB during many years for treating CR ch with UTI's, are high. New antimicrobial options for the management of these ch should be available at our institution.

P004

FOUR PEDIATRIC PATIENTS WITH THE IMIPENEM RESISTANT *ACINETOBACTER BAUMANII* (IRAB) INFECTION IN SINGLE INTENSIVE CARE UNIT

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Background and aims: *Acinetobacter baumanii* is known as an important cause of nosocomial infection, especially intensive care unit (ICU). The known risk factors are invasive procedures such as tracheal intubation, central venous catheter (CVC) insertion and overuse of broad-spectrum antimicrobials. We had 4 cases of IRAB and to investigate the route of infection, and describe their clinical characteristics.

Methods: We retrospectively reviewed the medical records of 4 pediatric patients of culture proven nosocomial *A. baumanii* infection which occurred in ICU of Kyunghee University Hospital between October 2007 and July 2008.

Results: The median age was 1.5 yrs, the median length of hospitalization was 162 days. The times of culture proven infection was 2, 15, 66, and 135 th hospital days, respectively. Their underlying diseases were all neurologic diseases. The three had mechanical ventilator. Only one received carbapenem before *A. baumanii* infection. The sites of infection were ventriculo-peritoneal shunt in 1, CVC in 1, tracheal intubation catheter in 1, and blood in 1. All were resistant to imipenem. Three were susceptible to colistin. Infection was not associated with clinical features such as fever or elevated C-reactive protein in our study.

Conclusions: It is thought that Imipenem resistant *A. baumanii* infection occurred due to nosocomial spread in ICU other than overuse of antimicrobials in our study. This study suggest that constant surveillance about IRAB and antimicrobial resistance is needed for patients with prolonged ICU care even in patients without fever or without increased acute phase reactants.

P005

COMPARISON BETWEEN BACTERIAL ANTIBIOTIC RESISTANCES IN THREE CHILDREN COHORTS WITH URINARY INFECTIONS

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The aim of the study was to compare the antimicrobial resistance of UTI causing bacteria in hospitalised children.

Methods: The three UTI children groups were: 36 in 2004 and 2005, 81 from 2006 to June 2007: 0-6 years-53, >6 years-28; 40 in 2008, 0-6 years-28, >6 years-12. They were treated with antibiotics and the antibiogram was performed.

Results: For the first group the cultures revealed 66,6% E.coli and 30,5% Proteus strains. 60% of E. coli and 86% Proteus were resistant to TMP/SMX. Best responses were obtained for cephalosporine and for Ciprofloxacin. In the second cohort: E.coli (40,74%), Proteus (12,31%), Klebsiella (2,46%). The intermediary resistant strains (54,54% -E.coli) were resistant to Ampicilin and TMP/SMX. Proteus and Klebsiella were resistant to Ampicilin, aminoglycozides, TMP/SMX, Colistin. Among the 40 cases of the 3rd cohort, 75% were with E. coli, 12,5% -Proteus, and 12,5% -Klebsiella. 45% of the cases received empirical oral antibiotics before admission and in those 84,6% of E. coli strains were resistant to Amoxyciline, 76,9% to TMP/SMX, and 30,7% to cephalosporine whilst 64,7% were resistant to Amoxyciline, 58,8% to TMP/SMX and 29,4% to cephalosporine in the other group. Klebsiella showed resistance to Ampicilin in patients previously treated and no resistance in the other group, and 60% of Proteus showed resistance to TMP/SMX in patients previously treated whilst 20% in the other group.

Conclusion is a modified resistance to antibiotics resistance in patients who received empirical treatment for UTI before admission and a disproportionate use of antibiotics that is still a problem.

P006

PREVALENCE OF DIFFERENT RESISTANCE PHENOTYPES OF HAEMOPHILUS INFLUENZAE ISOLATED FROM CHILDREN IN SPAIN: (SAUCE-4 PROJECT)

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Background and aims: Beta-lactamase (BLA) production in H. Influenzae is a well-known predictor factor for treatment failure in respiratory tract infections (RTI). Susceptibility patterns of H. influenzae and prevalence of resistance phenotypes are described.

Methods: This was a prospective, multicenter (34 hospitals) antimicrobial surveillance study performed between June-2006 and May-2007. A total of 2,736 H. influenzae isolates from patients with community-acquired RTI were collected and forwarded to a central laboratory. Susceptibility testing was performed by microdilution following CLSI M100-S18 guidelines and breakpoints. Chromogenic nitrocefin was used to test BLA-production. An ampicillin MIC of ≥ 2 mg/L was used to define BLA-negative ampicillin-resistant isolates (BLANAR). Capsular serotyping was performed with specific antisera against capsular antigen (Difco Laboratories).

Results: Up to 496 isolates from paediatric patients were identified. The origin of the samples was otical in 263 cases (53.0%), other respiratory samples in 224 (45.2%) and blood or pleural fluid in 9 cases. Ampicillin non-susceptible rate was of 21.4%. BLA-producing *H. influenzae* were 20.8%, whereas 3 isolates (0.6%) had a BLANAR phenotype. Another 2 isolates were found to be BLA-positive amoxicillin/clavulanate resistant (BLPACR) with 99.6% of isolates being susceptible to amoxicillin/clavulanate. Macrolide non-susceptibility was 0.2% for azithromycin and 1.2% for clarithromycin. The majority of isolates (98.8%) were non-capsulated, whereas serogroups a, b, and c represented 0.8%, 0.2%, and 0.2%, respectively. Six non-capsulated strains were isolated from blood and 1 from pleural fluid.

Conclusions: BLA-producing H. influenzae rate remains similar to previous SAUCE study (2001-2002).

BLNAR phenotype seems to be decreasing.

P007

ANTIMICROBIAL RESISTANCE TRENDS IN SHIGELLA SPECIES AMONG PATIENTS WITH ACUTE DIARRHEA IN CHILDREN HOSPITAL OF TABRIZ , IRAN

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Background & objectives: The study was carried out to determine the pattern of antimicrobial resistance of shigella species among patients with acute diarrehea in children hospital of Tabriz.

Materials & methods: The study included all of acute diarrhea patients who visited in the children hospital of Tabriz, Iran during 2002-2004 . All children whose fecal cultures yielded shigella species and antibiotic sensitivity testing was done were included in the study.

Results: A total of 45 isolated of shigella, 39 of which were shigella flexneri and 4 shigella sonnei. The rate of resistence in shiglla flexneri to ampicilin and trimetoprim - sulfametoxazol were 89.6% , 89.1% respectively. Multidrug resistance were in 65.7% cases. Almost all isolated shigella sonnei were resistant to ampicilin and 75% were resistant to trimethoprim sulfamethoxazol All of shigella species were found to be sensitive to third generation cephalosporins and nalidixic acid.

Conclusion: These results suggest the shigella flexneri is the important spp in this region with high rate of resistance to commonly prescribed antibiotic and the need to reassess the use of antibiotic agent in treatment of shigllosis.

Keywords: Shigella species, Shigllosis, Antibiotic sensitivity.

P008

EMERGENCE OF GES-TYPE EXTENDED-SPECTRUM BETA-LACTAMASE PRODUCING *ENTEROBACTERIACEAE* IN A PEDIATRIC LIVER TRANSPLANTATION UNIT

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Backgrounds and aims: Extended-spectrum beta-lactamases (ESBL) producing gram-negative bacteria are isolated with increasing frequency in pediatric populations. We report here for the first time in Belgium the emergence of *Enterobacteriaceae* carrying GES-type ESBL enzymes in a pediatric ward.

Methods: All patients admitted to this 14-bed ward mainly occupied by children hospitalized for liver transplantation were screened for multi-resistant gram negative bacteria in stools additionally to clinical samples. Identification and susceptibility testing of isolates were performed by BD Phoenix® automate and ESBL production was confirmed by double discs synergy test using Rosco® tablets. All phenotypic ESBL-producing strains were characterized by PCR targeting various ESBL genes.

Results: From January 2007 to January 2009, of the 2424 samples (562 stools) collected in 520 children, 50 ESBL-producing isolates (prevalence of 9.5%) were recovered including 10 GES-producing strains from 7 patients (6 fecal carriers). The GES ESBLs were found in 6 different *Enterobacteriaceae* species (two patients were colonized by more than one species) ; all isolates displayed identical resistance patterns. All patients but one were admitted for liver transplantation and originated from different countries of Eastern Europe. Patients and their families also stayed in the same hospital linked residency.

Conclusions: The diversity of the species, the multiple origins of the patients and the local clustering together highly suggest both cross-transmission and horizontal gene transfer of these GES plasmid-borne ESBL enzymes. Although no infection was diagnosed, GES ESBL-producing isolates may lead to outbreaks and represent a threat for fragile immunosuppressed patients such as liver transplanted children.

P009

SEROTYPES AND ANTIMICROBIAL SUSCEPTIBILITY OF STREPTOCOCCUS PNEUMONIAE FROM CHILDREN IN CYPRUS

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Background and aims: Resistance of streptococcus pneumoniae to antibiotics has increased in many countries. Since no previous data exist on the resistance of strep pneumoniae to antibiotics, our objective was to identify the resistance patterns and the circulating serotypes of strep pneumoniae in Cyprus.

Methods: A total of 150 nasopharyngeal isolates were recovered from 406 children younger than 5 years of age visiting the Government vaccination centers, the outpatient department of Archbishop Makarios Hospital and the offices of 4 private Paediatricians in Nicosia district. Sensitivity to penicillin, ceftriaxone, erythromycin, clindamycin, tetracycline, linezolid and vancomycin was tested by the disk diffusion and MIC tests. A questionnaire was also used to collect data including vaccination history.

Results: Forty percent of children involved were immunized by the conjugated pneumococcal vaccine. Resistance patterns of isolated strains were: Penicillin 39.4% Intermediate, 1.4% Resistant; Ceftriaxone 7.9% Intermediate, 5.8% Resistant; Erythromycin 40.6% Resistant, Clindamycin 30.8% Resistant, Tetracycline 31.9% Resistant. No resistant strains were detected to either linezolid or vancomycin. Twenty four percent of strains were multi-resistant. The most frequent serotypes identified were 15B (13.1%), 6B (12.3%), 23B (7.4%), 19F (6.6%) and 23A (6.6%). Of those serotypes 15B and 19F were associated with significant multi-resistance rates to antibiotics of 56% and 50% respectively.

Conclusions: The high prevalence of antibiotic resistant streptococcus pneumoniae strains colonising children under 5 years old in Cyprus, justify the need for systematic surveillance studies on the resistance characteristics of streptococcus pneumoniae in Cyprus in order to guide antimicrobial therapy and support the increase of vaccination coverage.

P010

ANTIMICROBIAL SUSCEPTIBILITY OF URINARY PATHOGENS IN CHILDREN WITH URINARY TRACT INFECTIONS

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Objectives: To determine the current antimicrobial susceptibility patterns of pathogens causing UTIs to pediatric patients from our Hospital during 2006-2008.

Methods: Data were collected from patients admitted in the paediatric unit during 3-year period (2006-2008). Identification and susceptibility testing were performed using the VITEK 2 system (BioMerieux(R), France). Susceptibility data were interpreted using CLSI breakpoint criteria. Double-disk synergy test and E-test were used for screening ESBLs.

Results: A total of 478 consecutive urine isolates from 465 children aged 1 month to 18 years with UTI were collected at our Hospital in 2006-2008. *E.coli* (n = 253, 52,93%) was the predominant pathogen, followed by *P.mirabilis* (n = 71, 14,85%) and *Ps.aeruginosa* (n = 31, 6,49%). Susceptibility rates to commonly used antimicrobial agents for *E.coli* and *P.mirabilis* were: ampicillin 58/73, amoxicillin/clavulanate 85/89, cefotaxime 94/97, ceftazidime 93/96, cefuroxime 80/85, ciprofloxacin 98/93, gentamicin 97/97, amikacin 97/100, netilnicin 97/96, trimethoprim/Sulfa 79/88. The susceptibility of *Ps.aeruginosa* was: amikacin 96, ceftazidime 93, ciprofloxacin 96, gentamicin 96, netilmicin 97, piperacillin/tazobac 100. ESBL produced 4% of *E.coli* and 0% of *P.mirabilis*.

Conclusions: *E.coli* is the primary bacterial pathogen causing UTIs in children, followed by Proteus mirabilis. Based on the resistance phenotype 15% of *E.coli* and 11% of *P.mirabilis* isolated from urine cultures in paediatrics patients were resistant to broad- spectrum beta- lactam antibiotics. The results reinforce the need for continuous local surveillance to show the current antimicrobial susceptibility data which can be used as aid to the empirical treatment of UTIs in children.

P011

DIFFERENCES IN ANTIBIOTIC SUSCEPTIBILITY PATTERNS OF BLOOD AND URINE *E. COLI* ISOLATES DERIVED FROM CHILDREN AND ADULTS

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Purpose: To compare antibiotic susceptibility patterns (ASP) of blood and urine *E. coli* isolates derived from children and adults with documented bacteremia and urinary tract infections.

Patients and methods: ASP data were collected over a 69 month period from computerized records of the Department of Microbiology, while demographic and clinical data were collected from the pediatric medical records. Duplicates were excluded. Only microbiological data were available for adults. *E. coli* identification and resistance testing was carried out by the Vitek 2 identification and resistance testing system. MICs were determined, and the results were reported as sensitive (S), intermediate (I), and resistant (R) according to CLSI standards. I and R isolates were grouped together. Susceptibility comparison per antibiotic in children vs. adults was carried out by Fisher's exact test.

Results: Pediatric (n=24) versus adult (n=259) *E. coli* blood isolates were more resistant against aminoglycosides [amikacin (p=0.03), gentamicin, netilmicin and tobramicin, p< 0.0001, for all three], ampicillin and ticarcillin (p=0.03 for both). Adult *E. coli* blood isolates tended to be more resistant against nalidixic acid (p=0.09). Pediatric (n=419) versus adult (n=838) *E. coli* urine isolates were more resistant against ampicillin (p=0.0009) and ticarcillin (p=0.003), while adult *E. coli* urine isolates were more resistant against quinolones (nalidixic acid, ciprofloxacin, norfloxacin, ofloxacin, p< 0.0001 for all four).

Conclusions: Significant differences exist in ASP of blood and urine *E. coli* isolates derived from children and adults. These differences likely reflect the more frequent use of ampicillin and aminoglycosides in children and of quinolones in adults.

P012

ANTIBIOTIC SUSCEPTIBILITY PATTERNS OF PEDIATRIC MRSA ISOLATES OVER A 67 MONTH PERIOD IN ALEXANDROUPOLIS, THRACE, GREECE

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Purpose: Methicillin-resistant *Staphylococcus aureus* (MRSA) isolates are on the rise, limiting the available therapeutic options. We studied the antibiotic susceptibility patterns (ASP) of pediatric MRSA isolates.

Patients and methods: We collected demographic, clinical and ASP data for children with MRSA isolates cared for in the Department of Pediatrics over the period 1/2003 to 7/2008. ASP data were collected from computerized data of the Department of Microbiology. Duplicates were excluded. MRSA identification and resistance testing was carried out by the Vitek 2 identification and resistance testing system. MICs were determined, and the results were reported as sensitive (S), intermediate (I), and resistant (R) according to CLSI standards. I and R isolates were grouped together.

Results: A total of 58 MRSA strains were isolated in 35 boys (60%) and 23 girls (40%) with a median age of 14 months (range 0.5 to 120 months). One isolate was from blood, 1 from pleural fluid, 4 from urine/urethra, 12 were from eyes/nose/ears, and 40 were derived from skin infections. Three of 58 (5.2%) isolates were resistant to clindamycin, 9/58 (15.5%) to erythromycin, 47/58 (81%) to tetracycline, 45/58 to fusidic acid (77.6%), 2/58 to tobramycin (3.4%) and 1/58 to both rifampin and TMP/SMX (1.7%). There was no resistance to glycopeptides, quinolones, and gentamicin. D-test performed in 5 erythromycin resistant and clindamycin susceptible isolates showed 3 to have inducible clindamycin resistance.

Conclusions: In our area, clindamycin, rifampin, and TMP/SMX resistance is low, while tetracycline and fusidic acid resistance is exceptionally high among pediatric MRSA isolates.

P013

PREVALENCE OF ANTIBIOTIC RESISTANCE OF STREPTOCOCCUS PYOGENES, STREPTOCOCCUS PNEUMONIAE AND HÄMOPHILUS INFLUENZAE IN AUSTRIA IN THE PAST TEN YEARS

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Background: Bacterial infections of the respiratory tract are an important topic in paediatrics. The most important bacteria are: Streptococcus pneumoniae, Streptococcus pyogenes and Haemophilus influenzae. In the past years resistance problems have increased worldwide but a significant regional fluctuation can be noticed.

Material and methods: Antibiotic resistance of isolates of all 0-16 year olds from the university hospital of Graz, and from settled paediatrics and general practitioners were analysed.

Results: In the 10 year period 1628 isolates of Streptococcus pneumoniae, 4197 Streptococcus pyogenes and 1843 Hämophilus influenzae could be detected.

Streptococcus pneumoniae: The number of penicillin-susceptibility has decreased considerably. While there were 99 % susceptible in the year 2000, there were only 94 % in 2008, but the number of high-level resistance was low. Macrolide resistance has shown some increase mostly combined with a decrease of susceptibility to penicillin and a resistance to Trimethoprim/Sulfamethoxazol.

No resistance was detected in Streptococcus pyogenes against penicillin. Macrolide susceptibility is subject to considerable fluctuations; nevertheless an overall increase of Macrolide-resistance can be noticed.

Haemophilus influenzae: An increase of the ß-lactamase-building isolates was registered from 6% in 2002 to 15% in 2007.

Conclusion: The number of the resistant strains is increasing considerably and a regional observance of the situation is definitely necessary. The trend of resistance in our region is emerging, but at a low level at the moment.

P014

PREVALENCE OF SEROGROUPS, SEROTYPES AND ANTIMICROBIAL RESISTANCE OF SHIGELLA ISOLATES AT GONDAR UNIVERSITY TEACHING HOSPITAL, NORTHWEST ETHIOPIA

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Background: The emergence and dissemination of multiple-drug resistance strains of Shigella are becoming a series global problem, particularly in developing countries. In Ethiopia, the diversity of Shigella strains and their antimicrobial susceptibility is not well studied.

Objective: This study was carried out to determine the prevalence of serogroups, serotypes & antimicrobial resistance of Shigella isolates from patients with acute diarrhea.

Methods: Consecutive stool specimens were received from patients and cultured for Shigella. Shigella isolates were confirmed by biochemical and serological tests. The antimicrobial susceptibility testing of all strains was carried using the single disc diffusion technique of Kirby and Bauer.

Result: Of the 1200 stool samples, 90(7.5%) yielded shigella isolates with the following serogroups:S. flexneri (72.2%), S. dysenteriae (10.0%), S. boydii (8.9%) and S. sonnei (8.9%). S. flexneri was found to be the predominant serogroup. The commonest serotypes were S. flexneri type IV (24.6%), S. dysentriae type 2 (33.33%), S. boydii types 2 and 5 (each 25%), and S. sonni phase I (75%). Eighty five (94.5%) of the isolates showed resistance to one or more drugs of which 71 (78.9%) of them were multiresistant. S. flexneri showed the highest multiresistance (91.2%) . Emergence of resistant S. flexneri serotypes to ciprofloxacin (2.2%) and norfloxacin (1.1%) has been observed.

Conclusion: We recommend ciprofloxacin & norfloxacin for empirical treatment of shigellosis with continuous monitoring of the distribution of serogroups, serotypes and antimicrobial resistance patterns and reservation of nalidixic acid and ceftriaxone for very severe cases of shigellosis.

P015

COMMUNITY ACQUIRED METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS SKIN AND SOFT TISSUE INFECTIONS IN CHILDREN IN GREECE. AN EMERGING EPIDEMIC?

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We present the results of skin and soft tissue abscesses in the children population of Athens Greece. These are patients who needed hospitalization because they needed sedation for the surgical procedure or because they were presented septic with fever and elevated markers of systemic infection.

A perspective study of hospitalized patients with skin and soft tissue infection due to Methicilline Resistant Staphylococcus aureus (MRSA) A total number of 28 patients from 1-1-08 to 31-12-08 were included in the study. The culture and identification were perfomed by conventional methods. A total of 23/28 (82%) had Staphylococcus aureus in the pus culture, 1/28 (3.5%) had Staphylococcal Coagulase Negative and 4/28 (14%) had infection from enterobacteriacae. From the Staphylococcal aureus infection 13/23 (57%) were detected Methicillin Resistant Staphylococcus aureus (MRSA) strain 9/13 (69%) of them had the phenotypic antibiotic patern characteristic of Panton - Valentine Leukocidin producing strain in Greece (Pen/Ox/kan/Tet/Fuci).

The age of the patients varied from 1 month old baby until 14 year old child. All cases were community acquired.

Our results show a possible emerging epidemic of the Panton - Valentine Leukocidin producing MRSA infection in the pediatric population in Greece and should be in consideration on the treatment of skin and soft tissue infections and on the other hand on the search for family endemics and Staphylococcal carriage.

P016

LONGER TIME SPENT FOR PATIENT IN OUTPATIENT SETTING IS ASSOCIATED WITH LOWER ANTIBIOTIC PRESCRIPTION

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Background and aims: In order to guide the improvement in the national judicious antibiotic use policy, the socioculturel, sociodemographic, economic, and cognitive factors which potentially influence the prescribing habits of pediatricians, family physicians and general practitioners were investigated with a questionnaire study.

Methods: The questionnaire study included demographic characteristics of physicians, antibiotic expectation of parents, case scenarios reflecting judicious antibiotic prescribing patterns for upper respiratory tract infections and antibiotic choice. The questionnaire were distributed by letters, web address, office visits, telephone calls, congress and society meetings. Responses obtained from 1477 physicians who had been practising in the different regions of the country were evaluated by multivariate analysis to demonstrate independent effect of each factor influencing the prescribing habits.

Results: Our results have shown that being a pediatrician, working in medical school, and spending enough time with patient were independently associated with less antibiotic prescription. Most of the physicians (%94) suggest antibiotics for a scenario case with pneumococcal pharynx colonization. Family physicians and general practitioners were more likely to prescribe antibiotics for viral upper respiratory infections.

Conclusions: Our findings suggest that spending enough time during ourpatient visits and level of education are the most important factors associated with rational antibiotic prescribing for upper respiratory infections.

P017

PREVALENCE AND MOLECULAR ANALYSIS OF INDUCIBLE CLINDAMYCIN RESISTANCE AMONG METHICILLIN SENSITIVE *STAPHYLOCOCCUS AUREUS* ISOLATES FROM PEDIATRIC PATIENTS IN ISRAEL

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Background: Clindamycin is considered an attractive empirical treatment for suspected *Staphylococcus aureus* infections. However, there is concern about the use of this antibiotic in the presence of erythromycin-resistance-mediated genes, leading to inducible clindamycin resistance (ICR), which is not detected by routine antibiogram testing. Little information has been reported about its prevalence among methicillin sensitive *Staphylococcus aureus* (MSSA) infections, and in Israel the prevalence of ICR is unknown.

Aims: To assess the prevalence of ICR among MSSA infections of pediatric patients in Israel, and evaluate the clonality of these isolates.

Methods: Retrospective analysis of MSSA infections during January 2006 to June 2007. A full antibiogram was performed for all isolates (including D-test to identify ICR), and phage typing was also determined. Selected isolates were subjected to pulsed-field gel electrophoresis (PFGE) to assess their clonality.

Results: The study included 240 MSSA isolates recovered during the study period (median age 52.5 months). Inducible clindamycin resistance was detected in 62/240 cases (25.8%). Phage type analysis demonstrated that 38/61 (62.3%) of ICR isolates were sensitive to group II, compared to 42/172 (24.4 %) of isolates not expressing ICR (P value < 0.01). Analysis by PFGE demonstrated that phage type II isolates expressing ICR belonged to the same clone, which was different from ICR isolates sensitive to other phages and different from phage II isolates not displaying ICR.

Conclusions: Clinicians should be aware of the ICR phenomenon when treating patients with suspected staphylococcal infections, and not rely on clindamycin only, especially in serious infections.

P018

EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL)-PRODUCING ENTEROBACTERIA - RISKFACTORS FOR INTESTINAL COLONIZATION AT THE NEONATAL INTENSIVE CARE UNIT (NICU)

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Background: Colonization and infection with extended-spectrum beta-lactamase producing Enterobacteriaceae (ESBL-E.) are a growing problem in Neonatal Intensive Care Units (NICU). Preterm low birth weight, prolonged mechanical ventilation, invasive devices and prior use of third generation cephalosporines were reported to be risk factors for colonization and/or infection with ESBL-E. In the last years several outbreaks of ESBL-E. colonization occurred at our NICU.

Methods: We retrospectively analyzed risk factors associated with colonization with ESBL-E. in newborns hospitalized at the NICU from Jan. 2005 to Jul. 2008. Patients were screened routinely at least twice a week for ESBL-E. in stool.

Fisher´s exact test and Mann-Whitney-U test (SPSS for Windows) were used for statistical analysis.

Results: 69 (5.9 %) out of 1164 patients have been colonized with ESBL producing *Klebsiella pneumoniae* (n=51), *Klebsiella oxytoca* (n=11), *Serratia marcescens* (n=6) and *Escherichia coli* (n=1). For details see Tab. I.

	ESBL non-colonised patients	ESBL colonised patients	
	n= 1095 (94.1%)	n= 69 (5.9%)	p-value
	number (%)		Fisher´s Exact Test
female sex	506 (46.2)	36 (52.2)	n.s.
cesarean section	712 (65.0)	55 (79.7)	0.013
Apgar 1 <9	563 (51.4)	57 (82.6)	<0.001
Apgar 5 <10	555 (50.7)	54 (78.3)	<0.001
Apgar 10 <10	427 (39.0)	49 (71.0)	<0.001
respirator therapy	366 (33.4)	44 (63.8)	<0.001
CPAP therapy	353 (32.2)	37 (53.6)	0.001
CVC	70 (6.4)	12 (17.4)	0.002
	median (range)		Mann-Whitney-U
gestational age	35 (23-43) weeks	31 (24-40) weeks	<0.001
birth weight	2365 (400-5215) g	1415 (540-3834)	<0.001
Respirator days	0 (0-66) days	3 (0-36) days	<0.001
CPAP days	0 (0-63) days	1 (0-86)	<0.001
CVC days	0 (0-37) days	0 (0-28)	<0.001
stay	15 (1-198) days	48 (3-194)	<0.001
clean stay	15 (1-198) days	22 (1-194)	0.005

CVC: Central Venous Catheter

clean stay: stay before/without ESBL colonisation

[Table I]

Cefuroxime/ampicillin were used as first line antibiotic combination. Third generation cephalosporines were not used during the observation period.

Conclusion: ESBL gene expression might be induced under therapy with second generation cephalosporines.

Factors associated with more severe illness (including lower gestational age and birth weight and more invasive therapeutic procedures) leading to longer stay at the NICU were significantly associated with colonization with ESBL-E. Longer hospital stay increases the risk of patient-to-patient transmission.

P019

EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL)-PRODUCING ENTEROBACTERIA - FAECAL CARRIAGE AND INTRAFAMILIAL TRANSMISSION AFTER INTESTINAL COLONIZATION AT THE NEONATAL INTENSIVE CARE UNIT (NICU)

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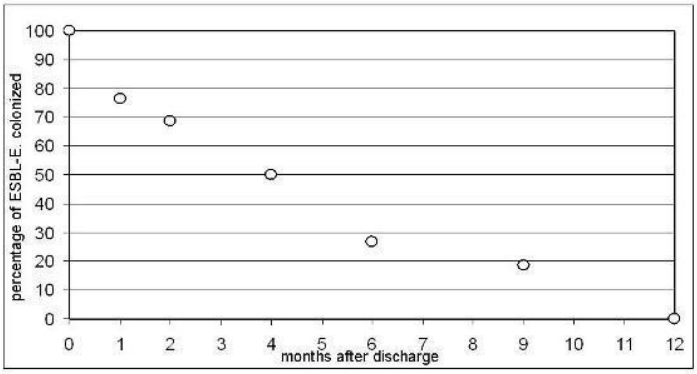
Background: Colonization and infection with extended-spectrum beta-lactamase producing Enterobacteriaceae (ESBL-E.) are a growing problem in Neonatal Intensive Care Units (NICU). In the last years an increasing number of patients colonized with ESBL-E. were observed at our NICU.There are no data on duration of faecal carriage and the risk of intrafamilial transmission after intestinal colonization with ESBL-E. in newborns.

Methods: Patients colonized with ESBL-E. at our NICU between June 2007 and October 2008 and the respective household members were screened for intestinal ESBL-E colonization 1, 2, 4, 6, 9 and 12 months after discharge.

Results: 23 colonized patients (gestational age 24+1 - 40+2, median 31+1 weeks; birth weight 500 - 3320, median 1380g; *Klebsiella pneumoniae* n=5, *Klebsiella oxytoca* n=11, *Serratia marcescens* n=7, *Escherichia coli* n=1) and 47 household members (16 mothers, 14 fathers, 16 siblings) were analyzed.

In former patients the percentage of colonized individuals showed a continuous decrease down to 0% 1 year after discharge (graph. 1).



months after discharge	0	1	2	4	6	9	12
pos./evaluated pts.	24/24	13/17	11/16	6/12	4/15	3/16	0/13
ESBL-E. pos. pts. %	100.0	76.5	68.8	50.0	26.7	18.8	0

Graph. 1 ESBL-E. colonization after discharge

[Graph. 1]

1 mother, 1 father and 5 siblings (including 2 twin siblings of former colonized patients) were colonized transiently with ESBL-E. During the observation period no infections with ESBL-E. were observed.

Discussion: After intestinal colonization with ESBL-E. at the NICU infants potentially remain carriers during the first year after discharge. Duration of carriage is varying. Intrafamilial transmission occurs infrequently.

P020

2.0 MCFARLAND ETEST METHOD FOR DETECTION OF HETEROGENEOUS VANCOMYCIN-INTERMEDIATE *STAPHYLOCOCCUS AUREUS*

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Background and aims: The population analysis profiles (PAP) method, the gold standard method for detection of heterogeneous vancomycin-intermediate *Staphylococcus aureus* (hVISA), is complicated, time-consuming, expensive, and needs well-trained microbiologists. Using a method with comparable sensitivity and specificity but more convenient, simpler, and cheaper would be a good alternative. We aimed to evaluate 2.0 McFarland Etest method in comparison with the PAP method for detection of h-VISA.

Methods: All methicillin-resistant *S. aureus* strains from clinical specimens obtained from consecutive patients at King Chulalongkorn Memorial Hospital (KCMH) and Siriraj Hospital, Bangkok, Thailand, from 2006 to 2007 were prospectively study studied.

Results: Of all 119 specimens, the PAP method detected 6 hVISA strains (5 and 1 from blood and pus cultures) from 4 patients at KCMH, accounting for the prevalence 6.35%. The MIC determined was in the range of 2-3 mg/mL. 2.0 McFarland Etest method detected 0 false positive and 5 false negatives (42%), and gave a sensitivity and a specificity of 16.7% and 100%. The one-point population analysis screening method detected 2 false positives and 1 false negative, and gave a sensitivity and a specificity of 83.3% and 98.2%.

Conclusions: This is the first prospective study to evaluate 2.0 McFarland Etest method for detection of hVISA without including homogeneous VISA. It has a very good specificity but a poor sensitivity for detection of hVISA. Due to its more convenience and less expensiveness in comparison with the PAP method, it may used as an alternative method to confirm the detection of hVISA.

P021

CLONAL SPREAD OF *S. PNEUMONIAE* AND *H. INFLUENZAE* ISOLATED FROM ACUTE OTITIS MEDIA IN JAPAN

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Clinical pictures of acute otitis media (AOM) have dramatically changed mainly due to high prevalence of antimicrobial resistant pathogens. *S.pneumoniae* and *H. influenzae* are leading causative pathogens responsible for AOM. Recently antimicrobial resistant pathogens, especially penicillin resistant *S. pneumoniae* (PRSP) and beta-lactamase non-producing ampicillin resistant (BLNAR) *H.influenzae*, have shown high prevalence and become the major causes of intractable clinical course of AOM.

In this study, we studied the acquisition and carriage rate of *S. pneumoniae* in the nasopharynx. Furthermore, we evaluated the genetic diversity of *S. pneumoniae* and *H. influenzae* isolated from children with AOM. Serotype 6B strains first colonize the nasopharynx; subsequently serotype 19F strains and serotype 23F strains colonize the nasopharynx. Contrarily serotype 3 strains less colonize the nasopharynx. While all of serotype 3 strains were susceptible to penicillin (PCG), most of serotype 19F and 23 F were resistant to PCG. The genetic diversities of these serotypes were different. Serotype 6B strains show different patterns and are considered as heterogeneous strains. Serotype 23F and 19F show some identical strains and their relatives. On other hand, all of serotype 3 strains are identical and less frequent colonize the nasopharynx. On the clonal evaluation of pneumococcal strains, there are some major clones such as Taiwan 19F-14, Taiwan 23F-15 and their relatives in Japan.

Although penicillin-resistant *S. pneumoniae* showed clonal diversity and dissemination depending on the serotypes, the most of BLNAR strains in Japan were genetically diverse. The three clusters of BLNAR strains were identified in Japan.

P022

EVIDENCE FOR TRANSMISSION OF VANCOMYCIN RESISTANT ENTEROCOCCI IN NICU AND PEDIATRIC WARDS IN IRANIAN HOSPITALS

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Background: Neonates, particularly those born prematurely, are at an increased risk of bacterial infection. *Enterococcus* spp. are a component of the human intestinal flora and may be found naturally in the birth canals of women. Intrapartum antibiotic prophylaxis of pregnant women with vancomycin, has led to increased VRE in the parturient and her child. As bacterial strains become increasingly resistant to antimicrobial therapy, measures to control this problem are essential. Current effort have focused on monitoring the VRE in NICU and Pediatric wards in Iran.

Method and material: The enterococci isolates were collected from patients in three hospitals in Tehran. The structure of vancomycin resistance genes of VRE isolates were studied by PCR amplification of the regions of ORF1, ORF2, *vanS-vanH, vanHAX*, *vanX-vanY*, *vanY-vanZ*, and *vanZ*. The isolates were typed by Pulsed- field gel electrophoresis (PFGE).

Results: Out of 50 VRE isolates, 4 were isolated from neonatal intensive care unit and Pediatric ward. All of 4 VRE isolates showed a high level vancomycin resistance (MIC≥128) and harbored *vanA* gene. The amplification of internal regions in *vanA* cluster exposed the presence of 3 types among the 4 isolates. Genotyping by PFGE using *Sma*I enzyme revealed the presence of 3 types.

Conclusion: The prevalence of VRE infections among NICU patients and Pediatric ward have been rare in Tehran. Two isolates collected from NICU and Pediatric wards showed two identical types with the same *vanA* gene cluster. This result may suggest a possibility of transmission of VRE isolates between two wards.

P023

ANTIMICROBIAL RESISTANCE AMONG UROPATHOGENS THAT CAUSE COMMUNITY-AQUIRED URINARY TRACT INFECTIONS IN CHILDREN IN HAMADAN, WEST OF IRAN

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Background and aim: Community acquired UTI (CA-UTI) causes significant illness in the first 2 years of life and it is considered as an common disease in school and pre-school children. The aim of study was to identify the most common of bacteria causing UTI, clinical manifestations and detection of antibiotics susceptibility of isolates in children who referred to hospital of Hamadan, western Iran.

Methods: Overall 912 pediatric patients clinically-suspected cases of UTI were investigated for urine cultures, urinalysis, clinical findings and antibiotic resistance patterns. Data were analyzed for four pediatric age groups: infants, toddler, preteens and teens. Antibiogram for twelve antibiotics test was performed by method of Kirby-Bauer. The required data of patients were analyzed using spss system.

Results: Out of 456 children suspected to UTI, 156 children (%34.2) had positive bacterial culture that %88.5 of isolates was Gram-negative .The most common isolates were *Escherichia coli* (%58.4), *Enterobacter sp.*(9.6%), *Kelebsiella sp* (6.4%), *Staphylococcus aureus* (5.8%), *Psuedomonas aeroginosa* (5.1%). Fever (72.8%), dysuria (58.3%), flank pain (47.4%), urgency (43.6%), urinary frequency (39.8%) were the commonest clinical manifestations of patients. The most effective antibiotics against isolates were nitrofurantoin, ciprofloxacin, naledixic acid, amikacin, ceftizoxime and co-trimoxazole while most of isolates showed high resistance against ampicillin, tobramycin, tetracyline and amoxicillin.

Conclusions: This study showed that Gram-negative bacilli in particular *E. coli* and *Enterobacter sp.* are predominant causes of bacterial agents of UTIs in children in this region. Most species showed high resistance against routine antibiotics such as tobramycin, amoxicillin, ampicillin and tetracycline.

P024

PENICILLINASE-LIKE ACTIVITY OF WHOLE HUMAN BLOOD SERUM

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Bacterial antibiotic resistance is known as one of the most challenging problems of up-to-date infectology, but this phenomenon is still analyzed from the side of bacteria only. Examining human blood serum for presence of catalytic antibodies (abzymes) we accidentally found high level of penicillinase activity, significantly higher than those expressed by polyclonal IgG studied before (I. Zhyltsou, 2001). Thus, our study was undertaken to assess the blood serum activity found and to associate it with some blood substance(s) and pathologic conditions. We examined 31 patient with erysipelas and 35 patients with pneumonia hospitalized to Vitebsk Infectious Hospital for 2007/08. To determine presence and level of beta-lactamase activity of blood serum, we applied modified neocuproine technique (A. Menashi, 1988), ampicillin and penicillin G were used as substrates. Beta-lactamase activity was found in 94,29% (95% CI: 86,6-100) of all pneumonia cases (average level of antibiotic destruction for 30 minutes of incubation is 51,38% for ampicillin and 81,76% for penicillin G). Also, beta-lactamase activity was revealed in 92,86% (95% CI: 83,32-100) of erysipelas cases (average level of destruction is 50,73% for ampicillin and 75,42% for penicillin G). No reliable differences between two groups were found. Dialysis experiments demonstrated the activity observed is mainly associated with light proteins (molecular weight below 12.000) and some non-protein substances (bilirubin?). Our results indicate that a large piece of penicillinase activity observed in clinical conditions may be explained by some properties of human blood, and this activity is definitely not associated with abzymes as it was assumed previously.

P025

ANTIBIOTIC RESISTANCE RATES IN PEDIATRIC BLOOD STREAM INFECTIONS BY ENTEROCOCCUS (2000-2006)

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Because of the emergence of multi-resistant *Enterococci* strains in pediatric patients the present study was aimed to analyze pediatric patients who had BSI (blood stream infection) due to *Enterococci* and determine their antibiotic resistance rates in a single-center experience from 2000 - 2006 (Department of Pediatrics I, Medical University Innsbruck, Austria).

Methods: Characterization of pathogens and susceptibility testing for the different antibiotics was performed according to standardized procedures in the laboratory of the Department of Hygiene, Microbiology and Social Medicine, Medical University Innsbruck, Austria.

Results: In the study period, 13 of 398 children (3.0%) (age mean 35.7 ± 65.7) had a BSI caused by *Enterococci*. Infants counted for 5 cases (38.5%), children older than 1 year of age counted for 8 cases (61.5%). *Enterococcus faecalis* was ascertained in 9 cases (69.2%), *Enterococcus faecium* in 4 cases (30.8%). *Enterococcus faecium* showed higher resistance rates according to ampicillin (100.0%), imipenem (100.0%), meropenem (100.0%) and vancomycin (25.0%) as *Enterococcus faecalis*. One patient died due to BSI with *Enterococcus faecalis* because of failure of empirical antibiotic treatment with a cephalosporine. Two patients died of *Enterococcus faecium* because of failure of empirical antibiotic treatment with vancomycin and macrolide.

Conclusion: Despite the low fraction of *Enterococci* in all BSI causing pathogens in the pediatric population, the present study demonstrated their clinical relevance. Increased alertness should be given to the occurrence of multi-resistant *Entercoccus faecium* and mechanisms causing its abundance, such as selection via antibiotic pre-treatement or ineffective empirical antibiotic treatment.

BACTERIAL INFECTIONS AND BACTERIAL VIRULENCE

P026

INVASIVE GROUP A STREPTOCOCCAL DISEASE BETWEEN 2003 AND 2008: CLINICAL AND EPIDEMIOLOGICAL ASPECTS

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Background and aims: Group A Streptococcus (GAS), a common cause of pharyngitis and uncomplicated skin/soft tissue infections, can also cause invasive disease, which may manifest as several clinical syndromes. The aim of this study was to describe epidemiological and clinical features of GAS invasive disease in children, in our area.

Methods: Cases of GAS invasive disease between January 2003 and December 2008 were detected by laboratory data. For each case, the hospital medical record was revised. GAS invasive disease was defined as Streptococcal Toxic Shock Syndrome (STSS), Necrotizing Fasciitis (NF) or sterile site infections that do not meet clinical criteria for STSS/NF.

Results: Twelve cases of GAS invasive disease were identified. The median age of the children was 5.5 years. Boys were affected more often than girls (8/12). The most common clinical presentations were bacteremia (4/12) and pneumonia with pleural effusion (4/12); one child was diagnosed STSS (probable). Five of the twelve patients had underlying chronic illness. Varicella virus infection preceded GAS invasive disease in two. Besides antibiotic therapy, 3/12 underwent surgery. The outcome was good in the majority (8/12) and there were no fatal cases.

Conclusions: Children with underlying medical conditions seem to be at greatest risk for GAS invasive disease, as are those with varicella virus infection. GAS infection should always be suspected when risk factors are present, and prompt institution of an adequate antibiotic should not be delayed. We ought to be aware of GAS potential to cause invasive infection, with its serious consequences.

P027

PANTON-VALENTINE LEUKOCIDIN PRODUCING STAPHYLOCOCCUS AUREUS - OUR EXPERIENCE

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Panton-Valentine leukocidin (PVL) is a necrotizing exotoxin produced by both methicilin - sensitive (MSSA) and methicilin - resistant Staphylococcus aureus (MRSA). PVL primarily causes skin infections, soft tissue infections and necrotizing pneumonia with high mortality. PVL producing strains are worldwide spread. In the Czech Republic have been monitored since the year 2004 when the first case was detected. Between the years 2004 - 2008 2981 strains of Staphylococcus aureus were examined in National referential laboratory for staphylococcal infections.190 strains were PV L+ (153 MSSA and 37 MRSA).7 strains of them were causative agents of pneumonia, four patients survived, three patients died. In our Department of Infectious Diseases University Hospital Bulovka two cases caused by PVL+ Staphylococcus aureus (both MSSA) were noted. Skin infection occurred in 27-year-old woman (recurrent furunculosis was caused by MSSA with significant production of PVL). We describe in detail the first case of fatal pneumonia with mediastinitis in 10-month-old boy who was treated consecutively in three Prague university hospitals. The disease began atypically with gastronitestinal symptoms and in causative agent (MSSA) hyperproduction of enterotoxin was prooved.

P028

PSEUDOMONAS AERUGINOSA ENDOCARDITIS IN A 3-YEAR-OLD BOY TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: *Pseudomonas aeruginosa* has been described as an uncommon cause of endocarditis in adults but to our knowledge no pediatric case has been reported in the literature for the past 20 years.

Clinical case: We describe a 3-year-old boy diagnosed with acute lymphoblastic leukemia who first developed a fully susceptible *Pseudomonas aeruginosa* bacteremia while he was in neutropenia. An initial antibiotherapy was started using piperacillin-tazobactam and amikacin. Recurrent bacteremias occurred during the following 101 days despite central venous access device replacements and multiple courses of antibiotics, including meropenem, ceftazidime, ciprofloxacin, rifampicin and colimycin. Several cardiac ultrasound were performed but evidence of endocarditis was observed only after 60 days of bacteremia when both transoesophageal and transthoracic ultrasound showed the rupture of a tricuspid cord and the presence of a millimetric image on the atrial side of the tricuspid valve. Due to failure of medical treatment, cardiac surgery was performed. Peroperative findings confirmed a purulent granuloma and perforations on the tricuspid valve.The abcess was removed and the valve repaired. The valvular biopsy yielded *Pseudomonas aeruginosa*. Antibiotics were extended for 30 days after surgery with no further positive blood cultures at 5 months of follow-up.

Conclusion: *Pseudomonas aeruginosa* is an exceptional cause of endocarditis in children. Prompt removal of central venous device should be performed in case of *Pseudomonas aeruginosa* bacteremia. Surgical intervention must be considered without delay if not responding to targeted antibiotics, particularly in leukemic patients with a greater risk of negative impact on their hematological outcome.

P029

EVALUATION OF CLINICAL, LABORATORY AND THERAPEUTIC FINDINGS OF BRUCELLOSIS AMONG CHILDREN HOSPITALIZED AT ARDABIL'S HOSPITALS

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Goal and precedents: Brucellosis is the common disease between human and animal and that is transmitted through contaminated animals. This study has been executed to determine clinical manifestation, laboratory findings and therapeutic approach of children afflicted by brucellosis, hospitalized at 2 hospitals (Aliasghar and Imam Khomaini) of Ardabil within 2000-2005.

Materials and methods: This study is a retrospective one, based on existing data of 51 medical units, belonging to patients that were hospitalized within 2000-2005 at these two centers diagnosed as brucellosis patients.

Results: From all 51 patients 76.5% were male. Familial history of brucellosis was positive among 38% of patients. Precedent of no pasteurized dairy consumption was seen among 62% of cases. 69% of patients were belonging to high risk families. Clinical manifestations of disease were fever (84.2%) arthralgia (81.2%) perspiration (60.2%)lackingappetite(54%)Hepatomegaly(31%)splenomegaly(21%)and lympadenopathy(18%).Laboratory findings were anemia(52.3%)leukopenia(41.2%)thrombocytopenia(4.5%)and leukocytosis(1.96%) . Treatment in the majority of patients (76.2%) was Cotrimoxazole beside Rifampin or Gentamycin. The brucellosis was the cause of FUO in the 17.6% of cases.

Conclusion and advises: According to findings it seems that among children with fever and Arthralgia and especially with precedent of no pasteurized dairy consumption and being male this is essential to evaluate brucellosis possibilities. On the other hand it is advised to perform programs to inform members of high risk families about this disease.

Keywords: Brucellosis, Children, Clinical and laboratory findings, Therapeutic findings.

P030

PREVALENCE OF CHLAMYDIA PNEUMONIAE, MYCOPLASMA PNEUMONIAE AND ACUTE EXACERBATIONS OF ASTHMA IN CHILDHOOD

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Background: Mycoplasma pneumonia and Chlamydia pneumoniae are frequent causative agent of acute respiratory disease and has been recently reported as a possible infectious triggers of asthma. In the present study we aimed to investigate the frequency of Mycoplasma pneumoniae and Chlamydia pneumoniae infections in asthmatic children. We investigated also whether there is a relationship between these agents and asthma attacks.

Method: Seventy asthmatic children were included in study. The study group was divided into two groups: group one consisted of 30 children with asthma attacks and group two consisted of 40children with stable asthma. As a control group we studied 30 healthy children.Serum samples were obtained and tested for C. pneumoniae and M.pneumonia specific IgM antibody by Enzyme-Linked Immuno Sorbent Assay (ELISA).

Results: There was a statistically significant difference for Mycoplasma IgM ($p < 0.05$).) and Chlamidia IgM ($p = 0.03$) between group one and the other two groups.

Conclusion: M. Pneumoniae and C. Pneumoniae may play a role in development of asthma exacerbations in childhood.

P031

C-REACTIVE PROTEIN AS A MARKER OF SERIOUS BACTERIAL INFECTION IN FEBRILE INFANTS AGED ≤3 MONTHS - A PROSPECTIVE STUDY

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Objective: To determine the utility of C-reactive protein as a marker of serious bacterial infection in hospitalized febrile infants aged ≤3 months.

Patients and methods: Data on blood C-reactive protein levels were collected prospectively for all infants aged ≤3 months who were hospitalized for fever at our center from 2005 to 2008. The patients were divided into two groups by the presence or absence of findings of serious bacterial infection.

Results: A total of 892 infants met the inclusion criteria, of whom 102 had a serious bacterial infection. Mean C-reactive protein level was significantly higher in the infants who had a bacterial infection than in those who did not (5.3±6.3 mg/dL vs. 1.3±2.2mg/dL, $p< 0.001$). Analysis of various cut-offs of C-reactive protein yielded better sensitivity, specificity, and positive and negative predictive values than for total white blood cell count in predicting serious bacterial infection.

Conclusion: C-reactive protein level is a valuable laboratory test in the assessment of febrile infants ≤ 3 months old and serves as a better diagnostic marker of serious bacterial infection than total white blood cell count.

P032

CORRELATION OF SIZE OF PURPURIC LESIONS ON ADMISSION WITH OUTCOME IN SYSTEMIC MENINGOCOCCAL DISEASE

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Background and aims: We have initiated a multi-centre prospective study in January 2000 including 97 paediatric hospitals from Germany, Southern Tyrol, Switzerland and Austria to analyse genetic polymorphisms in children with systemic meningococcal disease. In context with this study we were also testing for the correlation between extension and size of lesions on admission to the PICU and outcome.

Methods: Size of purpuric lesions on admission to the PICU was estimated and grouped into 6 classes (< 0.5 cm, 0.5-1 cm, 1-5 cm, 5-10 cm, 10-20 cm, >20 cm). 359 patients have been included into this study.

Results: The size of the largest lesion on admission correlated very strongly with outcome (overall $p = 1 \times 10^{-11}$, see Table 1). Group assessment was crosschecked on the basis of photographed patients by an independent dermatologist.

Diameter	Case fatality rate
< 0.5 cm	4/153 (2.6%)
0.5 - 1 cm	5/92 (5.4%)
1 - 5 cm	9/77 (11.7%)
5 - 10 cm	5/19 (26.3%)
10 - 20 cm	3/9 (33.3%)
> 20 cm	6/9 (66.7%)

Conclusions: The size of purpuric lesions on admission correlates strongly with mortality of patients with meningococcaemia. These findings demonstrate a high relevance of this parameter for the calculation of a prognostic risk score in the near future.

P033

THE THR164ILE POLYMORPHISM OF THE B2-ADRENERGIC RECEPTOR ASSOCIATES WITH SUSCEPTIBILITY IN CHILDREN WITH SYSTEMIC MENINGOCOCCAEMIA

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Background and aims: Meningococcal disease may present as sepsis, meningitis or a combination of both. The adrenergic system is a major factor for peripheral vascular resistance as well as cardiac output. 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 (B2AR) gene (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 this B2AR polymorphism.

Methods: Blood samples and clinical information of 287 previously healthy children with meningococcal infection were collected from 95 paediatric hospitals in Germany, Switzerland, Italy, and Austria between 2000 and 2004. Cord blood of 472 healthy newborns, all of Central European origin, served as population based healthy controls. The Ile164Thr polymorphism was analysed in all subjects using a TaqMan assay.

Results: The rare Ile164 variant was significantly more frequent in patients (2.8%) compared to healthy controls (0.6%, $p = 0.016$), resulting in a risk ratio for carriers of the Ile164 variant of 4.5 (95% CI: 1.2 - 17.0) for meningoccaemia.

Conclusion: In our study we provide first evidence that the Thr164Ile polymorphism of the human β_2 adrenergic receptor is associated with the risk for meningococcal disease. As the Ile164 allele is associated with decreased B2AR levels, further studies evaluating the impact of adrenergic receptor variants on meningococcal disease might be worth considering.

P034

EXTERNAL VALIDATION OF THE BACTERIAL MENINGITIS SCORE

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Background and aims: Sensitivity of the Bacterial Meningitis Score (BMS), based on five predictors (seizures, blood neutrophil count, cerebrospinal fluid (CSF) Gram stain, CSF protein and CSF neutrophil count) has been validated between 98.3% and 100% in four previous studies. To evaluate the BMS performance on our population of children hospitalized for meningitis.

Method: Retrospective cohort study including all children aged 29 days to 18 years who were admitted for meningitis between 1996-2006 and between 2007-2008 in two respective academic pediatrics departments. Inclusion criteria was meningitis (CSF white blood cells> 10 µL) without purpura, clinical sepsis, predisposing factor and antibiotic treatment before lumbar puncture.

Results: Among the 211 patients included, 23 (11%) had bacterial meningitis and 188 had aseptic meningitis. Out of the 121 patients categorized as very low risk of bacterial meningitis by the BMS (score = 0), 2 had bacterial meningitis (sensitivity 91%; negative predictive value 98.3%). The 2 patients with bacterial meningitis not detected by the BMS were 2.5 and 15 years old, both infected with Neisseria meningitidis; one had petechial rash.

Conclusion: Sensitivity of the BMS was lower than previously reported. Before evaluating the BMS in clinical setting (safely reduce hospital admission), further refinements of the BMS including petechial rash may be warranted to reduce the false negative cases.

P035

WELL APPEARING NEONATES WITH EARLY ONSET FEVER: WHAT RELIABILITY FOR LABORATORY MARKERS IN PREDICTING SEVERE BACTERIAL INFECTIONS?

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Background and aims: Few data exist on laboratory markers accuracy as predictors of severe bacterial infections (SBI) in febrile neonates. This study aimed to assess the diagnostic accuracy of white blood cell count(WBC), absolute neutrophil count(ANC), and C-reactive protein(CRP) in detecting SBI in well-appearing neonates with early onset fever without source (FWS) and in relation to fever duration.

Methods: Previously healthy neonates 7-28 days hospitalized with FWS from less than 12h to a Pediatric Emergency Department, were prospectively enrolled over a 4-year period. Laboratory markers were obtained upon admission and repeated after 12 to 24h from fever onset in those children with normal values on initial determination.

Results: Of the 99 patients finally studied, 25 had an SBI. ANC and CRP were significantly higher in patients with SBI compared to those without, while WBC did not differ between the two groups. Areas under ROC curves (AUC) at admission were 0.78(95%CI, 0.69-0.86) for CRP, 0.77(95%CI, 0.67-0.85) for ANC, and 0.59(95%CI, 0.49-0.69) for WBC. AUC for repeated determination obtained in 58 patients with normal values at admission resulted larger for all the parameters, with a significant improvement only for CRP, showing an AUC of 0.99(95%CI, 0.92-0.99; p=0.002). Laboratory markers values turned abnormal after >12h from fever onset for all the 5 patients with an SBI out of the 58.

Conclusions: In well appearing neonates with FWS laboratory markers studied were more predictive of SBI if fever duration was>12h. CRP seems a better predictor than both ANC and WBC especially after >12h from fever onset.

P036

CLINICAL PRESENTATION OF CHILDHOOD NEUROBORRELIOSIS: NEUROLOGICAL EXAMINATION MAY BE NORMAL

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Background: Neuroborreliosis has its highest incidence in children and elderly. Signs and symptoms are different between the different age groups. The aim of this study was to describe the clinical spectrum of neuroborreliosis in children.

Methods: The Dutch Pediatric Surveillance system registered cases of childhood neuroborreliosis during a two year time period. All Dutch pediatric hospitals took part in this surveillance. Criteria for reporting cases were strictly defined.

Results: Eighty-nine cases of neuroborreliosis were reported, in 75 cases, data were obtained and diagnosis was confirmed. The mean age at presentation was 8.5 years with highest incidence during summer months. Facial palsy was one of the presenting symptoms in 55 cases and the only symptom in 10 children. The five complaints most frequently reported were: malaise, headache, fatigue, fever, neck pain. Sixty children had one or more neurological signs at presentation, of which facial palsy, other cranial nerve abnormalities and meningeal signs were most frequent. Fifteen patients, however, had no neurological abnormalities at physical examination. These patients displayed more symptoms and had a significant delay until diagnosis was made.

Conclusions: In this study, 80% of pediatric neuroborreliosis patients presented with neurological abnormalities, most often consisting of facial nerve palsy. Twenty percent presented in an atypical way without objective neurological signs. A thorough neurological examination is essential once neuroborreliosis is considered in children. Even in the absence of neurological signs, neuroborreliosis may be suspected in children with typical antecedents and multiple subjective complaints. CSF investigations are then required to confirm the diagnosis.

P037

ETIOLOGICAL ASPECTS OF SEPSIS IN A PEDIATRIC INTENSIVE CARE UNIT

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Background and aims: We have studied Sepsis defined as the clinical characteristics that include systemic inflammatory response syndrome (SIRS) installed in bacterial infection context, intending to detect the etiological particularities in relationship with the patient's age and to study the context of Sepsis installing.

Methods: During an 8-year period of time, 82 patients (age between 4 days and 18 years old) with Sepsis were admitted in the ICU of Pediatrics III Clinic, Cluj. The bacteriological diagnosis was run in the laboratory of the Pediatrics III Clinic.

Results: Most of the cases subscribe to the 1-12 months category (35%), followed by 0-1 month category (21%). Out of 82 cases in study, 50 (61%) were with well known etiology, the rest being unknown. The identified bacterial agents were: Staphylococcus aureus (28 cases), Klebsiella (7), Escherichia coli (6), Enterobacter (4), Bacillus cereus (3), others (2).

The Sepsis etiology in the newborn and the infants is dominated by Staphylococcus aureus and Klebsiella.

From the total of 82 cases, 20 were identified with risk factors: premature rupture of membranes, chorioamnionitis, catheterization of the umbilical cord veins etc (0-1 month), prematurity, malnutrition, congenital infections (infants), immunodeficiency, invasive procedures etc (other age categories).

The portal of entry was identified in 37% of the patients. There were 2 cases of iatrogenic etiology.

Conclusions: In 61% of the cases, we were able to determine the etiology of Sepsis through bacterial determinations. The Sepsis etiology in the newborn and the infants is dominated by Staphylococcus aureus and Klebsiella.

P038

INVASIVE STREPTOCOCCAL DISEASE - A POSSIBLE EMERGENCE OF MORE AGGRESSIVE GAS STRAINS

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Background and aims: During the last two decades, the incidence of invasive streptococcal disease (ISD) has been increasing in Europe, probably associated with the emergence of more aggressive strains. During 4 consecutive years there were admitted 6 cases of ISD, with an increase during 2004 and 2007. The objective was to evaluate the characteristics of ISD and identification of risk factors in a paediatric population of a general hospital at Lisbon.

Methods: Retrospective analysis of Streptococcus pyogenes positive cultures (blood, cerebrospinal, pleural, sinovial fluid and pus), between April 2004 and December 2008. Epidemiological, clinical, laboratorial and evolution parameters were analysed.

Results: A total of six children, mean age was 5 years (min-29 months, max-14 years). Risk factors identified: viral infection (2), throat diseases (1), varicella (1). The diagnosis were bacteraemia (4), streptococcal toxic shock syndrome (1) and septic arthritis (1). 3/6 were treated with penicillin and clindamycin, 2/6 penicillin only and 1/6 additionally another antibiotics. There were complications in 5/6 patients: septic shock (1), acute respiratory distress (1), renal failure (1), subcutaneous tissue abscess (1), lymphadenitis (1), inflammatory streptococcal arthritis (1), pneumonia (1), pneumonia/empyema (1). 2/6 requires intensive care with: hemodynamic support (1), oxygen (1) and mechanic ventilation (1). Three children had to be submitted to a surgical intervention. There was no mortality.

Conclusions: Six cases of invasive group A streptococcal disease in a short period of time suggests a possible emergence of more aggressive GAS strains. Screening for different strains may be important to the identification of invasive clones.

P039

CHARACTERISTICS OF GROUP A STREPTOCOCCAL INVASIVE DISEASE IN CHILDREN

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Background and aims: The aim of this study was to review all cases of Group A Streptococcal (GAS) Invasive Disease (ID) admitted to our tertiary hospital.

Methods: Retrospective analyses of all cases of GAS ID (positive culture isolated from usually sterile sites), from January 1996 to December 2008 (13 years).

Results: There were 22 cases, with a maximum of 4 cases/year. In the second half of this period occurred 16 cases (73%). Fifteen were boys and the median age was 3,5 years. The most frequent clinical manifestations were fever (71%), rash (48%) and arthalgia/limbs' pain (43%). The diagnoses were bacteriemia (5), celulitis (3), osteoarticular infection (4), pyomyositis, surgical wound infection, streptococcal toxic shock syndrome (STSS), mastoiditis (2 each), necrotizing fasciitis and pneumonia (1 each). Four cases occurred during the course of varicella. Other risk factors were present in 5 cases. Median neutrophyl count was 9 427/µL (6 600-34 640) and median C reactive protein was 16.7mg/dL (0.3-42.5). Bacteria were isolated mainly from blood (71%). The outcome was good for most cases but there were 2 deaths due to STSS. M typing and the presence of virulence factors genes were not assessed.

Conclusion: Although the small number of cases limits the conclusions, there was an increase of invasive disease in the second half of the study. Microbiological investigation is essential to understand which M types or virulence factors genes are involved. Several cases occurred in the course of varicella or other risk factors and fatal outcome was associated with STSS.

P040

POSSIBLE MECHANISM OF IMMUNOSUPPRESSION DURING PEDIATRIC SEPSIS: ROLE OF MONOCYTES CD40L TOLERANCE

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Background: CD40-ligand (CD40L) is a membrane protein expressed primarily on activated T cells. CD40L stimulation induces monocytes to secrete immunomodulatory cytokines and to up-regulate surface molecules (CD80, CD86), which are important in promoting and maintaining adaptive immune response.

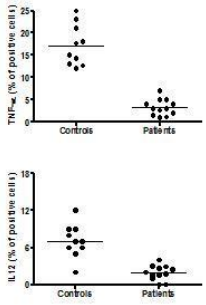
Objective: To analyse the response of monocytes to CD40L, in pediatric patients with Gram-negative sepsis.

Methods: Twelve patients were enrolled. Inclusion criteria: age >30 days, < 10 years and a diagnosis of sepsis. Exclusion criteria: congenital or acquired immunosupression. PBMC were stimulated in vitro with CD40L and analysed for TNF-a and IL-12 production, CD80 and CD86 surface expression and ability to induce interferon (IFN)-g production by autologous T lymphocytes.

Results: Cytokine production by monocytes during sepsis. (Fig. 1) TNF-a and IL-12 response of monocytes stimulated with CD40L from septic patients was significantly lower than that found in healthy controls.Effect of sepsis on the upregulation of surface molecules induced by CD40L. CD40L stimulation induced only a suboptimal CD80 and CD86 response in monocytes from septic patients (Fig 2).Sepsis interferes with the ability of CD40L to induce co-stimulatory functions in monocytes. PBMC were exposed to CD40L and then stimulated by immobilized anti-CD3 antibody. Significantly increased IFN-g expression was observed in T cells from control subjects as compared to septic patients. No selective defects of T cells were demonstrated in septic patients by anti-CD3 stimulation plus costimulation with anti-CD28 antibody.

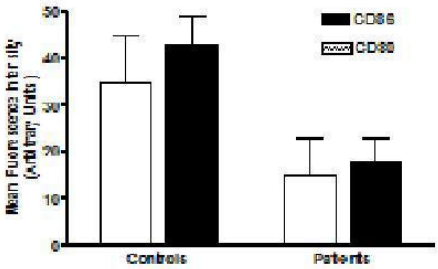
Conclusions: We conclude that in vitro CD40L tolerance may be a model of monocyte alteration observed during sepsis.

Figure 1



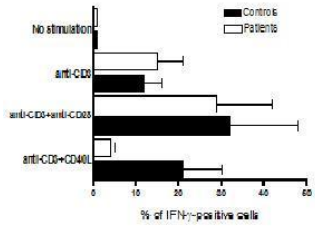
[figure 1]

Figure 2



[figure2]

Figure 3



[figure 3]

P041

CELL-MEDIATED IMMUNE RESPONSES AND PROTECTIVE EFFICACY AGAINST INFECTION WITH MYCOBACTERIUM TUBERCULOSIS BY HSP16.3 PROTEIN AND ITS SYNTHETIC PEPTIDE IN MICE

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Tuberculosis (TB) remains an urgent worldwide public health problem. Although some individuals initially control the infection by mounting a cell-mediated immunity, the majority of these individuals are latently infected. Several protein factors have been identified as contributing to latently infected. One of them is Heat shock protein 16.3 (Hsp16.3) of *Mycobacterium tuberculosis* (MTB), which plays an important role in the survival of MTB against macrophages. In this study, we compared the immune responses and protective efficacy against infection with MTB by Hsp16.3 protein and its synthetic peptide in mice. The results showed that both Hsp16.3 and its synthetic peptide induced specific antibodies in levels significantly higher than those of BCG. They also had similar stimulation indices in splenolymphocyte proliferation, which was remarkably higher than with BCG. Whether under Hsp16.3 or its synthetic peptide stimulation, the level of IFN-γ release of BCG was the highest with stimulation via the same two antigens, although BCG expressed a low Hsp16.3 level. A significant difference was observed between the IFN-γ levels of Hsp16.3 and its synthetic peptide groups stimulated by peptide, but not by those stimulated by Hsp16.3. In terms of resistance against H37Rv replication, BCG was more resistant than Hsp16.3 or the synthetic peptide in the spleens, but the difference in the lungs was not statistically significant. In conclusion, Hsp16.3 and its synthetic peptide had not only common immunological characteristics but also respective advantages, and so they should be considered new vaccines against TB, or components thereof.

P042

COMPARATIVE GENOMICS AND EXPRESSION OF PHENOL-SOLUBLE MODULIN-A OF TWO RELATED COMMUNITY-ASSOCIATED MRSA CLONES ASSOCIATION WITH NASAL COLONIZATION AND INFECTION

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Background and aim: A majority of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) strains in Taiwan were belonged to sequence type 59 (ST59) and can be divided into two pulsotypes with or without Panton-Valentine leukocidin (PVL) genes. PVL(-) clone was dominant in strains colonizing healthy children, whereas PVL(+) clone was commonly identified in clinical isolates. The factors associated with CA-MRSA nasal colonization and infections were explored by comparing strains of the two related clonal types.

Methods: Genetic compositions were compared in 7 PVL(-) and 7 PVL(+) strains of ST59 by DNA microarray with 3626 open reading frames. Expression of phenol-soluble modulin-α (PSM-α) was measured in log-phase of bacterial growth using real-time reverse transcriptase PCR in 20 PVL(-) and 25 PVL(+) strains of ST59 and 15 strains of a pandemic nosocomial clone, ST239. Values are presented as folds relative to the measurement of MRSA252 strain.

Results: Important genetic differences included the presence of an immune evasion cluster consisting of *sak* and *sep* genes in PVL(-) strains. Except for PVL, no known virulence determinant specific to PVL(+) strains was identified. Expression of PSM-α was significantly greater for ST59 than ST239 strains (560±610 vs. 5.5±8.4, $p < 0.0001$). Among ST59, PVL(+) strains produced a higher mean level of PSM-α than did PVL(-) strains (648±686 vs. 449±494), but not statistically significant ($p=0.2821$).

Conclusions: Harboring an immune evasion cluster may enhance the ability of nasal colonization of CA-MRSA ST59. PSM-α and PVL may both implicate in the CA-MRSA diseases.

P043

UNUSUAL HIGH FRECUENCY OF INTRACRANIAL COMPLICATIONS SECONDARY TO OTITIS MEDIA

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Introduction: Intracranial complications (ICC) secondary to otitis media are unusual but potentially life-threatening. We report an unusual high frequency of these events, and describe their clinical and epidemiological features.

Material and methods: A retrospective study of all pediatric patients with ICC admitted to our tertiary hospital from April 2004 through Nov 2007.

Results: Eight patients had ICC: sigmoid sinus thrombosis (4), lateral sinus thrombosis (1), meningitis (2), epidural abscess (1), otitic hydrocephalus (1). Four of the patients had acute mastoiditis. Pre-admission oral antibiotics were administered in 87.5% of the patients. Fever, otalgia, headache and VI and VII cranial nerves paralysis were the most frequent symptoms associated. The microorganism could be isolated in 3 patients: S pyogenes (2) and P mirabilis (1); the remaining patients had negative cultures. All of the patients received broad-spectrum parenteral antibiotics and 2 of them underwent a radical mastoidectomy.

Conclusions: We report a unusually high incidence of cranial complications secondary to acute otitis media. Multicentric studies are needed in order to asses a possible increase in the incidence of these events.

P044

SPREAD OF PVL POSITIVE *S. AUREUS* AMONG PATIENTS AT CHILDREN CLINICAL UNIVERSITY HOSPITAL

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Objectives: Althought S. aureus is considered to be an opportunistic pathogen certain clones are more prone to cause invasive disease due to the presence of virulence factors like Panton - Valentine leicocidin (PVL). PVL producing strains can cause severe skin infections and necrotizing pneumonia in previously healthy children and young adults.Aim of this investigation was to detect spread of invasive *S. aureus* among paediatric patients at hospital and presence of PVL.

Methods: Antibacterial susceptibility was determined according to CLSI standards (M2-A9, M100-S16). The *luk-PV* gene and the *SCCmec* type was detected by PCR. Chromatograms of the *spa* sequences were analysed by Ridom StaphType software (Ridom GmbH).

Results: Investigation of 370 invasive *S. aureus* (21 blood isolate, 349 - from pus) from patients, who were admitted to Children Clinical University Hospital in Riga from November of 2006 through November 2008, revealed that 241 (65%) isolates carried genes for PVL synthesis. 8 of them were identified as MRSA. Investigation of clonal relationship among the luk-PV positive S. aureus showed that majority of the typed strains belongs to the spa type t435. Retrospective analysis of patients medical cards from November 2006 throught March 2007 showed, that majority of patients were hospitalised in surgery department - 64%, others in therapeutical profile departments - 27%. Patients were hospitalised mainly with purulent skin and soft tissues infections like furunculosis, absceses, limfadenitis and mastitis.

Conclusions: Molecular investigation of S. aurues isolates showed that possibly there is nosocomial spread of S. aureus in hospital.

P045

THE PREVALENCE OF MIDDLE EAR PATHOGENS IN THE OUTER EAR, INNER EAR AND NASOPHARYNX OF OME PATIENTS

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Objective: The objective of this study was to investigate the prevalence of *Alloiococcus otitidis* (a putative middle ear pathogen) and the known middle ear pathogens *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pneumoniae* by means of species-specific PCR in OME-patients.

Methods: The patient group consisted of children which underwent surgical intervention at the ENT department of our hospital. During surgery middle ear fluid was collected using a Juhn tymp tap, and two swabs were taken from the nasopharyngeal cavity respectively the outer ear. In case the patient was treated for bilateral OME, samples were taken from both sides. DNA was extracted using the NucliSense EasyMag extractor.

Species-specific PCR was carried out on all samples for *A. otitidis, S. pneumoniae, M. catarrhalis* and *H. influenzae*.

Results: Percentage of positive PCR results

Species	Middle ear effusion fluid	Outer ear canal swabs	Nasopharyngeal swabs
[illegible]	40	40	25
A. otitidis	58	83	0
H. influenzae	35	18	56
M. catarrhalis	20	40	80
S. pneumoniae	13	23	48

[Table 1]

Conclusion: The prevalence of *A. otitidis* (58%) is indeed very high in middle ear fluids of OME patients, and even much higher than the prevalence of the other tested organisms. The prevalence of the known middle ear pathogens is high (48% to 80%) in the nasopharyngeal swabs, which could be expected because the throat is the reservoir for organisms infecting the middle ear by the Eustachian Tube. *A. otitidis* is however totally absent from the nasopharynx, but has a very high prevalence in the outer ear (83%).

P046

SEROPREVALENCE OF POLYSACHHARIDE SPECIFIC IGG AND BACTERICIDAL ACTIVITY TO *NEISSERIA MENINGITIDIS* SEROGROUP C: PRE- AND POST-VACCINATION PERIOD IN THE NETHERLANDS

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Background/aim: In 2002 a MenC conjugate (MenCC) vaccination was introduced into the National Immunization Program at the age of 14 months and a catch-up campaign was implemented targeting individuals between 1 and 18 years. We determined age specific seroprevalence of MenC polysaccharide (PS) IgG and MenC specific serum bactericidal antibodies (SBA) before and after introduction of MenCC vaccine.

Methods: Two population-based serum collections, established in pre- (1995/1996) and post-vaccination (2006/2007) period, were available. Using a multiplex immunoassay (MIA), MenC PS specific IgG was determined in 2303 and 6376 sera from pre-and post-vaccination period, respectively. In addition, in a subset of sera from both serum collections (735 and 1220 sera) MenC specific SBA titers were determined.

Results: Overall SBA seroprevalence was 22% [18.0-26.6.%] and 45% [41.1-49.3%] in pre- and post-vaccination period, respectively. SBA titers show a similar age-specific trend as MenC PS specific IgG (figure 1), except SBA titers are not significantly different between pre- and post-vaccination period in unvaccinated adult groups.

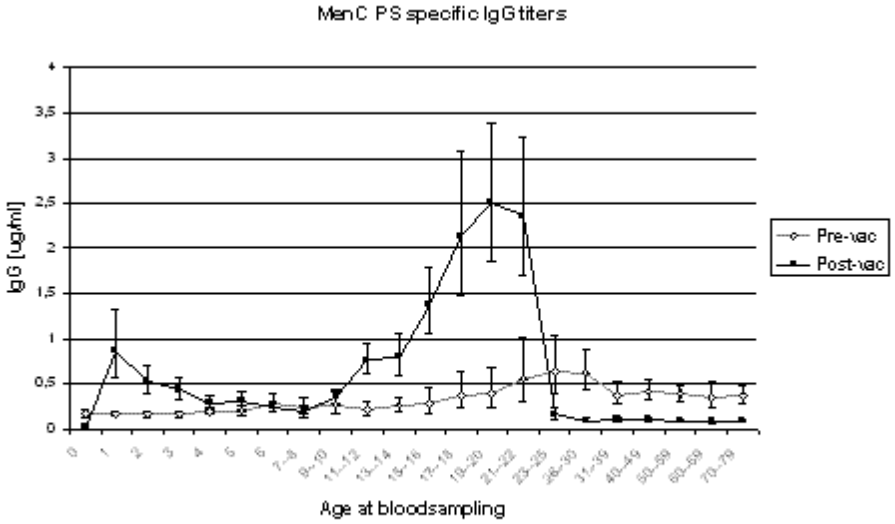

Figure 1. MenC PS specific IgG titers per age group for the pre- and post-vaccination period

[Figure 1]

Conclusions: MenCC vaccination induced higher IgG levels in vaccinated groups compared to natural exposure, but only older age groups seem to benefit from persistence of higher IgG levels. Due to mass vaccination, circulation of MenC probably decreased, resulting in lower IgG titers in unvaccinated adult groups. This may pose them at extra risk once MenC might start re-circulating.

P047

RECURRENT BACTERIAL MENINGITIS - CASE SERIES

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Background and aims: Recurrent bacterial meningitis (RBM) is an unusual entity and generally poses a considerable diagnostic challenge. Different conditions can predispose for recurrence of episodes and the isolated pathogen can guide the diagnosis. The aim of this study was to characterize all RBM admitted to a tertiary paediatric hospital.

Methods: Retrospective analyses of the medical records of all children with RBM, between January 1994 and December 2007 (14 years).

Results: During this period, 107 children with bacterial meningitis (BM) were admitted. Among those, 10 (9.3%) had more than 1 episode of BM; 6 were male. Six children had the first episode of BM in the first 6 months of age (range: 7 days-12 years). Twenty three episodes of BM were identified (7 had 2 episodes and 3 had 3 episodes). *N. meningitis* and *S. pneumoniae* were isolated in 4 episodes each and *Enterococcus faecium* in 2. Underlying conditions were identified in 9 cases: neurosurgery shunt implantation (6) and CSF leakage in 3 (skull fractures). A predisposing condition hasn't yet been identified in 1 child and no immunodeficiency was found.

Conclusions: It was identified a high proportion of BRM. An anatomical defect was the most frequent cause. In cases without an obvious predisposing condition an exhaustive evaluation, including search for anatomical and immunological defects, needs to be performed in order to prevent recurrence and improve the outcome.

P048

LEMIERRE SYNDROME CAUSED BY *ABIOTROPHIA DEFECTIVA* IN A CHILD

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Background: Lemierre syndrome (LS) is characterized by anaerobic septicaemia, internal jugular vein (IJV) thrombosis, and septic emboli following oropharyngeal infections.

Methods: We describe a previous healthy 12-year-old boy presented with a 5-day history of sore throat and fever. Physical examination revealed a temperature of 39.6°C, toxic appearing and painful swelling of the neck. Laboratory evaluation revealed leukocytosis and elevated C-reactive protein. Ultrasound of the neck demonstrated an abscess in the left side of the neck and thrombosis of the left IJV. A CT and a MRI scan of the neck confirmed the above findings. Two blood cultures specimens yielded a microaerophilic Gram-positive coccus which was phenotypically identified as *A. defectiva*. Intravenous dalacin, vancomycin and gentamycin were administered for a total of 4 wks, based on reported data on the resistance of A. defectiva to various antibiotics. Five days after initiation of therapy, he became afebrile. The course of the disease was uncomplicated. Follow up CT scan documented resolution of IJV thrombosis.

Conclusions: LS, a rare but potentially lethal complication of otolaryngological infections, is usually caused by Fusobacterium necrophorum. *A. defectiva*, originally known as a member of the nutritionally variant streptococci, is part of the normal oral and intestinal flora. It has been associated with various infections including bacteremia, endocarditis, brain abscess, septic arthritis and total knee arthroplasty infections. To our knowledge, A. defectiva has not previously been described as a cause of LS. This case expands the spectrum of disease caused by *A. defectiva* to include typical LS.

P049

WHAT WE KNOW ABOUT MALIGNANT WHOOPING COUGH?

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Background and aims: Increasing rates in incidence/mortality of whooping cough (WC) has been observed in nursing babies.

The aim was To evaluate the malignant WC risk factors, in patients admitted to pediatric intensive care unit (PICU).

Patients and methods: Retrospective-prospective observational study from patients with WC admitted to Sant Joan de Déu Hospital PICU (January 1999-December 2008).

Results: There were 252 WC cases, 38 (15%) admitted to PICU. From these, mean age was 6.23 weeks, 26 were females and nine patients had been premature. Microbiological confirmation was made in 24 patients by culture, in 8 by immunofluorescence and 5 by PCR. There was cyanotic cough in 85%, apneas 60% and acute respiratory failure (ARF) 54%. Thirteen patients need mechanical ventilation (MV).

Six patients (15.8%) died: were less than two months and had ARF and pulmonary hypertension. Five patients had pneumonia and one sepsis. All of them need HFOV and nitric oxide, and two required ECMO. There were found significant differences between fatal cases or not regarding to: oxygen treatment in intubated patients (FiO2>60% or < 60%, p=0,005), mean leucocytes number (69.957 leucocytes/mm^3 vs. 19.933, p=0.002) and platelets number (674.700 pl/mm^3 vs. 571.140, p=0.046), respectively.

Conclusions: Risk factors for WC malignant disease were: age; presence of pulmonary hypertension or ARF and pneumonia complication; leucocytosis or thrombocytosis and need of FiO2 in MV patients.

P050

INVASIVE NEONATAL GROUP B STREPTOCOCCAL INFECTIONS: STATISTIC REVIEW OF SANTO ANDRÉ HOSPITAL´S PEDIATRIC DEPARTMENT - PORTUGAL

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Background and aims: Group B Streptococcus (GBS) remains an important cause of serious neonatal infection despite great progress in perinatal GBS disease prevention. The goal of this study was to describe the population of children admitted to our department for GBS disease.

Material and methods: Retrospective review of all cases of GBS infection admitted to Pediatric Department from 2000 to 2008. Cases of GBS infection were defined as isolation of GBS from blood or cerebrospinal fluid and/or clinical evidence of disease in a colonized infant with GBS (detection of bacterial antigen in urine with latex agglutination test after first 24 hours of life).

Results: Data from 46 infants (39% girls and 61% boys) were collected and analyzed. 80% of the infants suffered from early-onset disease of whom 43% presented with septicemia, 22% with pneumonia and one with meningitis. Regardless of the site of involvement, respiratory signs were the initial clinical findings in almost 60% of neonates with early-onset disease. Main presentation of late-onset disease was also septicemia (50%) however, 38% presented with meningitis and there were no cases of pneumonia. Nearly 46% of infants had risk factors for GBS infection being intrapartum fever the most common (30%). There was no fatality but 50% of those who had meningitis suffered permanent neurologic sequelae.

Conclusions: No data of neonatal invasive GBS infections are available for Portugal. Nevertheless, our results are similar to those available in international literature. The serious sequelae encountered enhance the importance of guidelines compliance in prevention of perinatal GBS disease.

P051

CLINICAL PROFILE OF SERIOUS BACTERIAL INFECTION IN YOUNG FEBRILE INFANTS

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Background and aims: Identifying febrile infants at risk of serious bacterial infection (SBI) continues to challenge clinicians. The aim of our study was to evaluate the clinical features associated with SBI in febrile young infants.

Methods: We retrospectively evaluated all infants aged 31-180 days, admitted for fever >38ºC without a focus between 2000 and 2007. As SBI were considered all cases of occult bacteremia, urinary tract infection (UTI), bacterial meningitis, pneumonia and bacterial gastrenteritis.

Results: Of the 786 infants studied, 256(32.5%) had SBI: 217(27.6%) UTI, 19(2.4%) bacteremia, 14(1.8%) pneumonia, 4(0.5%) bacterial meningitis and 2(0.25%) bacterial gastrenteritis. The most common historical and physical findings on presentation were: decreased feeding 41.5%, ill contact 31.2%, nasal congestion 26.6%, cough 16.9%, grunting 15.6%, irritability 14.1%, diarrhea 12.5%, tachypnea 12%, lethargy/hypotonia 5%, mottled skin 3.9%, vomiting 3.4% and rash 2%. Completely asymptomatic were 99 infants with SBI (42.4% of SBIs) from which 88(96.6%) had UTI. Fever>39ºC, tachypnea, and absence of upper respiratory symptoms (nasal congestion and/or cough), were identified by logistic regression as possible clinical predictors of SBI. The absence of upper respiratory symptoms was associated with UTI, whereas fever >39ºC, decreased feeding, and grunting were associated with bacteremia. However, all these logistic regression models had poor goodness-of-fit coefficients.

Conclusions: The clinical profile of SBI in febrile infants was non-specific and an important number of these (especially with UTI) had a falsely reassuring well appearance. Physicians should not be based on historical and physical findings for assessing the risk of SBI in febrile young infants.

P052

AFTER ALL, IT WAS A MYCOBACTERIOSIS!

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Background: Mycobacterial infection, despite rare in developed countries, is still common in low socioeconomic level populations. The forms of presentation can be protean and constitute a real diagnostic challenge.

Aim: To analyse the cases of mycobacterial infection whose diagnosis was not straight forward.

Methods: Descriptive study, from January to December 2008, of mycobacterial infections admitted in our hospital. Demographic data, origin, vaccinal status, contacts with tuberculosis, cause of admission and final diagnosis, mean length of stay and evolution were analysed.

Results: Seven children were identified, 2-14 years old with African origin (6/7) predominance. In all cases the final diagnosis was different from the original. The initial unfavourable clinical course prompted a detailed investigation to get the final diagnosis. The initial diagnosis were: chronic osteomyelitis (3), lymphoprolipherative disease (1), parotid neoplasm (1), encephalitis (1) and chronic facial ulcer (1). The final diagnosis were osseous tuberculosis (3), ganglionar tuberculosis (2), meningeal tuberculosis (1) and cutaneous tuberculosis (1) by *Mycobacterium tuberculosis* (5) and *Mycobacterium africanum* (2). The vaccinal status was unknown in three patients and four children had BCG vaccine. Four patients had history of contact with tuberculosis. Six had tuberculinic test over 15mm. The mean length of stay was 38 days. Six patients had a favourable evolution and one died (tuberculous meningitis).

Conclusions: In all these patients, the initial diagnosis was unclear and the etiological investigation revealed a mycobacterial infection. This entity should always be sought in patients with risk factors or with positive tuberculin test.

P053

PSEUDOMONAS AERUGINOSA AMONG BULGARIAN CYSTIC FIBROSIS PATIENTS TREATED WITH TOBI 300®

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Background and aim: There is increasing consensus in using antibiotics threw inhalation against Pseudomonas Aeruginosa (PA) lung colonization in cystic fibrosis (CF) patients. To assess the influences of TOBI 300 on PA in sputum, the drug tolerance and changes in lung functional parameters, body mass index (BMI) and quality of life while using TOBI 300 in Bulgarian cystic Fibrosis (CF) patients.

Methods: 18 CF children aged 6-18y and 25 CF adults aged 19y-28y have received TOBI 300 through inhalation, twice daily for 4 weeks, followed by interrupting the treatment during the next 4 weeks. All CF patients have received their common CF treatment and PA in their sputum had been established more than 3 times for the last two years. Clinical status, lung functional tests (LFT), PA in sputum, BMI and quality assessment of CF life have been followed.

Results: During the observation period (>4 months) PA in sputum has disappeared in 10 adult CF (40.0%) and in 12 CF children (66.7%). LFT's have shown improvement in a half of the CF children (n=9) and in 28% of the adults (n=7). Appetite in most patients has improved, nevertheless significant changes in BMI have not been found. Better quality of CF life (answering positive on 7 or more questions from the questionnaire) has been found in more than 80% of the CF patients. Drug adverse effects have not been noticed in any of CF patients.

Conclusions: Treatment with TOBI 300 has been well tolerated and shown adequate therapeutic results.

P054

VARICELLA AND STREPTOCOCCUS - A TOXIC COMBINATION. SYNDROME OF CELLULITIS TO NECROTISING FASCIIITIS

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We describe 6 cases seen over a period of one month - all developing culture-positive Group A Streptococcus subsequent to varicella infection. All of the cases of varicella infection were mild to moderate.

2 cases developed necrotising fasciitis (one of whom subsequently developed leukaemia). 4 cases developed varying degrees of cellulitis - one affecting the under-chin area sufficiently that a period of intensive are was required.

All were treated with antibiotics including clindamycin when culture results were known. All of the cases showed variable levels of infection markers including C-reactive protein / erythrocyte sedimentation ratio.Both cases of necrotising fasciiitis required extensive surgery though both survived. Of the cellulitis cases all made a full recovery.

The combination of these pathogens is well-recognised and has been used as an argument for varicella vaccination in a climate of viewing varicella as a benign childhood infection.

Clinicians should be alerted to the possibility of these skin complications as they occur in previously healthy subjects. Also that varicella is the most common precipitant of necrotising fasciitis in adults - Streptococcus accounting for 50% of cases. They should also be alerted to the need for rapid and radical surgery to reduce spread in necrotising fasciitis.

P055

INTESTINAL YERSINIOSIS IN CHILDREN

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Background and aims: Nowadays the problem of yersiniosis infection remains vital. Disease indicators intestinal yersiniosis, caused Y.enterocolitica among children till 14 years in our country last years remain stable and make from 4.6 in 2006 to 9,78 in 2008 (on 100 thousand). The purpose of our research was the analysis of clinico-laboratory features of yersiniosis with determination of tactics for therapies.

Methods: There were 89 patients age 1 - 17 yo under supervision. The diagnosis was based on the epidemiological anamnesis, the general clinical examination, bacteriological and serological studies.

Results: The symptomatic form of disease began from fever (100 %), vomiting (35.5%) and diarrhea (68%). Clinical manifestation include colicky abdominal pain (39 %), headache (47 %), anorexia (28 %), exanthema (12%) and pain at joints (12 %). Phenomena of enteritis and gastroenteritis are prevailed. 2 children have pseudoappendisitis syndrome and need consultation of surgeon. One boy with asymptomatic form of disease had such complication as arthritis. The following changes in the general analysis were determined: leucocytosis (83.8), increase of SSR (71%) and CRP (95%), neutrophilia (68%). High level of sensitivity to anitbiotics Y.enterocolitica had to carbopenem group (100 %), cephalosporins of 3 generations (≥ 90 %), aminoglycosids 2 and 3 generation (≥90 %), fluorochinolons (≥96 %) and just 53 % for nalidixic acid.

Conclusions: Thus, polymorphism of clinical manifestations is characteristic for intestinal yersiniosis, and high sensitivity of microbes is kept to cephalosporins of 3 generations, aminoglycosids 2 and 3 generation, fluorochinolons and carbopenems.

P056

ICD-10 SURVEILLANCE OF INVASIVE PNEUMOCOCCAL DISEASE (IPD) IN HOSPITALIZED CHILDREN IN BAVARIA 2005/2006

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Objective: To estimate the burden of IPD complications in Bavarian children ≤16 years before the introduction of general pneumococcal conjugate vaccination.

Methods: ICD-10 data specific to IPD (G00.1 meningitis, A40.3 sepsis) were reported from 28 out of 41 (68.3%) Bavarian paediatric hospitals from 01/01/2005 to 31/12/2006. Reports were matched to data of pneumococcal isolates sent to the National Reference Center for Streptococci (NRZ) for serotype distribution and capture-recapture analysis.

Results: In 2005/2006, 98 children with IPD were reported by ICD-10 from 28 hospitals (mean 3.5/hospital; range 0 to12). There were 41 IPD cases with meningitis (41.8%) and 57 with sepsis (58.2%). During the same period, 87 S. pneumoniae isolates from 85 children with IPD (meningitis: 25/29.4%; sepsis: 60/70.6%) were reported to NRZ from 25 hospitals. Thirty datasets could be matched and serotype information was available. The most frequent serotypes were 14 (n=5; 16.7%), 1 (n=3; 10.0%) and 19F (n=3; 10.0%). Fifteen serotypes (50.0%) are covered by 7-valent, 19 (63.3%) by 10- valent and 23 (76.7%) by 13-valent pneumococcal conjugate vaccination. By using the capture-recapture method, we calculate a number of 278 IPD corresponding to a yearly incidence of 3.2/100,000 for 2005/2006.

Conclusion: ICD-10 is a reliable surveillance instrument of hospitalized IPD, which can be used to monitor the effects of general pneumococcal conjugate vaccination. These results, however, show that ICD-10 can be combined to a second case source to account for potential underreporting.

P057

NOVEL HYPOTHESIS FOR UNEXPLAINED SUDDEN UNEXPECTED DEATH IN INFANCY (SUDI)

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Background and aims: In 2008, two key retrospective studies independently reported typically pathogenic bacteria in normally sterile sites of infants succumbing to sudden unexpected death, questioning whether a proportion of unexplained SUDI were simply undetected cases of bacteraemia. In these instances, evidence of bacteraemia was presumably overlooked in the investigation of death. On the other hand these findings pointed to an asymptomatic “bacteraemia” limited to a restricted period of development. We aimed to collate the data to formulate this hypothesis.

Methods: Using pathologic and epidemiological clues, an hypothesis is introduced that is based upon three contributing factors: Transient bacteraemia, pathogen pattern recognition insufficiency, and a prenatal infectious event.

Results: Sterile site infection with *Staphylococcus aureus* or coliforms was found in about 1/4 SIDS cases. Polymorphisms in key innate immune response genes were demonstrated. Organ growth anomalies (thymomegaly and megencephaly and cardiac growth retardation associated with SIDS (not sudden unnatural comparison deaths) were shown to have prenatal origins.

Conclusions: Sterile site infection could represent a "footprint" of a transient bacteraemic event. Prenatal infection is likely to explain organ growth anomalies in SIDS/SUDI. These, together with innate immune system gene polymorphisms could provide a coherent explanation for SIDS/SUDI.

P058

STAPHYLOCOCCUS LUGDUNENSIS INFECTIVE ENDOCARDITIS: REVIEW OF THELITERATURE, CLINICAL PROFILES AND OUTCOME

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Background and aims: Infective endocarditis Staphylococcus lugdunensis is rare. We conducted a retrospective cohort study to identify the prognostic factors of this disease.

Methods: We retrospectively reviewed articles reported from 1988-2008.

Results: The mean age of all cases was 53.88 years. Left-sided valves endocarditis represents 82.5% (52/67) and native valves endocarditis was 78.7% (48/67). Although most strains (80.4%) of staphylococcus lugdunensis were penicillin susceptible but 66.7% (42/67) patients received valve replacement operations. 41.3% (26/67) of cases fully recovered.

Conclusions: The virulence of S. lugdunensis differs from other coagulase negative staphylococci with its rapid and destructive course and caused a higher mortality. Detailed microbiology identification, echocardiography evaluation and early surgery may improve outcome.

P059

FRONTAL MASS: A CHALLENGING DIAGNOSIS WITH AN UNEXPECTED CAUSE

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Background and aims: *Capnocytophaga* spp. are gram-negative bacteria, normal constituents of the oral flora in humans and in some animals, which can be responsible for systemic infections, most frequently in immunocompromised patients.

Methods: The authors describe a case of an unusual *Capnocytophaga* infection in an immunocompetent child.

Results: A previously healthy 12-year-old boy was admitted to the Emergency Service with a 5-day history of frontal headache and fever. Amoxicillin-clavulanate was prescribed for a suspected sinusitis and moxifloxacin was added later because of persistent headache. He presented 1 month later with fever, left retro-ocular pain and a frontal mass. The CT scan showed a frontal abscess (44,7x41mm) with extra-axial endocranial and extracranial component, with underlying destruction of bone tissue. Surgical drainage was performed and *Capnocytophaga* spp. was isolated in the purulent content. He was treated with amoxicillin-clavulanate with a good outcome. The detailed clinical history revealed a dog bite some days before the first clinical symptoms and a visible scar was still present in his dorsal region. It was not possible to confirm that this species was from the canine species. Dental examination was normal. An immunodeficiency was excluded. One year later he is still clinically well.

Conclusions: This is an unusual infection, with a rare clinical manifestation, that could be related to the dog bite. *Capnocytophaga canimorsus* is one of the most common agents of infection after dog bite. The microbiological identification of these bacteria facilitates appropriate antimicrobial therapy but it is somewhat difficult and a clinical guidance is important.

P060

ATYPICAL PRESENTATION OF TUBERCULOSIS IN A 15-YEAR-OLD GIRL: A CASE REPORT

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Introduction: Active tuberculosis primarily involves the lungs. Peritoneal tuberculosis is a rare presentation of tuberculosis particularly in children. Because of the diversity of the demonstrations, the diagnosis is often delayed and the complications and mortality increase.

Case report: We report the case of a 15-year-old girl with past medical history of asthma, who presented to the Emergency Department with low fever, respiratory distress and increased abdominal diameter. Examination revealed an hypoventilation of the left lung and an abdominal distension with an ascitic wave. The chest radiograph and the CT scan of the thorax showed a pleural effusion and an ascite partitioned. We first suspected a tumoral process. This diagnosis was not confirmed by laboratory exams. The partitioned ascite directed us towards a tuberculosis. The tuberculosis skin test and the first polymerase chain reaction (PCR) for the Mycobacterium of Tuberculosis were negative. The interferon gamma release assays and the next PCRs in the pleural and abdominal fluid confirmed the diagnosis of Tuberculosis. Anti-tubercular therapy was initiated.

Conclusion: This case underlines the diversity of presentation of tuberculosis. The partitioned ascite is an essential element of orientation. Also a negative tuberculosis skin test does not exclude the diagnosis. The interferon gamma release assays can be a good alternative to the tuberculosis skin test when this one is negative and there is however a strong clinical suspicion. In case of doubt, not hesitate to repeat the laboratory exams like the PCR.

P061

BACTERIAL AND VIRAL INFECTIONS INDUCE ALTERATIONS IN ZINC PLASMA CONCENTRATIONS

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We studied the correlation of zinc with procalcitonin (a highly specific marker for the diagnosis of bacterial infections) plasma concentrations and also evaluated the alterations of Zn concentrations in children with infections. 151 children were included in the study: 73 children with bacterial infections (Group A) and 78 children with viral infections (Group B). Serial blood samples were taken from almost 1/3 of patients of each group. Blood samples were collected the morning of day 1(on admission), day 4 (after admission), and after recovery . PCT concentration was determined by chemiluninescence, while Zn concentration was measured with AAS.The main results of the study showed that: a) patients with viral and bacterial infections had significantly lower Zn concentrations on admission ($p< 0.03$ and $p< 0.0003$, respectively) b) patients with bacterial infections had significantly lower Zn concentrations than those with viral infections ($p< 0.03$), while no such correlation was calculated in the day 4 (after admission) and after recovery ($p>0.73$ and $p>0.15$, respectively) c) PCT and Zn levels correlated significantly in patients with bacterial infections ($p< 0.00001$, $r=-0.518$) and d) no such correlation observed in children with viral infections.The lower zinc levels observed in patients with bacterial infections may be due to the action of IL-1, which released by granulocytes and mediates a redistribution of body zinc during the acute phase response. The latter results in increased hepatic zinc sequestration and urinary excretion of zinc. Zinc may also be utilized from the immune system in order to develop an optimal host defense.

P062

MICROORGANISMS ISOLATED FROM BLOOD CULTURES OF CHILDREN AND THEIR ANTIMICROBIAL SUSCEPTIBILITIES AT A KOREAN HOSPITAL (2007-2008)

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Background and aim: Analysis of blood culture results and antibiotic susceptibilities provides valuable information for the empirical treatment. The aim of the study was to identify the frequent causative microorganisms in bacteremia of children and their antibiotic susceptibilities at a Korean Hospital.

Methods: The blood culture results of 9,789 children less than 10 years old were analyzed. Bactec 9240 blood culture systems and Bactec Peds Plus F bottles were used. Identification of organism and antimicrobial susceptibilities were determined by Microscan LabPro system.

Results: Among the 9,789 blood cultures, 594 (6.1%) were positive. Among the isolates, 98.0% were aerobic and facultative anaerobes and 2.0% were fungi. Coagulase-negative staphylococci (CNS) were frequently isolated (68.2%, 405/594)). Excluding CNS, *Staphylococcus aureus* was isolated most frequently, followed by viridans streptococci, *Enterococcus* spp., *Escherichia coli*. 52.8% of *S. aures* isolates were methicillin-resistant *S. aures* (MRSA). All isolates of *Enterococcus faecalis* and *Enterococcus faecium* were vancomycin-susceptible. 33.3% of *E. coli* isolates were cefotaxime-resistant.

Conclusion: *S. aureus* is the most common etiologic agents of bacteremia in children. MRSA is frequently isolated. Gram negative bacteremia is relatively uncommon in children.

P063

EDUCATION AS KEY FACTOR IN INVASIVE BACTERIAL INFECTION OUTCOME - OUR EXPERIENCE WITH "RED FLAG" SYSTEM IN LOWER SILESIA, POLAND

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Background and aims: Invasive bacterial disease (IBD) is a life-threating condition. Recognizing early symptoms could shorten the time to hospital admission which is critical for outcome. We focused on educational activities in hope to rise awareness and attain better outcomes.

Methods: "Red flags" are concept which is used to identify potentially serious pathology by recognizing key symptoms originally used in low back pain. We adapted this system to IBD focusing on hemorrhagic rash, lethargy, drowsiness, nausea, vomiting, cold hands and feet and prolonged capillary refill.

Results: About 100 doctors were trained during lectures, 3000 posters were distributed and a campaign in media (TV, Internet) had been carried on for 2 months. In the following 2007 year we hospitalized 60 children referred as IBD confirming the diagnosis in 28 (11 purulent meningitis, 7 sepsis and 10 mixed infection). 23/28 children were pretreated with antibiotics, 4/28 were referred to ICU and there was no fatal outcome. It is worth noting that two parents in their two children and one of the patients, a boy aged 12 y diagnosed sepsis himself. The etiology was identified in 14/28 cases (N.menigitidis: 9/14, S.pneumoniae: 2/14, H.influenzae 2/14, S.aureus 1). The main red flag symptom was hemorrhagic rash observed in 14/28 children (8/9 N.meningitidis, 1/2 S.pneumoniae, 1/1 S.aureus and 4/14 unknown etiology).

Conclusions: Education of parents & doctors seems to be the best way of reducing mortality in children with IBD. Haemorrhagic rash with fever is the main symptom raising suspicion of IBD.

P064

ETIOLOGY OF BACTERIAL INFECTIOUS DISEASES IN PRE-TERM NEWBORN INFANTS

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Introduction: Maternal, environmental, and host factors determine which infant exposed to a potentially pathogenic organism will develop serious or other potentially invasive infections, causing significant mortality and long-term morbidity in neonates, especially for premature infants , higher in infants with very low birth weight.

Aim/material: The purpose in this retrospective study was to identifications the bacterial microorganisms caused neonatal infectious diseases in pre-term newborns hospitalized in the Center of Neonatology ,during the period of 2002 ,2003 and 2004.We used clinical, microbiological, laboratory and radiology methods.

Results: 682 pre-term newborns (PTNB) were treated at the Center of Neonatology in Podgorica during the period 2002-2004. In 98 PTNB were proven infections (14,3%). Most frequent infectious diseases were: omphalitis (36,7%), sepsis (30,6%),pneumonia (15,3%), cutaneus infections (12,2%) , diarrhea (2,0%), conjunctivitis (2,0%) and urinary tract infection (1,0%).

Dominant pathogens in all infections diseases 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 marscensens*(13,3%), then *Streptococcus alfa haemolyticus group A*, *Acinetobacter* spp. and *Pseudomonas spp.* (3,3%).

Conclusions: There are significant regional differences in pathogens of neonatal infections.It is important to identifications the bacterial microorganismsims in our region, analysis of longitudinal trends assist in the formulations of strategies to treat and prevent neonatal serious infections.

P065

GROUP A STREPTOCOCCAL MENINGITIS IN 5-YEAR-OLD BOY: A CASE REPORT

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Streptococcus pyogenes (SP) is an agent rarely associated to meningitis and corresponds to 0.2-1% of the cases, usually as a contiguous infection site, such as otitis, sinusitis and mastoiditis.

A previously healthy 5-year-old child presented to our service with fever, vomiting, ear ache and headache starter four day before. During initial examination, the patient appeared to be in a toxic condition and his neck was stiff. The patient was submitted to a lumbar puncture and the cerebrospinal fluid (CSF) was indicative of bacterial meningitis and therapy with ceftriaxone and dexamethasone was immediately instituted. Laboratory investigation revealed a white blood cell count of 23,200 leukocytes/µL with 22.100 neutrophils, ESR 109 mM, CSF with 2,400 cells/mm3 (60% neutrophils), protein of 56,6 mg/dL, glucose of 25 mg/dL, positive Gram stain and negative latex test. Blood culture was negative and CSF culture identified SP and the strain was sensitive to penicillin.

The clinical presentation of SP meningitis is not different from the other bacterial meningitis. SP has to be considered as a cause of bacterial meningitis in childhood: approximately 50% of cases reported during the neonatal period. In older children meningitis due to SP seems to be associated sometimes with a focus of infection in the middle ear. The antibiotic of choice for the treatment of SPM is penicillin and there have been no reports of resistance of this agent to this drug.

Our purpose is to emphasize that this agent is also a cause of meningitis in healthy children.

P066

UNUSUAL CLINICAL PRESENTATION OF A PATIENT WITH BARTONELLA HENSELAE INFECTION

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Background and aims: Cat scratch disease is a loco-regional infectious disease, produced by Bartonella spp(henselae, claridgeaiae, quintana), usually with a benign evolution and complete recovery.

Methods: The authors present a clinical case of acute encephalitis, produced by Bartonella henselae, in an immunocompetent patient, with complete recovery and no neurological sequelae after etiologic and supportive treatment.

The diagnostic was established: clinical symptoms (fever, headache, seizures, vomiting and lethargy), laboratory findings and epidemiological diagnostic (a bite on right hand). Also, the diagnostic was completed with serologic test in cat that was positive.

Results: The patient was a girl, 8 ages old, was admission in our intensive care unit for: fever, headache, seizures, vomiting, lethargy and coma. Also, on the right hand, the child has a wound produced by cat. Serological diagnostic on the cat was positive for Bartonella Henselae. CRF was normal on lumbar puncture. IRM cerebral was normal. EEG show focal abnormalities, such as spike and slow sharp-wave patterns. The treatment was and etiologic (ciprofloxacin), pathogenic (dexamethazone) and symptomatic. The evolution was favorable with complete recuperation.

Conclusions: The presentation wanted to point out the possibility of this particular rare etiology in a clinical setting of acute encephalitis, especially in a patient with a positive history of animal exposure (the most probable etiology including rabies, cat scratch disease, choriolymphocytic meningitis).

P067

A FATAL CASE OF INFECTIVE ENDOCARDITIS CAUSED BY COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS ST 72 IN KOREA

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Background: Community-associated methicillin-resistant Staphylococcus aureus.

(CA-MRSA) has now emerged on five continents over the last decade. CA-MRSA is usually associated with young healthy individuals in the community, who have no risk factors for acquisition of HA-MRSA. CA-MRSA is primarily associated with skin and soft tissue infections however, there have been severe cases of CA-MRSA infection associated with septic shock, bacteraemia and necrotizing pneumonia.

More recently, infective endocarditis (IE) due to the involvement of CA-MRSA has been described.

Case: We report a fatal case of infective endocarditis caused by a non-US 300, Panton-Valentine leukocidin toxin- negative CA-MRSA clone without risk factors associated with HA-MRSA. This is a serious case of CA-MRSA infectin caused by a sequence type 72 clone, which is one of the common CA-MRSA clones in Korea where serious infections have been rare.

The patient was died by worsening cerebral hemorrhage with thrombocytopenia due to infective endocarditis.

P068

COMMUNITY-ACQUIRED METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (CA-MRSA) IN THE LAST DECADE IN A PAEDIATRIC HOSPITAL

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Background and aims: CAMRSA infections are a common and serious problem in some countries. Local and national surveillance is needed.

Methods: Retrospective review of all cases admitted to our Emergency Service (ES), between 1998 and 2008 (11 years), with a clinically relevant infection and *S. aureus* positive culture, obtained within 48 hours of admission. Isolates from sputum were excluded.

Results: CA *S. aureus* infection was diagnosed in 343 cases. MRSA was found in 17 cases (5%) with no increase over the years; 53% were male, the median age was 1,5 years and 58,8% were hospitalized. Diagnoses were: skin/soft tissue infection (11), urinary tract infection (3), sepsis (2) and osteomyelitis (1). Five children had traditional risk factors: indwelling catheter (3), recent hospitalisations/surgery (2), previous antibiotic use (2) and immunodeficiency (1). All received medical treatment (b-lactam in 7) and surgical drainage was performed in 6. The outcome was good in all. Resistances were: 56% to macrolides, 50% to aminoglycosides, 12,5% to cotrimoxazole and 5,5% to clindamycin. All were susceptible to vancomycin. Isolates were not typed.

Conclusion: The increased incidence of CA-MRSA referred in many countries was not found in our institution over the last 11 years. Some MRSA may still be healthcare associated making the number of community associated MRSA lower. Skin/soft tissue infections were the most frequently found and some children who received inactive antimicrobial therapy had outcomes similar to those who were treated with antimicriobial agents to which the organism was susceptible.

P069

MENINGOCOCCAL PURPURA FULMINANS: HYPOCALCEMIA A RISK PROGNOSTIC FACTOR

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Despite progress in patient management, purpura fulminans remains a severe disease, and risk prognostic factors have been described by many authors. Our group has extensively researched hypocalcemia because cardiovascular consequences demonstrated in animal modes, point to immunoreactive hypocalcitoninema (E. Mallet, Lancet 1983) which was later found to be procalcitonin.

Aim: We attempted to access hypocalcemia as a prognostic factor and were prompted to conduct a retrospective local series (25 year period) on purpura fulminans, prior to current hyperendemia.

Main results: 75 cases were collected (44 boys and 31 girls) aged from 1 month to 15 years. Most cases occurred between 6 months and 4 years (53 children ie 70 % less than 4 years) with a peak between 1 and 2 years (18 children ie 25 %), bacteria was identified 50 times out of 75, with 39 meningococcus B, 10 C, 6 unidentified. 18 deaths occurred and 11 severe sequelae (2 cutaneous, 2 neurological, 1 renal; 1 combination neurological and renal). Hypocalcemia occurred in 53 % of cases (< 2.2 mM/l) with rates falling to 1.56 mM/l. Multivariate analysis using logistic regression showed 4 variables very significantly involved in our series regarding lethal issue: well known as the presence on DIVC p 4.10^{-2}, rapid evolution of purpura and kaliemia p 3.10^{-3}, and the new factor hypocalcemia (calcemia or adjusted calcemia) p 3.10^{-2}.

Conclusions: This hypocalcemia, previously reported by one author (Baines) may be added to the prognostic risk factors for purpura fulminans. Nevertheless etiology and consequences warrant further research.

P070

STAPHYLOCOCCAL SCALDED-SKIN SYNDROME IN A 2-YEAR OLD CHILD

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Background and aims: Staphylococcal scalded-skin syndrome (SSSS) is a toxin-mediated condition occurring in neonates and young children, which is characterized by blistering and superficial desquamation of the skin. SSSS is caused by two staphylococcal exfoliative toxins (ETA and ETB) produced by *Staphylococcus aureus*, which split the granular cell layer of the skin. It is usually diagnosed by its characteristic exfoliating rash, however diagnostic dilemmas can cause delay in the treatment of children with SSSS. Early diagnosis and treatment with parenterally administered beta-lactamase resistant penicillins are important to prevent life threatening complications of SSSS.

Methods: In this report we present a case of suspected child abuse, later diagnosed as SSSS.

Results: A 2-year old girl was referred to hospital with perioral erythematous rash. She had coryzal symptoms with rhinitis and malaise. On examination three small round ulcerations on her sternum resembling cigarette burns were noted and hospitalization was decided. On the 2nd day of her admission, perioral exfoliation and new bullous lesions on her trunk, nose and right arm were observed. The bullae were tender with positive Nikolsky sign and they could rupture easily revealing a moist erythematous base. No mouth or anal mucosa was involved. Infection control measures were implemented instantly including isolation of the infected child. The desquamation ceased 3 days after the initiation of antibiotic therapy and the skin lesions resolved within 10 days.

Conclusions: This case reflects the importance of clinical observation during hospitalization in the early diagnosis of SSSS, so appropriate treatment can be initiated.

P071

BACTEREMIC VS NON-BACTEREMIC PNEUMONIA IN CHILDREN

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Background and aims: In order to enhance current knowledge of community-acquired bacteremic pneumonia in children, its characteristics were elucidated and compared to non-bacteremic pneumonia.

Materials and methods: A 7-year (2000-2006) retrospective evaluation of the clinical and laboratory features of all children hospitalized with bacteremic pneumonia in a tertiary pediatric center. These were matched to 27 children hospitalized for pneumonia without bacteremia.

Results: Of 6653 children hospitalized with pneumonia, 57 (0.8%) had proven bacteremia. The causative bacteria were: *S. pnuemoniae* - 44 (77%), non-typable *H. influenzae* - 6 (10.5%), *S. aureus* - 3 (5.3%), *Streptococcus* group A - 2 (3.5%), *Psuedomonas* Spp and *Klebsiella pneumoniae* - 1 (1.8%) each. In the 5 cases of aspiration pneumonia, the causes of bacteremia were *S. pneumoniae* (2), *H. influenzae* (2) and *S. aureus* (1). The median age was 2 years with a male predominance. There was no mortality. As compared to children with non-bacteremic pneumonia, bacteremic children required hospitalization in pediatric intensive unit more often, had a longer hospitalization, higher white blood cell count and higher C-reactive protein, and higher rates of hyponatremia and hypoalbuminemia.

Conclusions: Children with bacteremic pneumonia present a more severe clinical course, and higher rates of laboratory abnormalities as compared to children with non-bacteremic pneumonia.

P072

THE RISK OF SERIOUS NOSOCOMIAL INFECTION BY STAPHYLOCOCCUS

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Objectives: A study was done at Damanhour Teaching Hospital (1300 Bed) to evaluate handwash practice among medical staff using staph. Aureus presence or absence as a serious measure for infection control.

Patients and methods: 56 of hospital physicians and nurses from Haemodialysis unit and from Heamatemesis unit were subjecteal to a questionaire about hand washing and Infection control also tests for the presence of staph. aureus in their hand flora swabs culture directly after handwashing before and after patients contact.

Conclusion & recommendation: The study showed knowledge about the mode of viral B & C hepatitis transmission between physicians 70% while nurses 21%. The percentage of vaccinated staff against HBV infection was very bad 36% of physicians & 47% nurses. Usage of gloves & masks and goggles during contract with patients was very low, this was explained by pressure of work Bad system of medical waste disposal (needles. Syrings & Scaples …) was discovered in the questionaire.

There was a very high rate of positive staphylococcus Aureus hands swabs cultures from hands of physicians & nurses (50% in Heamodialysis unit & 75% in Haematemesis unit. Which have alarm about the high risk of severe nosocomial infections development in the future.

Educational programs along with training courses on infection control and proper handwashing already have been started in the hospital by the author.

P073

THE OUTCOME OF BACTERIAL MENINGITIS IN CHILDREN

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Background: Bacterial meningitis (BM) is an emergent disease which even if early treated has a high mortality rate and neurologic complications(NC).

Patients and method: Over a period of six years we have analyzed the outcome of BM in 277 children treated in Hospital of Infectious Diseases in Prishtina.

Results: From 277 children with BM, NC occurred in 21,7% of cases while from 63 adults NC occured in17,5% of cases (p>0,005). The overall mortality rate was much higher in adults (M=19%) comparing with children (M=5,4%)(p>0,001). The outcome of BM was the worsest for the youngest group-ages (the highiest mortality rate in neonates and the highiest rate of NC in children in first year of life)(p< 0.001). We didn't find significant difference in frequency of NC and mortality rate occording to gender and between children who came from rural places (NC=22,4%, M=5,6%) and children from urban places (NC=20,7%, M=5,2%) (p>0,005). The outcome of BM in children was unfavorable for cases admitted after 3 days of illness (p< 0,001), for cases previously hospitalized (NC=25,3%, M=11,5%) and treated with antibiotics (NC=26%,M=10%), in cases with primary focus (NC=24,7%, M=5,7%), in cases caused by pathogen agents resistant to antibiotics(NC=50%, M=16,7%), in unconfirmed cases(M=7,8%) and in hospital acquired infection(M=15%). Factors that mostly influenced the worst outcome of BM in children were: presentation of severe clinical forms on admission (NC=26,9%, M=16,1%), alteration of mental state (NC=31,2,M=10,6%), presentation of neurologic deficit on admission (NC=52,3%, M=18,2%), presentation of seizures before admission (NC=68,7%, M=14,6%) and after admission(NC=75,6%, M=24,4%), presentation of purulent thick CSF (thick pus in 40% of death cases).

P074

OCCULT BACTEREMIA - A 3 YEAR REVIEW ON THE ADMISSIONS OF CHILDREN WITH FEVER WITHOUT FOCUS CONSIDERED AT RISK

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Background and aims: Currently, occult bacteremia (OB) has become a rare event and with better outcome due to vaccination against its most frequent and lethal agents. In Portugal, vaccination against Group b *H. influenzae* and Group C Meningococcus has become universal since 1996 and 2006 respectively. Heptavalent-Conjugated Pneumococcal Vaccine (PCV7) has been available since 2001 for private purchase only, still there´s a coverage of over 60%.

We aimed to identify the OB rate in children admitted to our hospital with fever without focus for being considered at high risk due to age or clinical appearance, and attempt to characterize the group in terms of its clinical and laboratorial profile.

Methods: A retrospective review of clinical files of children admitted with fever without focus for up to 7 days and 0-5 years old from 2005 to 2007.

Results: We found 53 cases. There was documented bacteremia in 6 of them (11,5%). 4 had incomplete vaccination (< 3 months old). One had complete PCV7. All had symptoms for less than a day. 5 were considered ill appearing. Laboratory values, in the group, had no significant changes. Group B Streptococcus (GBS) was isolated in 2/4 below 3 months old. In those 3-36 months old (2), the agents were Pneumococcus and Meningococcus. 2 had meningitis (GBS and Meningococcus).

Conclusions: Clinical appearance and duration of fever were the only predictors of OB. GBS was an important agent up to 3 months old. In those 3-36 months, the agents encountered were those described in the literature.

P075

PNEUMONIA IN CHILDREN OVER THAN 3 YR.-ETIOLOGY, ANTIBIOTIC SENSITIVENESS, TREATMENT AND DRUGS HYPERSENSITIVITY REACTIONS

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The aim of this study was to analyze etiology, antibiotic sensitiveness and treatment of pneumonia in children over 3 years old, as well as drugs hypersensitivity reactions.

Material and method: In the period 2006-2008yr. 750 children at the age 3-16yr. were treated in our Department for acute respiratory diseases with pneumonia. Diagnosis were made by means of clinical picture, some biological parameters, chest x-ray findings and microbiological investigations.

Results: Before hospitaliziation 91% of the patients were treated with antibiotics. 89% of them have had anamnestic data for cough, 67% - fever and 9% - drugs hypersensitivity reactions. Chest x-ray showed consolidations in 51%. Etiologic agents were investigated in 85% of the patients and a positive identification was made in 32% of them. The most commonly isolated bacteria Streptococcus pneumoniae- 48%, Haempohilus influenzae- 34%, and Moraxella catarrhalis -9%. Analyze of antibiotic sensitiveness confirmed that S. penumoniae was sensitive on Penicillin - 91% and Ampicillin- 86%. H. influenzae was sensitive on Penicillin- 72% and Ampicillin 76%. M.catarrhalis was sensitive on Penicillin- 69% and Ampicillin-84%. Isolated bacterial agents showed sensitivity on Amoxycillin- clavon acid in above 96% and Cephalosporines(III generations) in above 99%. The treatment consisted of antibiotics, parenteral hydration and respiratory physiotherapy. Cephalosporins applied as initial treatment in 51%, ampicillin in 30% and macrolides in 15%. Drugs hypersensitvity reactions confirmed in 4.0%.(ampicillin-2%, cephalosporins and macrolides -1%).

Conclusion: Pneumonia constitute a major health problem in our country and very often there are diagnostic and therapeutic problem(particulary if the children have drugs hypersensitivity reactions).

P076

BACTERIAL MENINGAISIS INFECTION IN KENYA

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Objective: Kenyan village children are casualties to bacterial meningaitis. Early diagnosis and appropriate antibiotic treatment are perhaps the most important initiatives towards eradication of this great pendamic and its management in Kenyas rural villages. Though published datas suggest that fewer than half of the cases of childhood meningitis are identified at first assessment in hospitals in this region. The objective of this study indicates and brings to awareness that bacterial meningaitis kills many children from poor and desperate Kenyan villages without access to hospitals or clinics.

Methods: Nyando Sub District Hospital, serving 300 000 people in a rural, malaria-pendemic area of the Western Kenyan , was studied. A Kenya Medical Research Institute research center is located at Kisian near Kisumu city. All pediatric admissions aged 60 days between June 2001 and July 2002 were eligible.

Results: A total of 91 (2.0%) of 4582 admissions had meningitis, including 77 (4.0%) of 1929 of those who met the IMCI referral criteria for meningitis at admission.Independent indicators of the presence of meningitis were a bulging fontanel, neck stiffness, cyanosis, impaired consciousness, partial seizures, and seizures outside the febrile convulsions age range.

Conclusions: The presence of 1 of a bulging fontanel, neck stiffness, cyanosis, impaired consciousness, partial seizures, and seizures outside the febrile convulsions age range is a clear indication for lumbar puncture and/or presumptive treatment.

Keywords: Meningitis • Kenya • sub-Saharan • rural.

P077

INVASIVE E.COLI SEPTICAEMIA COMPLICATED BY ACUTE HEPATIC FAILURE AND HAEMOLYTIC UREMIC SYNDROME IN A FOURTEEN YEAR OLD MALE

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Background/purpose: Some cases of E.coli septicaemia in neonates,infants and younger children are complicated by HUS.This complication is uncommon in adolescents from developing countries, except those in septic shock, mortality and multiple organ failures are usually higher in this age group.The pathogenesis of AHF in E.coli septicaemia is from dysfunction following hepatitis, kupffer cell hyperplasia which causes poor biliary excretion/free radical scavenging role/hepato-renal syndrome. Gram negative endotoxaemia sustains the vicious cycle of DIC, complement activation/kinin liberation/renovascular spasms, anoxia, leaky capillaries/hypotension associated with HUS. A case where a good outcome was achieved by a timely intervention is described.

Case/intervention: A fourteen year old child was admitted with a six days history of fever, vomiting dysentery, abdominal pains, oliguria and epistaxis. He was icteric, acutely ill looking, lethargic, pale and febrile. He had no features of chronic liver or renal dysfunction. He had no significant lymphadenopathy. He had a significant hepatomegaly without other visceromegaly. His urinalysis was significant for bilirubinuria, proteinuria,haemoglobinuria and erythrocyturia. He was severly anaemic at 4.4g/dl, leucocytotic at 14.1x10 6, thrombocytotic at 50x10 9, hyperlactinaemic at 12mmol/l. He had a significantly deranged hepatic and renal function indexes. He had no Hepatitis B antigaenaemia or malaria parasitaemia. Hepatomegaly/nephromegaly were demonstrated at USS. The blood/urine/stool cultures were positive for O157H E.coli. Timely intervention with renal replacement therapy, antimicrobial therapy and transfusion lead to rapid complete laboratory/clinical recovery.

Conclusion/importance: ARF in HUS following septicaemia in older children has a high mortality rate, experimental models showing renal injury well before deranged biochemistry, cystatin an earlier indicator of ARF will identify cases which will benefit from prophylactic interventions with fenoldapam a nephroprotector thereby precluding invasive interventions and progression to chronic renal failure/transplantation and sudden death.

P078

MASSIVE COMPOSITE ASCITES DUE TO CRYPTOGENIC CIRRHOSIS AND OCCULT MYCOBACTERIUM TUBERCULOSIS INFECTION IN A 13 YEAR OLD GIRL

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Background & purpose: In most cases of ascites, basic evaluation is usually adequate for achieving a diagnosis, however this may not be applicable in cases of composite and diverse aetiologies. In such cases a methodological diagnostic approach will be rewarding. Infective causes should always be considered in children living between the Tropics of cancer and capricorn. A case where a diagnosis was achieved with this technique is described.

Case & intervention: A 13 year old girl came to the ED with a 5 months history of fever, a 3 months history of abdominal swelling, respiratory difficulty and yellow eyes. Her history was significant for occasional coughs, ingestion of raw cow's milk, herbs, but not for TB contact, transfusion or any individual /familial ill health. She was pale, mildly icteric with pedal oedema.She was afebrile, acyanosed, had no clubbing or adenopathy. She had a massive ascites,cirrhosis, portal hypertension, normal ovaries at USS.CT revealed loculated, encysted, septated ascitic fluid. The serum albumin& liver enzymes values were normal. Her SAAG was < 1.1and her ascitic fluid was positive for MTB.

Intervention: Anti-TB drugs, diuretics, multivitamins and follow up.

Conclusion & Importance: The aetio-pathogenesis of ascites in cirrhosis has been reviewed. Portal hypertension definable by a hepatofugal flow at USS has been implicated. The diagnosis of Paediatric TB has always been debatable and ambigous. A high index of suspicion in the appropriate clinical setting and and the application of well selected investigations was invaluable in achieving a timely diagnosis.The use of methodological approach in the study of complex cases is highlighted.

P079

A METHODOLOGICAL STUDY OF CASES OF CLINICAL TETANUS AND THE IMPACT OF MODERATED SEDATION AND BETA BLOCKAGE ON THEIR OUTCOME

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Background/purpose: The management of paediatric clinical tetanus is critical, given its high mortality rates at 20-58%. Application of a sedative, anxiolytic, muscle relaxant, anticonvulsant and nursing care is imperative. However, overenthusiastic sedation leads to respiratory depression/death whereas inadequate sedation contributes to ventricular arrhythmias due to spasms of cardiac muscles, and sympathetic dysautonaemia which could lead to hypertension / tachycardia/hypotension.Therefore, sequential moderated sedation/ beta blockade will be a logical management strategy; a series where this regimen was used to achieve an utmost outcome is described A prospective review of cases of clinical tetanus managed in the ED/ PICU from September 1999 to September 2008 is described.

Cases/interventions: 47 cases, 31 males, 16 females aged below 15 years. The mean duration of hospitalization was 7.1 days. The immunization status was indeterminate in most cases. Lower limbs injuries 64.85%, unhygienic circumcisions 21.73%, ear piercing/infections/scarifications/ tattooing 13.42%. The 3.86% mortality figure was associated with late presentations/bad prognostic factors. Interventions: Diazepam/chlorpromazine or phenobarbitone, Tetanus Immunoglobulin/toxoid, antibiotics, vitamin A/standard nursing care. Interestingly most severe cases needing aggressive interventions were not lost. Surviving the first 96 hours was usually followed by a complete recovery without sequelae.

Conclusion/importance: Good intensive care during the early periods of hospitalization reduced mortality significantly. Survivors have no sequalae; intensive care had a good cost benefit ratio. In comparison, a relatively moderated sequential sedation strategy applied in these series improved the mortality figures considerably. The role of reimmunisation of children to maintain protective antibody levels/adequate care of accidental, incidental/coincidental wounds is re-emphasized.

P080

THE APPLICATION OF ULTRASONIC ECHOGRAPHIC AND ROENTEGENOGRAPHIC FEATURES IN THE DIAGNOSIS OF PAEDIATRIC PULMONARY AND EXTRAPULMONARY TUBERCULOSIS AND ITS COMPLICATIONS

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Background/importance: Paediatric TB implying cases below the age of 5 is common and of public health importance by providing evidence of ongoing transmission. Anecdotal evidence intimates that these group are not infectious because they lack cavitary lesions,however recent investigations casted doubts on this hypothesis. Even with the novel diagnostic aids, the distinction of active Paediatric TB from Latent TB still remains challenging in most settings, being based mainly on opinions/results of chest x-rays interpreted in a standardized way by referenced ID Paediatricians/Roentgenologists in appropriate clinical settings.

The Spectra of Radiologic features associated with possible/probable/definite PaediatricTB is itemised.

Clinical/imaging details: USS/CXRs of 29 children below 5 were reviewed,22 males, 17 females. Imaging was undertaken, evaluated, interpreted/ reported in a standardized manner by Roentgenologist/Paediatrician, contact history 11, abdominal tumefaction 9, hepatomegaly 7, splenomegaly 9, lymphadenopathy 7, Icterus with deranged LFTS 3 TST positivity 5.

Radiologic features: pPrihilar opacities 21. Right apical opacities 5, Miliary mottling 3, liquefying consolidations 3, bilateral patchy infiltrates 8, Hydrocephalus 1, left lobar consolidation 2, Unilateral para pneumonic effusions 3.mediastinal widening 17,atelectasis 1, hydropneumothorax 1, On AbdominalUSS, peri-hepatic, mesenteric lymphadenopathy 4, Transthoracic USS complemented X-rays for the demonstration of aerodynamically/haemodynamically/rheologically significant pleural effusions and for the elucidation of the pleural fluid micro anatomical environment, consistency, loculations septations / encystments which directed approach at diagnostic/therapeutic thoracocentesis.There were no cavitory lesions.

Conclusion/importance: Although the diagnosis of Paediatric TB remains ambiguous, enigmatic and debatable especially in resource restricted settings, a methodologic approach to its investigation by well referenced teams could rapidly achieve a diagnosis /management by clarifying indeterminate and enigmatic cases.

P081

PURPURA AND ABDOMINAL ADENOPHATY BY BARTONELLA HENSELAE INFECTION

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We present two atypical cases of infection by Bartonella Henselae.

1) A seven year old child presented with an extensive purpura over his limbs and trunk, a spleen palpable 2 cm below the costal margin and cervical lymphoadenopaty. Laboratory test revealed a leukocyte count of 7.9x109 per liter, with 0.28 neutrophilis, 0.67 lymphocytes. The haemoglobin level was normal and platelet count was 6x109 per liter. PT, aPTT, RSV, RCP were normal. Chest roentgenogram and abdominal ultrasound examination were unremarkable, while neck ultrasound examination evidenced a diffuse cervical lymphoadenopaty with reactive characteristics. Treatment with intravenous gamma-globulin 1g/Kg/die was prolonged for two days. After 48 hours the platelet count was $69x10^9$ per liter and on day seven the count was $222x10^9$ per liter with a total regression of purpura IgG antibodies to *Bartonella henselae* was performed using an indirect immunofluorescence assay and resulted positive (1: 2348, >128). Treatment with clarithromycin (15 mg/Kg/die) was prolonged for 14 days, obtained the regression of lymphadenopaty.

2) A fifteen year old child presented with a five days history of fever and abdominal pain, without superficial lymphoadenopaty. She presented a spleen palpable 1 cm below the costal margin. Laboratory test revealed a leukocyte count of 11.9x109 per liter, 0.25 neutrophilis, 0.64 lymphocytes. RCP was 303 IU/L (< 5). Abdominal ultrasound examination evidenced a diffuse lymphoadenopaty with reactive characteristics and two ipoecogen lesions in the spleen. IgG antibodies to *Bartonella henselae resulted positive (1:4600). Clarithromycin*-therapy (15 mg/Kg/die) was prolonged for 21 days, obtained the normalization of ultrasound examination.

P082

STAPHYLOCOCCUS AUREUS NASAL CARRIAGE AND VITAMIN D RECEPTOR POLYMORPHISMS IN INDIVIDUALS WITH TYPE 1 DIABETES

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Background: Polymorphisms in the vitamin D receptor (VDR) gene have been associated with susceptibility to several infections. The purpose of this study was to investigate whether polymorphisms in the VDR gene may influence nasal carriage of Staphylococcus aureus in individuals with T1D.

Methods: VDR polymorphisms FokI F>f, BsmI B>b, ApaI A>a, and TaqI T>t were determined and nasal swab was obtained to detect colonization of S aureus in 93 T1D patients. A repeat nasal swab was obtained in 76/93 individuals for estimation of persistent S aureus carriage.

Results: S aureus nasal colonization was observed in 31% and persistent carriage in 25%. TaqI T allele was related to S aureus colonization more than TaqI t (37.0% vs 20.9%; p 0.016; OR 2.22, 95% CI 1.11 to 4.46) as was to persistent S aureus carriage (29.3% vs 17.0%; p 0.068; OR 2.02, 95% CI 0.88 to 4.68). ApaI a allele was related to S aureus colonization more than A (38.5% vs 27.2%; p 0.081; OR 1.67, 95% CI 0.88-3.16). No differences were observed for BsmI and FokI genotypes.

Conclusion: VDR polymorphisms may be associated with nasal carriage of S aureus in individuals with T1D.

P083

STAPHYLOCOCCUS AUREUS COLONIZATION IN CHILDREN AFFECTED BY ATOPIC DERMATITIS

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Background and aims: Atopic dermatitis is a chronic inflammatory skin disease associated with colonization of the skin with *Staphylococcus aureus* known to produce toxins with superantigen activity. In this study we determined the prevalence of *S. aureus* and MRSA in the lesional and nonlesional skin, and in the anterior vestibule of the nose in children with atopic dermatitis. We also examined the relationship between *S. aureus* skin lesion and nasal colonization, the production of toxins and the presence of nasal colonization in patient's cohabitants.

Methods: Nasal and skin (lesional and nonlesional) swabs cultures for bacterial isolation were obtained from 94 children affected by atopic dermatitis. Nasal swabs were taken from 15 patients' cohabitants. *S. aureus* strains were tested for detecting the toxins SEA, SEB, SEC, SED, EXT and TSST-1.

Results: In the lesional skin we found 36% prevalence of *S.aureus*, in the same group of patients the nasal colonization was 94,4%. The presence of MRSA was 7% in the lesional skin and 3% in the nose. 65% of *S. aureus* strains isolated from patients releases toxins. We observed that all positive patients to *S. aureus* had at least one positive cohabitant and that the presence and the kind of toxins in strains isolated coincide to 100%.

Conclusion: This data focus the importance of the nasal carriage as risk factor for the development of skin lesions in atopic dermatitis patients and indicates that in the current diagnostic practice is appropriate to include the research of *S. aureus* in the patient's cohabitants.

P084

DIAGNOSTIC MARKERS FOR IDENTIFYING SEPSIS IN PATIENTS WITH SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS)

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Background and aims: Sepsis caused by infection remains a major cause of mortality and morbidity among children. According to available evidence the measurements of combinations of biochemical markers offer the best prospects for early diagnosis of sepsis. The aim of this study was investigate the value of measuring changes in C reactive protein (CRP), procalcitonin (PCT), interleukin 6 (IL6) and lipopolysaccharide-binding protein (LBP) for the early diagnosis of sepsis in SIRS patients.

Methods: Children with SIRS (n=52) treated in the Children's Clinical University Hospital were enrolled in prospective study. At time 0 and at the 24th and 48th hours of the study inflammatory markers were evaluated.

Results: Sepsis was recognized in 21% of the SIRS patients. The difference in PCT levels between the sepsis and SIRS patients was statistically significant ($p < 0.05$). In SIRS patients at time 0 the mean IL6 level was 51.3 ± 137.2 pg/ml and the mean LBP level was 29.21± 36.2µg/ml, which was significantly less than mean values of IL6 and LBP for sepsis patients (accordingly 476.68 ± 955.1pg/ml and 46.15± 27.4µg/m). The mean level of CRP at time 0 was 136.7±89.7µg/ml in sepsis patients which significantly different ($p < 0.05$) from the mean level in the SIRS patients (58.8±56.8µg/ml).

Conclusions: The levels of CRP, PCT, IL 6, LBP differed significantly in SIRS and sepsis patients. Those inflammatory indicators could be used to identify sepsis patients and particular attention should be paid to SIRS patients with elevated levels of above-mentioned inflammatory indicators.

P085

INTERACTIONS BETWEEN *STREPTOCOCCUS PNEUMONIAE* AND *MORAXELLA CATARRHALIS* IN AN IN VITRO MODEL OF NASAL COLONISATION

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Background and aims
Both *Streptococcus pneumoniae* and *Moraxella catarrhalis* have the ability to elaborate a range of pathologies from their common niche in the nasopharynx. Synergistic or antagonistic interplay between these bacteria has the potential to influence both colonisation and pathogenesis. This study aims to investigate the effect of pneumococcal components on the subsequent adhesion of *M. catarrhalis* using an *in vitro* model of nasal co-colonisation.
Methods
Detroit 562 cells were incubated with filtered culture supernatant from encapsulated pneumococci (D39) (or culture medium as a control) for 24 hours. Two different *M. catarrhalis* strains, MX2 (high adherence) or A2 (low adherence) were subsequently added to the cells for 1 hour. Non-adherent bacteria were removed by washing and adherent bacteria labeled for immunofluorescence microscopy using appropriate antibodies. Samples were blinded and bacterial adherence quantified by counting.
Results
Prior pneumococcal stimulus increased subsequent adhesion of the MX2 *M. catarrhalis* by 2.55 times compared with controls ($p<0.001$), but did not significantly affect adhesion with the A2 strain.
Conclusions
Prior incubation with pneumococcal proteins increased adherence of *M. catarrhalis* to pharyngeal cells via a mechanism that is currently unknown, but may act via adhesins expressed by MX2 and not by A2. This synergistic interaction may explain the increased co-occurrence of these organisms that has been reported in some epidemiological studies of acute otitis media. Future experiments will explore the role of specific pneumococcal antigens and validate the findings using primary respiratory epithelial cells in culture.

P086

STREPTOCOCCUS VIRIDANS INVASIVE INFECTIONS IN A PEDIATRIC POPULATION

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Background and aims: *Streptococcus viridans* (SV) is a heterogeneous group of facultative anaerobic a hemolytic streptococci found as a normal mouth commensal. SV growing in blood cultures are often considered as contaminants. However this pathogen may rarely cause invasive infection in non immunocompromised paediatric patients.

Methods: Retrospective review of cases of SV recovered from January 2006 to January 2009. Cases were identified by laboratory records, retrieving all SV isolated from a normally sterile site from children aged 0 to 17 years, admitted in our 170-bed paediatric teaching hospital. Contamination was defined as a single positive sample in a child which had otherwise not been treated for SV infection. SV cultured in blood from patients with malignant disease and in peritoneal fluid collected during appendicectomy were excluded.

Results: 115 children were identified. For 105, culture was contaminated. 3 patients presented non complicated abscesses (1 subcutaneous, 1 retropharyngeal and 1 retrotonsillar). 7 children previously healthy or with mild co-morbidities had a severe invasive infection: 1 endocarditis, 1 osteomyelitis (two focus), 1 mediastinitis, 1 catheter related septicaemia and 3 surgically treated empyema. Antibiotic resistances were noted in 3 cases. Some SV strains were sent for speciation by 16S rRNA sequencing, 3 were already identified as *S. anginosus*.

Conclusions: SV invasive infections in our pediatric population are rare and can occur in healthy children. Identification of SV with conventional microbiology tests is difficult and molecular technique can be used to identify species. Finally, antibiotic resistances observed should lead to improve the use of antibiotics.

P087

EXTRACRANIAL FRONTOORBITAL ABSCESS WITH SYSTEMIC INVOLVEMENT ASSOCIATED WITH *BARTONELLA HENSELAE* INFECTION

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Systemic infections caused by *Bartonella henselae* are very rare and most of cases are found in immunocompromised patients. We report a case of a $1^{1/2}$-year-old girl admitted to the hospital with a supraciliar mass. Two months earlier she presented fever of unknown origin (FUO) for two weeks receiving various antibiotics without clinical improvement. An interciliar abscess appeared which was drained surgically. Afterwards, another mass in the right frontal supraciliar area developed. On arrival, physical exam showed a fluctuant, not painful supraciliar mass (4 cm), with enhanced osseous rim. No swelling of lymph nodes noted. Close contact with cats was denied. She was afebrile and blood tests, including CRP were normal. Serology for *Leishmania*, *Borrelia, Coxiella, B. quintana* and *Rickettsia* were negative. The mass was drained of purulent fluid. Cultures for aerobic, anaerobic and mycobacterias were negative. Immunodeficiency was excluded (lymphocyte subpopulations analysis and granulocyte function test were normal). Malignancy was excluded. Cranial CT scan showed a cystic lesion of the extracranial soft tissue in the right frontoorbital area with irregularity and thickness of the underlying parietal bone and hyperechoic areas surrounded by a thin rim highly echogenic. Chest X-ray showed areas of calcification in mediastinum. Abdominal ultrasound showed multiple echogenic areas in spleen, pancreas and liver. Anti *B. henselae* antibodies was detected (IgG titre 1:256 in IFA). The diagnosis of *B. henselae* abscess with systemic involvement was made. The girl was treated successfully with clarithromycin for 8 weeks. *B. henselae* infection should be considered in the initial evaluation of FUO.

P088

INFECTIOUS INCIDENCE IN CHILD BURNS

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Background: Burnt wounds present high risk of infection. Despite significant advances in the treatment, sepsis remains the major cause of the morbidity.

Aims: We intend to establish the infectious incidence in burnt wounds, locally treated with Silversufadiazine and conventional antibiotherapy.

Methods: We evaluated 35 children - 22 male and 13 female - admitted in ICU Department of Pediatric Surgery, between 2005 and 2008.We studied the thickness of lesions and the bacteriological status affecting the burnt wounds.

Results: To an amount of 30 patients (85,7%), the lesions were partial thickness.For the others, we obtained the following bacteriological datas:v 4 patients with Gram +;v 11 patients with Gram - (3 with Pseudomonas Aeruginosa);v 3 patients had Gram + and Gram - ;v to 6 patients we discovered fungal infection;v sepsis was encountered in 10 patients; septic shock appeared in 8 patients.Mortality was 5, 43 % (2 patients).

Conclusions: Even with correct local therapy, infectious incidence in pediatric burns remains important. Pseudomonas Aeruginosa represent nosocomial infection (8,57%).Burn lesions requires supplementary surgical measures in order to limit the damage produced by bacteria and fungus.

P089

USE OF SEROSURVEYS TO REFLECT EPIDEMIOLOGICAL CYCLES OF BORDETELLA PERTUSSIS INFECTION

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Background: Large serosurveys in the EU (ESEN) and in the US (NHANES) have established reliable data about the overall distribution of anti-pertussis toxin (PT) antibodies in the population. We tried to detect, whether small serosurveys would detect epidemiological cycles in the circulation of B.pertussis that occur every 3-4 years.

Methods: Adult plasma and blood donors aged between 18 and 60 years were screened for IgG-anti-PT by a standardized ELISA method using the CBER/FDA reference serum. A value of ≥100 EU/ml was regarded as indicative for a recent contact to B.pertussis antigens. Nasopharyngeal swabs received from children (< 16 years) with suspected pertussis from a similar catchment area were tested for Bordetella-DNA by real-time PCR amplyfing the IS 481 of B.pertussis and the IS 1001 for B.parapertussis.

Results: In 2002, 600 donors were screened and 4 had an IgG-PT of ≥100 EU/ml (0.7%), and a total of 306 swabs were tested from which 12 were positive for Bordetella-DNA (3.9%). In 2003, a total of 1,500 plasma donors were tested and 6 of them had an IgG-PT of ≥100 EU/ml (0.4%). In the same year 330 swabs yielded 15 positive results (4.5%). In 2005, a total of 2,000 plasma donors were tested and 70 of them had an IgG-PT of ≥100 EU/ml (3.5%). In that year, from a total of 470 swabs 161 were positive for Bordetella-DNA (34.2%), indicating an epidemiological cycle.

P090

METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS ISOLATES IN A TERTIARY SPANISH CHILDREN´S HOSPITAL: CLINICAL AND MICROBIOLOGIC EVALUATION

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Background and aims: Methicillin-resistant Staphylococcus aureus (MRSA) has emerged as an important cause of infection among healthy children in many areas of the world in recent years, but this tendency has not been confirmed in Spain. The aim of this study was to evaluate the incidence and resistance pattern of MRSA.

Methods: We reviewed charts of children with an MRSA isolate between 2005 and 2008. Clinical and microbiological parameters were analyzed and compared between community-acquired (CA-MRSA) and hospital-acquired MRSA.

Results: MRSA was isolated from 34 patients. Seventeen (50%) were CA-MRSA: 10 skin and soft-tissue infection (58,8%), 6 ear exudates and 1 from a complicated sinusitis and meningitis. Hospital-acquired MRSA was isolated from respiratory tract (7 cases), spinal fluid (3 cases), wound exudate (2 cases) and other locations (5 cases). We did not find an increased number of isolates of CA-MRSA during the study period (10 in 2005-2006 vs 7 in 2007-2008). One CA-MRSA and 7 hospital-acquired MRSA were resistant to macrolides (7% vs 41%; p=0,02), and 7 CA-MRSA and 15 hospital-acquired MRSA to fluoroquinolones (41% vs 88%; p=0,005). Five CA-MRSA were resistant to clindamycin (29,4%) without change in recent years. Only one isolate was resistant to cotrimoxazole. All MRSA isolates were susceptible to vancomycin and rifampin.

Conclusions: In our study we have not found an increased incidence of CA-MRSA in the last years. CA-MRSA was significantly more susceptible to macrolides and fluoroquinolones than hospital-acquired-MRSA. According to our findings cotrimoxazole may be the best option for the treatment of CA-MRSA infections.

P091

THREE CHILDREN OF A FAMILY WITH TUBERCULOUS LYMPHADENITIS

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Tuberculosis is a major problem health in the Southeast of Iran. This area is near by Afghanistan and the incidence of TB is high. The clinical presentation of TB disease is very different and we observe very rare cases of diseases in this region. But, tuberculous lymphadenitis of the neck is common in Zahedan (a city in Southeasetrn Iran).

Hereby, We report three cases of TB lymphadentitis in a family (two brothers and one sister). What was surprising in our patients was that three cases of a family were symptomatic in one time.They had 3, 5 and 8 years old.

All cases referred to our hospital because of fever, weight loss, and multiple lymph nodes in their necks. Duration of symptoms was about 2 months. Diagnosis was performed by histopathological examination and they treated with antituberculous drugs according to national guideline.

P092

FAILURE RATE OF TREATMENT AMONG SMOKER CHILDREN WITH NEW CASE PULMONARY TUBERCULOSIS, ZAHEDAN, SOUTHEASTERN IRAN

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Introduction /aim: Smoking damages the lung´s defence mechanism against infections including tuberculosis(TB) and the other infections. Association between smoking, tuberculosis disease and complications have been reported among adults patients, but there are a few reports on the influence of smoking on pulmonary diseases in children. The aim of this study was to evaluate the effect of smoking on the treatment of TB among children with pulmonary TB.

Materials and methods: From May 2005 to November 2007, we evaluated all TB patients < 18 years in Zahedan Tuberculosis Center (Southeastern Iran). Nobody was immunosuppressed, or drug resistant.

Results: Thirty nine tuberculous patients, including 15 cases who were smokers, evaluated. Except 3 cases, the others had an age range between 15-18 years. All smokers were male. Smokers had a longer duration of clinical symptoms including chronic cough than non-smokers. Smoker had a delay in sputum smear conversion time. Among non-smokers one patients had failure (4%), but in smokers failure rate was 18%.

Conclusion: Based on the results from this study, smoking is associated with a delay in the response to treatment and an increasesd failure rate among children with PTB.

Keywords: Failure rate, Children, Pulmonary TB, Cigarette smoking, Treatment.

P093

SPECTRUM OF CLINICAL MANIFESTATIONS OF BRUCELLOSIS IN CHILDREN AND ADOLESCENTS IN THE SOUTHEAST OF IRAN

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Background/aim: Brucellosis is an ancient infectious disease and has a worldwide distribution. It has a different clinical manifestations and can cause chronic debilitating illness with extensive morbidity and sometimes, it can be fatal. Familiarity with this re-emerging zoonosis is essential for physicians to recognize it. In this study, we present different clinical features of the disease in children and adolescents in Southeatern Iran.

Material and method: During two years, from 2005 to 2007, we evaluated the patients with brucellosis who referred to our hospital and had an age less than 18 years.Diagnosis was made by serologic tests including wright and 2ME . A titer more than 1:160 in two tests was diagnostic.

Results: Among 59 cases who referred to our clinics, 17 cases were between 7-18 years. Almost, disease in adults had not a specific feature and the symptoms were fever , constitutional symptoms or bone pain. But, disease had a more specific feature in children . A 17-old-year boy had osteomyelitis (L2-L4) with cold abscess. An 11-year-old girl had pancytopenia and other girl patient who was 15 years old, presented with seizure and with more evaluations during hospitalization, the diagnosis of brucella meningitis confirmed. Another boy patient had septic artheritis and the diseae was confirmed by culture in the last patient.

Conclusion: Our study showed that brucellosis in children has more specific clinical manifestations than adults.

Keywords: Brucellosis, clinical manifestations, children.

P094

GROUP A STREPTOCOCCUS NECROTIZING FASCIITIS IN INFANT WITH A SECONDARY CASE OF NECROSIS IN CAREGIVER

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Background: Necrotizing fasciitis (NF) is a soft tissue infection usually caused by Group A Streptococcus (GAS). The last 2 decades have brought an increase of invasive GAS infections, including NF. GAS streptodornases are exotoxins playing a central role in GAS spreading in connective tissues.

Methods: NF diagnosis was based on consensus definition (J. Ped, 2007; 151; 79-84). Bacterial identification and antibiogram were performed using Vitek2. GAS *emm*-typing, MLST and PCR detection and sequencing of 14 GAS exotoxins were carried out using standard protocols.

Results: A 7 months-old girl presented a cellulitis of the arm complicating a varicella. Despite of early treatment by clindamycin and penicillin, she evolved towards a decompensated shock justifying intensive care therapy. Simultaneously, NF appeared rapidly and aggressive surgical debridement was decided. During the surgery, the nurse pricked one's finger with contaminated sharp. Despite of immediate disinfection, she presented 24 hours later a cellulitis with necrosis of the finger. Multisensitive *emm*-type 5.44 GAS strains were isolated from wound samples of both the child and the nurse, indicating that the strains most likely belong to the same GAS clone (MLST under progress). Moreover, the virulence factor genes were identical in the 2 isolates. Only one superantigen-encoding gene (*speC*) was found but a rather high number of streptodornase-encoding genes (*spd1, spd3, spd4 and sdn*) was detected.

Conclusions: The high number of streptodornase-encoding genes in this GAS isolate might account for its high virulence which explain most likely the rapid evolution towards necrosis in the two different hosts.

P095

EVALUATION OF CLINICAL FINDINGS AND TREATMENT OF CHILDHOOD BRUCELLOSIS IN IRAN

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Retrospectively we evaluated the records of 45 children with brucellosis; 31 males (68.8%) and 11 females (24.4%).only 16.3% (8/42)of the patients were < 5years. 24% (12/42) were older the 5 years but ≤10 years and 59.7% (22/42) were older than 10 years but ≤15 years. Twenty eight of the children were living in rural areas and the remaining living in urban areas. Ingestion of unpasteurized milk was reported in 24 (53.3%) children animal contact in 15 (33.3%), while 19 (42.2%) children appeared to have no history of exposure to either. There was the most common symptom 32 children presented with high fever reaching 39.5◦c,4 of there with chills intermittent and night fever was observed in 10 children respectively. sweating in (76.4%) and artheralgia or arthritis involved mianly the knee and hips was observed in 30 (83%) children. Sacroileitis was seen in 2 children (4.8%). Antibiotic treatment lasted for 28 days on average. There were no complications or relapses, except one, and the final outcomes were excellent.

P096

LUNG ABCESS IN CHILDHOOD: RETROSPECTIVE ANALYSIS OF 32 CASES

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Background and aims: Lung abscess is defined as localized necrotizing inflammation of lung parenchyma that rarely occurs in childhood. Staphylococcus aureus is the most common isolated microorganism. This study aimed to review the clinical and laboratory findings, and prognosis of children with lung abscess.

Methods: We reviewed the medical records of 32 children (22 males and 10 females) hospitalized with a diagnosis of lung abscess between 1986 and 2008. The information was obtained regarding age, gender, presenting symptoms, underlying conditions, microbiological data and treatment modalities.

Results: Eight of the 32 patients had primary lung abscess, while 24 had secondary lung abscess due to comorbidities. Fever and cough were the most common presenting symptoms. Five of 32 patients had neuromotor retardation. Immune deficiency was diagnosed in three cases. Thoracocentesis or percutaneous drainage was performed to twenty-five of 32 children and the most common pathogen isolated from the abscess was S.aureus (21.8%). All patients were initially treated with antibiotics, and twenty-seven of 32 were treated with multiple antibiotics. Cephazoline, vancomycin or teicoplanin were the first choice of treatment due to their Gram positive coverage and in case of persisting fever meropenem, imipenem or aminoglycosides was added to therapy due to their Gram negative spectrum.

Conclusion: In children with pneumonia, persisting fever or auscultation findings must alert the physician about accompanying or developing lung abscess. Antibiotics having Gram positive coverage must be the first choice of treatment due to the most common organism isolated, S.aureus.

P097

IINVASIVE MENINGOCOCCAL DISEASE (IMD) IN COSTA RICAN (CR) CHILDREN (CH)

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Background and aims: Meningococcus is the second leading cause of bacterial meningitis in CR ch. Reports about IMD in Latin American (LA) ch are scarce and the real burden is unknown. Our objective was to describe the epidemiology and microbiology of IMD in ch admitted to the only paediatric tertiary referral and teaching hospital (H) of CR.

Methods: Retrospective chart review of ch aged < 14 yrs with a laboratory-confirmed IMD episode, period Nov 15, 2000 to Nov 5, 2006.

Results: 31 patients (pts) were identified, of which 6 had an incomplete chart and were excluded. 12/25 (48%) pts were boys. Mean age was 2.9 yrs (range 12 days to 13.8 years); overall, 80% were < 5 yrs of age. The most common clinical presentations were meningitis in 84% pts and meningococcemia in 16% pts. The most common symptoms were: fever, 100%; decreased consciousness, 84%; neck rigidity, 64%; and purpuric/petechial rash, 64%. Only 1 isolate was penicillin-resistant and none were cefotaxime-resistant. Serogroup distribution was as follows: B, 61.5%; A, 15%; W-135, 15% and C, 7.6%. 28% pts were admitted to the PICU. Complications included secondary seizures in 24%, septic shock in 20%, and amputations in 4% (1 pt) No deaths occurred.

Conclusions: Compared to other countries, the mortality rate of IMD in CR ch is low. Most cases wouldn't have been prevented with the current vaccines available in CR.

P098

LESSONS LEARNT FROM A FATAL TUBERCULOSIS CASE

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Background and aims: In industrialized countries it is believed that generalized tuberculosis (TB) in children is rare due to universal vaccine availability and rather low incidence rate in adults. However, in the past few years a dramatic reemergence of TB all over Europe has been noticed. One possible reason could be increased rate of TB among immigrant populations. A child who represents nearly natural history of miliary TB is being presented.

Methods: A case report.

Results: A one-year-old boy, born in Poland, vaccinated at birth against TB disease and living in a refugee camp was admitted to the Pediatric Intensive Care Unit (PICU) due to dyspnea, tachycardia and opisthotonus. History revealed that the child had previously been hospitalized for pneumonia (at the age of 4 months) and generalized lymphadenopathy (at the age of 10 and 12 months). Each time hospitalization was interrupted by his parents who declined diagnostics and requested early discharge. A formal statement in their own native language was filed with medical records. At admission to PICU child's vital signs were abnormal. Chest X-ray revealed miliary tuberculosis, cerebrospinal fluid examination showed lymphocytic pleocytosis (87 cells) when intra-cranial tuberculomas were visualized on MRI. Tuberculin skin test stayed negative. TB diagnosis was confirmed by gastric culture. The child died on 22nd day of hospitalization despite proper anti-tuberculosis treatment from miliary tuberculosis with CNS involvement. Thorough investigation revealed contact with fresh adult TB case in a refugee camp.

Conclusions: Neither negative TST nor vaccination history should exclude TB from differential diagnosis.

P099

SUILYSIN PREVENTS INVASION AND TRANSLOCATION OF *STREPTOCOCCUS SUIS* ACROSS THE BLOOD-CEREBROSPINAL FLUID BARRIER IN VITRO

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Background and aims: Previous experimental studies in a standard Transwell culture system have shown *Streptococcus suis* ability to compromise barrier function of porcine choroid plexus epithelial cells (PCPEC). The development of an 'inverted' Transwell filter system of PCPEC enables us with this model to investigate bacterial invasion and translocation from the physiologically relevant basolateral (blood) to the apical (cerobrospinal fluid) side. Previously we could show specific invasion and translocation of *S. suis* across the PCPEC exclusively from the basolateral side. During this process, bacterial viability and the presence of a capsule as well as cytoskeletal regulation of PCPEC seemed to play an important role.

Methods: Now, we analyzed the effects of the thiol-activated hemolysin suilysin on *S. suis* invasion and translocation rate across PCPEC and its influence on PCPEC barrier function.

Results: Cell viability and barrier function were not significantly affected after infection of suilysin mutants and the *S. suis* wildtype. Interestingly, we observed a lower invasion and translocation rate in three different suilysin deficient mutants compared to the *S. suis* wild-type. In contrast previous published results show that suilysin promotes invasion into the endothelial cells.

Conclusions: Thus, possibly regulated by the presence of a suilysin, *S. suis* induces signals in PCPEC that prevent cellular uptake during the bacterial transcellular translocation process. Further experiments have to clarify the mechanisms for our observations. Still, our data underline the relevance of the blood-cerebrospinal fluid barrier as a gate for bacterial entry into the central nervous system.

P100

GRANULOMATOUS CERVICOFACIAL LYMPHADENITIS - *N*OT *T*HAT *M*ANY?

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Introduction: Granulomatous cervicofacial lymphadenitis (GCL) is not uncommon in children. We sought to determine their epidemiologic profile and identify features that aid management.

Methods: We retrospectively analyzed epidemiologic, clinical, laboratory, imaging and histopathological data for patients who had lymph node biopsies performed between 1998 and 2006, from the cervicofacial region that showed granulomatous lymphadenitis.

Results: We identified 60 children with GCL, noting a rising incidence from 2003 (>75% cases occurred after 2003). Mean age was 67 months, mean symptom duration before presentation was 7 weeks. Most had single (73%) and unilateral (97%) lymphadenopathy, without features suggestive of acute bacterial lymphadenitis. Forty-two percent of children had Tuberculin Skin Test (TST) reading of ³10mm. There were 10 (19%) positive node cultures, including 7 isolates of Non-Tuberculous Mycobacteria (NTM; 4 *Haemophilum*, 2 *Fortuitum*, 1 not identified), 2 isolates of *M.Tuberculosis* (TB), and 1 of *M. Bovis* (BCG strain). Subgroup analysis suggested that patients with NTM GCL (compared to TB GCL) were younger (56 months vs. 99 months) and had lymphadenopathy in the parotid/ pre-auricular or submandibular regions, but did not reach significance. Younger age predicted recurrence after any initial treatment (mean 42 months of age vs. 73 months, p=0.05), while initial complete excision of affected nodes predicted no recurrence (8% recurrence vs. 43%, p=0.03).

Conclusions: The incidence of GCL appears to be rising. While microbiological yield is low, most were due to NTM; our isolates were predominantly *M. haemophilum*. Initial complete excision of affected nodes (if possible) remains the best mode of treatment.

P101

SUBTLE NEUROLOGICAL AND FUNCTIONAL PROBLEMS IN SCHOOL AGE SURVIVORS OF BACTERIAL MENINGITIS

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Background and aims: Bacterial meningitis is a serious infection with high morbidity and a significant risk for neurological sequelae. Additionally to major disabilities, meningitis survivors could develop subtle problems in many functional areas, including motor and sensory performance, dexterity, competence and behavior. The aim of this study was to assess the presence of such problems in children and teenagers with a history of bacterial meningitis.

Methods: Thirty children and teenagers with a history of bacterial meningitis were compared to 30 healthy controls for neurological soft signs (NSS), dexterity, competence and behavior problems. For the assessment of the NSS, the protocol of Shafer and colleagues was used. Dexterity was assessed with the Grooved Pegboard Test and competence and behavior problems were tested with the Child Behavior Checklist (CBCL).

Results: Meningitis survivors performed worst than controls only in one out six NNS tested. In that item (motor speed), subjects needed more time to complete the timed tasks of the examination (P=0.019). There was no significant difference in performance on the Grooved Pegboard Test and the items assessed with the CBCL.

Conclusions: Children and teenagers with a history of bacterial meningitis showed no significant differences when compared to healthy controls with respect to the presence of NSS, dexterity, competence and behavior problems.

P102

A COMPARISON OF REAL-TIME PCR AND CONVENTIONAL CULTURE-BASED METHODS FOR THE DIRECT DETECTION OF GROUP B STREPTOCOCCI FROM CLINICAL SPECIMENS

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Background and aims: Group B streptococci (GBS) are the principal cause of sepsis and meningitis in neonates. Development of a rapid and sensitive method to detect GBS from clinical specimens may improve healthcare for expectant women and newborns and allow appropriate antibiotic prophylaxis/therapy to be implemented. The objective of this prospective study was to evaluate the utility of a non-culture based method for GBS diagnosis. This molecular detection method involves real-time amplification of a novel target gene, the GBS-specific *cylB* gene, using Roche's fluorescence resonance energy transfer LightCycler PCR system.

Methods: To compare the sensitivity of *cylB* PCR and conventional culture-based methods for GBS detection, a collection of 100 clinical specimens (ear swabs) were analysed. The specimens were obtained from newborns undergoing sepsis screening on the neonatal units of two UK hospitals. Swabs were examined for GBS by LightCycler PCR amplification of *cylB* and by culture on GBS selective media (Granada agar).

Results: A total of 100 ear swabs were analysed. PCR and culture-based methods were positive for 7 specimens and negative for 84 ear specimens. Only one ear swab was negative for GBS by PCR, but positive by culture. GBS were detected in an additional 8 ear swabs by PCR, but not by culture.

Conclusions: PCR amplification of *cylB* enabled detection of GBS in 8 specimens from which GBS could not be detected by culture. The superior sensitivity and reduced time-to-result of this molecular assay makes it an attractive option for GBS detection, particularly in the urgent intrapartum setting.

P103

PREDOMINANCE OF NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* IN THE NASOPHARYNX AND MIDDLE EAR OF CHILDREN WITH RECURRENT ACUTE OTITIS MEDIA

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Introduction: *Streptococcus pneumoniae* (Pnc), non-typeable *Haemophilus influenzae* (ntHi) and *Moraxella catharralis* (Mc) are traditionally the main pathogens associated with recurrent acute otitis media (rAOM). The aim of this study was to investigate carriage patterns and the presence of bacteria in the middle ear of children with rAOM.

Methods: Nasopharyngeal (NP) swabs and middle ear effusions (MEE) of children with rAOM were cultured for Pnc, ntHi, Mc using conventional culture methods. In addition, samples will be analysed using pathogen specific PCR. Pneumococcal serotyping was performed by the Queensland Pneumococcal Reference Laboratory. NP samples are also being collected from healthy age-matched controls.

Results: Bacterial culture results in children with rAOM (n=109) showed that ntHi was the most frequently carried pathogen in the nasopharynx (60.8%), followed by Mc (51.7%) and Pnc (35.0%). Of the 42 Pnc isolates cultured from NPS, only 4 (9.1%) were PCV-7 serotypes whereas 19 (43.2%) were vaccine related types, predominantly 19A (n=12) and 6A (n=5). The remainder 21 (47.7%) were non vaccine types with 11A (n=6) and 15C (n=3) the most common serotypes. 131 MEE samples have been cultured in which ntHi was found in 17 (13%), Mc in 10 (7.6%) and Pnc in 4 (3.1%) samples.

Conclusions: Introduction of PCV-7 has reduced the prevalence of Pnc in children with rAOM, however an increase in ntHi and Mc is observed. New vaccines for rAOM may need to include additional bacterial antigens. Furthermore, surveillance of bacterial NP carriage and MEE isolates may help inform vaccine policy.

For the Gromit Study Research Team, Vaccine Trials Group, Telethon Institute for Child Health Research, Perth, Australia

P104

DETECTION OF ANTIBIOTICS RESISTANCE PATTERNS IN ISOLATED STRAINS FROM VARIOUS BACTERIAL INFECTIONS IN CHILDREN IN HAMADAN, WEST OF IRAN

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Background and objective: Antibiotics resistance of pathogens is one of the main problems for pediatric infections in the third world countries. Therefore, the aim of study was the evaluation of frequency of bacterial infections in children and detection of antibiotics resistance patterns of bacteria in Hamadan, during 2002 to 2007.

Methods: This is a cross-sectional study that performed on 6391 children under 14 years of age who admitted at pediatric wards from 2002 to 2007. All children which were diagnosed with meningitis, septicemia, pneumonia, gastroenteritis, and urinary tract infections (UTI) were evaluated. Disk agar diffusion method was used to determine the isolated bacterial resistance to 12 antimicrobial agents. Data were analyzed using spss system.

Results: From 6391 samples, 27.7% were positive culture. 65.4% of isolated bacteria were gram negative and 34.6% (613) were gram positive. The most common infections were: urinary infections (36.8%), gastroenteritis (34.9%), sepsis (17%), pneumonia (9.2%), and meningitis (2.1%). Isolated bacteria were: *E. coli* (36.3%), *Staphylococcus aureus* (18.2%), *Staphylococcus epidermidis* (13.3%), *Klebsiella* spp.,(10%), *Enterobacter* spp., (6%), *Shigella spp.*, (3.9%), *Pseudomonas auroginosa* (2.8%). The most effective antibiotics on both gram positive and gram negative isolates were ceftriaxone, imipenem, nitrofurantoin, cefepime, kanamycin and gentamicin. Most strains were resistant against cephalexin, ampicillin, erythromycin and co-trimoxazole.

Conclusions: This study showed that the most common bacterial infections were gastroenteritis, UTI and sepsis. *E.coli* and *Kelebsiella* spp., were the most common gram negative bacteria and *Staphylococcus aureus* was the most common gram positive one, which were resistant to the wide spectrum antibiotics.

P105

SEROLOGICAL RESPONSE IN CHILDREN WITH GROUP A STREPTOCOCCAL PHARYNGITIS IN THE UNIVERSITY HOSPITAL IN LATVIA

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Antibody tests have no value at the time of diagnosing acute GAS sore throat; however, they are crucial in providing evidence for antecedent streptococcal infection in terms of rheumatic fever prevention.

Objectives: To detect the serological response in children having GAS acute pharyngitis with episode of sore throat in Children's Clinical University Hospital in Latvia.

Methods: With the support of WHO a total of 340 patients between 2-12 years of age with complaints of sore throat were screened at the emergency setting of the University hospital. Throat swabs were obtained for GAS culture, rapid Biostar Strep A OIA MAX GAS antigen detection tests (RADT) were done and serological response was measured by having at least double elevation in antistreptolysin O (ASO) and/or antiDNase B titres in pair seras. According to all three above-mentioned criteria episode of acute GAS pharyngitis was defined.

Results: From 340 children having complaints of sore throat, 94 (27.6%) had positive RADT and 75 (22%) of the latter - positive GAS culture. Serological response was detected to 36 (48%) children who met acute GAS pharyngitis criteria, from which 22 (61%) had both tests elevated twice or more, 9 (25%) individuals had elevated only ASO titres and 5 (14%) had only antiDnaseB titres.

Conclusions: Serological testing indicates that half (52%) of those having positive RADT and GAS culture, are GAS carriers with sore throat of unknown origin. To verify serological response it is desirable to perform both of the serological tests, in order to reveal acute GAS pharyngitis.

BONE, JOINT AND SOFT TISSUE INFECTIONS

P106

GRADENIGO´S SYNDROME COMPLICATED BY *S. PNEUMONIAE* MENINGITIS

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Background and aims: Gradenigo´s syndrome, the association of acute otitis media (AOM), headache/facial unilateral pain and sixth nerve paralysis, is a rare presentation of petrositis and a very rare complication of AOM.

Methods: We describe a case of Gradenigo´s syndrome complicated by *Streptococcus pneumoniae* meningitis.

Results: A 8-year-old girl, with recurrent AOM, was admitted to the Emergency Service (ES) with a 2-months history of intermittent fever and unilateral headache. At the beginning of the symptoms an AOM was diagnosed. A month later a sixth nerve palsy was observed. A computerized tomography (CT) was performed and showed osteitis of the right petrous apex, suggesting petrositis or a tumoral lesion and mastoiditis. Two days later, she was admitted to the ES with meningeal signs, severe headache, vomiting and fever. A lumbar puncture was performed and meningitis was confirmed. She was started on ceftriaxone and vancomycin. *S. pneumoniae*, serotype 3, susceptible to penicillin was isolated. Because of a suspected allergic reaction, with severe pruritus, antibiotics were changed and treatment was completed with levofoxacin. During treatment a magnetic ressonance imaging was performed showing an improvement. The outcome was good. A year later she has a normal physical examination and the CT shows resolution of the infection.

Conclusions: Life-threatening complications of AOM, although rare, still occur, as it happened with our case. In the presence of unilateral pain and sixth nerve palsy, Gradenigo´s syndrome should be evocated and treatment should not be delayed in order to avoid other complications. Conservative medical treatment without surgery was successful.

P107

SEPTIC ARTHRITIS (SA) IN COSTA RICAN CHILDREN (CH)

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Background and aims: Publications about SA in Latin American ch are scarce, and this is one of the largest series in the Americas. Our main objective was to describe the epidemiology and microbiology of SA in ch hospitalized at the only paediatric tertiary referral and teaching hospital of Costa Rica.

Methods: Retrospective chart review of patients (pts) aged < 13 yrs with a hospital discharge diagnosis of SA, from January 1, 2003 to December 31, 2007.

Results: 110 pts were included, 64% were male. Age distribution was the following: newborns, 8% pts; 1-24 months, 25%; 2-5 yrs, 22%; and >5 yrs, 45%. The most common symptoms were: fever, 88 (80%) pts; pain, 100 (91%) pts; and functional limitation, 97 (88%) pts. The main affected joints were: hip (48%), knee (42%), ankle (3.6%), and elbow (3.6%). The 3 most common agents were: S. aureus, 33 (30%) pts (half were MRSA); S.agalactiae, 2 (1.8%) pts; and K.pneumoniae, 2 (1.8%) pts. Cultures were sterile in 64 (58%) pts. Arthrocentesis and arthrotomy were performed in 85% and 64% of pts, respectively. Complications and sequelae occurred in 13.6% and 9%, respectively. No deaths occurred.

Conclusions: Empirical initial antibiotic therapy for Costa Rican ch with SA should include drugs effective against MRSA. The high rate of sterile cultures in our series prompts urgent improvement in detection procedures for establishing the etiologic role of Kingella kingae.

P108

OSTEOMYELITIS: EPIDEMIOLOGY, CLINICAL MANIFESTATIONS AND MANAGEMENT

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Background: The aim of this study was to describe the epidemiology, clinical and laboratory data and management of ostemyelitis in our hospital.

Methods: All patients younger than 15 years admitted in our center with osteomyelitis between 2000 and 2008 were retrospectively reviewed.

Results: Forty eight patients were identified (52% female), with median age of 2 years (range 6-150 months). Main onset manifestations were pain (96%), functional impairment (89%) and fever (75%). Mean time since onset until admission was 6,5 days ± 6,6. Femur (25%), tibia (25%), tarsus (20%) and pelvis (14%) were the most affected bones. Leukocytosis (>13.000/mm^3) was found in 52% cases and elevated PCR (> 30 mg/L) in 50%. Procalcitonin was elevated (0,5-2 ng/ml) in two out of seven patients. Blood cultures were positive in 21%, goup A streptococcus was the bacteria most frequently isolated (13%). Gammagraphic bone scan, performed with mean time since onset of 8,2 days ± 6,8, was diagnostic in all cases. Patients received antibiotic treatment, initially i.v. (mean time 10,2 days ±3,4), later switched orally (17,4 days ± 6,6). Surgical treatment was required in 3 cases. Only one patient had chronic osteomyelitis criteria, the rest of them had a favourable outcome.

Conclusions: Ostemyelitis is often difficult to diagnose due to absence of specific clinical and laboratory findings and the young age at presentation.

Although X- rays are useful, gammagraphic bone scan was the best imaging test for diagnosis in our series. Early diagnosis and treatment are essential to avoid chronic osteomyelitis and skeletal disabilities.

P109

MULTIDRUG-RESISTANT SKELETAL TUBERCULOSIS: REPORT OF TWO CASES

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Background and aims: The increasing emergence of drug-resistant strains is a serious problem in the management of tuberculosis. Few cases have been reported of multidrug-resistant skeletal tuberculosis in children.

Methods: Two cases of multidrug-resistant skeletal tuberculosis diagnosed at Hospital La Paz (Spain) are described.

Results:

Case 1: A 4-year-old immigrant Chinese girl presented with a 6-month history of a fluctuant mass at her right ankle. MRI revealed cortical tibio-talar irregularities and synovial hypertrophy. An open synovial biopsy was performed, which showed tubercular granulomas. Tuberculin skin test was positive. PCR for M. tuberculosis in biopsy sample and synovial fluid were positive. Multidrug-resistant M. tuberculosis was isolated from synovial biopsy and gastric aspirates. Case-contact evaluation revealed tuberculosis in a grandfather in China. Treatment with five drugs led to complete healing of tibio-talar erosions.

Case 2: A 4-year-old girl presented with a 4-month history of progressive kyphosis. MRI showed dorsal spondilytis and paravertebral abscess. Tuberculin skin test was positive. She underwent surgery and abscess material culture yielded multidrug-resistant *M. tuberculosis*. Case contact study was negative, but further questioning of the family revealed a household contact with a young immigrant from Morocco who had died from tuberculosis. Both strains were identical by RFLP analysis. Currently she is being treated with good evolution.

Conclusions: Skeletal tuberculosis is an emergent disease that requires a high index of suspicion for diagnosis. Rapid identification of multidrug-resistant strains is necessary for an adequate management of cases. Case contact studies should be conducted whenever a case of tuberculosis is identified.

P110

RIB TUBERCULOSIS IN A CHILD: CLINICAL, RADIOLOGICAL, HISTOPATHOLOGICAL FINDINGS AND UTILITY OF THE QUANTIFERON-TB GOLD TEST FOR DIAGNOSIS

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Introduction: Skeletal tuberculosis (TB) accounts for 1-5% of all TB and involvement of the rib is extremely uncommon. Clinical and radiological features of bone TB may resemble other conditions such as infections and bone tumors.

Case report: A 3.5 year-old boy was referred to our clinic with the local swelling at the right side of the pectoral region during last 9 months. On physical examination, he had pectus excavatum, and there was slightly tender palpable mass measuring 5x5 cm on left chest wall. BCG scar was present. He had no history of fever, weight loss, trauma and family history for chronic conditions including tuberculosis. He was initially considered as to have Ewing sarcoma with ultrasonography. Computerized thorax tomography revealed mild destructive lesions of the rib and hypodense lesion measuring 8x5x6 cm. There was no evidence of pulmonary TB with radiological findings, and early gastric aspirates were negative for AFB on three occasions. Histopathological examination of incisional biopsy showed granulomatous inflammation. Ziehl-Nielsen-stained smears for AFB were negative. PPD produced 20-mm induration at 48 hours. The QuantiFERON-TB Gold test was positive. He had been treated with isoniazid, rifampicin, pyrazinamide. Mass lesion completely disappeared after first month, and there was no recurrence after finishing 9-month-therapy.

Conclusion: Diagnosis of extra-pulmonary TB is difficult and high index of suspicion is required in children. The QuantiFERON-TB Gold test may hold promise for use when conventional workup including microbiological tests is not diagnostic when tuberculosis is suspected.

P111

OSTEOMYELITIS IN CHILDREN-A PORTUGUESE HOSPITAL STUDY

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Background: Despite diagnostic and therapeutic advances, osteomyelitis continues to cause significant disease burden, presenting a challenge to physicians.

Objectives: Review the experience and outcome of osteomyelitis in children from a suburban area outside Lisbon.

Methods: Retrospective study of children with osteomyelitis, between July 1996 and December 2008. Osteomyelitis was classified as acute (AO) or chronic (CO), if symptoms were present for less or more than two weeks before diagnosis. Demographic, clinical, laboratory, imagiologic, therapeutic data and outcome were analysed.

Results: Total of 47 children, 34(72%) with AO and 13(28%) with CO. Median age was 6,9±4,6 years and 26(55%) had risk factors: sickle-cell disease (10), preceding fracture (5), immunodeficiency (2), paraplegia (2), varicella (2) and others (5). The mean duration of symptoms was 9±16 and 146±143 days in AO and CO, respectively. The most affected bones were the femur (25%) and tibia (25%). Etiologic diagnosis was made in 25(53%) cases, by blood culture (47,6%), pus aspiration (80%) or both (25%). *Staphylococcus aureus* (56%) and *Salmonella* (16%) were the predominant organisms. Skeletal scintigraphy confirmed diagnosis in 64% cases. The median duration of parental therapy was 29,5 days and surgical procedure was performed in 16(34%) patients. Complications included: abscess (14), fistula (4) and chronic osteomyelitis (3). Children with AO had higher leukocyte count (16930vs9277;p=0,007) and serum C-reactive protein (11,15vs4,18;p=0,048). None of the patients who switched to oral therapy within 2 weeks was rehospitalized.

Comments: Despite the longer duration of symptoms prior to diagnosis, the overall outcome was similar to that reported by others.

P112

SALMONELLA OSTEOARTICULAR INFECTION IN CHILDREN WITH SICKLE CELL DISEASE

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Background and aims: Salmonella osteoarticular infection is a severe condition in children with sickle cell disease (SCD).

Methods: Retrospective analysis of patients hospitalized in our institution between 1997 and 2008. *Salmonella* was isolated from the blood, pus or articular aspirates.

Results: 12 cases were analyzed. The median age was 3 years (SD ±5.7, range 15 months to 14 years) and 67% of children were under 5 years. Before admission, gastro-enteritis symptoms were present in 66% of cases and vaso-occlusive crisis in 83%. Median duration of symptoms was 3 days (SD ± 8.8, range 0 to 31 days). The predominant presenting symptom was pain in 92% of cases, 33.3 % of the patients have multifocal infection and 70% involved bones of the arm. The initial CRP was greater than 30mg/L in 75% (median: 51 mg/L, SD ± 30.4,). 50% of the 20 osteoarticular samples isolated *Salmonella spp* despite the initiation of the antibiotherapy (from 1 to 25 days). Initial ultrasound was the most contributing exam pathological in 80% of cases. Parenteral antibiotics associating a third generation cephalosporin and ciprofloxacin were given in all cases during a long period (mean: 17 days; range 8 to 26 days). Ten patients (83.3%) undergone surgical therapy. Control of infection was difficult: 50% of the patients needed more than one operation for subsequent arthritis, osteomyelitis or sub periostal abscess.

Conclusions: Salmonella osteoarticular infections remain a therapeutic challenge in children with SCD: dissemination of the infection occurs frequently despite medico-chirurgical treatment.

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PEDIATRIC OSTEO-ARTICULAR INFECTIONS CAUSED BY *STREPTOCOCCUS PNEUMONIAE*

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Background and aims: Pediatric pneumococcal osteo-articular infections (OAI) are uncommon (5-10% of pediatric OAI). The objective of this study was to describe their clinical and microbiologic characteristics.

Methods: Data were retrospectively collected from children aged < 16 years, who were hospitalized for pneumococcal OAI between 1997 and 2007 in 4 pediatric hospitals in Paris.

Results: A total of 42 children were included: 30 arthritis, 8 osteomyelitis and 4 osteomyelitis with arthritis. The mean age of the 42 infected children was 12 months (range 3 months to 14 years) and 74% of the patients were < 2 years. Six of 39 children (15%) were immunized with 7-valent pneumococcal conjugate vaccine (PCV7).

Twenty-three of 42 strains (55%) were intermediate or resistant to penicillin. Fifteen of 42 serotypes (36%) were available: two serotypes 1, one 6A, one 6B, one 9, three 14, one 15B and six 19A (40%). Five of 6 serotypes 19A were intermediate or resistant to penicillin. Vaccine strains were isolated in 3 not vaccinated children and in a child who received only one vaccine injection. The 19A serotype was the only strain isolated in the 3 children with complete vaccination. The evolution was favorable for all children but 5 children required one secondary surgical revision (3 arthritis, 1 abscess, 1 peritonitis).

Conclusion: The epidemiology of pediatric pneumococcal OAI is changing with the widespread of the PCV7. In this study, the most common serotype was 19A. Children > 2 years of age are also affected.

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CONSENSUS FOR OSTEOARTICULAR INFECTIONS' DIAGNOSTIC CRITERIA IN CHILDREN, USING A DELPHI METHOD

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Purpose: There are many diagnostic criteria for osteoarticular infections in the literature, without consensus. This study aimed to determine consensual definition criteria for arthritis, osteomyelitis, and any osteoarticular infections in children, using a Delphi method.

Methods: A group of 12 French-speaking experts (paediatric infectious diseases physicians and paediatric orthopaedic surgeons) were contacted for participating to an e-mail Delphi process in the year 2008. Diagnosis criteria identified in a systematic PubMed research were proposed to the Delphi participants for consensus for an epidemiological definition (definite diagnosis) and for a clinical definition (probable diagnosis). Five definition criteria for arthritis, eight for osteomyelitis and five for any osteoarticular infection were included in a 3-rounds process. Exclusion of the worst definitions was performed in the first round. A classification of the remaining definitions was performed in the second round. A selection of the best definition within the two most accurate was performed in the third round. An a priori consensus threshold of at least 70% was required for each round.

Results: Eleven experts (from Switzerland [n=1], Belgium [n=5] and France [n=5]) participated. A consensus was obtained for an epidemiological definition of arthritis, osteomyelitis, and any osteoarticular infection. A consensus was also obtained for a clinical definition of any osteoarticular infection. However, no consensus was found for a clinical definition of arthritis and osteomyelitis, for which two definitions have been retained.

Conclusion: This Delphi process has provided consensual definitions for osteoarticular infections that could be used for either epidemiological or clinical next studies.

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OSTEOMYELITIS IN CHILDREN: COMPARATIVE STUDY BETWEEN GROUP A BETA-HEMOLYTIC *STREPTOCOCCUS* (GABHS), METHICILLIN-SUSCEPTIBLE (MSSA) AND METHICILLIN-RESISTANT (MRSA) *STAPHYLOCOCCUS AUREUS*

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Background and aims: Acute hematogenous osteomyelitis (AHO) is caused by *Staphylococcus aureus* in most cases. GABHS usually is next in frequency.The objective of this study was to compare the clinical manifestations, laboratory findings and outcomes of children with AHO caused by GABHS, methicillin-susceptible and methicillin-resistant *Staphylococcus aureus*.

Methods: Medical records from children admitted at Santa Casa de São Paulo Hospital with a diagnosis of AHO between February 2007 and December 2008 were reviewed. Diagnosis of AHO was based on clinical and imaging criteria. Antimicrobial susceptibilities were determined by disk diffusion tests.

Results: A total of 21 patients with AHO were included during the 23 months study period. *S. aureus* was the etiologic agent in 10 (47%) cases being 3 of these MRSA. GABHS was identified in 5 (23,8%) patients. Polymicrobial infection occurred in two cases. Patients with MSSA and MRSA AHO had a mean duration of fever of three days whereas patients with GABHS had a mean of two days of fever. On admission, mean white blood cell (WBC) count was 16986/mm³, 18842/mm³ and 21283/mm³ and mean erythrocyte sedimentation rate (ESR) was 87.3mm/h, 67.8mm/h and 117mm/h in patients with GABHS, MSSA and MRSA AHO, respectively. The median total duration of antibiotic therapy was 18.0, 24.0 and 44.0 days for GABHS, MSSA and MRSA AHO, respectively.

Conclusions: MRSA AHO was associated with a higher WBC count and ESR than MSSA and GABHS AHO. Moreover, patients with MRSA OHA needed longer antibiotic therapy than those with MSSA and GABHS AHO.

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CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO) DUE TO *COXIELLA BURNETTI* INFECTION- IS THERE A ROLE FOR INTERFERON (INF)- Γ THERAPY?

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Q fever is a zoonosis caused by *Coxiella burnetti*, an obligate intracellular bacteria. It is rare in children and osteoarticular involvement in chronic Q fever has only been described in six children (1). There is uncertainty regarding the optimal treatment and monitoring of these patients.

We present a 3-year-old girl with a 12-months history of painful swelling of her wrist, followed by a pseudo-paralysis of her arm, a chronic abscess of the chest wall and finally back pain. MRI of the spine revealed destructive vertebral lesion at T10 level with extradural extension and X-rays showed additional bone destructive lesions in the humerus and femur. Histopathology of the humerus biopsy was normal; blood and biopsy cultures remained negative. Flucloxacillin was given with good clinical response; however a new lesion developed in the navicular bone 3 months after stopping antibiotic treatment. At this point, the diagnosis of Q fever was established serologically (anti-phase I IgG titer: 1/32000) and by PCR from bone biopsy. Antimicrobial therapy with rifampicin and ciprofloxacin was started; immunology studies including the Interleukin-12 and INF-γ/INF-γ receptor pathway were normal. Two years later the disease has not been satisfactory controlled and therapy with INF-γ (12.5mcg/m^2 s.c. 3-times weekly) was initiated to enhance killing of *C. burnetti* through monocytes/macrophages; so far no new lesions have occurred.

C. burnetti infection should be considered in paediatric patients with chronic recurrent multifocal osteomyelitis. Optimal therapy remains to be established and may consist of prolonged antibiotic therapy and adjuvant immunotherapy.

1. Nourse, CID 2004

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SEPTIC ARTHRITIS: A 5 YEAR RETROSPECTIVE STUDY

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Background: Septic arthritis (SA) is a disabling and potentially life-threatening condition requiring prompt diagnosis and treatment.

Aims: Comparing results after the implementation of management guideline in our department in January 2007 and compliment evaluation.

Materials and methods: Retrospective study of children with SA, admitted between January 2003 and June 2008. Demographic, clinical, laboratory, imagiologic, therapeutic data and outcome were analysed.

Results: 56 patients, with median age of 23 months (max 15 years; min 17 days). Risk factors were present in 19,6% (congenital heart disease and trauma) and co-morbidities in 16,1% (varicella, meningococcal sepsis, pneumonia, piomyositis, bursitis and Kawasaki disease). Microbiological diagnosis was achieved in 32,1%, by blood culture (11%), pus aspiration (5.4%) or both (16%). *Staphylococcus aureus* was the predominant organism (17,9%).After guideline introduction we verified: a slight increase in laboratory data (WBC 90,5 vs 100%, p=0,5; CRP 88 vs 100%, p=0,3; ESR 40,5 vs 64,3%, p=0,1); synovial fluid analysis (0 vs 21,4%, p=0,01), imaging (US 88 vs 92%,p=0,6; bone cintigraphy 19 vs 35,7%, p=0,25) and microbiologic studies (pus aspiration cultures 59 vs 78,6%, p=0,3). There was no significant change in therapeutic arthrocentesis (83,3-85,7%, p=1). Antibiotic use according to the guideline was 71% and the duration was accomplished in 64%. There was no significant reduction on median in-hospital stay (14± 13,2 vs 13,5± 8,7days, p=0,5) and in 50% the follow-up was insufficient.

Conclusion: Our audit identified deficiencies in standards of care of SA, despite a management improvement after guideline implementation.

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OSTEOARTICULAR INFECTIONS IN BELGIAN CHILDREN : A SURVEY OF CLINICAL, BIOLOGICAL, RADIOLOGICAL AND MICROBIOLOGICAL DATA

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The aim of this study is to report the most frequent pathogens which were found to be responsible for osteo-articular infections in infants and children in Belgium, and to propose an appropriate empirical antibiotic therapy to apply before identification of the responsible pathogen. Clinical presentation, imaging and blood biology are also reviewed and analysed.

Fifty-six cases of osteo-articular infections (acute/subacute osteomyelitis, osteo-arthritis, septic arthritis, spondylodiscitis, sacro-iliitis) treated between 2001 and 2007 were retrospectively reviewed, focusing on clinical, biological, microbiological and radiological data.

Septic arthritis, acute osteomyelitis, septic osteo-arthritis and sacro-iliitis often have a loud clinical (fever, pain, inflammatory signs) and biological presentation. Subacute osteomyelitis and spondylodiscitis are almost asymptomatic, but for functional impairment. The responsible pathogen was isolated in 38% of the cases. The most frequent pathogen was *Staphylococcus Aureus*, followed by *Pneumococcus*, *Streptococcus* A and B, *Kingella Kingae*, and *Haemophilus*. None of them had resistance to usual antibiotics.

Functional impairment is the only constant symptom of osteo-articular infections. Other clinical and biological symptoms may be absent, making the diagnosis often difficult. We recommend oxacillin (>5 years) or a combination of oxacillin with cefotaxime (< 5 years) in the empirical treatment of osteo-articular infection, and a total of 4 weeks of treatment.

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SALMONELLA PARATYPHI B SKULL OSTEOMYELITIS AND SICKLE CELL DISEASE

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We report the case of a 17 year-old teenager with an uncommon site of chronic osteomyelitis.

She had been followed up for severe sickle cell disease (SCD). She was hospitalized for an acute febrile illness. Her physical examination was unremarkable. Her laboratory findings were normal, without elevated inflammatory markers. Blood culture results revealed an occult bacteremia due to *Salmonella paratyphi B*. She was first treated by 48 hours of IV ceftriaxone, followed by 8 days of oral ciprofloxacin. Her clinical evolution remained satisfactory and she was discharged after 6 days. She was rehospitalized 3 months later for severe headache. A 2 cm local tumefaction of the skull close to the right parietal bone was noticed. New laboratory exams were again normal. MRI demonstrated parietal osteomyelitis with severe lesions of the right parietal bone spreading to the soft tissue and complicated by extradural abscess. Percutaneous aspiration of this collection was positive for *Salmonella paratyphi B*. The collection aspirated twice and the bone abscess was first treated by oral ciprofloxacin. The clinical and diagnostic imaging response was very poor during the first weeks of antibiotic treatment. Surgery was performed after 2 months of oral therapy to drain the collection and incise the necrotic bone. Oral ciprofloxacin was given during 6 months and a good clinical and radiological outcome was obtained.

Osteomyelitis of the skull is a rare disease, even in immunocompromised patients such as SCD subjects. This infection is frequently complicated by extradural abscess. Treatment must include surgery and antibiotic therapy.

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SEPTIC ARTHRITIS AND OSTEOMYELITIS IN CHILDREN: A REVIEW OF CASES FROM 1997-2006, OXFORD, ENGLAND

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Background: Osteomyelitis (OM) and septic arthritis (SA) are serious bacterial infections with potential long-term morbidity. There is a paucity of evidence upon which to base treatment recommendations. We reviewed management of all cases of SA and OM in children aged < 10 years at the John Radcliffe and Nuffield Orthopaedic Hospitals, Oxford during 1997-2006.

Methods: Cases of SA and OM were identified through clinical discharge coding and subsequent chart review.

Results: Forty six cases of OM (30 < 5 years of age) and 56 cases of SA (45 < 5 years of age) were identified. Duration of presenting symptoms for OM was 1-42 days (median = 5.5) and for SA 1-14 days (median =1). Positive bacterial cultures were obtained for OM in 11/35 (31.4%) with surgical samples and for SA in 25/52 (48%) with joint aspirates. Of 36 positive cultures the most frequent organisms were Staphylococcus aureus (10), Group A streptococcus (9) and Streptococcus pneumoniae (3). Empiric treatment with beta-lactam antibiotics was used in 93% of cases, median total treatment duration of 44 days for OM and 29 days for SA. Of 86.9% OM patients with a recorded outcome, complete recovery occurred in 95 %. Outcome for patients with septic arthritis was recorded in 73% of patients treated, with complete recovery in 93.2%.

Conclusion: For OM and SA the causative organism was identified in under half the cases with microbiological specimens. Despite variable practice with respect to antibiotic choice, route and duration of treatment, most patients achieved complete recovery.

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HIP AND KNEE PAIN IN A CHILD WITH BACTEREMIC PNEUMOCOCCAL PNEUMONIA AND EMPYEMA

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Background: *Streptococcus pneumoniae* is a leading cause of pediatric invasive infections including bacteremia, meningitis and pneumonia. However arthritis is a scarcer manifestation of pneumococcal disease.

Clinical case: A 3-year old girl -healthy and properly vaccinated- presented with fever and dyspnea. Laboratory and radiographic data indicated an acute inflammatory syndrome with pulmonary consolidation and pleurisy. Empiric IV cefotaxime was started. After 2 days, computed tomography identified a loculated empyema requiring surgical drainage. Blood cultures isolated a penicillin-susceptible pneumococcus (serotype 1); the antimicrobial regimen was therefore switched to IV penicillin. Meanwhile the girl developed pain and reduced mobility of the left leg. Ultrasonography showed small effusions of hip and knee joints. Scintigraphy excluded other bone involvement. Pneumococcal arthritis was confirmed by PCR analysis of the joint fluid. Protracted fever lasted for 2 weeks, but serial blood cultures remained negative. CRP level and leukocytosis remained high for 3 weeks. The chest drain was retrieved after 5 days. Antibiotics were administrated during 6 weeks with a parenteral-oral sequence. Despite pulmonary recovering, residual joint dysfunction persisted after 1 month.

Conclusion: We report an unusual manifestation of pneumococcal disease, including complicated pneumonia, bacteremia and polyarticular arthritis. Septic arthritis might be underestimated since the diagnosis of joint infection is mostly performed by culture and direct fluid examination. PCR is a sensitive method to distinguish septic from reactive arthritis without requiring viable pathogens. In presence of invasive infections, molecular diagnosis may be helpful in case of negative culture results or prior antibiotic use.

CONGENITAL INFECTIONS

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FETAL VARICELLA EMBRYOPATY: CASE REPORT

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Background: Fetal Varicella Embryopaty is a rare disorder in which affected infants have multiple congenital abnormalities due to the mother´s infection with varicella zoster virus early during pregnancy.

Objectives: To detect the prenatal ultrasound findings associated with Fetal Varicella Embryopaty and to specifythe most appropriate safety method of Fetal Varicella Embryopaty prenatal diagnosis.

Patient selection: A 21-year-old female,exposed accidentally to varicella zoster virus during the first weeks of pregnancy, was referred at 20 weeks´ gestation for aselective ultrasonography for detection of fetal abnormalities.

Methods: Ultrasonography at 16 weeks of pregnancy; selectiveultrasonography for detection of fetal abnormalities, triple test and amniocentesis.

Results: Ultrasound examination revealed a single fetus with an abnormal fetal development: microcefaly, microphthalmia and cataracts, bilateral clubbed feet, abnormally positioned handsand polyhydramnios. Fetal chromosomal analysis showed normal male karyotype: 46,XY. After an extensive counseling the parentsdecided to terminate the pregnancy. The pathology exam confirmed all the malformations.

Conclusions: The necessity of ultrasound examination for the prenatal detection of fetal abnormalities to all pregnancies and especially for the risk categories.

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LONG-TERM FOLLOW-UP OF TOXOPLASMA GONDII CONGENITAL INFECTION: STUDY OF 11 MOTHER/CHILD PAIRS IN A SINGLE CENTER

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Background and aims: The clinical pattern of congenital Toxoplasma gondii (Tg) infection ranges from asymptomatic to severe manifestations. The risk of late complications has been extensively described. Aim: to evaluate long-term outcome of vertically transmitted Tg infection.

Methods: Retrospective study (January 1997 - December 2007) of all children in which Tg infection was microbiologically confirmed during pregnancy or in the first year of life.

Case definition: positive IgM and/or IgA, persistence of positive IgG beyond 12 months of age or positive PCR in amniotic fluid or blood. Yearly ophthalmological and clinical follow-up was performed in all cases.

Results: Eleven children were included. Median age: 9 years (2-22). Vertical infection was dated in the third trimester in 6/11 cases (undetermined in 5). Amniocentesis was performed in 2/11 cases, with positive PCR to Tg in both. In the resting 9 cases diagnosis was established by serological methods. Spyramicin was given to 7/11 mothers, and 8/11 children received treatment with pyrimethamine-sulphadiazine and folinic acid for one year. 4/11 newborns were clinically asymptomatic and 7/11 symptomatic. Sequelae were detected in both groups (2/4 and 6/7): chorioretinitis (7), severe neurological sequelae (3, 1 died) and partial hearing loss (1). Late onset and reactivation of chorioretinitis were detected at a median age of 3,5 years (4 cases).

Conclusions: The risk of late onset complications (mainly chorioretinitis) even in asymptomatic Tg infected newborns confirms the importance of a long-term ophtalmological follow-up. Significant efforts should be done to standardize the management of Tg infection during pregnancy.

P124

CONGENITAL ANOMALIES AMONG NEONATES BORN TO WOMEN WITH ACTIVE CYTOMEGALOVIRUS INFECTIONS

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Background and aims: Cytomegalovirus (CMV) can cross the placenta and cause fetal infections. This study was sought to follow-up a number of pregnant women with serological evidence of active CMV infection until delivery to determine the incidence and types of symptomatic congenital CMV infections among the neonates.

Methods: Sixty women with and 50 women without serological evidence of active CMV infection were enrolled in this study. Infection was diagnosed by utilizing specific ELISA kits to detect the specific CMV-IgM and IgG isotypes in serum of the participant women and CMV-IgM marker in cord blood samples obtained from the neonates after delivery.

Results: Specific CMV-IgM isotype was detected in cord blood samples of 6 (10%) overtly sick infants (with different congenital anomalies) born to mothers with serological evidence of active CMV infection. Central nervous system abnormalities were detected in all six cases (2 with microcephaly and 4 with hydrocephaly).

Conclusions: Congenital CMV infection should be suspected in infants born with congenital abnormalities, especially those of the central nervous system. Moreover, the detection of more cases of hydrocephalus in this region is worthwhile and notable.

P125

PERINATAL TRANSMISSION OF HEPATITIS C VIRUS - HOSPITAL SANTO ANDRÉ, LEIRIA-PORTUGAL 2002-2006

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Background: The vertical transmission of hepatitis C virus (HCV) is the main route of infection in children, occurring in rare cases (0-10%). Current recommendations for HCV screening include anti-HCV testing at age >18 months to reduce false positives and false negatives.

Aims: To characterize the population of children born to HCV-positive mothers in Hospital Santo André. To identify risk factors for perinatal HCV transmission and improve approach to HCV screening in our department.

Methods: Retrospective descriptive study of children born to HCV-positive mothers between January 2002 and December 2006. New anti-HCV testing were performed in cases that didn't meet recommendations for HCV screening.

Results: We included 59 children born to HCV-positive mothers in a total of 12 985 births, corresponding to a prevalence of 0.45%. We identified a child with HCV infection without any risk factor for perinatal transmission. Of the children with negative anti-HCV at age 18 months, half had done anti-HCV prior to age 9 months, all positive. Children discharged because of negative anti-HCV at age 9 months were called in a 2nd phase of the study, for new anti-HCV at age > 18 months, beeing all negative.

Conclusions: The perinatal HCV transmission rate was 2.9%. There were no identified risk factor for perinatal transmission in the single case of HCV infection. Regarding anti-HCV at age 9 months, there was a high rate of false positives but no false negative. This study has enabled the detection and correction of mistakes in our approach to HCV screening.

P126

CONGENITAL TUBERCULOSIS: REPORT OF TWO CASES

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Background and aims: Congenital tuberculosis is a rare disease, fatal when untreated and with non specific signs and symptoms.

Methods: Two cases of congenital tuberculosis diagnosed at Hospital La Paz (Spain) in the last year are described. Both children were born in Madrid but their mothers came from Morocco.

Results:

Case 1: A 3-month-old boy presented with cough from the first month of life. Chest radiograph showed hilar adenopathy and tuberculin skin test was positive. After 12 days of treatment, the patient's condition worsened developing respiratory distress and cyanosis. CT scan and bronchoscopy revealed left main bronchus compression. Gastric aspirate culture was positive for *M. tuberculosis*. The mother suffered from primary sterility due to tubal obstruction and pregnancy was achieved by in vitro fertilization.

Case 2: An 8-day-old preterm neonate presented with fever and respiratory distress. He received broad-spectrum antibiotics with no improvement. Chest radiograph showed miliary pattern. Tuberculin skin test was negative. Bronchial washings yielded acid-fast-bacilli (AFB) on smear microscopy and *M. tuberculosis* by polymerase chain reaction (PCR) and by culture.Both children were successfully treated with antitubercular drugs and corticosteroids.Both mothers had normal chest radiograph and negative sputum AFB smear and culture. Tuberculin skin test was positive in case 1 1and negative in case 2. Endometrial biopsies demonstrated tubercular granulomas and PCRs were positive for M. tuberculosis.

Conclusions: Congenital tuberculosis can mimic many perinatal diseases making the diagnosis difficult. It is important to consider it, particularly if the mother is at risk for tuberculosis, or suffers from tubal sterility.

P127

THE CORRELATION BETWEEN ASYMPTOMATIC CONGENITAL CYTOMEGALOVIRUS (CMV) INFECTION AT BIRTH AND LATER OUTCOMES IN CHILDREN

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The correlation between asymptomatic congenital CMV infection at birth and later physical and developmental outcomes of children remain unclear.

Objectives: This study was undertaken to ascertain whether children with congenital cytomegalovirus (CMV) infection at birth, but without neurologic symptoms, differed in somatic, neurologic, developmental, or intellectual status from matched control children at 4-6 years of life.

Study design: Retrospective cohort study. 32 of all the 44 children with asymptomatic congenital CMV infection at birth were investigated at age of 5-6 years for surveying physical growth and intellectual developments. The neurologic status was assessed with the Stott test and intellectual development with the Wechsler Intelligence Scale for Children.

Results: no significant differences were noted between the asymptomatic congenital CMV infection children and the controls in average weight, height and head circumference (both $p>0.05$). However, the intellectual development was disproportion in asymptomatic congenital infected children. Compared with the control group, both global development quotient (DQ) and full-scale intelligence quotient (IQ) scores of asymptomatically infected children were worse ($t=2.19$, $p=0.031$; $t=2.48$, $p=0.015$), especially on language DQ scores ($t=3.25$, $p=0.002$) and verbal IQ scores ($t=3.88$, $p=0.001$), as the incidence rates of mental retardation (DQ/IQ< 70), ($p>0.05$).

Conclusions: Although asymptomatic congenital CMV infection did not have significant influence on the later physical development, it is obviously an important factor correlating with long-time intellectual and cognitive outcomes, especially on the development of language. It is necessary to survey CMV congenital infection and monitor the early intellectual development of children with asymptomatic congenital CMV infection.

P128

GANCICLOVIR TREATMENT OF CONGENITAL CYTOMEGALOVIRUS DISEASE IN TERM AND PRETERM NEWBORNS

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Background and aims: Ganciclovir (GCV) is used in the treatment of serious congenital cytomegalovirus disease in the newborns. The treatment needs to be started early after birth and be extended to obtain adequate therapeutic effect.

A total of 57 newborns with a history congenital CMV disease, hospitalized at the Neonatology Department between January 2002 and December 2006, treated with GCV, were analyzed.The aim of this study was to estimate the safety of ganciclovir therapy in term and preterm newborns.

Methods: The individual doses of GCV were used and its blood levels were analyzed with HPLC method.In the study group there were 47 (82,46%) term newborns and 10 (17,54%) premature babies (~ 37 weeks).

Results: In the study group the mean body weight in the start up point of GCV therapy was 3188,60 g ± 747,65 g (1400-4865 g). The treatment was started in the 14th (5-35) day of life. The mean duration of therapy was 21 (13-44) days. The mean daily dose of GCV was 12,28 ± 4,82 mg/kg/day. In 36 (63,16%) newborns the doses were increased to obtain appropriate therapeutic levels of the drug in the blood.

The following side effects were noted both in term and preterm newborns during the GCV treatment: neutropenia in 19 (33,33%), anemia in 30 (52,63%), elevated aminotransferase levels in 8(14,04%).No thrombocytopenia was observed. Renal function during and after treatment was normal.

Conclusions: GCV is well tolerated in newborns with congenital cytomegalovirus infection, both mature and premature,if its serum concentration monitoring and its individual doses are used.

P129

SINGLE CENTRE EXPERIENCE WITH CONGENITAL TOXOPLASMOSIS: ANALYSIS OF PATIENTS MANAGED IN OUR DEPARTMENT (WROCLAW, POLAND) IN LAST 8 YEARS

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Background and aims: Congenital Toxoplasmosis may involve the retina and brain with long-life sequelae. Signs and symptoms are similar to other congenital infections and the disease is often diagnosed late. The aim of the study was to sum up single centre experience with management of toxoplasmosis and analysis of patients (age, sex, manifestations, mode of diagnosis) treated in our department in last 8 years.

Methods: Descriptive retrospective study; 13 children with congenital toxoplasmosis attending the Department of Pediatrics Infectious Diseases in Wroclaw, Poland between 2000 and 2007 were enrolled.

Results: 33 children suspected of congenital *Toxoplasma gondii* infection were referred to our department (about 0,4-0,5% of all admissions) in analyzed period. The diagnosis was confirmed in 13 children (8 girls and 5 boys) aged 5 days - 3 years (median 3 months), Toxoplasmosis was responsible for 0,1-0,3% of all admissions per year. Disease was diagnosed with serological tests in all patients but two: in one the diagnosis was made by PCR and in the other during autopsy. The most frequent manifestation were: intracranial calcifications, dilatation of ventricles and retinochoroiditis observed in 6/13, 6/13 and 5/13 patients respectively. 12/13 children were treated with pirymethamine/sulpha with 100% survival but sequelae were found in 10/12 children in follow up ranging from 1 to 8 years.

Conclusion: Though congenital toxoplasmosis is rarely responsible for hospitalizations in children, it results in sequellae in the vast majority of children and should be considered in any child with unexplained abnormalities of eye or CNS.

P130

MONITORING THE HIGHS AND LOWS OF CONGENITAL CMV

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Background: During treatment for congenital CMV (cCMV) clinicians may monitor viraemia but there is currently no information to support its superiority to viruria. No published studies to our knowledge report on viral load (VL) in saliva or the relationship between VL in different body fluids.

Aims: To observe and compare changes in VL in different body compartments during treatment for cCMV.

Methods: VL of samples of blood, urine and saliva was measured using CMV PCR as part of a prospective study. VL data for blood and urine were also available from a national treatment registry, set-up with ESPID funding, and from clinical samples received in our laboratory.

Results: A total of 207 samples (83 blood; 86 urine; 38 saliva) were obtained at a mean of 9 time points from 12 babies treated for cCMV. 10/12 babies were viraemic at birth. Mean VL from specimens within 7 days of commencing treatment was 3.2 ± 0.94, 7.1 ±1.1 and 7.4 ±1.0 in blood, urine and saliva respectively. Urine and saliva VL followed a similar declining trend that was distinct from that seen for blood. Complete viral suppression was uncommon during a 42 day course of treatment.

Discussion: Despite a lower baseline, full suppression of viraemia during treatment was rare. Preliminary results show that saliva may be a useful tool for monitoring viral response to treatment. The relevance of viral suppression in each of these body compartments and how they relate to VL in the central nervous system are yet to be determined.

P131

MOTHER-TO-CHILD TRANSMISSION OF CYTOMEGALOVIRUS IN CHILDREN OF HIV-POSITIVE MOTHERS

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Infections with cytomegalovirus (CMV) remain significant clinical problem especially concerning immunodeficient patients. Children of HIV-positive mothers undergo panel of diagnostic test for possible vertical infections. The aim of the study was to analyse the rate of CMV-transmission in these children in addition to routine monitoring.

Forty newborns of HIV-positive women were enrolled in the study, 26 girls and 14 boys, gestational age 33-39 week (mean 36.8±1.8 week), birth weight 2060-3820g (mean 2700±366g). Children were tested for HIV, HCV, CMV in week 1, 4 and 16 after birth. In all children HIV viral culture with detection of p24 antigen and HIV-RNA was preformed. Children positive for anti-HCV antibodies were tested for the presence of HCV-RNA in the blood by RT-PCR. Patients with the presence anti-CMV antibodies were tested for the presence of CMV-DNA in blood and urine by quantitative PCR assay. History data, birth parameters and clinical findings were compared between CMV-positive and negative children.

No child from the study group was found to be HIV-positive. One HCV infection was detected. However CMV-DNA was found in the blood in 12 patients (30%) and in the urine in 30 children (75%). Children with CMV-DNA in the urine had lower birth weight (2607.6±268.0 vs. 2996±493.9; p=0.03). In 2 children CMV-DNA was detected in the blood late the week 16 with significant peripheral lymphadenopathy.

CMV-infection is relatively common among children of HIV-positive women. Test should be therefore included into standard monitoring for early detection of possible symptomatic cases.

P132

SEROPREVALENCE FOR TOXOPLASMOSIS OF MATERNAL SEROLOGY FOR COLLECTION OF UMBILICAL CORD BLOOD IN BRAZIL

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Background and aims: Umbilical cord blood (UCB) is an important source of stem cells. In Brazil, although the storage do not requires maternal serological screening for Toxoplasma gondii, sometimes IgG and IgM anti-toxoplasma are done. We aimed to describe the percentage of TOXO (IgG and IgM) reactive samples in mothers who decided to store UCB in a private umbilical cord blood bank.

Methods: Descriptive, transversal and retrospective study of 1931 blood samples. Results of IgG and IgM anti-TOXO had been carried through.

Results: All 1931 samples analyzed were obtained from high socioeconomic class women collected by a private UCB bank. IgG negative 1359 (70,4 %), IgG positive 571 (29,6%), inconclusive 1 (0,1%), IgM negative 1918 (99,3%), IgM positive 11 (0,6%), inconclusive 2 (0,1%).

Conclusions: The seroprevalence of anti-toxoplasma IgG in this group was 29.6% , lower than in general Brazilian pregnant women´s population, that varies from 32.4% to 77.1%, depending on the region. That can be explained by the higher socioeconomic conditions of the this group. The seronegative leads to the risk of the women infection during pregnancy. Only 0.6 % had probably recent infection (demonstrated by the presence of IgM anti-toxoplasma), what places the newborns at risk of infection. The risk of transmission to the fetus on an acute infection is 20- 50%, and can cause hydrocephaly, corioretinitis, mental retardation, cerebral calcification and death.

P133

SEROPREVALENCE FOR CYTOMEGALOVIRUS OF MATERNAL SEROLOGY FOR COLLECTION OF UMBILICAL CORD BLOOD IN BRAZIL

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Background and aims: Umbilical cord blood (UCB) is an important source of stem cells. In Brazil storage requires maternal serological screening, including IgG and IgM anti-cytomegalovirus (CMV). We aimed to describe the percentage of CMV (IgG and IgM) reactive samples in mothers who decided to store UCB in a private umbilical cord blood bank in Brazil.

Methods: Descriptive, transversal and retrospective study of 3779 blood samples, collected by a private UCB bank. Results of IgG and IgM anti-CMV had been carried through.

Results: All 3779 samples analyzed were obtained from high socioeconomic class women. IgG negative 1163 (30,8%), IgG positive 2578 (68,2%), inconclusive 38 (1,0%), IgM negative 3665 (96,9%), IgM positive 61 (6,1%), inconclusive 52 (1,4%), not available 1 (0,02%)

Conclusions: The seroprevalence of CMV infection in this group was 68.2%, lower than in general

Brazilian population (80%), which can be explained by the higher socioeconomic conditions of this group. However, 1.6 % had probably recent infection or reactivation of the virus (demonstrated by the presence of IgM anti-CMV). Intrauterine CMV infection is the most common of all recognized intrauterine infections, occurring in an estimated 0.4%-2.3% of all live births, and it can have a variable outcome. Although studies on long-term follow-up are needed for a better understanding of the effectiveness of mass screening, identifying the women under risk of primary CMV infection may help to prevent congenital infection and to provide early treatment for the neonates affected.

P134

MATERNAL SEROLOGIC PROFILE FOR COLLECTION OF UMBILICAL CORD BLOOD IN BRAZIL

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Background and aims: Umbilical cord blood (UCB) is an important source of stem cells. According to RDC- resolution #153/04 of ANVISA, in Brazil, storage requires maternal serological screening, obtained during the partum. We aimed to analyze and describe the serologic profile of mothers who decided to store UCB in a private cord blood bank.

Methods: Descriptive, transversal and retrospective study of 3780 blood samples collected by a private UCB bank. These serologies had been carried through: HBsAg, anti-HCV, Lues (VDRL and FTA-abs), HIV I/II, HTLVI /II.

Results: From 3780 samples, 21 (0.6%) were positive for HBsAg, and only 6 (0.2%) were positive to anti-HCV. For HIV, 2 (0,1%) were positive, confirmed by other exam. For HTLVI /II, from 3778 samples, 6 (0.2%) were positive. The same result was found for Lues, using the VDRL test, although only one (0.03%) was confirmed in the FTA-abs test.

Conclusions: All samples were obtained from high socioeconomic class women, who probably are concerned about diseases prevention, as they pay for a private cord blood bank. Therefore, the good results found in this study, probably does not represent the serologic profile for general population. Other researches among this topic must include other segments of the population, including mothers from different social levels. In this way, we can build effective strategies to prevent infectious disease in pregnant women and their children.

P135

CT/ECHOCARDIOGRAPHIC/TRANSCRANIAL TRANSFONTANELLE/ABDOMINAL ULTRASOUND FEATURES IN PAEDIATRIC NON SYNDROMIC ISOLATED CONGENITAL OPHTHALMOPATHIES,IMPLICATIONS FOR THE DETECTION OF A COVERT CONGENITAL RUBELLA SYNDROME

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Background/purpose: In Congenital Rubella syndrome there are constellations of clinical features implicationg the Central nervous system,Cardiovascular system,Eyes and the heamato-lymphatic systems.Embryological , the optic vesicles/cups are derived from the fore brain, hence it will be plausible to infer that causalities will involve the two structures synchronously. Cardiovascular defects are commonly associated with other congenital structural anomalies with quality of life and mortality implications.A review where an interplay of imaging modalities was applied to explore causality factors related to congenital rubella syndrome in a case series of clinically congenital isolated opthalmopathies is described.

Imaging details: The Computer assisted tomographic /Echocardiographic /Transcranial Transfontanelle Ultrasound features in 15 cases of congenital Ophthalmopathies presenting in infancy and childhood were reviewed.

Cases: Congenital developmental cataracts 2, familial,5 non familial ,5 congenital glaucoma /buphthalmos, 3 nystatgmus.The High Resolution CT 2D/M mode Echo/Transcranial Transfontanelle Ultrasound were undertaken,evaluated,validated and interpreted in a standardized manner by the Radiologist /Cardiologist.The study concerned 9 females and 7 males all aged below one year.

Results: The features were piquantly unremarkable in all cases. This Potpourris of imaging modalities will be most relevant in settings where causality by Rubella is plausible but may be very clinically covert. The unyielding imaging features in these cases intimates that structural defects within the limits of these imaging modalities are unlikely to be related defects, it is possible that on progression to MRS/SPECT/Electroretinogram/ Visual Evoked Potentials more eloquent implicating or associated lesions could be deciphered which could direct genetic counseling, generate hypothesis and could also direct management and research.

P136

CONGENITAL SYPHILIS - A PREVENTABLE DISEASE STILL OCCURRING - REPORT OF FOUR CASES

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Introduction: Congenital syphilis is preventable by serological screening and correct treatment of pregnant women. However it is still a significant public health issue and increasing incidence has been reported in several European countries.

Procainic-penicilin is not currently available in our country and choosing to treat suspected cases implies admission for 10 days of IV-treatment.

Case report: We report four cases fulfilling the CDC case definition of congenital syphilis, admitted to our unit in one-month period for IV-treatment with penicillin.

Two newborns had unsupervised gestations. One mother refused treatment while the others received adequate penicillin regimen. One mother was treated in the last month of pregnancy, and in one other case the partner refused treatment. Only in one child the non-treponemic titre was fourfold greater than maternal titre. In the other cases decision to treat was based on presence of symptoms, absence of expected decrease in maternal non-treponemic titre after treatment, and mother treated one month before delivery.

Two of the newborns were born prematurely and small for gestational age, one of them had severe disease with hepatosplenomegaly, ascitis, thrombocytopenia and conjugated hyperbilirrubinemia.

None of the children had alterations in the long bone X-ray and LCR examination was not conclusive.

Discussion: These four cases illustrate the clinical implications of a preventable disease. Current guidelines result in treating many non-infected children. Appropriate prenatal measures can not only avoid the consequences of dramatic symptomatic cases as well as prevent the long hospital stay needed to complete treatment of suspected cases.

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ANTENATAL DIAGNOSTIC PROBLEM OF CONGENITAL RUBELLA

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Rubella infection in the mother during pregnancy can lead to congenital rubella syndrome characterized by microcephaly, growth retardation, cataracts, patent ductus arteriosus, mental retardation and hepatosplenomegaly especially if rubella is acquired in the 1st trimester. With adequate prenatal screening tests and use of rubella vaccine, perinatal transmission of rubella has almost been abolished in developed countries. During pregnancy, several laboratory tests such as amniotic fluid analysis and fetal blood sampling for rubella polymerase chain reaction (PCR) or presence of rubella IgM have been used to diagnose fetal affection and then determine about continuation or medical termination of pregnancy.

Case report: A 30 day old preterm neonate presented with jaundice and clay coloured stools since Day 7 of life. He was second of twins with birth weight of 800 grams and delivered at 7 months of gestation. Mother had fever with rash at 5 months of gestation and her TORCH titres at that time were positive for Rubella IgM. She underwent amniocentesis and amniotic fluid rubella PCR was negative following which she continued her pregnancy. Both babies were tested for Rubella IgM at birth and both had a positive Rubella IgM though urine for rubella PCR were negative. On presentation, the child had jaundice, Ascitis, hepatosplenomegaly, dilated abdominal veins. Other systemic examination was normal. Investigations showed thrombocytopenia, hyperbilirubinemia, elevated liver enzymes and peripheral pulmonary Stenosis suggestive of congenital rubella syndrome. Subsequently the child had decreasing jaundice and normalization of liver enzymes after 2 months.

EMERGING AND RE-EMERGING INFECTIONS

P138

HUMAN METAPNEUMOVIRUS AND HUMAN CORONAVIRUS INFECTION AND PATHOGENICITY IN SAUDI CHILDREN HOSPITALIZED WITH ACUTE RESPIRATORY ILLNESS

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Background and aims: Human metapneumovirus (hMPV) and the Netherland human coronavirus (HCoV-NL63) have been isolated from children with respiratory tract infection. The prevalence of these viruses has not been reported from Saudi Arabia. We sought to determine whether hMPV and HCoV-NL63 are responsible for acute respiratory illness and determine clinical features and severity in hospitalized pediatric patient population.

Methods: Nasopharyngeal specimens from children less than 16 years old who were with acute respiratory diseases were tested for hMPV and HCoV-NL63 by reverse transcriptase-polymerase chain reaction. Samples were collected from July 2007 to November 2008.

Results: Both viruses were found among Saudi children with upper and lower respiratory tract diseases during the autumn and winter of 2007 and 2008, contributing to 141.1% of all viral diagnoses with individual incidences of 9.4% (hMPV) and 1.3% (HCoV-NL63) among 489 specimens. Initial symptoms included fever, cough, nasal congestion. Lower respiratory tract disease occurs in immunocompromised individuals and those with underlying conditions. Clinical finding of respiratory failure and culture negative shock have occurred in 7 children infected with hMPV and have of hematologic malignancies, mylofibrosis, Gaucher disease, and congenital immunodeficiency: 2 of the 7 patients died with acute respiratory failure. All children infected with HCoV-NL63 had underlying condition, one of the 4 patients developed respiratory failure.

Conclusion: hMTP and HCoV-NL63 are important cause of acute respiratory illness among hospitalized Saudi Children. hMPV infection in the lower respiratory tract is associated with morbidity and mortality in immunocompromised children. HCO-NL63 may cause severe lower respiratory disease in those with underlying condition.

P139

ESBL (EXTENDED SPECTRUM BETA LACTAMASE) INFECTIONS - AN EMERGING PROBLEM IN CHILDREN

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Background and aims: There is an emergence of infections with ESBL-producing micro-organisms recently. They remain poorly characterised in children. We sought to characterise children in a teaching hospital from whom an ESBL-producing organism had been isolated.

Methods: We identified all children under sixteen years of age who had ESBL-producing organism isolated in the year 2007.The referral source was contacted for further information where possible. Clinical details and treatment were analysed to determine likelihood of infection or colonisation.

Results: Fifteen children were identified, aged three months to nine years. Thirteen isolates were obtained from urine, one each from a wound swab and a cough swab. Three isolates were obtained from hospitalised children, but only one of these needed treatment. This child presented with lymphadenitis and continued to be pyrexial and irritable despite treatment with cephalosporin. Subsequently ESBL producing organism was isolated from the urine and she responded to appropriate antibiotic. Data was available for nine out of twelve patients originating from the community. Of these, four had repeat specimens which didn't grow ESBL-producer again. Three were treated and two remained asymptomatic and well. Two asymptomatic children had recently visited the Indian subcontinent.

Conclusions: ESBL-producing organisms are increasingly isolated in children, but from our review appear frequently to be colonisers rather than pathogens. However, it is very important to be vigilant about the possibility of ESBL infection in children especially if they fail standard antibiotic therapy or they had recent visit to Indian subcontinent which has high reservoir of resistant organisms.

P140

TICK-BORNE LYMPHADENOPATHY, A RICKETTSIAL DISEASE IN CHILDREN. DESCRIPTION OF 34 CASES IN SPAIN

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Background: A newly recognized rickettsial disease, named TIBOLA (tick-borne lymphadenopathy), was first identified twelve years ago. The aim of this study was to describe the epidemiological and clinical aspects of patients with TIBOLA diagnosed in children in Catalonia (North-eastern Spain)

Methods: The study included all patients < 14 years treated in our hospital who presented characteristic clinical symptoms of TIBOLA (the presence of an inoculation lesion after a tick bite with regional lymphadenopathies). Inclusion period: 2000 - 2008. Serology tests: for *Rickettsia conorii* and *R. slovaca*. The presence of Rickettsia was assessed by PCR in blood, skin biopsy and ticks from patients.

Results: Thirty four patients fulfilled the inclusion criteria. Mean age: 7.2 years (2-13). 23 males. 26 cases appeared from October to April. 33 patients were tick bite on the scalp. A necrotic eschar was observed in 27 cases and was surrounded by a perilesional erythematous halo in 21. All patients had painful regional lymphadenopathies. Serology for *R. conorii* was positive in 4 cases. Serology for *R. slovaca* and PCR were negatives.The tick, identified as *Dermacentor marginatus*, was studied in six patients. Three out of them were positive for sequences compatible with *R. slovoca* as determined by DNA sequencing. 30 patients received antibiotic treatment. Progress was satisfactory in all cases.

Conclusion: TIBOLA is present in Catalonia. Although clinical and epidemiologic manifestations are very specific microbiologic confirmation is difficult.

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P141

SITUATION OF CRIMEAN-CONGO HAEMORRHAGIC FEVER IN IRANIAN CHILDREN IN 2008

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Background and aims: Crimean-Congo Haemorrhagic Fever (CCHF) disease is one of the most important infectious diseases in Iran. This viral zoonotic disease has a mortality rate around 50%, its agent is a virus of the genus Nairovirus and family Bunyaviridae. It is transmitted to humans by infected tick bite, handling of infected blood or tissues or nosocomially. CCHF has been reported from Africa, Eastern Europe, Asia and the Middle-East.

Methods: The laboratory of Arboviruses and Viral Haemorrhagic Fevers of the Pasteur Institute of Iran (National Reference Center) has collected Iranian CCHF probable children's sera (aged from 2 months to 14 years) in 2008. They were all checked by specific ELISA for detecting antibodies against CCHFV and by RT-PCR assay for detecting the genome of the virus.

Results: In 2008 , the number of confirmed cases is 9 and 2 ended to death. Among the 9 confirmed cases, 5 were boys and 4 were girls. Two of confirmed cases had a history of contact with the blood or tissue of infected livestock.6 were of rural origin and 3 were of urban origin.

Conclusions: Our studies demonstrate that CCHF is one of the children infectious diseases in rural areas in Iran. These studies also show the fact that in rural areas children who had contact with blood and exudates of infected livestock (as CCHF is asymptomatic in livestock) are more at risk. So informing children and their parents about routes of transmission and prevention of this disease is really crucial.

P142

SCREENING OF CHAGAS DISEASE IN BOLIVIAN PREGNANTS AND FOLLOW UP OF THEIR CHILDREN IN A NON-ENDEMIC AREA

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Introduction: Spain is the first country in bolivian immigration all over the European Union. The aim is to determine the prevalence of Chagas Disease in bolivian pregnant to find cases of vertical transmission and its associated characteristics

Methods: Prospective, cross-sectional study. Percentage of immigrations: 20%. Group of study bolivian pregnants attended at tertiary hospital in the south of Madrid. As screening test a immunochromatographic one was used, and confirmed by ELISA/IFI when positive. Case was defined by positive serology with two different techniques. In the child: Mother infected and positive parasitologic assay or positive serology at the seventh month of life.

Results: 327 pregnant and their 328 children were studied. Median age 27 (range 15-44). Median gestational age: 39wk (range 26-42). By regions, from Cochabamba were 63%. The 54% came from rural areas. The 5% has received blood donations in Bolivia. The 67% had seen triatomids at home. The 54% had lived in adobe houses. The 62% of them has been travelling to Spain since 2004. Almost 80% has never returned to their country. Any direct relative with Chagas Disease: 28,3%. Relatives infected and dead: 6,6%.Prevalence of Chagas Disease in the study population: 18%. The rate of vertical transmission was 2%. There is statistical difference between infected and non-infected pregnant and living in urban or rural area but not comparing apgar, weight or gestational age.

Conclussions: Screening of Chagas´Disease should be considered in bolivian pregnants due to the high rate of infected women in this population and the possibility of vertical transmission.

P143

DETECTION OF HUMAN RHINOVIRUS C IN CHILDREN WITH ACUTE LOWER RESPIRATORY TRACT INFECTIONS, SOUTH KOREA

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Backgroud and aims: Human rhinoviruses (HRV) are common causes of respiratory disease, but their molecular epidemiology has been poorly investigated. Recently, new HRV genotype, HRV-C, was identified, which clinical spectrum is still not clear. The purpose of this study was to investigate the molecular epidemiology of rhinovirus in children hospitalized with acute respiratory disease in Korea.

Methods: From the 148 HRV positive samples, a total of 54 samples which were negative for other respiratory viruses were included in the study for subsequent sequence analysis from January 2006 to December 2006. All specimens were tested for the presence of human respiratory syncytial virus (hRSV), influenza virus A, influenza B, parainfluenzavirus, and adenovirus using direct immunofluorescent assay, and for human metapneumovirus (HMPV) by RT-PCR. For genotyping of hRV, primer P1-1 were used as the forward primer and multiple primers were used for reverse primer; P3-1, P2-1, P2-2 and P2-3.

Results: Upon 5'-NCR gene analysis of HRV, 26 HRV strains were HRV-A, 11 were HRV-A2, 6 were GAC, and 2 were HRV-B. HRV-C was detected in 9 patients. The HRV-C positive patients had variable diseases including pneumonia, bronchiolitis, and asthma exacerbation. None of the HRV-C patients required admission to intensive care unit. HRV-C infection was at their peak in September.

Conclusion: HRV-C was detected in children hospitalized with LRTIs in Korea, which suggest the possible role of HRV-C in children. The standardization of diagnostic method for HRV-C is needed, becasue diverse strains of HRV are co-circulating including HRV-C and GAC.

P144

THE SEVERITY OF PERTUSSIS IN YOUNG INFANTS IN THE UNITED ARAB EMIRATES

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Background: Pertussis is one of the vaccine preventable diseases that can potentially be fatal. Despite the availability of a vaccine, the disease continues to pose a significant risk to infants. The case fatality varies but generally ranges between 2-3 percent in infants. Risk factors for death need to be identified and addressed before the disease progresses to death.

Objectives: To evaluate the clinical course of pertussis presented to Shaikh Khalifa Medical City (SKMC). To identify the risk factors for mortality in this group of children.

Methods: We conducted a retrospective case review of children < 2 years admitted to SKMC with PCR proven pertussis over the period 2004 to 2008.

Results: Forty patients were admitted during this period. The mean age was 63.3 days. Mortality rate was 12.5 % (5 deaths). The median length of stay was 6 days. Co-infection with other viruses occurred in 16% of the patients (RSV, Parainfluenza, and Influenza). Using step wise logistic regression analysis for mortality the only variate came out significant for death was absolute lymphocyte count (P = 0.008, OR 5.11, 95% CI 1.5-17.1). Prematurity, pneumonia, and age, as predictors were not found to be statistically significant.

Conclusion: Our mortality figure was higher than reported benchmarks. Amongst other postulates it remains possible that our PCR testing provided us with a more sensitive diagnostic tool in infants that may previously have been missed. Our small sample size possibly prohibited known predictors from being statistically significant.

P145

FIRST TIME INVESTIGATED CHOLERA OUTBREAK IN THE INDIAN STATE OF UTTARAKHAND 2007: THE DANGER OF DRINKING UNPROTECTED, UNTREATED SPRING WATER

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Background: Outbreak of Cholera and other water borne diseases is quiet common and continue to be public health problems in Indian. These outbreaks are rarely investigated. We received information about increased number of diarrhea cases with four deaths in a village of Uttarakhand state of India during July 2007. We investigate this outbreak to identify risk factors and propose recommendations.

Methods: A retrospective cohort study was conducted to identify risk factors used a questionnaire. We collected rectal swabs and water specimen for microbiological studies. We describe the outbreak in terms of time, place and person.

Results: We identified total 85 cases (Median age: 27 years) among 416 villagers (Attack rate 20%), starting 22nd June to 17th July 2007, cases peaked on 11th July. The age specific attack rate was highest among 50 years and older (30%). Case Fatality Rate was (CFR = 4.7%) and highest (24%). among 50 years and older age group. The attack rate was higher among those who using spring tank water than the other water source (21.8% vs. 3.1%, $P < 0.001$, relative risk: 7, 95% confidence interval [C.I.]: 2.8 - 17). The Attributable risk was 85 % among those who using spring tank water. Laboratory isolated Vibrio Cholerae 01 Eltor Ogawa from one of the two rectal swabs and two out of three water samples showed fecal contamination.

Conclusion: An outbreak of Cholera was due to unprotected spring water supplied into community without any treatment including chlorination for drinking water was the source of outbreak.

P146

LYMPHATIC FILIARIASIS (LF) PRESENTING AS HYDROCOELE IN A CHILD FROM ENDEMIC AREA

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Lymphatic filiariasis is considered as one of most devastating disease under the Neglected Tropical Diseases by WHO.In Malaysia,there are still some areas in northern states and East Malaysia that are endemic for LF.

Disease associated with LF infections in children is poorly understood.We report here a case of asymptomatic microfilaremic boy who was found to have hydrocoele and lymphadenopathy during ultrasound.

This 6 years old boy was found to have positive Brugia rapid test during screening in his village in Gua Musang, Kelantan. He was otherwise well with no symptoms of recurrent fever, leg or genitals swelling. On examination, he was afebrile with mild pallor and noted to have right inguinal lymphadenopathy with no limb or scrotal oedema. There was no palpable lymphnode over axilla, epitrochlear, crural or popliteal region.

His hemoglobin was 10g/dL and his white blood cells was $11x10^3$/uL(EO-35%).His Brugia rapid test (Anti-filiarial Ig G antibody) was positive for Brugia Malayi. Night blood examination using nuclear pore technique detected 22 microfilaria/1 ml of blood.Ultrasound examination showed bilateral hydrocoele with right inguinal and left axillary lymphadenopathy. No filarial dance sign noted.

He was treated with DEC and albendazole and during follow up ultrasound showed resolution of hydrocoele and lymphadenopathy.

Unlike adults,lymphatic filariasis presents with non-pathognomonic syndromes as clinical presentations in children like fever, lymphadenopathy or arthropathy and high index of suspicion is needed to look for infected children during mass screening.

Acknowledgement to Filiariasis Division, Institute for Medical Research, Jalan Pahang, Kuala Lumpur.

P147

CHANGING CLINICAL MANIFESTATIONS OF DENGUE INFECTION IN NORTH INDIA

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Background & aims: We have observed a changing clinical picture of dengue infection over the last 2 years and describe here clinical features observed in the last season in a teaching hospital in Northern India.

Methods: Children admitted to the CSM Medical University Hospital, Lucknow from August to December 2008 with suspeced dengue infection were enrolled and their clinical and laboratory findings charted. IgM capture ELISA was done in serum using commercial kits. Those testing positive for dengue IgM were considered 'probable' dengue infection. WHO case definitions were used for Dengue Hemorrhagic Fever (DHF). Those with altered sensorium were classified as Dengue Encephalopathy (DE).

Results: Eighty children were dengue IgM positive. Mean age was 5.9 (± 3.1) years, male: female ratio was 1.6:1 and 87.5% were from rural areas. History of seizures was present in 45%, altered sensorium in 51.2%, vomiting in 41.2%, hemorrhage in 38.8%, skin rash in 37.5% and jaundice in 2.5% cases. Edema was present in 47.5%, hepatomegaly in 62.5%, splenomegaly in 60%, meningeal signs in 8.7% cases and generalized increase in muscle tone in 13.7%. Investigations revealed low platelet count (< 100,000/ cu mm) in 60.3%, pleocytosis in cerebrospinal fluid in 17/ 38 (44.7%) and raised sGOT and sGPT in 76.9% and 66.7% respectively. DE and DHF were present in 53.7% and 22.5% cases respectively. Mean duration of fever was 14.9± 7.3 days. Mortality rate was 13.7%.

Conclusions: A significant proportion of children presented with little described features of encephalopathy, edema, splenomegaly and prolonged fever.

P148

CONGENITAL TUBERCULOSIS: A RARE FORM OF AN EMERGING DISEASE

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Congenital tuberculosis (TB) is considered a rare entity and diagnosis is usually delayed due to the non-specific presentation.

A 62-day old girl was admitted with fever and broncho-pneumonia. She was delivered, vaginally, at 33 week's gestation to a HIV negative mother emigrated from Pakistan and living in Belgium for the last six years. The pregnancy was complicated by fever and preterm labour 3 days before the birth. The baby did well until day 60 when she developed fever, light cough and poor feeding. On Physical examination she seemed moderately ill with aural discharge, normal chest sounds and slight abdominal distension.

Laboratory evaluation revealed mild inflammatory syndrome, chest X-Ray showed bilateral reticulo-nodular opacities and narrowing of the left main bronchus. After an unsuccessful 2 days cure of broad-spectrum antibiotics, tuberculin skin test (TST) and three gastric aspirates were performed. TST demonstrated a 15 mm induration and positive acid-fast stain was detected on the gastric aspirate. Anti-tuberculosis treatment was initiated. Cultures grew *M. tuberculosis* resistant to nicotibine.

Mother's disease was prompted because of child´s disease and she was diagnosed with miliary and meningitis TB. An endometrial biopsy revealed inflammation with non necrotic granuloma.

Tuberculosis should be considered when diagnosing infants with aspecific symptoms of infection and/or pneumonia that are non-responsive to conventional antibiotics. Careful evaluation of the mother is required when analyzing illnesses in an infant. The incidence of neonatal TB might increase in industrialized countries as a result of immigration from countries with higher TB incidence among women of childbearing age.

P149

WHOOPING COUGH: RE-EMERGING INFECTION

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Background and aims: Whooping cough, a highly contagious disease caused by *Bordetella pertussis*, is re-emerging, despite the widespread use of vaccines during the last decade.

Our aim was to analyze the pediatric cases of confirmed pertussis infection, in the last year.

Methods: Retrospective review of medical records from children with positive *Bordetella*-specific polymerase chain reaction, at Centro Hospitalar do Porto, from January to December 2008. Data collection included the age of presentation, sex, pertussis immunization status, household contacts, presenting symptoms and signs, duration of hospital stay, clinical course, treatment and complications.

Results: Six children were identified, five were less than 6 months old (median 53 days) and one was14 years-old. Four children needed hospitalization, one of them in the intensive-care unit. Cough was present in all cases, paroxistic cough and cyanosis in 5 (83%). Two patients had apnea episodes: one, a preterm child, needed reanimation; the other, had also a Parainfluenza 2 bronchiolitis and developed central sleep apnea during the convalescence stage.

Three cases had possible sick contacts, which were adults in two of them.

Half of the children had not received any pertussis vaccine, and the older child received the 5 doses.

Conclusions: The 6 cases in only one year may suggest a significant resurgence of the infection, which can be fatal in early life. The clinical presentation can be atypical in the adolescence group, and the disease is often misdiagnosed. The authors agree with the need to review the immunization schedule to protect the vulnerable pre-immunisation group.

P150

PERTUSSIS COMPLICATED BY CENTRAL SLEEP APNEA - CASE REPORT

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Background and aims: Vaccination against pertussis has led to significant decline in morbidity and mortality, however this disease is far from controlled. Newborns and infants too young to be fully vaccinated are highly susceptible to infection and at risk of severe disease and death.

Methods: Case report.

Results: The authors present a clinical case of a 6-week-old female infant with *Bordetella pertussis* infection associated with *Parainfluenza 2* bronchiolitis admitted in the intensive-care unit after a prolonged apnoeic episode reversible with stimulation. Following transfer to pediatric nursery, the paroxistic cough improved but, during sleep, she presented repeated apnoeic episodes with mild dessaturation. Many apnoeic episodes, mostly of central type, without paroxistic or epileptic activity, were recorded by electroencephalography (EEG). Polysomnographic study preformed 7 weeks after the beginning of symptoms revealed many episodes with periodic breathing, particularly on REM, with slight reduction of cardiac frequency. Two months after discharge she repeated the EEG which was normal.

Conclusions: This case suggests that, beside the fact that the periodic breathing could be normal in young infants, the transitory apnoeic and cyanotic episodes could be facilitated by pertussis. However, the underlying mechanisms responsible for this dangerous complication are still unknown.

P151

CO-INFECTION CCHF AND MALARIA

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Southeast of Iran is an endemic region for CCHF. In 1999, we faced with an outbreak of CCHF in Sistan and Baluchestan, where is near by Pakistan and Afghanistan.The most cases of Malaria in Iran are also reported from this area. Hereby, we report a 17-year-old woman who admitted to our hospital because of acute fever, headache, epistaxis, petechia and vaginal bleeding. The patient treated with ceftriaxone for probable diagnosis of Typhoid fever and Ribavirin for CCHF because she had a history of animal contact in a rural area during the last 5 days. Laboratory results showed pancytopenia. On 2 th day of hospitalization, blood test revealed the M. Falciparum and quinine (IV) started. Unfortunately, she died due to massive GI and vaginal bleeding in ICU. Three weeks later, we received a positive test (Rt-PCR and IgM-ELISA) for CCHF.We recommend every physician should be aware of co-infection Malaria and CCHF in endemic area.

Keyword: Co-infection CCHF and Malaria.

P152

KIDS PROPHYLAXIS POST- EXSPOSURE RABIES INFECTION IN BOSNIA AND HERZEGOVINA

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Objective: Rabies virus in neurotrophic RNA virus that causes an acute encephalitis with atypical focal neurological signs and paralyses. Although rabies infections in childhood are rare, they can cause serious health problems. The recommendations for children given here are intended as a general guide but child has its specifics caracteristics.

Methods: Post-exposure prophylaxis (PEP) is any prophylactic treatment started immediately after exposure child to a rabies disease in Bosnia and Herzegovina . The treatment consists of repeated injections of rabies vaccine and immunoglobulin.

Results: Post-exposure treatment, which consists of local treatment of the wound, followed by vaccine therapy (with human rabies immunoglobulin) should be initiated immediately with contacts of categories II and III, but for category I (touching or feeding animals, licks on the skin) , no treatment is required in ours cases in Bosnia. PEP is commonly used, and very effective, to prevent the outbreak of rabies after a bite by a rabid animal.

Discussion: Only the cell-derived vaccines that meet the WHO requirements regarding safety, potency and efficacy for this application may be considered for intradermal use.

Conclusions: It has been shown that purified equine rabies immunoglobulin products cause adverse reactions in 3% of vaccinees in Sarajevo, even when sensitivity tests are performed prior to their administration.

Keywords: Rabies, Post-exposure prophylaxis (PEP), Management, Children.

P153

WHOOPING COUGH: A RE-EMERGING DISEASE

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Despite the high vaccination coverage in most of the Western world, the incidence of whooping cough has increased in all age groups during the last decades. The introduction of acellular vaccines nor the introduction of booster vaccinations in toddlers has changed this trend. Current vaccines are not well equipped to overcome the rising incidence of whooping cough for various reasons. Therefore, an improved whooping cough vaccine is needed.

The required characteristics of such an improved vaccine are that it

(1) allows all age groups to be vaccinated with *B. pertussis* circulating strain antigens,

(2) protects against whooping cough induced by *B. parapertussis*,

(3) enables infants to be vaccinated earlier,

(4) causes minimal adverse events after repeated vaccination, and

(5) protects longer than currently registered vaccines.

Consequently, vaccine compositions that can fulfill these requirements were examined, using time to market, costs and risks as constraints. The most likely candidates to succeed are oral or intranasal vaccines consisting of inactivated *B. pertussis* cells, since an oral vaccine has already shown proof of protection in a phase III study without adverse events, and an intra-nasal vaccine has shown proof of concept in a phase I study. Live attenuated vaccines are also promising, but may take longer to commercialize. At this point it is not clear if *B. parapertussis* cells should also be included in an improved whooping cough vaccine, and what the cost-benefit ratio would be.

EPIDEMIOLOGY

P154

LACK OF MOTHER-TO-NEWBORN TRANSMISSION OF HEPATITIS C VIRUS IN IRAQI WOMEN: A PROSPECTIVE STUDY WITH HEPATITIS C VIRUS RNA TESTING

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Background: What has been published about the risk of mother-to-infant transmission of hepatitis C virus (HCV), shows variation according to the population studied and the test used. Polymerase chain reaction (PCR) was used for the first time in Iraq in a prospective study.

Aims: To asses the risk of vertical transmission in an unselected population of Iraqi pregnant women.

Material & methods: HCV antibodies (Abs) were sought with third generation enzyme immunoassay (EIA-3) in 3491 pregnant women. A positive reaction was then confirmed by a third-generation immunoblot assay (LiaTek-III). This last test was confirmed positive in 112 serum samples . we followed 26 babies of 25 anti-HCV positive mothers at first month of life. Eight of these children could be followed for six months postnataly.

Results: All the 26 neonates were positive for HCV Antibodies (with EIA-3 and Lia Tek-III) during the first month of life and it completely disappeared within the following six months. HCV RNA was consistently negative in 22 sera (14 infants at first months and 8 of repeated at 6 months later) regardless of the hepatitis C virus polymerase chain reaction status of their mothers (9 of whom were positive for HCV RNA).

Conclusion: The study showed the absence of vertical transmission of HCV from pregnant Iraqi women to their offspring.

Acknowledements:

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ANTIBIOTIC PRESCRIPTION AT DISCHARGE IN A FRENCH PEDIATRIC EMERGENCY DEPARTMENT IN 2008

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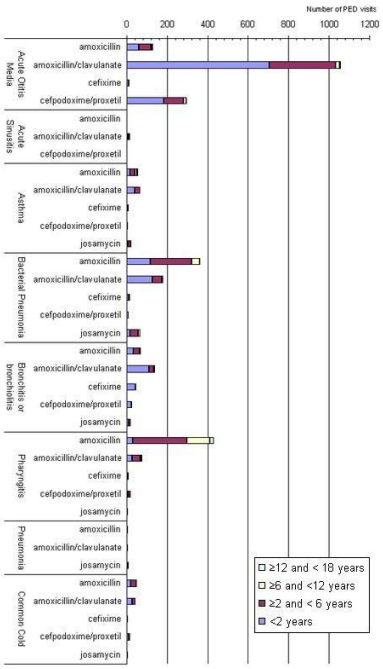
Background: Respiratory Tract Infection (RTI) is very common among children seen in a Paediatric Emergency Department (PED). Our aim was to evaluate the antibiotic prescription at discharge for RTI in our PED.

Methods: We studied the database of the 73 875 PED visits in 2008.

Results: During 2008, RTI accounted for 15410 (20,5%) of PED visits.

	< 2 years	≥2 and	≥6 and	≥12 and	Total
Common Cold	3333	1408	267	57	5065
Bronchitis or Bronchiolitis	3502	785	236	42	4565
Pharyngitis	187	774	261	59	1281
Acute Otitis Media (AOM)	1196	603	55	22	1876
Asthma	583	794	338	77	1792
Acute Sinusitis	3	10	15	7	35
Bacterial Pneumonia	351	347	82	16	796
Total	9155	4721	1254	280	15410

There were 3206 antibiotic prescriptions for RTI at discharge in our PED. The diagnosis of AOM was the main reason for antibiotic prescription at discharge. Amoxicilin/clavulanate was the most used antibiotic. Cefpodoxim/proxetil accounted for 20% of antibiotic prescription in AOM.



[Antibiotic prescription at discharge]

Conclusion: These results suggest a good appliance of national guidelines by physicians in our PED. The high number of AOM questions about the criteria used in our PED to identify properly AOM.

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EPIDEMIOLOGICAL PROFILE OF BLOODY DIARRHEA AMONG CHILDREN LESS THAN TEN YEARS OF AGE IN BAGHDAD

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Background and aims: Because of the high incidence of bloody diarrhea in Baghdad, we tried to study and to evaluate these cases.

Our aims were to evaluate the prevalence of bloody diarrhea among children with diarrhea less than 10 years old, to identify the most commonly causative agents and to detect factors that may be associated.

Material & method: A sample of 1500 children was collected. All children aging less than 10 years with diarrhea. Mother interviewing and clinical examination of each child was carried-out. Then general examination and cultured of stool was performed.

Result: The prevalence of bloody diarrhea was (28%) of the patients presented with diarrhea. The male to female ratio was 1.42:1, with no significant association. Children whose age ranged between (7-9 years) constituted significantly higher rate (66.6%), although (1-3years) children are largest age group attendants 270 (30.6%).

Entamoeba Histolytica was the main causative agents for all age groups, with significant higher prevalence among age group (1-3years), followed by Non-typhoid salmonella and Shigella.

Higher prevalence of bloody diarrhea was detected among those residing rural areas, children on exclusive bottle-feeding and children who use teats & have thumb sucking habit.

Their were highly significant between the clinical signs and bloody diarrhea like fever in (33.3%), vomiting in (29.7%), dehydration in (45.9%), tenesmus in (45.2%) and convulsion in (50%) of cases.

Conclusion: Parasitic infection as well as bacterial infection is serious public health problem among Iraqi children mostly related to environmental sanitation and personal hygienic conditions.

P157

CLIMATIC FACTORS ASSOCIATED WITH ROTAVIRUS INFECTIONS IN CHILDREN UNDER 5 YEARS OF AGE IN ENGLAND AND WALES

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Background: Rotavirus is the most common cause of gastroenteritis in children under 5 years. In England and Wales, rotavirus incidence is highly seasonal; the peak in late winter/ early spring suggests a role for meteorological factors in the epidemiology of the virus.

Methods: Poisson regression adapted for time-series data was used to investigate the short-term effects of mean weekly temperature, relative humidity and total rainfall on number of reported laboratory-confirmed rotavirus infections in children under 5 years between 1993 and 2008. Separate models were constructed for each of the 10 regions of England and Wales. We adjusted for long-term trends, seasonal patterns, other climate factors and public holidays. We estimated the percentage change in number of rotavirus reports per unit decrease in temperature, humidity and rainfall. Region-specific estimates were pooled across regions in a meta-regression to provide a combined estimate.

Results: There was strong evidence for a linear relationship between mean weekly temperature and reported rotavirus infections. The pooled estimate for England and Wales was a 16% (95% CI 9% to 24%) increase in number of reports per 1°C decrease in temperature above a threshold of 5°C. A 2% (95% CI 1% to 4%) rise in number of reports was observed per 10mm drop in total weekly rainfall. There was no overall effect of relative humidity on number of rotavirus reports.

Conclusion: Climate variability can affect the incidence of rotavirus infections. An understanding of the links between climatic factors and rotavirus infections can help predict the demands on health services.

P158

GLOBAL CHANGES IN PNEUMOCOCCAL SEROTYPE EPIDEMIOLOGY - VACCINE EFFECT, ANTIBIOTIC USE EFFECT OR SECULAR TREND?

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Background: Since the introduction of PCV7 pneumococcal conjugate vaccine, increases in the prevalence of serotype 19A have been attributed to vaccine. However, similar changes have been seen for this serotype and other serotypes in countries not using vaccine. Furthermore, 19A increases have not been seen in all populations using vaccine.

Methods: Pneumococcal serotype epidemiology was reviewed in several countries.

Results: Epidemiologic surveillance in Spain over the 25 years before PCV7 reveals dramatic changes in the absolute and relative prevalence of various serotypes. Recent UK data demonstrates substantial increases in serotypes 1, 7F and 19A prior to PCV7. In Denmark, there has been a four-fold rise in serotype 1, but 19A accounts for only 1% of cases in children. In Korea, increases in serotype 19A predate PCV7 introduction. In the US, serotype 19A increases in the country overall occurred following PCV7. However, surveillance in the American Indian population, with extensive PCV7 use before and after licensure, reveals 19A disease incidence has decreased in this population. This contrasts with substantial increases in 19A disease in Native Americans in Alaska. Interestingly, macrolide use is uncommon in the American Indian population and common in the Alaskan Native, Korean, Spanish and UK populations.

Conclusions: Pneumococcal serotype epidemiology varies substantially over time and place. Antibiotic use patterns may have a stronger influence on emergence of new strains than vaccine. The focus of attention on one serotype, 19A, has hindered recognition of increases in incidence and morbidity due to other serotypes such as 1 and 7.

P159

THE OUTBREAK OF VIRAL HEPATITIS A IN THE CZECH REPUBLIC IN 2008: THE NEED FOR ACTIVE CONTROL OF CONTACTS

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Backgorund: The incidence of viral hepatitis A (VHA) decreased considerably in the Czech Republic in last years. In 2008 occurred the outbreak of VHA in Prague and Central Bohemian Region. Out of 1103 cases, 197 were diagnosed in children. The aim of our study was to evaluate the epidemiological and clinical characteristics of VHA cases.

Materials and methods: We are presenting retrospective analysis of paediatric patients with VHA admitted to our department in 2008.

Results: 100 children (56 males and 44 females) with the median age of 8 years were enrolled to the study. The length of hospital stay was 6 days at average. Contact with the infection in family members was noted in 57 patients; 23 patients negotiated any contact with VHA. The most frequent symptoms were: icterus (in 48 cases), nausea (45), fever (44), emesis (36) and abdominal pain (32). Asymptomatic course was observed in 33 patients. Medians of AST and ALT levels were 10,58 µkat/l (ranging from 0,56 to 139) and 27,19 µkat/l (0,35 to 109,7) in symptomatic patients; 0,91 µkat/l (0,44 to 32,77) and 0,98 µkat/l (0,28 to 41,19) in asymptomatic patients. Medians of bilirubin levels were 59 µmol/l in symptomatic and 10 µmol/l in asymptomatic patients. The relapse of the disease occurred in 3 patients.

Conclusion: Active control of VHA contacts in our country proved to be important because the course of VHA was asymptomatic in one third of our cases. But in many patients without clinical symptoms the elevation of aminotransferases was detected.

P160

THE TREND OF BACTERIAL MENINGITIS IN ITALIAN CHILDREN AFTER THE INTRODUCTION OF THE VACCINES AGAINST MENINGITIS

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Background: In Italy, data on bacterial meningitis are available from the 1994. They derive from statutory notification of meningitis (since 1991 only for Neisseria meningitidis) and from the "national surveillance of bacterial meningitis" (since 1994) based on clinical notifications. Vaccines against *N.meningitidis,* Streptococcus pneumoniae, Haemophilus influenzae are available, in Italy, respectively from 2002, 2001, 1995. Up today only HIB vaccine is recommended for all newborns whereas for the others the recommendation is at regional level. We describe the epidemiology of meningitis due to these three pathogens, in Italy, in years 1994-2008.

Methods: In both surveillance systems, cases are notified to the Local Health Units, that transmit the data to the regional and national authorities. Laboratory confirmation for all cases is required. A convenience sample of isolates is sent to the National Reference laboratory, at the National Institute of Health, for confirmation, serotyping and molecular typing.

Results: The trend of incidence in agegroup 0-5:N.meningitidis: it is almost stable from 1994 (2.19*100.000) to 2007 (2.02*100.000). A peak is present in period 2003-2005 (in 2004 4.35*100.000). In 2008(data not definitive) there is a small decrease (1.18 *100.000). However this decrement is not present in children under the first year of life.S.pneumoniae: it is stable from 1994 (1.76*100.000) to 2007 (1.60*100.000). H.influenzae: it shows a significantly decrease from 1994 (2.70*100.000) to 2007 (0.11*100.000).

Conclusion: A strong impact of the Italian vaccination policy is evident only for HIB whereas for the other two vaccines the coverage in Italy is not enough to achieve a significant decrease.

P161

COXSACKIE VIRUS RELATED WITH ONYCHOMADESIS. COHORT STUDY

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Background: An outbreak of Onychomadesis started on June last year and related with Hand Food and Mouth Disease (HFMD). More than 311 infants were affected in Valencia. (Eurosurveillance, http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18917) Isolated viruses were identified as Coxsackievirus A10 as principal agent related with.

Retrospective study has some bias and misclassification in order to evidence. Our aim was supporting those observations by a prospective cohort study toward a major evidence.

Methods: A Prospective observational study is carrying out. Population from nursery (n = 58) Three month following-up. Age: 14 to 46 months old. Information about children are from diagnosis by paediatricians and complementary data from parents. Stool samples were collected for onset at the beginning - HFMD- Onychomadesis. Data processed with SPSS.

Results: HFMD was identified in 18 children (31%) and others 11 (19%) as unspecified skin rash viral. Latency period between HFMD and Onychomadesis reach a mean of 43 days (Pct 25%: 37/ Pct75%: 52). Eleven Onychomadesis cases have had previous HFMD diagnosis and four (25%) were previously diagnosed by unspecified exanthema. Viruses identified at current were CVA-6 in initial samples.

Conclusions: Previous skin rash symptoms were found in all Onychomadesis cases. Currently the stool samples are being processed in the laboratory. Initial results show that 8 cases of HFMD Coxsackievirus A6 has been isolated. 5 of these subjects developed Onychomadesis. Cohort study and their following activities will finish on May 2009.

P162

ROTAVIRUS DISEASE BURDEN AND THE COST-BENEFIT OF ROTAVIRUS VACCINE IN TAIWAN

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Rotaviral gastroenteritis was a common disease both in developing anddeveloped countries. Well established medical system can only avoid the severe complication and mortality. It was quite different in epidemiology and disease burden among each countries and area. Rotaviral vaccine had been licenced in 1998, and was now re-on marketing 2006, which was proved to have good efficacy in preventing mortality and morbidity and was also cost saving. This study was introduced to evaluate the cost-effectiveness of rotavirus vaccine in Taiwan, which combined with the data base of National Health Institute (NHI), surveillance system of Taiwan CDC, those published data and the ongoing active surveillance study.

Those useful data for cost-effectiveness of rotavirus disease included:

(1) Epidemiology of rotavirus in Taiwan: peak age of infection, mortality, prevalence of RV related outpatient and inpatient medical visit and circulating genotypes;

(2) Disease burden of rotavirus, which include direct and indirect medical cost, including those outpatient clinics and inpatient service;

(3) Pyschological stress of family during the course disease.

The age of rotaviral gastroenteritis in Taiwan was older than those developing countries, with the onset of 1 to 2 year-old (similar to Hong Kong and Singapore). Rotavirus vaccines were proved to be still active before children age of 2. The economic burden of rotaviral diarrhea was estimated around 1 billion NTD. Once the rotavirus vaccine is recommended by ACIP of Taiwan, the cost-benefit for the price 2 or 3 doses RV vaccine is evaluated.

P163

INCIDENCE RATE AND ATTRIBUTABLE MORTALITY OF NOSOCOMIAL INFECTION IN PEDIATRIC INTENSIVE CARE UNIT

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Background and aims: Nosocomial infections (NIs) in critically ill patients is an increasingly prevalent problem. Nosocomial infections have been linked to increases in morbidity, length of hospitalization, increased healthcare costs, and increased mortality. Our study was to examine the proportion of sites of NIs and prognostic factors of mortality in pediatric Intensive care unit (PICU).

Methods: A retrospective cohort study was conducted at a PICU with 14 beds in a 2,900-bed tertiary refer medical center. All patients admitted to the PICU who had developed NIs from 2007 to 2008 were eligible. The definitions of the Centers for Disease Control and Prevention were used to categorize specific NIs as bloodstream infection (BSI), respiratory tract infection (RTI), urinary tract infection (UTI), surgical-site infection (SSI), or other.

Results: Seventy and one NIs occurred in 1,455 screened patients. The incidence rate was 4.9%. The most frequent NIs observed were BSIs 30.3%, UTIs 25.8%, RTIs 15.2%, SSIs 12.1%, and others 16.7%. The most common organisms were Escherichia coli 15.7%, Staphylococcus aureus 8.6%, coagulase negative Staphylococci 8.6% and Pseudomonas aeruginosa 8.6%. The crude **mortality** rate were 31%. Logistic regression analysis of prognostic factors of mortality, Neoplasm (Odds Ratio [OR] 12.89, 95% confidence interval [CI] 1.34-12.62), used day of mechanical ventilator (OR 1.05, 95% CI 1.02-1.09), and used day of Foley catheter (OR 1.43, 95% CI 1.16 - 1.76) were independent factors ($p < .05$).

Conclusions: BSIs were the most site of NIs in PICU. Invasive devices and underlying diseases were the important prognostic factors.

P164

LATENT TUBERCULOSIS INFECTION AND DISEASE IN CHILDREN, IN CRETE, GREECE

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Background and aims: The purpose of this study was to investigate the epidemiological characteristics of latent tuberculosis infection (LTBI) and Tuberculosis disease in children in Heraklion region.

Methods: Data was collected from the Anti TB Unit of Venizelion General Hospital from years 2006-2008, involving the evaluation of tuberculin skin test (TST) in 7043 children. Ages ranged between 15 months to 14 years old. In all cases a TST was performed with a 0,1 ml (2TU) tuberculin PPD RT 23 SS1 interdermally. The transversal diameter of induration was evaluated in 48-72 hours. A result of ≥ 7mm induration in unimmunized children was considered positive result, as well as a result of a ≥15mm induration with prior BCG.

Results: 41 children were diagnosed with LTBI (91%) and 4 (8,8%) had pulmonary disease. 16 (35%) were boys and 29 (65%) girls. The tuberculin index was found 0,34%, 0,98% and 0,62% respectively for the years 2006, 2007 and 2008. 36 (80%) of them had not been immunized and 9 (20%) were immunized with BCG. At diagnosis the mean age was 6,1 years old and median 6. In 12 (27%) cases at least one adult from their environment was discovered. 11 (24,4%) children were immigrants and 34 (75%) were Greek. All children in the study were treated for tuberculosis.

Conclusions: Tuberculosis infection remains a serious health issue. Tuberculin index is still high in Heraklion, Crete. The majority of cases discovered had latent tuberculosis infection. A considerable proportion of patients were immigrants.

P165

INCIDENCE OF ACUTE OTITIS MEDIA (AOM) AND COMMUNITY ACQUIRED PNEUMONIA (CAP) IN A BRAZILIAN COMMUNITY LEVEL PRIMARY CARE SERVICE (PCS)

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Background: AOM is the most important cause for pediatric consultations and CAP is an important marker of respiratory infections and we lack of precisely data on those in Brazil. Our objective was to describe the incidence of those diagnoses in a two consequent year clinical surveillance in a large PCS in Brazil.

Methods: Weekly review of all outpatients visits in a PCS in Brazil. The incidence by age range was calculated dividing the total number of each diagnose by the population attended by the center.

Results: Total numbers of outpatients' visits were 104,101 and 114,229 in 2006 and 2007 respectively. The incidences of AOM per 1000 patients according to the age range in 2006 and 2007 were: 0 to 4y = 181 and 150; 5 to 14y = 29 and 24 ; from 16 to 65y+ all had incidence under 8/1000. For CAP the incidences were in 2006 and 2007, : 0 to 4y = 89 and 81; 5 to 14y = 16 and 10; 15 to 24y = 8 and 11; 25 to 59y = 9 and 13; 60 to 65y = 21 and 35 ; 65y+ = 34 and 46.

Comment: Incidence of AOM and CAP were similar between the two years, with a slight reduction of AOM in 2007 and increase of CAP. Overall incidence by age range showed AOM in children under 4y and CAP in the young and the elderly. This data will help to calculate the impact of interventions such influenza and/or pneumococcal vaccinations.

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EPIDEMIOLOGY OF *STREPTOCOCCUS PNEUMONIAE* INFECTIONS IN PARIS AREA: PREDOMINANCE OF SEROTYPE 19A

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Background: We have studied 457 Streptococcus pneumoniae isolated in 2007 from adults and children living in the west area of Paris. For all isolates we performed capsular typing and determined the antibiotic resistance patterns.

Results: *S. pneumoniae* 19A was the most frequently isolated serotype (34.7%) both in children and adults. It represented 12.8% (28/219) of the strains isolated from invasive infections in adults and 17/63 (27.0%) in children. Among isolates responsible for meningitis, *S. pneumoniae* 19A was isolated once in adult. Interestingly, *S. pneumoniae* 19A was isolated in 5/10 pleural fluids from children and 4/12 from adults. Among the 173 isolates from acute otitis media (AOM), 110 (63.6%) were *S. pneumoniae* 19A.No difference concerning antibiotic resistance were observed between children and adults. The susceptibility of *S. pneumoniae* to penicillin, amoxicillin, cefotaxime, erythromycin, pristinamycin and rifampicin was 61.2%, 83.9%, 91.9%, 56.5%, 100% and 100%, respectively in children and 64.4%, 83.1%, 84.9%, 68.9%, 100% and 100% in adults, respectively. However, strains isolated from AOM, were significantly less susceptible to b-lactams (3.2%) and erythromycin (4.5%). This decreased susceptibility was correlated with the prevalence of the serotype 19A. Furthermore, two 19A strains presented a high level of resistance to b-lactams (MICs: penicillin ≥6 mg/L; amoxicillin ≥6 mg/L cefotaxime ≥4 mg/L).

Conclusion: We confirm the predominance of serotype 19A among S. peumoniae responsible for invasive and non-invasive diseases either in children or adults in France.

P167

SEASONALITY OF THE RESPIRATORY SYNCYTIAL VIRUS IN BELGIUM, 2000-2008

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Background and aims: Respiratory syncytial virus (RSV) is a major cause of respiratory tract infection during the child's first year of life, as well as in subsequent years. In some infants, infection with RSV can lead to lower respiratory tract infection and result in hospitalization.

The present eight-year retrospective analysis aims to describe the seasonality of RSV in Belgium, especially the changes observed in 2008.

Methods: RSV is one of the respiratory viruses weekly monitored by the sentinel laboratory network (62% of all microbiology laboratories), coordinated by the Scientific Institute of Public Health. This study describes the seasonality of RSV in Belgium during a period of 8 years, particularly the changes observed in 2008.

Results: RSV infections begin generally to increase in October and decrease in March, with a peak in mid-December (week 50). In 2008, the onset of RSV infections began 3 weeks earlier and the peak was observed in mid-November (week 46). This change was observed in some other European countries.

The analysis of meteorological parameters such as temperature, humidity and the particulate matter concentrations in ambient air can not explain the changes of the epidemiology of RSV.

Conclusions: Surveillance of RSV should be emphasized and if further changes in epidemiology should persist, it will be necessary to discuss modification of prevention rules.

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PEDISURV, A WEB APPLICATION TO REGISTER PEDIATRIC DISEASES

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Background: In 2002 the network PediSurv (**Pedi**atric diseases **Surv**eillance) was developed in order to collect information about some vaccine preventable diseases according to European Decision (2119/98/CE). Mumps, measles, rubella, acute flaccid paralysis (AFP) and invasive pneumoccocal diseases (IPD) in 2007 were included since they were not registered by other networks or under mandatory notifications. All Belgian paediatricians and GP working in Brussels were invited to participate to this network. Participation is voluntary and requests a monthly reporting of the diseases even in case of a zero case notification. Since data entry from paper form induced mistakes, a web application was developed also to reduce this time consuming activity. Participants can directly enter the data. PediSurv was born.

Methods: PediSurv is a secured web based application developed by the Institute of Public Health with ASP.Net language linked at a SQL database. PediSurv is also an alert system, when a case of measles is notified; an email or a sms is sent to the public health authorities at Community level.

Results: In 2007, 811 GP and paediatricians participated to the network and among them 40% used the PediSurv application.

Conclusions: PediSurv is a user friendly tool allowing registering of cases and zero case notification as well. This system offers rapid notification permitting Health Authorities to take adapted control measures.

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A DETERMINISTIC EPIDEMIOLOGY MODEL TO STUDY PERTUSSIS IN ARGENTINA

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Background and aims: Vaccination against pertussis started in Argentina in the 70s, coverage being estimated as 90% in average. Despite this, disease incidence is rising, registering a 6-fold increase since 2002. Though a clear increase is observed at all age groups, children < 6 months old had the highest proportion of cases. In this age group a delay in vaccine application was registered: around 30% of infants had fewer vaccine doses than they should. To estimate how this delay may contribute to the observed increase in disease incidence, an epidemiological model was used.

Methods: Starting from a SIR-type model we introduced the age-dependent vaccination scheme currently employed in Argentina. The model contains 9 epidemiological classes and 30 age groups. Parameters were taken from literature and local epidemiological data.

Results: We followed a deterministic approach. The steady state was reached by allowing temporal system evolution to constancy of all age epidemiological class sizes. Delay in vaccine application was simulated by modifying the coverage rates of each dose. By setting vaccine efficacy in 90% for all doses, the model estimates that a delay in the first vaccination comparable to that observed caused a 12% increment in infected individuals aged 0-2 year-old. This value went to 22% by simulating such delay also in the second and third doses. If non-uniform vaccine efficacy were considered for each dose the relative impacts changed.

Conclusions: Based on mathematical model analysis, a delay in vaccine application might be related with the observed disease incidence increase.

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PERTUSSIS EPIDEMIOLOGY IN ARGENTINA OVER 2006-2008: TRENDS BY AGE GROUP AND STATUS OF VACCINATION

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Background and aims: Pertussis is a vaccine-preventable disease caused by *Bordetella pertussis*. Despite good vaccination coverage in Argentina, disease incidence increased 6-fold since 2002. Here we describe pertussis epidemiology in Argentina during 2006-2008 and discuss possible reasons for increase.

Methods: Proportion of pertussis cases by age, immunization status, and immunization coverage rate evaluated at the Argentinean National Pertussis Reference Center are reported. CDC criteria were used for diagnosis. *B. pertussis* isolates were characterized by pulse filed gel electrophoresis (PFGE) and *prn* and *ptx* genotypes. Comparisons with vaccine strains are included.

Results: From 8,176 patients with pertussis clinical signs, 22.9% were confirmed: 523 in 2006, 617 in 2007, and 734 in 2008. Approximately 55% occurred at Buenos Aires and Córdoba, the most populated regions. Though a clear increase is observed at all age groups compared to previous data, children < 6 months old had the highest proportion of cases. In this age group a delay in vaccine application was registered, 30% of infants had fewer vaccine doses than they should. In addition, molecular characterization of the isolates revealed a genotypic divergence between them and the vaccine strains. PFGE profiles of vaccine strains had only 64% relatedness with all Argentinean isolates analysed. Moreover, while vaccine strains contain *prn*1/7 and *ptxS1* B/D alleles, local isolates have *prn*2 and *ptxS1*A.

Conclusions: Pertussis is an important problem for public health in Argentina. Delay in vaccine application, and divergence between vaccine strains and local isolates could contribute to the described pertussis epidemiology.

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ACUTE OTITIS MEDIA BURDEN DURING THE FIRST SIX YEARS OF LIFE IN FRANCE IN 2008

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Background and aims: Acute Otitis Media (AOM) is one of the most common childhood diseases, but its clinical and economic burden is not well characterized. The primary objective of this study was to describe the management of AOM. The secondary objectives were to evaluate the impact of AOM on quality of life of their parents and to evaluate the economic costs.

Methods: This is an observational prospective epidemiological study. Patients aged between 0-6 years, suffering from AOM (GP or pediatrician diagnosis) were eligible. This study was performed in France using CSD's LPD panel. Severity was evaluated by the Faces Pain Scale (FPS rating 0-10) and the quality of life by the PAR-ENT-QOL scale (rating scale 0-100).

Results: 439 children were included. 10.5% included by GP were aged 0-1 year (25.3% by pediatrician), 40.9% 1-3 years (vs 48.5%) and 48.6% 3-6 years (vs 26.3%). 18.2% had recurrent AOM, 45% received pneumococcal vaccination (75.4% in the 0-1 year).

The AOM diagnosis was associated mainly with otalgia (72.4%) and fever (71.0%).

Antibiotic were prescribed in 89.8%, and analgesic-antipyretic drug in 72%. 57% of the parents reported a severity (FPS) between 2 and 4, with a significant difference for age and between GP/Pediatrician. The mean total score of the PAR-ENT-QOL was 25.4 (SD= 17.8).

Direct medical costs (with hospitalization) were 97.3 euros from a societal perspective for GP (vs 93 euros in pediatrician). 31.4% of the parents reported absenteeism from work.

Conclusions: The burden of AOM is substantial in terms of severity and societal impact.

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INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN LOWER 5 YEARS OLD. GRAN CANARY 2004-2008

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Background and aims: It considers to know the epidemiological decriptive characteristics, the temporary distribution and the mostly prevalents serotypes in Invasive Pneumococcal Disease in children lower 5 years in Gran Canary Island, during the temporal period 2004-2008.

Methods: Prospective study of the Invasive Disease confirmated cases and notified to the Gran Canary Microbiological Informative Sistem, between 2004-2008 that were hospitalized in Gran Canary with laboratory diagnosis as S. Pneumococcal in blood, Cerebral Spinal Fluid, or in other usvally steril places and acute disease with a compatible clinic of Pneumococcal Disease.

Results: There were notified 80 cases, 12 (15%) in 2004, 17 (21%) in 2005, 19 (24%) in 2006, 9 (11%) in 2007, and 23 (29%) in 2008. Also the 37,5% of sickness were below 1 year old, the 50% between 1 and 2 years and the 12,5% older 2 years. Only rested 10 processes without tipifying. Of the 70 tipified, 67,14% were not prepared by the 7-valent conjugate vaccine. The serotype most identified was the 19A (29%), and the 14 (13%).

Conclusions: The appearance of the isolated vaccinal serotypes could be conditioned by the mentioned use of the vaccine in a high percentage of lower 5 years old population. In 2006, 2007 and 2008 was detected a higher numbers of serotypes not predictables for the vaccine (69%,87,5%, 77,2%). We have to increase the knowledge of this disease with a continued alertness, remarking the need of to confirmate the diagnosis and have isolations to identify the causer serotypes.

P173

MENINGOCOCCAL DISEASE IN CHILDREN LOWER 10 YEARS OLD. GRAN CANARY 2004-2008

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Background and aims: It considers to know the epidemiological decriptive characteristics, the temporary distribution and the mostly prevalents serogroups in Meningococcal Disease in children lower 10 years in Gran Canary Island, during the temporal period 2004-2008.

Methods: Prospective study of the Meningococcal Disease confirmated cases and notified to the Gran Canary Compulsory Disease Reporting system, through individualised notification of cases, and the microbiological data from the Microbiological Informative Sistem, between 2004-2008.

Results: In the studied period, there were notified 22 cases, 5 (23%) in 2004, 6 (27%) in 2005, 4 (18%) in 2006, 2 (9%) in 2007, and 5 (23%) in 2008. Also the 14% of sickness were below 1 year old, the 68% between 1 and 5 years and the 18% older 5 years. Only rested 4 processes without tipifying (18%). Of the 18 tipified, 64% were Serogroups B, 9% W135, one case, C, not vaccinated, and 1 case, A, imported.

Conclusions: We have to increase the knowledge of this disease with a continued alertness, remarking the need of to confirmate the diagnosis and have isolations to identify the causer serogroups.

P174

FIVE YEARS OF ACUTE OSTEOMYELITIS IN A BELGIAN PAEDIATRIC TERTIARY HOSPITAL

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Background: Acute osteomyelitis is scarce in Paediatrics. In 36 to 70% of the cases, no germs are found and this raises the question of the choice of the first line antibiotherapy.

Aim: To identify main etiologies of osteomyelitis in our population and to correlate with clinical and biological presentation.

Method: Retrospective study of all files of children admitted for acute or subacute osteomyelitis or arthritis from January 2003 to December 2007.

Results: Thirthy-eight children were included. Mean age was 5.8 years (median 2.4). Delay between first signs and first consultation was 7 days. Pain was present in 36 patients, fever in 26, functional impairment in 31, redness and swelling in 20. Fourteen/22 patients had a contributive ultrasonography, 20/36 children had a positive X-Ray. Five/6 CT scan, 21/21 scintigraphy and 16/16 MRI were positive.

Median of Sedimentation rate was 63 mm/H, CRP was 3.6 mg/dl. Thirteen/33 (36%) blood and 9/24 (37%) osseous biopsy or articular fluid cultures were positive forStaphylococcus Aureus (9), Streptococcus A/B types (6), Kingella Kingae (1), salmonella (1), mycobacterium tuberculosis (1) and negative in 20 children.

Intravenous antibiotics were shifted to oral forms when CRP was negativated. According to this principle, mean duration of intravenous treatment was 11.9 days (median 9) with no relapse.

Conclusion: In our population, first line antibiotherapy must still target staphylococcus and streptococcus. Echography and radiography can be negative and should be completed by scintigraphy and MRI in doubtfull cases. Short intravenous treatment according to SIRS is possible.

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MENINGOCOCCAL INFECTIONS: EPIDEMIOLOGICAL SITUATION IN BELARUS

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Background and aims: Meningococcal infection is still one of the main cause of childhood morbidity and mortality. The aim of this study is to learn epidemiology and evidence to vaccination from meningococcal infection.

Methods: During 3 years epidemiological situation of meningococcal infection was analysed in children under 15 yo.

Results: In our country the lowering sick rate of meningococcal infections from 2,84 (2006 y) to 1,63 (2008 y) per 100000 is indicated. The high level of sick rate is among children younger 15 yo - 10,39/100000 (IC 95%: 7,7 - 13,08). We estimated the prevalence of illness among child aged under 2 yo - 73,5 % (IC 95 %: 67,7 - 79,2).Thanks to early diagnostic and treatment the level of death decreased from 6,9 % to 1,8 %. Among admitted to infectious hospital children 52 meningococcus were identified. The structure was following: serogroup A - 23,6%, B - 27,1%, C - 30,1%, nontypical - 19,2%. It was estimated high level sensitivity all group of microbes to β-lactam antibiotics.

Conclusions: This study confirms prevalence of patients under 2 yo with meningococcal infection. It is a sign for starting vaccination against meningococcal infection for young children.

P176

EPIDEMIOLOGY OF HOSPITALIZATIONS DUE TO NOSOCOMIAL ROTAVIRUS IN YOUNG CHILDREN IN SPAIN (1998-2007)

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Background and aims: This epidemiological survey was undertaken to estimate the burden of nosocomial rotavirus in children up to 5 years of age in Spain during a ten year period (1998-2007).

Methods: Retrospective survey by reviewing all hospitalizations related to nosocomial rotavirus in the National Surveillance System for Hospital Data (Conjunto Mínimo Básico de Datos). Codes were selected by using the 9th International Classification of Diseases codes: ICD-9-CM 008.61. The annual incidence, average length of hospitalization, mortality and case-fatality rate were calculated by using municipal register data.

Results: A total of 10,990 hospital discharges for nosocomial rotavirus in children up to 5 years old were reported during the study period. The annual incidence was 59.02 cases per 100,000 (CI 95%: 57.91-60.12). The average length of stay was 12 (SD 19) days. A total of 30 deaths were reported. The mortality rate was 0.16 deaths per 100,000 (CI 95%: 0.10-0.22) and the case-fatality rate was 0.27% (CI 95%: 0.18-0.37).

Incidence decreased significantly with age from 226.11 per 100,000 in children up to 1 year old to 1.78 per 100,000 in 4 year old children, respectively. Maximum case-fatality rate was found in children up to 1 year old (0.33%).

Annual average cost for National Heath Care System was 351,965,194 € with a mean hospitalization cost of 32,026 €.

Conclusions: Nosocomial rotavirus infections in children up to 5 years of age pose a significant health threat in Spain. Special attention and public health measures as vaccination are required to reduce their incidence.

P177

TEMPORARY EVOLUTION OF PNEUMONIA AND COMPLICATED PNEUMONIA ADMISSIONS IN PAEDIATRIC POPULATION OF NAVARRE (NORTHERN SPAIN)

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Background and aims: In Navarre the pneumonia causes paediatric population morbidity and the pneumococcus is the most frequent agent. In 2001 began not systematic pneumococcal vaccination(PCV7). There are studies that indicate decrease of income for pneumonia and others increase of complicated pneumonias. Our aims are to describe the temporary trend and to evaluate the possible effects of the vaccine.

Methods: Total pneumonia admissions (TP), pleural effusion (PE) and empyema (EP) were analyzed retrospectively in our hospital from 1995 to 2006. The population figures were obtained of Navarre census. The statistical analysis was realized by t student, R pearson and logistic regression. We considered as pneumococcal pneumonias (PP) those with: a culture(+) in blood or pleural liquid (PL) or Ag/pcr(+) in PL.

Results: Total of 1365 TP were registered, with correlative increase with the years (Rp=0.804;p=0.002), also in PE (154,Rp=0,886;p< 0.001), EP (38,Rp=0,878;p< 0,001) and PP (32,Rp=0,809;p=0,001). Comparing the incidence/100.000 children in prevacunal (1995-2001) and postvacunal (2002-2006) period, a significant increase was observed in admissions by TP (176vs254,p=0,018), PE (8vs27;p=0,02), EP (1vs8;p=0,019) and PP (2vs9;p=0,012), diminishing however the number of admissions/100000/year (3748vs3191;p=0,014). Therefore, the TP admissions percentage increase in the postvacunal period (4,75%vs7,96%; p=0.004). Analyzing TP hospitilzation risk in periods 1 (1995-1998), 2 (1999-2001) and 3 (2002-2006) it was obtained: 1-2:OR=1,2(CI95%:1,02-1,4); 1-3:OR=1,62(CI95%:1,4-1,87).

Conclusions: Pneumonia admissions and its complications have been clearly increased, more evidently in the postvacunal period. The differences found between this and other studies might been explained for epidemiological and microbiological reasons.

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EPIDEMIOLOGY OF HOSPITALIZATIONS DUE TO *BORDETELLA PERTUSSIS* IN CHILDREN UP TO 12 MONTHS OF AGE IN SPAIN (1999-2005)

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Background and aims: This epidemiological survey was undertaken to estimate the burden of *Bordetella Pertussis* in children up to 12 months of age in Spain during a seven year period (1999-2005).

Methods: Retrospective survey by reviewing data of the National Surveillance System for Hospital Data (Conjunto Mínimo Básico de Datos), including more than 98% of Spanish hospitals. All hospitalizations due to *Bordetella Pertussis* for children up to 12 months of age, reported during 1999-2005 period, were analysed. Codes were selected by using the 9th International Classification of Diseases codes for *Bordetella Pertussis*: ICD-9-CM 033 (033.0-039.9). The annual hospitalization rate, average length of hospitalization, mortality and case-fatality rate were calculated by using municipal register data.

Results: A total of 3277 hospital discharges for *Bordetella Pertussis* in children up to 12 months of age were reported during the study period. The annual hospitalization rate was 139.41 cases per 100,000 children (CI 95%: 134.64-144.18). The mean age of the patients was 2.68 months (SD 1.81). The average length of stay was 8.85 (SD 8.3) days. A total of 12 deaths were reported among the total of patients hospitalized. The mortality rate was 0.51 deaths per 100,000 children up to 12 months years (CI 95%:0.22-0.80) and the case-fatality rate was 0.37% (CI 95%: 0.16-0.57).

Conclusions: *Bordetella Pertussis* infections concentrate in children up to 12 months in Spain. Public health measures as vaccination of care takers, health care professionals and relatives, especially young parents, are required to reduce the *Bordetella Pertussis* related hospitalizations.

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MOLECULAR CHARACTERIZATION OF GROUP A HUMAN ROTAVIRUSES IN SALENTO, ITALY, DURING 2006-2007 REVEALS THE PREDOMINANCE OF UNUSUAL STRAINS

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Background and aims: The distribution of rotavirus (RV) genotypes circulating throughout the world changes over time.

The purpose of the present study was to monitor the prevalence of the different G and P genotypes of rotaviruses circulating in Salento and detect any uncommon types.

Methods: During the period from January 2006 to December 2007, a total of 243 RV positive stool samples were collected from children with diarrhoea admitted to four Hospitals in the province of Lecce (Copertino, Galatina, Gallipoli and Tricase). All the specimens were tested for RV by real time PCR and genotyped for VP7 (G-type) and VP4 (P-type) gene by reverse transcription (RT) and multiplex PCR using different type specific primers.

Results: We identified 4 common G&P combinations viz. G2P[8], G1P[8], G2P[4] and G9P[8] amongst 59.8% of the typeable rotavirus positives. Rotavirus G2P[8] was recognized as the most widespread genotype during the sentinel-based survey in Salento.

The detection of other novel and unusual strains, such as G2P[10], G4P[10], G8P[4], G9P[11] and G10P[8] is noteworthy. Furthermore, a significant number of mixed infections were observed during the survey period but G3P[8] rotaviruses were not detected.

Conclusions: This study highlights the genetic diversity among rotaviruses isolated from children in Salento and the emergence of some novel strains. Therefore, it is highly essential to continuously monitor for these strains so as to assess the impact of vaccines on RV strains circulating in Salento and understand the effect of strain variation on efficacy of presently available vaccines.

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ROTASCORE EXTENSION STUDY: FREQUENCY AND CLINICAL CHARACTERISTICS OF ROTAVIRUS GASTROENTERITIS IN GREECE"

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Background and aims: Rotavirus Gastroenteritis (RVGE) is the most frequent cause of acute gastroenteritis (AGE) in children up to 5 years old worldwide. Aim was to determine the proportion of RG in Greece and compare its clinical burden to that of AGE due to other pathogens.

Methods: The study was conducted in 5 Hospital Emergency Units (HEU) between January 2007 and June 2008. Children up to 5 years of age with AGE were included. A rapid stool immunochromatographic test for rotavirus antigen detection was performed. Symptoms severity score was calculated using Clark scale.

Results: 393 children participated in the study (median age 23 months, 216 boys- 55.1%). RVGE proportion was 42.3% (CI 95%, 37.4-47.1%) in HEU and 47.8% (CI 95%, 41.7-53.9%) in hospitalized patients. Most children with RVGE (77.8%) were between 3 months and 3 years old. The 78.6% of RVGE was in winter months between December and April. Behavioral changes, signs of dehydration, weight loss, fever ≥38°C, vomiting and duration of diarrhea were more prevalent in RVGE ($p< 0.01$). In children with RVGE a higher severity ($p< 0.01$), hospitalization rate ($p< 0.05$) and clinical reevaluation ($p< 0.05$) was observed, as well as longer hospitalization stay (median 4 vs 3 days) and parents' days of absence from work ($p< 0.05$).

Conclusions: It is confirmed that RVGE causes major clinical burden in Greek children up to 5 years and it is responsible for nearly half the cases visiting HEU or requiring hospitalization due to AGE.

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FURUNCULOSIS CAUSED BY COMMUNITY-ACQUIRED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* IN A SCHOOL IN BRUSSELS, 2008: A POSSIBLE OUTBREAK

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Background and aims: Methicillin-resistant *Staphylococcus aureus* (MRSA) is an emerging pathogen outside health-care settings. In December 2008 a case of furunculosis caused by MRSA was identified school with 800 children in Brussels. The isolated strain expressed genes coding Panton-Valentine Leukocidin (PVL). PVL-positive *S. aureus* can cause severe invasive infections.Three cases of skin infection had occurred in the same classroom. A quick response was organized by health authorities in order to assess the extent and control a possible outbreak provided that a potentially life-threatening microorganism had been isolated.

Methods: Risk factor questionnaires, and nasal swabs were obtained for 38 persons, children and adults, of the affected classroom. Education and hygiene measures were implemented. A case control study was conducted. Cases were defined as confirmed (positive culture for MRSA) and probable (compatible clinical symptoms). Odds ratios (OR) and 95% confidence intervals were calculated for different exposures.

Results: There were 1 confirmed and 3 probable cases; all of them girls; We did not find any significant association between cases and exposures.* No nasal carriers for MRSA were found.

Conclusions: A case of furunculosis by MRSA and 3 clinical cases in the same school led to a successful public health response. Information, education and communication, remain the cornerstone of public health interventions. Clinicians should be aware of emerging pathogens causing skin infection outbreaks.

*

Table 1.Exposures and their association with furuncles in a school in Brussels, 2008.

Exposure	OR	[95% Conf. Interval]	*P* (Fisher's test)
Being a girl	N.S.	0.83 - ∞	0.10
Having taken oral antibiotics during last three months	11	0.11 - 888.10	0.20
Hospital exposure or having a health-care related father or mother	2.40	0.15 - 36.55	0.37
Being a child (<11 years)	1.08	0.08 - 62.91	0.72
Having pets at home	0.70	0.01 - 9.98	0.63
Group leisure activities	0.42	0.03 - 6.66	0.37

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SERIALLY DIFFERENCED MARKERS FOR PATHOGENETIC STAGES EXPRESS THE UNDERLYING TENDENCY FOR OTITIS MEDIA TO CONVERT TO HEARING LOSS

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Background and aims: OM pathogenesis is a probabilistic cascade (viral exposure > URTI > bacterial colonisation > (R)AOM > lasting effusion with possible biofilm formation > hearing loss (HL). Risk factor and treatment studies could be strengthened by better reflecting the consequent co- variability patterns.

Methods: We modelled later auditory function (HL or tympanometric equivalent) using untreated occasions and cases in two large OME trial databases: TARGET and GNOME. Across four available occasion-pairings separated by 3 months, generalised linear models adjusting for age and season compared three approaches:

(i) co-optimised coefficients for two earlier independent covariates, namely the prior baselines in HL and a 5-item RAOM questionnaire score; the same information, but as

(ii) the normalised difference [Z(HL)−Z(RAOM score)]; and

(iii) separate univariate predictors.

Results: Within these selected samples, coefficients for prior HL/tympanometry measures were always positive as expected, but for RAOM scores were negative, and mostly significant. Hence normalised differencing (ii) gave prediction generally not inferior to co-optimised covariates (i), and for GNOME, actually superior prediction. Imposed differencing thus reflects a stable and relevant underlying conditionality: the tendency to convert any (further) AOM to HL (again).

Conclusions: Sequential normalised differencing (ii) has already clarified whether atopy is a risk factor in OM and enhanced the prediction of treatment benefit. That appears due in part to the general prediction of non-resolution (in controls) shown here, hence is relevant to selecting persistent cases for targetting interventions. The imposed constraint reduces degrees of freedom (2 to 1), assisting power in small studies.

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NEW PENICILLIN SUSCEPTIBILITY BREAKPOINTS FOR *STREPTOCOCCUS PNEUMONIAE* AND THEIR EFFECTS ON SUSCEPTIBILITY CATEGORISATION IN GERMANY FROM 1992 TO 2008

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Objectives: This study was performed to analyse the penicillin susceptibility of all isolates of *S. pneumoniae* with IPD that were sent to the German National Reference Center for Streptococci (NRCS) between 1992 and 2008 and to evaluate potential differences in susceptibility categorisation when applying the new and the old CLSI guidelines, respectively.

Methods: A population and laboratory based surveillance study of invasive pneumococcal disease was conducted in Germany. Cases from January 1, 1992 to November 27, 2008 were included in this study.

Results: From 1992 to 2008, 13554 invasive isolates were obtained. Data on penicillin susceptibility were available for 13216 isolates. 2311 isolates (17.5 %) originate from patients with meningitis, and 10905 isolates (82.5 %) are from non-meningitis cases. Penicillin susceptibility categorisation according to the former Clinical and Laboratory Standards Institute (CLSI) guidelines results in 4.3% intermediate resistant and 1.3% resistant isolates. When the new CLSI guidelines (2008) are applied, considerably higher resistance rates are observed in the meningitis group (6.7% resistant, 0.0% intermediate resistant) than among the non-meningitis cases (0.0% resistant, 0.3% intermediate resistant). Irrespective of the guidelines used, a slight increase in pneumococcal penicillin resistance can be noticed in Germany from 1992 to 2008.

Conclusions: Despite the different effects of the new guidelines on meningitis and non-meningitis susceptibility categorisation, their application results in a lower overall rate of penicillin resistant pneumococcal isolates due to the numerical predominance of non-meningitis cases. This should be kept in mind when interpreting surveillance studies on pneumococcal penicillin resistance.

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THE DIRECT WET MOUNT EXAMINATION - A FOUR MONTHS PERIOD EVALUATION

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Background and aims: The direct wet mount examination is a microscopic review of a fresh fecal specimen to detect parasites (including motile protozoan trophozoites). The authors have evaluated the incidence of intestinal parasites in feces among hospitalized children using direct wet mount microscopic examination. The direct examination of stool is beneficial to assess the worm burden of a child and provides a quick diagnosis.

Methods: There were performed in pediatric clinic laboratory 863 parasitological stool exams during a 4 months period using direct wet mount microscopic examination in Lugol´s iodine (100 ml distilled water, 1 gram iodine and 2 grams potassium iodide). The examinations were performed using optic microscopy by the same investigator under x100 and x400 magnification.

Results: From 863 parasitological exams, 123 specimens (14,25%) were positive: 18 specimens - Ascaris lumbricoides (2,08%), 10 specimens - Entamoeba coli (1,15%), 38 specimens - Giardia intestinalis (4,4%), 40 cases - Blastocystis hominis (4,63%), 6 cases - Trichiuris trichiura (0,69%) and 2 specimens Enterobius vermicularis (0,23%) and 9 cases (1,04%) have presented combined parasitic infections.

Conclusions:

1. We have noticed the low incidence of positive specimens using direct wet mount microscopic exam;

2. Giardia intestinalis and Blastocystis hominis have almost same prevalence;

3. The routine parasitological stool exam has revealed a low prevalence for whipworm infection (0,69%);

4. The direct wet mount is not useful for Enterobius vermicularis infection diagnosis (the Graham test is useful).

P185

COMPARISON BETWEEN QUELLUNG REACTION AND SEQUENTIAL MULTIPLEX PCR FOR THE DETERMINATION OF STREPTOCOCCUS PNEUMONIAE CAPSULAR SEROTYPES AMONG CARRIAGE ISOLATES

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Background and aims: The gold standard for S. pneumoniae serotype determination is the Quellung reaction determined with specific antisera. The high cost of these antisera, the technical expertise requirements and subjectivity in interpretation are drawbacks of this method. Current sequential multiplex PCR was developed for the detection of serotypes associated with IPD in USA (Pai and al JCM 2006). A S. pneumoniae carriage study was carried out and 317 strains were collected. Both serotyping methods were compared to evaluate the accuracy of PCR in carriage studies.

Methods: S. pneumoniae were isolated from nasopharyngeal aspirates in healthy children in Brussels and identified as recommended by CLSI. Serotyping was performed using the PCR-based method and the Quellung reaction.

Results: 317S. pneumoniae were collected. PCR-based serotyping allowed serotype determination of 188 strains (60%). Concordance between PCR and Quellung reaction was observed for 70% of the isolates (131 out of the 188 strains). Although the specificity was globally excellent (>95%), the sensitivity varied widely among serotypes (6% for serotype 15 to 84% for serotype 19A). At the bioinformatics level, the number of cps sequences available for each serotype in databases is low for most of the serotypes and probably precludes for optimal design of specific primer pairs.

Conclusions: PCR-based serotyping is undoubtedly a promising method even epidemiological differences may play an important role. To increase the sensitivity of the method, primers may have to be designed based on a larger sample of cps sequences from the same serotype.

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EPIDEMIOLOGY OF NASOPHARYNGEAL FLORA IN 299 HEALTHY CHILDREN ATTENDING KINDERGARTEN IN BRUSSELS

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Background: A cohort study in healthy, 3 to 6 year old children was conducted in Brussels over 2 school years to determine nasopharyngeal carriage rates and antimicrobial resistance of 5 different bacteria: *S. pneumoniae, S. aureus, H. influenzae, M. catharralis* and *S. pyogenes.*

Methods: Demographic data were collected. Three sequential naso-pharyngeal aspirates were performed (autumn, winter, spring). Identification of the 5 bacteria was performed as recommended by CLSI. Antibiotics resistance profiles were determined by disc diffusion and E-tests. S. pneumoniae serotyping was carried out by the Quellung reaction.

Results: 299 healthy children (median age 4.4 years) were included. 19% children had received at least one dose of PCV7. Carriage rate was 42% for *S. pneumoniae*, 33% for *S. aureus*, 58% for *H. influenzae*, 40% for *M. catarrhalis* and 3% for *S. pyogenes*. 87 patients showed a dual carriage of *S. pneumoniae* and *S. aureus.* 110 children presented a carriage of both *S. pneumoniae* and *H. influenzae*. 23 different *S.pneumoniae* serotypes were determined; the most frequent ones were: 6B, 19F, 23F,19A, 6A, 15A, 11A, 23A, 1 and 29. Among 317 pneumococcus isolates, 15% were penicillin non susceptible, 24% were erythromycin resistant, 11% were coresistant to penicillin and erythromycin.4% *S. aureus* were MRSA.25% *H. influenzae* and 100% *M. catarrhalis* were beta-lactamase producers.

Conclusions: These data provide a dynamic overview of naso-pharyngeal flora in healthy children in Brussels. Unusual *S. pneumoniae* serotypes (eg 1, 7F) were isolated in this population. Antibiotic resistance rates are globally comparable to clinical isolates exept for MRSA.

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AGE SPECIFIC SEROEPIDEMIOLOGY OF DIPHTHERIA, TETANUS AND PERTUSSIS AMONG KOREANS

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Background: This study was conducted to make the strategy of preventing diphtheria, tetanus and pertussis through age specific seroepidemiology of diphtheria, tetanus and pertussis among Koreans.

Purpose: The primary focus of this study was to assess the usefulness of DTaP and Td vaccination and get the basic data for making the strategy of DTaP and Td vaccine policy. Secondary focus was to find out the changes of defense immunity against diphtheria and tetanus in adolescents and adults after the introduction of Td vaccine.

Methods: We detected the anti-diphtheria and tetanus toxoid antibodies from the age specific samples by using ELISA, and compared those levels between age groups. Also, we detected and compared the anti-PT antibody levels with same methods.

Results: We found that the immunity against diphtheria and tetanus were well maintained in children with age below 10 years old, but the level of anti-diphtheria and tetanus Ab. were markedly decreased after 20 old aged persons. Also, anti-PT antibody levels in the group with age below 10 years old were statistically higher than the levels in other aged groups. And there were no different anti-PT levels between other aged groups.

Conclusions: We concluded that the usefulness of DTaP vaccination was acceptable through confirming the high antibody levels of diphtheria, tetanus and pertussis in the group with age below 10 years old. However, we found the necessity of active Td vaccination in persons with age more than 30 years, because of very low anti-diphtheria and tetanus antibody levels in those people.

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PRIMARY AND SECONDARY PROPHYLAXIS OF RHEUMATIC FEVER - OUR EXPERIENCE

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One of the most important contributing factors for the decline in rheumatic fever (RF) is the successful primary, as well as secondary prevention of RF.

Objectives:

1. to stress the role of prophylaxis in the appearance of first atack and RF recurrences and

2. to underline some problems with RF prophylaxis we are faced with.

Material and methods: Retrospective study of patients with group A beta haemolyticus streptococcal infections (GABS) and RF treated at University Children´s Hospital, Prishtina, between 1974/2007. A total number of 1254 children, aged from 5 to 16 yrs have been treated from RF (first attack and recurrences) for that period. After first attack of RF, the secondary prophylaxis was performed at all patients with benzathin penicillin G. Many years ago, the interval between two injections was 1 mo, but our experience revealed that despite the regular monthly prophylaxis certain number of RF recurrences ocurred. Then the interval between two injections was shortened to three weeks which results in lowering of FR recurrences.

2. Like in secondary prophylaxis, the medicament of choice for the treatment of GABS infections was also benzathin penicillin G, in one doses or repetitive ones (for months or years) in chronic throat infections. Following ASO titer in such patients, some of them manifested high ASO titer, despite regular benzathine penicillin injections every three weeks.

Conclusion: Fail to benzathin penicillin therapy in some patients with GABS means GABS carriers or maybe something unmentioned before: streptococcal rresistance to penicillin therapy?

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RHEUMATIC FEVER AND ITS NEW IMAGE

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Despite the fact group A beta streptococcus infections(GABS) remain the same, rheumatic fever (RF) in our country, like many, developed and developing countries in decreasing too.

Objective: To present RF during last eight years and to stress some changes ocurred in RF.

Material and methods: Retrospective study of in, and out patients, treated at Univesrity Childrens Hospital, Prishtina, between 2000/ 2007. Study group consists of 153 patients with RF, aged from 5 to 16 yrs. Diagnosis of RF was established using history, revised Jones criteria, laboratory, including echocardiography with its modalities. Diagnosis of GABS was performed using throat culture and following antistreptococcal antibodies for ASO.

Results: Analysis a group of 153 pts with RF, diagnosed at Prishtina Childrens Hospital, revealed some changes occured in RF features, in comparison with earlier period (twenty years ago). According to clinical features: arthritis remains the same , 36.8% as pure and in 37.5% in combination with carditis, chorea is decreasing (20% vs 7.6%), while carditis is increasing (63.1%, as pure, or in combination with arthritis or chorea).

The most dramatic change in RF appearance is the number of recurrences, which are rapidly decreasing, from 20% to 8.3%, underlying that the number of RF recurrences for the last four years was zero.

Conclusion: Like many reports, RF is becoming less prevalent and is changing its features - manifested mainly with mild and moderate cases and low number of recurrences.

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HOSPITAL BASED EPIDEMIOLOGICAL STUDY OF INFLUENZA VIRUSES AMONG CHILDREN

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Surveillance effort is being implemented that monitors the antigenic changes of influenza virus isolates in India. Since March 2003 to Janaurary 2009, total 3000 Nasopharyngeal swab (NPS) and Throat swab (TS) specimens have been collected from the Kalawati Saran Children's Hospital (KSCH), New Delhi, Clinical Research Centre (CRC), VPCI, New Delhi, Lok Nayak Jai Prakash Hospital (LNJP), India. All the clinical specimens were inoculated in MDCK cell lines after processing of the specimens. Positive isolates were typed and sub-typed by HAI and confirmatory test has been done with RT PCR using strain specific primers for HA gene. Out of 3000, 241 specimens were found positive for H1N1, H3N2 or Influenza B. The monthly distribution of influenza viruses revealed the peak season for influenza virus circulation to be during the month of January-March and June-July. According to meteorological data influenza virus isolation rate increases as the temperature decreases, humidity increases and in rainy season. The data indicates that Influenza A and B are co-circulating in the community with characteristic marked seasonality.

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MOLECULAR EPIDEMIOLOGY OF MEASLES VIRUS IN THE CONTEXT OF GLOBAL MEASLES CONTROL

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The genetic diversity of recently identified measles virus (MV) strains from Europe and Africa was analysed in the context of regional measles elimination and global measles mortality reduction programs led by the WHO.

In Europe, the prevalence and genetic diversity of indigenous MV genotypes (C2 and D6) was considerably lower than during the 1990s. However, multiple importations of other genotypes from Africa and Asia as well as their introduction into highly mobile and unvaccinated communities caused a major spread of MV in Europe during recent years. Many of the imported MV genotypes originated from regions with high measles lethality but in Europe case fatality rates remained low.

In Kinshasa (DRC), different MV genotypes, B3 and B2, were found in two consecutive epidemics (2002-03 and 2004-06), suggesting that MV circulation had been temporarily interrupted despite sub-optimal vaccination coverage in the local population. The small genetic distance (0.2%) between B2 strains from Kinshasa 2005 and those identified 20 years earlier in Gabon revealed a remarkable genetic stability of the corresponding viruses. In contrast a high genetic diversity of genotype B3 viruses (1.8-2.9%) was found within different cities of Nigeria, even though they were collected within a period of maximum 2 months. The co-circulation of many genetically distinct MV strains suggested that measles remains highly endemic in Nigeria.

Molecular epidemiology of MV is a powerful tool to monitor virus transmission within and between regions with different vaccination coverage and thus helps to develop optimized strategies for global measles control.

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THE ROLE OF INTERNATIONAL TRAVEL AND VACCINE EXEMPTORS IN THE EPIDEMIOLOGY OF MEASLES IN THE U.S., 2008

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Background and aims: Measles was declared eliminated in the United States (U.S.) in 2000. In 2008, the U.S. reported its highest number of measles cases since 1996. We describe the characteristics of measles cases reported in the U.S. during 2008.

Methods: Measles cases, reported to the Centers for Disease Control from state health departments, are categorized as internationally imported (II) if they resulted from exposure to measles virus outside the U.S., import-linked (IL) if they were epidemiologically linked to an II case, or associated with imported-virus (IV) [viral evidence indicating an imported measles genotype]. An outbreak was defined as ≥3 cases linked in time or place.

Results: During 2008, 140 measles cases and seven outbreaks were reported. The majority (126 [90%]) were associated with importations (24 II, 29 IL, 22 IV, 51 linked to IV); 60% of these were associated with Europe. Fourteen cases were of unknown source. Case-patients ranged in age from 5 months to 71 years; 14% were under 12 months, 20% were 1-4 years, and 42% were school-aged (5-19 years). Among U.S. residents (127 case-patients), 91% were unvaccinated. Of the 98 case-patients eligible for vaccine, 67 (68%) were unvaccinated because of personal or religious beliefs.

Conclusions: In the U.S., measles elimination has been maintained through high vaccination coverage. However, measles importations into the U.S. will continue to occur until global control of measles is achieved. Unvaccinated or under-vaccinated individuals, including infants and school-aged children whose parents refuse or defer vaccination, remain at risk for infection.

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BACTERIAL COLONISATION AND ASTHMA-LIKE SYMPTOMS IN INFANTS. THE GENERATION R STUDY

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Background and aims: An association between early bacterial colonisation and childhood asthma has recently been described in high-risk infants. Our aim was to investigate, in a population-based prospective birth cohort, nasopharyngeal colonisation with bacterial pathogens in early life and asthma-like symptoms in young children.

Methods: A group of 1,079 infants participated in the Generation R Focus Study: a cohort study from fetal life onwards. Nasopharyngeal swabs were cultured for the airway pathogens *Streptococcus pneumoniae, Moraxella catarrhalis* and *Haemophilus influenzae* and a nasal swab was cultured for S*taphylococcus aureus*. Swabs were obtained at 1.5, 6 and 14 months of age. Questionnaires on asthma-like symptoms and potential confounders (gestational age, birth weight, gender, maternal smoking, maternal educational level, breast-feeding, day care and siblings) were obtained at 6, 12 and 24 months of age.

Results: Infants who were culture positive for any of the airway pathogens at least four times in the first year of life had an increased risk to develop asthma-like symptoms in the second year of life (aOR 3.62 95%CI 1.51-8.68). Colonisation with *M. catarrhalis, H. influenzae* as well as any of the three airway pathogens together at 6 months carried the highest risk (aOR 1.54 95%CI 1.13 - 2.09). *S. pneumoniae* alone and *S. aureus* did not significantly associate with the development of asthma-like symptoms.

Conclusion: The frequency of airway pathogen colonisation during the whole first year of life, rather than colonisation as such, determines the risk of asthma-like symptoms in childhood.

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CHANGING EPIDEMIOLOGICAL PROFILE OF LEPROSY IN CHILDREN IN THE NAMPULA DISTRICT (MOZAMBIQUE) AT THE TURN OF THE ELIMINATION CAMPAIGN

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Background and aims: Leprosy detection rate in children is an indicator of disease prevalence and transmissibility in general population. Mozambique achieved the WHO elimination target of < 1 case of leprosy per 10.000 inhabitants in 2007; however, endemic pockets still present a threat to public health in some remote and low resource areas. The aim of this study is to analyse the disease's epidemiological profile in children in the Nampula district during the 2006-2008 period.

Methods: From January 2006 to December 2008 APARF cooperated closely with the Health Ministry in the active search of new cases in the Nampula district (>200.000 inhabitants), providing access to disease information, diagnosis and multidrug therapy.

Results: During 2006 144 new cases were detected, and thedetection rate decreased to 45 in 2008 (estimated prevalence fell from 8 to 2 cases per 10.000 inhabitants, the difference being very close to statistic significance [p=0,057]). The proportion of children < 18 years decreased from 32 to 20% (p=0,14) during the same period and there was a trend towards new cases being detected in older children, suggesting decreased transmissibility. The multibacillary proportion increased from 77 to 89% and the cumulative proportion was a significant 71% (p< 0,001), which is a phenomenon observed when leprosy is close to elimination.

Conclusions: This changing epidemiological profile in children, although still not statistically significant, suggests that leprosy is decreasing as a result of a sustained effort towards elimination, but a strong commitment is still required to achieve this goal.

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CLINICAL PROFILE OF LEPROSY IN CHILDREN IN THE NAMPULA DISTRICT (MOZAMBIQUE) DURING THE 2006-2008 PERIOD

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Background and aims: Leprosy is a devastating disease in children, because, along with the physical disabilities it may cause, the stigma too often undermines the child's opportunities to live a normal live. From January 2006 to December 2008, APARF underwent active search of leprosy cases in the Nampula District (> 200.000 inhabitants), working in close cooperation with the Health Ministry.

Methods: A descriptive retrospective study was conducted, based on the clinical files of children diagnosed with leprosy during the project period.

Results: Since inception of the project, there were diagnosed 85 leprosy cases in children and adolescents under 18 years (median 13 years), with no significant preponderance between sexes. All of them received the WHO-recommended multidrug regimen. Multibacillary forms were a significant majority (71%, p< 0,001) and the peak incidence (48%) was observed in the 10-14-year old age group. Complications such as type 1 and 2 reactions were observed and treated with steroids in 10% and 12,5% of the patients, respectively, and physical disability at the time of presentation was observed in an alarming 11% of children. Among the latter, 4% were found to have WHO Grade 1 and 7% Grade 2 disabilities, with only 22% having improved with physical therapy, or steroids or surgery as needed. The abandon rate fell from 17% in 2006 to 0% in 2008.

Conclusions: At present there are still many children living with physical disabilities and many more stigmatized by the disease. Leprosy complications were unusually high in this population.

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PREVALENCE, CUMULATIVE INCIDENCE AND SOCIO-DEMOGRAPHIC DETERMINANTS OF VARICELLA ZOSTER VIRUS (VZV) INFECTION IN EARLY CHILDHOOD IN THE UK

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Background: Germany is the only European country to have introduced universal childhood varicella vaccination. In the UK, age-related data on susceptibility to VZV infection are lacking to inform vaccination policy and optimal timing of vaccine schedules.

Aims: To report prevalence, cumulative incidence, and socio-demographic determinants of VZV infection acquired by age 5 years.

Methods: 12509 UK Millennium Cohort Study members. Maternal report of: VZV infection at age 3 and 5 years; maternal ethnicity, socio-economic status, education; family size; pre-school day-care attendance. Weighted prevalence and cumulative incidence were calculated and Poisson regression used to estimate adjusted relative risks (aRR; STATA v9).

Results: 5350 children acquired VZV infection by age 3 (44.8%; [95% CI: 43.5%, 46.0%]), and a further 3989 (32.2%; [95% CI: 31.1%, 33.3%]) between 3 and 5 years of age, giving a cumulative incidence to age 5 of 76.9% [95% CI: 75.9%, 78.0%]. Children of mothers from professional backgrounds (aRR 1.04; [95% CI: 1.02, 1.05]), and those from larger families (aRR 1.03; [95% CI: 1.02, 1.05]) or who attended pre-school day-care (aRR 1.05; [95% CI: 1.03, 1.07]) were at higher risk of VZV infection by age 5, while those with mothers from ethnic minorities (aRR: 0.95; [95% CI: 0.92, 0.98]) were at lower risk.

Conclusions: Three quarters of UK children acquire VZV infection by 5 years of age; almost half by age 3 years. The risk of VZV infection is higher in children attending day care or from larger families. An infant vaccination schedule would be optimal for the UK.

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STUDY OF FOOD POISONING IN NAVODARI CAMP, IN THE SUMMER OF 2007

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Introduction: Food poisoning is a problem specific for the summer season, given that 90% of the total patients hospitalized at our hospital during summer present digestive pathology and 50% of them are tourists. The camp was closed because of the food poisoning epidemic.

Objectives: The work aims to study epidemidemiologic, clinical, biological and therapeutic aspects related to food poisoning in Navodari camp.

Material and method: Retrospective study of 72 patients with food poisoning.

Results: Out of the 101 patients who showed up at the emergency room, 72 were hospitalized. The debut was within a few hours (less than 10 hours) from the food ingestion (cooked in the camp's kitchen). Over 90% of the patients had general toxic symptoms and vomiting; 95% had mild and severe dehydration symptom. 40% cases were diagnosed with Salmonella group D identified in fecal samples; in 11 % of the cases, the fecal samples had both Salmonela as well as E. Coli. In 2/3 of the cases, the inflammation was high. Many patients being rehospitalized in their own city.

Conclusions:

1) Association of Salmonella and E Coli in so many cases make us believe that, beside food, some of the kitchen personnel had E. Coli.

2) Navodari camp had epidemic outbreaks each year, which proves that the measures taken along the years to combat it were insufficient. The camp closure is not a happy measure for the children whose families have average or low income.

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DESCRIPTIVE EPIDEMIOLOGY OF DOG BITES/MAULINGS& RABIES/ RELATED INFECTIONS IN PICU /ED WITH IMPLICATIONS FOR A MORE CRITICAL/ HOLISTIC EVALUATION/MANAGEMENT STRATEGIES

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Background/purpose: Dogs bites/ maulings, particularly affecting children could be fatal, causing global public health concerns. 50% of children are affected at some point, predominantly males. Related infections are polymicrobial, Pasturella/ Bacteroides represents earlier pathogens, staphylococcus invades latter, its aetio-pathogenic nomenclature gets exponentially grotesque .Mortality was significant at >2%. Teenagers survived most. Deaths were newsworthy, made headlines and were acceptable indicators. Anecdotally direct attributive mortalitiy were unduly contingent on rabies, without adequate re-appraisal of simulating co-morbidities causing encephalopathies in dog maulings, such as severe infections/trauma. This misconception could espouse uninterventional management strategies, given its even/uniform case fatality. Accurate mortality figures were poorly documented /difficult to decipher. Its evaluation is more difficult in developing countries, making revisiting the investigation/management of dog bites/victims worthwhile.

Cases/interventions: Review of cases at an ED/ PICU from September 1999 to September 2008. Most cases presented within 24 hours .213 were admitted, most of the dogs were unknown, boys were mostly afflicted 65.4%, most cases were < 10 years, most bites involved the head, face, scalp/neck. Wound sepsis in 35%, encephalopathies 5.23%, hydrophobia /compatible rabies/death 1.41%.

Interventions: Radiography/Wound cultures, tetanus toxoid/rabies vaccine, broad spectrum antibiotics, analgesia / appropriate nursing/critical care with sedatives if encephalopathic. Co-amoxiclav/tetracyclines were not used.

Conclusion: Managing dog bites/maulings is complex/critical. Rabies should not be implicated in all encephalopathies related to dog maulings.Most critical/holistic evaluation / management strategies should be applied to eschew preventable fatalities from its simulating co- morbidities. Ongoing antibiotic policies are more appropriate for latter onset infections than earlier onset ones.

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A PREDICTION RULE FOR PNEUMONIA IN CHILDREN WITH FEVER AND COUGH FOR PEDIATRIC ASSESSMENT UNITS AND EMERGENCY CARE

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Background and aim: To develop and validate a prediction rule for identification of children at risk for pneumonia to support clinical decisions in emergency care.

Methods: Patients aged 1 month - 16 years with fever and cough at the emergency department of the ErasmusMC-Sophia, Rotterdam, The Netherlands (n=504, 2003-2005; median age 1.6 year; interquartile range (IQR) 0.8-2.9) and at the paediatric assessment unit at the University Hospitals Coventry and Warwickshire NHS Trust, UK (n=237, 2005-2006; median age 2.1 yr; IQR 1.2 - 5.2) were included. Independent predictors for pneumonia assessed by multivariable logistic regression were derived in the Dutch cohort and validated in the UK cohort.

Results: The derivation cohort included 78 (16%) children with pneumonia; the validation cohort 34 (14%). Laboratory tests were performed in 51% of the patients (259/504 and 120/237). Predictors for pneumonia included illness duration, ill appearance and tachypnea (ROC-area 0.74; 95% CI 0.63-0.85). These clinical signs remained diagnostically useful when applied to the validation cohort (ROC-area 0.71; 95% CI 0.53-0.89). Using these predictors children can be categorized into low, intermediate and high risk for pneumonia to guide management. C-reactive protein significantly improved risk estimation of pneumonia in those with intermediate risk.

Conclusion: The risk of pneumonia can reasonably be assessed by general appearance, illness duration and breathing rate. Serum CRP contributes to risk prediction in particular in children with an intermediate risk of pneumonia. Children categorized as having low risk of pneumonia do not require antibiotics or further investigation and can be safely discharged.

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THE OUTCOMES OF UNIVERSAL PCV-7 IMMUNISATION IN INFANTS IN KIELCE REGION

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The aim of study was to evaluate the effect of PCV-7 on incidence of pneumonia.

Methods:

- On the 1st of January 2006 there was initiated program of common PCV-7 vaccination in infants founded by authorities of city of Kielce.
- There was applied a modified 3-dose vaccination program 2+1 (3/12-6/12-13/12)
- There was compared a frequency of hospitalization due to pneumonia in children in age groups of 0-1 and 2-4 years in the period before (2004-2005) and after implementation of universal immunization (2007 and 2008).

Results:

- Compared to 136 children with pneumonia in age group of 0 -1 year in a control period (2004 and 2005) there were hospitalized 53 and 51 children in the year 2007 and 2008 respectively.
- Compared to 30 children with pneumonia in age group of 2-4 year in a control period (2004 and 2005) there were hospitalized 23 and 19 children in 2007 and 2008 respectively.

Conclusions:

- A number of pneumonia hospitalizations in vaccinated children (aged 0-1 year) was reduced by 61% in 2007 and by 62.5% in 2008. In 2007 in unvaccinated children aged 2-4 years a reduction in pneumonia hospitalization was 23%. In 2008 the reduction rate in this age group increased to 37% and was result of vaccination started in 2007.
- PCV-7 vaccination schedule 2+1 was effective in reduction of pneumonia hospitalization in children.

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TICK-BORNE ENCEPHALITIS IN CHILDREN AND ADOLESCENTS IN THE WEST BOHEMIAN REGION (CZECH REPUBLIC) BETWEEN 1960 AND 2008

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Background and aims: After lyme borreliosis, tick-borne encephalitis (TBE) is the second most common infection transmitted by ticks in Europe. The West Bohemian Region ranks among the highest incidence areas in the Czech Republic.

Methods: The retrospective survey analysed 0-19-year-old patient´s records with serologically established TBE as reported to the Hygienic Service of West Bohemian Region from 1960-2008.

Results: During the surveyed period 420 cases of TBE in children and teenagers were confirmed by laboratory testing (3.4 per 100,000 inhabitants p.a.). The highest incidence rate for both male and female sexes (6.2 and 4.1 respectively) concerns the same age group of 15-19 years old. Of all the reported cases, one case was fatal (a 15-year-old boy, 0.2%). None of the sick reported TBE vaccination. Over the years the risk of transmission in particular areas of the region has changed. The current highest incidence rate is reported in the Klatovy District (14.9 per 100,000 inhabitants p.a.). In 5.2% cases patient's anamnesis showed data on the consumption of non-pasteurized milk or non-pasteurized diary products. As a result of the gradual prolongation of the infection season, the transmission period currently falls between March and November. The preschool category reported the highest incidence in June and September, while schoolchildren fall predominantly in the standard summer holiday months of July and August. Based on officially available data, 13.7% of the Pilsen Region´s young population has been vaccinated, so far.

Conclusions: Low vaccination coverage may hardly influence the unfavorable TBE epidemiological situation.

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HIGH RATES OF ANTIBIOTIC PRESCRIBING DURING PREGNANCY WITH POTENTIAL CONSEQUENCES FOR CHILDHOOD OUTCOMES: UK PRIMARY CARE DATABASE STUDY

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Background and aims: To evaluate antibiotic prescribing patterns in pregnancy.

Methods: Primary care data for 4% of patients in the UK between 1992 and 2007 were analysed for pregnant women aged 15 to 45 years.

Results: Overall, 37,494/114,734 (33%) women received at least one antibiotic prescription during pregnancy. Two-thirds (65%) received just one prescription and less than 5% received more than three antibiotic prescriptions. The most frequently prescribed antibiotics were broad-spectrum penicillins (48%), cephalosporins and other betalactams (21%). Erythromycin accounted for 7% of all prescriptions and was prescribed at the same rate throughout pregnancy. Trimethoprim, tetracyclines and quinolones, and metronidazole were prescribed in the first four weeks of pregnancy, but the number of prescriptions of these antibiotics declined substantially thereafter. In the four weeks *before* delivery, 3,041 (8%) women received an antibiotic prescription and 337 (1%) women received Erythromycin. The level of antibiotic prescribing declined from nearly 40% in 1997 to 35% of pregnant women in 2007. Young maternal age and social deprivation were associated with increased antibiotic prescribing: relative risk 1.34 (95% CI 1.29 -1.38) for women in most deprived v least deprived area, adjusted for age.

Conclusions: Antibiotic prescribing is common in pregnancy. Further research into prescribing of antibiotics in primary care during pregnancy is urgently needed in view of emerging evidence that maternal antibiotics can potentially affect long term neurological outcomes, gut flora and immune development in children.

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SEROTYPE-SPECIFIC CLINICAL OUTCOMES OF INVASIVE *PNEUMOCOCCAL DISEASE* IN HOSPITALIZED PEDIATRIC PATIENTS IN MADRID (MAY 2007 - APRIL 2008)

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Background: The PCV7 vaccine was only available privately in Spain from October 2001. Use of this vaccine increased from 2002 onwards, with reported coverage in 2006 below 50%. In October 2006, the Madrid local health authority approved its inclusion in the childhood vaccination schedule. This 3-year hospital-based surveillance study (21 centres) aimed to assess changes in pneumococcal serotype distribution and clinical outcomes in Madrid after the introduction of PCV7.

Methods: Inpatient cases younger than 15 years old with confirmed invasive pneumococcal disease (IPD) confirmed by culture or PCR were included. Conventional serotyping was performed by an agglutination test (Pneumolatex) and Quellung reaction. Cases of culture-negative empyema were serotyped using real-time PCR.

Results: 163 cases were identified. The Table shows the distribution of clinical outcome by serotype focus on STs: 1, 3, 5, 6A, 7F, and 19A.

	Meningitis (n=23)	Bacteraemic pneumoniae (n=59)	Pleural empyema (n=64)	Bacteraemia (n=19)	Others (N=8)
ST 1	0 (0%)	16 (27%)	20(37%)	0(%)	0(0%)
ST 3	0 (0%)	1 (2%)	3(6%)	0(%)	1(12,5%)
ST 5	3(13%)	17(29%)	11 (20%)	4(21%)	0(0%)
ST 6A	3(13%)	0(0%)	0(0%)	1(5%)	0(0%)
ST 7F	1(4%)	6(10%)	3(6%)	5(26%)	0(0%)
ST 19A	5(22%)	4(7%)	7(13%)	3(16%)	4(50%)
Total	12(52%)	44(75%)	44(82%)	13 (68%)	5(62%)

[cases by clinical outcome and serotype]

Conclusions: Serotypes 19A and 5 did not appear to favor a particular site, whereas serotypes 1 and 3 were only involved in lung disease. As previously reported, ST 1 was the most prevalent serotype in patients with empyema, and ST 19A was the most prevalent in patients with meningitis.

For Heracles Study Group, Madrid, Spain

P204

SEROTYPE DISTRIBUTION OF INVASIVE *STREPTOCOCCUS PNEUMONIAE* AMONG HOSPITALIZED PEDIATRIC PATIENTS IN MADRID (MAY 2007 - APRIL 2008)

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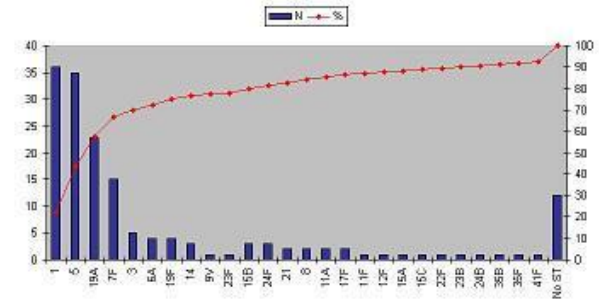
Objectives: This 3-year active hospital-based epidemiological study aimed to assess the changes in pneumococcal serotype distribution, clinical syndromes, and underlying conditions associated with invasive pneumococcal disease (IPD) after the introduction of the PCV7 vaccine in Madrid in November 2006 (21 centres involved).

Methods: Inpatient cases younger than 15 years old with laboratory-confirmed IPD or culture-negative empyema were included. Pneumococci were identified using microbiologic and molecular genotyping methods. Conventional serotyping was performed by an agglutination test (Pneumolatex) and Quellung reaction. Cases of culture-negative empyema were serotyped using a real-time PCR that targeted different capsular locus genes. Data for the period May 2007-April 2008 are presented.

Results: 163 cases were identified during this period. The Figure shows the serotype distribution of cases.

Figure 1: serotype distribution of cases (n=163). May 2007-April 2008



[serotype distribution of cases]

Conclusions: Only three serotypes (1, 5, and 19A) were responsible for 60% of the cases. Only a very low proportion of IPD cases were due to one of the PCV7 serotypes after the introduction of the PCV7 vaccine (6%). The high number of IPD cases due to serotype 5 could suggest an outbreak in Madrid. Continuous surveillance is needed to monitor the development of this strain.

For Heracles Study Group, Madrid, Spain

P205

PROSPECTIVE POPULATION-BASED SURVEILLANCE OF BACTERIAL MENINGITIS IN CHILDREN < 5 YEARS OF AGE IN NINE RUSSIAN CITIES

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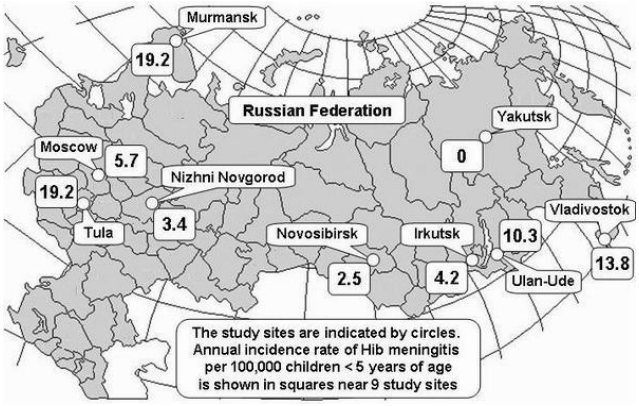
Background and aims: The burden of meningitis caused by *Haemophilus influenzae* type b (Hib) in Russia was estimated only by hospital-based surveillance or by retrospective Hib-RAT assessment. In this study the incidence rates of bacterial meningitis per 100,000 children < 5 years of age (U5-children) was evaluated prospectively in the capital cities of 9 Provinces of Russia (Map).

Methods: Both bacteriological culture and non-cultural methods (latex agglutination, PCR) were used for diagnostics.

Results: Etiological agent was identified in about 85% of 343 probable bacterial meningitis cases. Hib caused 27% of all bacterial meningitis cases on average (Table), whereas *N.meningitidis* caused about 54% of cases. The annual incidence rate of Hib-meningitis varied greatly (Map). The mean incidence rate of laboratory confirmed Hib-meningitis in these 9 cities was equal 8.8 cases per 100,000 U5-children. The incidence rate of systemic meningococcal disease in the same populations ranged from 17 cases/100,000 U5-children in Ulan-Ude to 77 cases in Murmansk with the mean value 30.

Conclusion: Hib-meningitis ranks after meningococcal meningitis in Russian U5-children. The introduction of Hib-vaccine may be considered, at least in such Provinces with high Hib-incidence as Murmansk, Tula, Vladivostok, and Ulan-Ude.



[Map]

City of surveillance	Moscow	Mur-mansk	Tula	Nizhni Novgorod	Novo-sibirsk	Irkutsk	Ulan-Ude	Yakutsk	Vladi-vostok	Total or mean
Years and duration of surveillance	2000-2001, 24 mo.	2004, 12 mo.	2004-2005, 24 mo.	2004-2005, 24 mo.	2004-2005, 24 mo.	2007-2008, 18 mo.	2007-2008, 18 mo.	2007-2008, 18 mo.	2007-2008, 18 mo.	180 mo.
Number of children < 5 years of age in the city	344000	15608	19812	58293	60247	31561	19379	18253	29029	596182
Number of probable bacterial meningitis cases	209	10	15	30	35	16	10	6	12	343
Number of confirmed bacterial meningitis cases	180	9	15	24	30	13	8	4	11	294
Number of Hib meningitis	39	3	8	4	3	2	3	0	6	68
Number of meningococcal meningitis	117	5	7	10	20	8	4	2	5	178
Number of pneumococcal meningitis	14	0	0	8	7	3	1	2	0	35
% of laboratory confirmed bacterial meningitis cases	86%	90%	100%	80%	86%	81%	80%	67%	92%	85%
% of Hib meningitis among all confirmed bacterial meningitis cases	22%	33%	53%	17%	10%	15%	38%	0.0%	55%	27%

[Table]

For The Russian Hib Study Team, Regonal Russian Hospitals, Moscow, Murmansk, Tula, Nizhni Novgorod, Novosibirsk, Irkutsk, Ulan-Ude, Yakutsk, Vladivostok, Russia

P206

CHANGING EPIDEMIOLOGY OF PERTUSSIS IN SÃO PAULO, BRAZIL, 2000-2008

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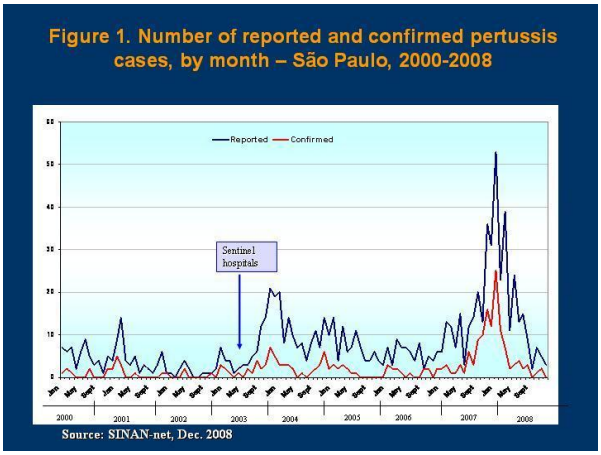
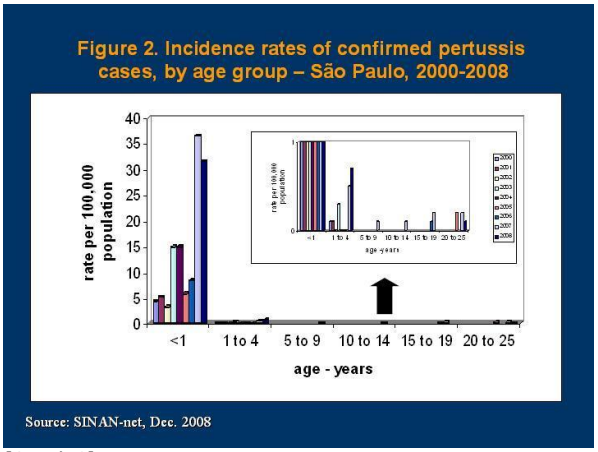
Background and aims: In the last decades many countries reported pertussis resurgence, but data from São Paulo were lacking. The aim of this study is to describe the epidemiology of pertussis in the city of São Paulo, Brazil, from 2000 to 2008.

Methods: The study was conducted in São Paulo, a city with 11 million people including 170,000 infants. Vaccination coverage for 3 doses of DTP in the first year of life is over 95% in the last 5 years. Until 2002 the surveillance system was passive and thereafter active in sentinel hospitals. The data sources were the on-line National Information System of Reporting Diseases (SINAN-net) and Brazilian Institute for Geography and Statistics. We adopted the case definition recommended by WHO. The information analyzed in each case was: age, date of onset of pertussis symptoms, vaccination status, and outcome. Incidence rates by age group and year and case fatality ratio were calculated.

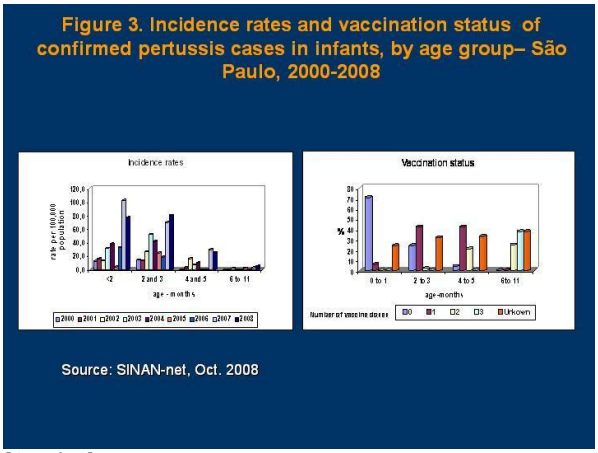
Results: During the period, a total of 883 suspects and 236 confirmed pertussis cases were reported, 41% from sentinels. Figure 1 show 2 peaks of cases: one in 2003 after active surveillance implementation, and another in 2008. 90% of cases occurred in infants < 1 year old (Figure 2 and 3) with incomplete vaccine basic series. The case-fatality ratio in infants was 5%.



[Graph 1]



[Graph 2]



[Graph 3]

Conclusions: Pertussis continuous to be a significant public health problem in São Paulo, mainly in infants < 6 moths. The surveillance system is not sensitive to detect pertussis in adolescents and adults.

P207

SCREENING TO DETERMINE THE PREVALENCE OF RHEUMATIC HEART DISEASE IN ASYMPTOMATIC CHILDREN IN GUYANA SOUTH AMERICA

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Background and aims: The prevalence of Rheumatic Heart Disease (RHD) in tropical rural Western Hemispheric settings is unknown.

Methods: A Canadian medical team visited six remote Amerindian villages along the Upper Mazzaruni River of Guyana. Teachers randomly selected 68 healthy children in the villages. The children were asked basic questions about symptoms and past history of rheumatic fever, underwent clinical examination and echoDoppler (ED) study using portable equipment to determine the prevalence of RHD. 2 cardiologists using pre-specified criteria reviewed all ED studies. If RHD was detected, a long-term supply of penicillin for secondary prophylaxis was provided.

Results: 68 children between the ages of 8 and 17 years were assessed: 11 recalled an illness of fever with joint soreness and 21 felt that they were unable to keep up with their peers on exertion. Four asymptomatic children had definite echo evidence for RHD (6%). Only one child with RHD on ED had a systolic ejection murmur and this was related to an incidental small muscular VSD.

Conclusions: Screening for RHD in remote areas of developing countries using portable ED equipment is feasible. Stethoscope auscultation is not helpful in identifying asymptomatic rheumatic heart disease in children but may be helpful in identifying congenital heart disease. There is a very high prevalence of asymptomatic RHD in this population. Approaches to the diagnosis and management of streptococcal pharyngitis in the developing world need to be reassessed and appropriate treatment algorithms formulated to reduce the prevalence of RHD.

P208

THE BELGIAN PAEDIATRIC SURVEILLANCE UNIT "PEDISURV": MORE THAN COUNTING CASES

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Background: In several countries, Paediatric Surveillance Units have been established to facilitate surveillance for a range of conditions. In Belgium, a network "PediSurv" was set up to contribute to polio-free certification and measles elimination goal of the World Health Organization.

Methods: As of October 2002 a prospective surveillance is carried out by 40% of the Belgian paediatricians and 37% of the general practitioners in Brussels. 80% of the hospitals with a paediatric department participated. Participation is voluntary with monthly reporting of cases of Acute Flaccid Paralysis (AFP), measles and mumps. Invasive pneumococcal disease (IPD) was added in October 2005 following introduction of the 7-valent pneumococcal conjugate vaccine and congenital rubella syndrome (CRS) in 2007. A standardized form is used to obtain case-specific information. Notification is done by mail or Internet and zero-reporting is requested.

Results: Between 2003 and 2007 approximately 550 clinicians participated monthly (response rate 64% - 70%). Non-polio AFP rate ranged from 0.06 to 0.50. Measles incidence remained above the elimination threshold of < 1 per million. Besides a measles outbreak in 2007, several clusters of measles and mumps were identified every year. Incidence of IPD in children < 5 year was estimated at 67/100 000 in 2006 and 58/100 000 in 2007. No cases of CRS were reported.

Conclusions: Although PediSurv is not an exhaustive surveillance system, the stable participation allowed to observe trends and to detect clusters and outbreaks. Information is being used for decision-making in public health and monitor progresses in different elimination goals.

P209

SEROPREVALENCE OF TOXOCARIASIS IN SCHOOLCHILDREN IN NORTHERN IRAN

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This cross-sectional study was carried out on 1210 randomly selected schoolchildren, attending sixteen primary and secondary schools, during the period between November 2005 and June 2006. Students who accepted to include their children were requested to be present at sampling time and to fill in a simple questionnaire with personal and epidemiological data. Three ml of venous blood were taken by vein puncture under sterile conditions from each subject for detection and titration of antibodies to *T.canis* and eosinophil counts. Total IgG anti-*Toxocara* antibodies study was carried out by *T.canis* IgG ELISA kit. According to the manufacture recommendations, an index positivity >11 U was considered positive. Of the 1210 serum specimens tested, an overall seroprevalence for *Toxocara* antibodies of 25% was obtained. There was no association between positive seroprevalence and age (P=0.69). Boys and girls differed significantly with regard to *Toxocra* titre (P < 0.001). Eosinophilia in peripheral blood (≥5%) was detected in 24.5% (297/1210) of the population studied, 97/297 (32.8%) of whom were seropositive for toxocariasis. The findings of this study confirm that infection with *Toxocara* is quite high and widespread in children in Northern Iran. Therefore health promotion efforts must be directed at increasing the awareness of the population about the potential zoonotic hazards associated with the disease and how to minimize them.

P210

PARETIC COMPLICATIONS OF ASEPTIC CNS INFECTIONS IN CHILDREN AND ADULT PATIENTS IN THE CZECH REPUBLIC

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Background: Arboviruses (tick born encephalitis - TBE), Borrelia burgdorferi sensu lato (neuroborreliosis-NB) and enteroviruses are the most frequent causes of aseptic CNS infections in the Czech Republic. All of these diseases can have the same complication- paresis. We evaluated a frequency, severity and clinical recovery of palsies depending on age.

Methods: Four hundred thirty patients (144 children, 286 adults) hospitalized in Bulovka University Hospital (2005-2007) with final diagnosis of neuroborreliosis,(60 adults, 34 children), TBE (204 adults, 15 children) and enteroviral meningitis (22 adults, 95 children) were enrolled to the retrospective study. They were monitored during stay in hospital and after 1 and 6 months.

Results: Seventy eight patients suffered from palsies. Most of them was in NB group, 16 children (41%) had facial nerve palsy, 45 adults (71%) had affected facial nerve or other cranial or peripheral nerves, in 5 cases quadruparesis or paraparesis was present. In followed period no changes of palsy frequency had appeared. Clinical recovery was generally good. In TBE group no child had palsy, 15 adult patients (6,8%) had serious paretic complications with long lasting sequelae. The frequency of palsies 6,0% in 2005 and 3,3% in 2006 increased to 15,2% in 2007. Enteroviruses caused mild palsies in 2 cases (1,5%), only.

Conclusion: Cerebrospinal fluid examination is recommended in every patient with facial nerve palsy to exclude neuroborreliosis. Our results confirm the importance of TBE vaccination especially in elderly persons.

P211

EPIDEMIOLOGY OF TUBERCULOSIS AMONG KIDS IN BOSNIA AND HERZEGOVINA AFTER WAR

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Introduction: Tuberculosis in childhood is different from that in adults, and requires different expertise. Children generally have a much smaller bacterial population and there is less secondary resistance. Treatment was usually with isoniazid, rifampicin, and pyrazinamide for Bosnian children.

Methods: Authors analyzed data from the national tuberculosis surveillance database. Evaluated risk factors and kids patient characteristics included demographics, social contacts, economic status, travel history,living and social environment, medical history, family history, and exposure to tuberculosis.

Results: This study demonstrates that the incidence of tuberculosis children in Bosnia and Herzegovina has followed this pattern with a clear resurgence in childhood tuberculosis occurring between 1995 and2008. Bosnian incidences of tuberculosis are decreasing, but it is one of the most highest in Europe (20 to 30 on 100.000 children until 19 years, before more than 60).

Discussion: Poverty was strongly associated with tuberculosis in this study. This confirms earlier estimates and counters thoughts that those estimates were high. The diagnosis of TB in children, particularly in children younger than five years, remains difficult.

Conclusion: These findings point to an unrecognised burden of kids disease, ongoing community transmission, and missed opportunities for prevention. To reverse the current trend of increasing tuberculosis morbidity, both a more aggressive search for cases and the use of preventive therapy among high-risk kids populations will be necessary. Tuberculosis is presently one of the major kids problem in Bosnia and Herzegovina.

Keywords: Tuberculosis, Epidemiology, Children, Prevention.

P212

EPIDEMIOLOGY OF VARICELLA AFTER INTRODUCTION OF GENERAL VARICELLA VACCINATION - FIRST RESULTS FROM THE 'BAVARIAN VARICELLA SURVEILLANCE PROJECT' 2006-2008

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Background and aims: Since July 2004, varicella vaccination has been recommended for all children aged 11-14 months in Germany. An epidemiology surveillance project was initiated in 2006.

Methods: Monthly reports of varicella patients (≤16 years of age) and varicella vaccinations were collected from 88 (67%) of 132 paediatric practices in the Munich area (Bavaria). Detailed information was collected for varicella complications and vaccinated cases. Vaccine coverage was determined yearly, in random samples (n=600) of children 18-36 months of age.

Results: From October 2006 to April 2008, practices reported a total of 8,795 varicella cases (5.7 cases per month and practice; 64% in children < 5 years of age), and 13,828 (first) varicella vaccinations (8.9 per month and practice). Vaccine coverage increased from 38% in 2006/2007 to 51% in 2007/2008. From October 2006 to April 2007, there were 3,913 varicella cases (7.2 cases per month and practice), compared to 2,661 cases (5.0 cases per month and practice) from October 2007 to April 2008. In 42 (0.5%) of all varicella cases, a total of 57 complications were reported (skin complications 51%, otitis media 11%, pneumonia 9%, central nervous system 7%, others 22%). Ten (0.1%) children were hospitalised; 3 (0.03%) showed permanent scars. There were 379 (4.3%) cases in varicella-vaccinated children.

Conclusions: Further follow-up is necessary to confirm the observed decrease of about 30% in the burden of varicella disease, which currently is still dominated by mostly unvaccinated cases.

P213

CHARACTERISTICS OF VARICELLA DISEASE IN VACCINATED CHILDREN FROM THE 'BAVARIAN VARICELLA SURVEILLANCE PROJECT' 2006-2008

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Background and aims: Long-term surveillance studies on varicella vaccination generally show a large decrease of varicella disease burden, but indicate an increase in annual rates of varicella in vaccinated children. In Germany, after general recommendation for vaccination (one dose at 11-14 months of age) in 2004, a varicella surveillance project was initiated in 2006.

Methods: Detailed reports on vaccinated varicella cases (VVC) in children ≤16 years of age were collected from a network of 88 paediatric practices in the area of Munich City and County.

Results: From October 2006 to April 2008, the paediatricians reported a total of 8,795 varicella cases; of those, 379 cases (4.3%) occurred in vaccinated children. In VVC, age (median, IQR) at varicella vaccination was 1.9 years (1.1-3.1); age at varicella disease was 3.8 (2.6-4.9) years; the delay (median, IQR) from vaccination to disease was 16.9 months (9.6-25.9). About 91% of the VVC were varicella breakthrough cases (VBC), occurring more than 42 days after vaccination. Four (1%) children of the VBC had received 2 doses. Out of 199 VBC with reported counting of lesions, 186 (93.5%) showed less than 50 lesions indicating mild varicella disease. Complications were reported for 5 VBC (including 1 hospitalisation); 1 child showed few permanent scars.

Conclusions: Correspondingly to a 30% decrease of varicella cases (see separate abstract), a small increase in varicella breakthrough cases with mostly mild clinical presentation has been observed. Continued surveillance is necessary to determine the optimal age for a second dose of varicella vaccine.

P214

CLINICAL AND MOLECULAR EVIDENCE OF INFLUENZA TRANSMISSION WITHIN HOUSEHOLDS

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Background and aims: Influenza virus is associated with significant morbidity and mortality, causing 83 pediatric deaths during the 2007-08 season. The understanding of influenza transmission is critical to pandemic influenza preparedness. This report focuses on the transmission of influenza virus within households, as children are the primary source of family infections.

Methods: Children with influenza-like illness during the 2007-08 influenza season had nasal washings submitted for rapid antigen testing, culture and PCR. Accompanying parents or siblings, regardless of clinical illness were also enrolled. Transmission was defined as 2 or more family members developing influenza with onset at least one day apart.

Results: 118 children (114 symptomatic) and 104 adults (56 symptomatic) from 89 families were enrolled. Forty-four families had at least one member who was influenza PCR-positive (1 H1N1, 27 H3N2 and 16 Influenza B), including 3 families with one asymptomatic influenza-positive person.Suspected transmission of influenza was noted in 16/28(57%) families with influenza A versus 4/16(25%) families with influenza B (p=0.05)Transmission was molecularly confirmed (conserved sequence homology in two PCR-positive family members) in 14/28(50%) families with influenza A versus 2/16(12.5%) families with influenza B (P=0.02). 11/16(68%) confirmed transmissions originated from a child (ages 10m-17y, mean 6.6y).

Conclusions: Influenza is highly transmissible within families, with young children being the most common source. Transmission of influenza A was significantly more common than influenza B. Subclinical influenza infections occur in contacts of clinically ill patients, and molecular diagnostics have the potential to identify pre-symptomatic patients during an influenza pandemic.

P215

SEROPREVALENCE OF VACCINE-PREVENTABLE DISEASES IN BELGIUM

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Background and aims: To evaluate the susceptibility to vaccine-preventable diseases in Belgium, a seroprevalence study was carried out in 2006 and compared to a previous study in 2002.

Methods: Residual sera from 3974 Belgian inhabitants (aged 1-65 years), stratified for age and gender, were collected through hospital laboratories and blood transfusion centres that were geographically well distributed.

The IgG antibody titers for measles, mumps, rubella (MMR) and diphtheria (D) at all ages, for tetanus (T) from the age of 40 years on, and hepatitis B (HBV) markers in up to 19-year-olds were defined by different ELISA's.

Results: In 2006 and in 2002, ≥10% of 5-9 year-olds, and ≥5% of 10-29 year-olds were seronegative for measles and 12-13% of women of childbearing age (15-40 years) had < 10IU/ml rubella-antibodies. In under-20-year-olds, 2% were seropositive for anti-HBc+ and 1% for HBsAg.

In the infant and adolescent age cohorts targeted by the universal HBV vaccination campaign, 89% and 66% respectively had anti-HBs >10 IU/ml in 2006 versus 75% and 56% in 2002.

In 2006, the proportion with anti-D ≥0.1IU/ml was 75-80% in 1-29 year-olds, but diminished steeply with age to 24% in 50-65 year-olds. The proportion of adults with anti-T ≥0.1IU/ml diminished little with age (40-65 years) from 92% to 85%.

Conclusion: A remaining risk for circulation of measles and for Congenital Rubella Syndrome was demonstrated in Belgium. Universal HBV vaccination was well implemented in both targeted age cohorts. At adult age, immunity against tetanus was much better than against diphtheria.

P216

COVERAGE OF RECOMMENDED VACCINES IN INFANTS IN FLANDERS, BELGIUM, ANNO 2008

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Background and aims: Previous surveys in Flanders demonstrated a high coverage of vaccines recommended in infancy, though not yet optimal for MMR. To evaluate any trends, including the uptake of the recently introduced pneumococcal (PCV-7) vaccine, and to obtain more information on reasons for non-vaccination, a new EPI-based survey was performed in 2008.

Methods: The study population consisted of 1002 infants aged 18-24 months selected randomly by EPI cluster sampling (S1) and 404 infants (S2) selected for having incomplete vaccination data in Vaccinnet, Flanders' web-based vaccine registration system. Their parents were interviewed at home, vaccination documents were checked and if they were incomplete, additional information was asked and vaccination data were updated from medical files if possible. Coverage rates were measured for poliomyelitis (IPV) (mandatory), tetanus-diphtheria-pertussis (DTP), H. influenzae type b (Hib), hepatitis B (HBV), measles-mumps-rubella (MMR), PCV-7, and meningococcal C (MENC) vaccine.

Results: In S1 the coverage rate was 95% or above for IPV, DTP, Hib, HBV ,MMR and MenC; 80.0% were fully vaccinated with PCV-7. Nevertheless 2-13% of vaccine doses were administered more than 2 months after the recommended age, and 8% of infants had not yet completed the primary course of IPV-DTP-Hib-HBV by 6 months of age.

In S1+S2, infants who were not immunised in well-baby clinics or who had more older siblings were more at risk for not (yet) being fully vaccinated by 18 months of age.

Conclusions: Universal vaccination reaches infants very well in Flanders, but compliance to recommendations on timing leaves room for improvement.

P217

TRANSMISSION OF ROTAVIRUS TO HOUSEHOLD MEMBERS OF SWEDISH CHILDREN HOSPITALIZED FOR SEVERE ROTAVIRUS GASTROENTERITIS RESULTS IN LOSS OF PARENTAL PRODUCTIVITY

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Background and aims: Rotavirus Gastroenteritis (RV GE) is responsible for > 500,000 deaths and millions of hospitalization annually among younger children worldwide. A larger prospective hospital-based surveillance estimates the incidence for hospitalization due to rotavirus infection in Sweden to range from 300 to 500/100,000 children < 5 years. Information regarding household transmission of rotavirus and its impact is limited. In this sub-study, we aimed to investigate the transmission pattern of rotavirus among household members of hospitalized children and subsequently the impact on parental productivity.

Methods: Household members of children hospitalized for RV GE at the Astrid Lindgren Children's Hospital during winter season 2007/2008 were asked whether they developed GE symptoms in association with the child being hospitalized. Stool samples from family members, collected within 14 days after discharge of their child, were tested for rotavirus by ELISA (Oxoid).

Results: 155 households of the RV GE children were interviewed of which 97 provided stool samples for testing. In 51% of these (n=49), rotavirus was detected in at least one additional family member who either was symptomatic or asymptomatic. Among the household members 32 of 96 mothers, 17 of 86 fathers and 18 of 64 siblings excreted rotavirus. All rotavirus positive siblings were < 5 years of age and no difference between genders was noted. Significant loss of parental productivity was observed.

Conclusions: In more than 50% of households, at least one additional family member of children hospitalized for RV GE excreted rotavirus most likely contributing to further spread of the virus.

P218

SYSTEMIC ANTIMICROBIAL DRUGS USAGE IN A PEDIATRIC UNIVERSITY CLINIC FROM BUCHAREST, ROMANIA

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Background: Antibiotic use significantly contributes to increasing rates of resistant pathogens and hospitals are advised to measure antibiotic use and monitor its relationship to resistance. The aim of this study was to describe the antimicrobial consumption (ABC) in pediatric inpatients of Bucharest, Romania.

Methods: A random sample accounting 895 (≈30%) out of the 2917 patients discharged from “Grigore Alexandrescu” Emergency Hospital for Children, during October 2008, has been draw first. By reviewing medical charts of enrolled patients, appropriate demographic, clinical, and pharmacological data have been captured and filled in an Epi6 software database. ABC have been expressed as usage density rate where the nominator was the pooled number of days of therapy (DOT) with each type of antimicrobial agent and the denominator the pooled number of patient days (PDs), respectively.

Results: The patients' median age was 5 years, the median duration of hospitalization was 3 days and the pooled number of PDs accounted 4049.

The exposure to overall antibacterial agents accounted 2607 DOT and the correspondent ABC density rate was 64.44 DOT/100 PD. Fifty-two percents of patients received at least one antimicrobial agent. The top five antibacterial agents used were ceftriaxone, gentamicin, cefoperazone, cefazolin and cefuroxime.

Discussions: ABC density rate found by us is consistent with values recently reported abroad in similar settings; however, the high prevalence of patients exposed to antibacterial agents and the cephalosporins' overuse are matters of concern.

Conclusion: ABC density rate based on DOT metric appears as a value indicator for driving antimicrobial usage proper stewardship.

P219

HOW TO DETERMINE URGENCY FOR CHILDREN WITH FEVER IN EMERGENCY CARE? A RISK CHART FOR TRIAGE

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Background and aims: Triage aims to identify patients who benefit most from immediate medical care. According to the Manchester Triage System, a commonly used triage system in Europe, all children with fever are triaged as high urgent, and have to be seen within 10 minutes. We aimed to assess the value of body temperature alone and combined with age and presenting problem to predict high urgency in children.

Methods: Prospective observational study. Children attending the emergency department of two hospitals were included. Missing values on temperature were imputed (14.7%). Data were analyzed using logistic regression analysis. As a predefined reference standard for urgency we used a proxy, consisting of a combination of vital signs at presentation, presence of a potentially life threatening condition, performed diagnostics and therapy, and scheduled follow-up. We developed a score chart based on the final model to decide on urgency.

Results: 12,562 patients were eligible. In 1,407 (11.2%) patients the reference standard for urgency was missing. Temperature alone had a moderate discriminative ability to predict urgency, but its combination with presenting problem and age led to better performance. The influence of temperature (75^{th} versus 25^{th} percentile) on high urgency is high for patients presenting with urinary tract problems (OR 3.0, 95% C.I.1.0-9.2) and low for neurological problems (OR 0.8, 95% C.I.0.6-1.1).

Conclusions: Body temperature combined with age and presenting problem is an important discriminator in triage to predict urgency in children. However, the presence of fever itself is not sufficient to classify children as highly urgent.

P220

REPLACEMENT OF PNEUMOCOCCAL SEROTYPES AMONG COLONISED CHILDREN FOLLOWING INTRODUCTION OF PCV-7 IN THE NORWEGIAN VACCINATION PROGRAMME

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Background and aims: The seven-valent conjugated pneumococcal vaccine (PCV-7) was introduced in the Norwegian childhood vaccination programme in July 2006. A cross-sectional study of nasopharyngeal carriage of *Streptococcus pneumoniae* among children attending day-care centres (DCC) was performed in the autumn of 2006. In order to evaluate the changing epidemiology of pneumococci colonising children, a follow-up was performed in the autumn of 2008, two years after start of widespread use of PCV-7.

Methods: Cross-sectional studies of nasopharyngeal carriage of pneumococci among children attending DCC, using a sensitive sampling method. Briefly, nasopharyngeal swabs were transported to the laboratory in a serum broth and plated within 3-4 hours. Pneumococci were identified directly from the broth by serotyping, and confirmed by growth on blood agar.

Results: Nasopharyngeal swabs were obtained from a total of 1213 children, 611 in the 2006-study and 602 in the 2008-study. The proportion of children vaccinated at least twice with PCV-7 increased from 3.4% in 2006 to 39.2% in 2008 ($p < 0.001$). In total, 475 (77.7%) and 484 (80.0%) children carried pneumococci in 2006 and 2008, respectively. The proportion of isolates belonging to PCV-7 serotypes decreased from 235 of 539 isolates (43.6%) in 2006 to 116 of 563 isolates (20.6%) in 2008 ($p < 0.001$).

Conclusions: The rate of nasopharyngeal colonisation with pneumococci among children attending DCC remains high and unchanged after introduction of PCV-7 in the childhood vaccination programme. The ecological niche vacated by the PCV-7 serotypes has been replaced by non-PCV-7 serotypes.

P221

PRESENCE OF ROTAVIRUS AND ADENOVIRUS ANTIGENS IN OUTPATIENT WITH GASTROENTERITIS IN PRIVATE HOSPITAL IN ANKARA-TURKEY

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Aim: Especially in childhood, one of the most important causes of mortality is infectious diarrheas. We aimed to determine distribution of gastroenteritis case occurred due to rotavirus and adenovirus factors according to various age groups, months and years, epidemiology of which is not well-known in our country.

Materials and methods: Antigens of rotavirus and adenovirus were investigated by immuno-chromatographic method (CerTest Biotec-Spane; rota-adeno blaster) in stool samples of 2,962 patients, who applied to various clinics of our hospital between January 2005 - June 2008 and who had the diagnosis of acute gastroenteritis.

Results: Viral antigens were determined in 605 (20,4%) of 2,962 stool samples. Of those 2,962 samples, 483 (16,3%) were found to be positive for rotavirus and 77 (2,6%) for adenovirus. Combination of positivity of rota and adenovirus was determined in 45 (1,5%) samples. Cases of viral gastroenteritis (rota and adenovirus) are observed most frequently in 0-5 years-old group, and rotavirus is seen more during winter and adenovirus throughout the year.

Conclusions: It is observed that rotavirus and adenovirus are important factors in gastroenteritis developing in the region where our hospital gives service and in 0-5 years-old group. Preventing empirical use of antibiotics for patients, whose test results are positive by rapid and valid (specific and sensitive) diagnostic methods such as the immuno-chromatographic method, is important for reducing development of antibacterial resistance.

FUNGAL INFECTIONS, INFECTIONS IN THE IMMUNOCOMPROMISED AND HIV/AIDS

P222

MICAFUNGIN: OVERVIEW OF SAFETY IN CHILDREN

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Background and aims: Children at risk of invasive fungal infections are often fragile hosts with multiple underlying conditions. Since drug safety is critical in such patients, we evaluated the safety of micafungin, a novel antifungal agent, by pooling pediatric safety data from clinical trials.

Methods: Adverse event (AE) data were pooled from clinical trials conducted in Europe, the Americas and Asia.

Results: 296 patients received at least one dose of micafungin. The mean ±SD age was 6.5±5.1 years; 66 patients were < 1 year. Common underlying conditions were malignancies (37.5%) and hematopoietic stem cell transplantation (33.8%). Neutropenia (ANC< 500 cells/µL) at baseline was present in 40% of patients. Overall, the median maximum daily micafungin dose was 1.7 mg/kg (interquartile range [IQR]: 1.0-2.4 mg/kg). Median treatment duration was 15 days (IQR: 6-29 days). Consistent with the multi-morbid underlying conditions of this population, AEs, irrespective of causality, were experienced by most (93.2%) patients, and a large proportion of these (34.1%) were serious. Few AEs were considered by the investigator to be treatment related or led to treatment discontinuation (see table). No trends were seen with analysis of AEs by dose or duration of treatment.

Conclusions: Micafungin has a favorable safety profile in pediatric patients with complex and life-threatening underlying conditions.

All causality (≥20%)	vomiting (31.8%), pyrexia (22.3%), diarrhea (21.6%), nausea (21.3%), hypokalemia (20.9%)
At least possibly related* to micafungin (≥2%)	hypokalemia (3.0%), ALT increased (3.0%), hyperbilirubinemia (2.0%), AST increased (2.0%), LFT abnormal (2.0%), AP increased (2.0%), hypertension (2.0%)
At least possibly related* to micafungin and leading to treatment discontinuation (7 patients)	neutropenia, AST/ALT increased, rash, (3 patients with underlying leukemia/ANCT); jaw and joint pain, hyperbilirubinemia, creatinine increased (3 patients with underlying HSCT); creatinine increased (1 patient with premature birth)
ALT/AST: alanine/aspartate aminotransferase; ANCT: antineoplastic chemotherapy; HSCT: hematopoietic stem cell transplant; LFT: liver function tests; *Investigator-assessed causal relationship.	

P223

MICAFUNGIN: OVERVIEW OF EFFICACY IN CHILDREN

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Background and aims: Invasive fungal infections are a major source of morbidity and mortality in immunocompromized children; however, information on new antifungal therapies in children is limited. We evaluated the efficacy and pharmacokinetics (PK) of micafungin, a novel antifungal agent, by reviewing pediatric data from micafungin clinical trials.

Methods: A retrospective review of pediatric data from clinical trials was performed.

Results: A total 296 children received micafungin (MICA) for invasive candidiasis (IC), refractory IC, refractory invasive aspergillosis (IA), prophylaxis in hematopoietic stem cell transplantation (HSCT) patients, or to assess PK. Most patients age < 1 year were premature (38/66), whereas most children age >1 year were HSCT recipients or malignancy patients (181/230). Median maximum daily dose for patients < 1, 1 to 4, 5 to 8, 9 to 12 and 13 to 15 years were 2.0, 1.5, 1.5, 1.9 and 1.5 mg/kg, respectively. Treatment success rates are shown in the table. MICA showed linear PK, with a higher clearance in neonates than in older children and adults.

Conclusions: MICA is an efficacious agent for the treatment and prophylaxis of pediatric invasive fungal infections.

Therapeutic Category	Treatment	N	Treatment Response, n/N (%) by Age Group (years)				
			0 to 2	3 to 7	8 to 12	13 to <16	Overall
Phase III							
Invasive candidiasis or candidemia	Micafungin	52	24/30 (80.0)	5/7 (71.4)	3/8 (37.5)	4/7 (57.1)	36/52 (69.2)
	Liposomal Amphotericin B	54	31/40 (77.5)	6/9 (66.7)	1/3 (33.3)	2/2 (100)	40/54 (74.1)
Prophylaxis of fungal infections	Micafungin	39	6/7 (85.7)	10/14 (71.4)	7/12 (58.3)	4/6 (66.7)	27/39 (69.2)
	Fluconazole	45	6/13 (46.2)	4/7 (57.1)	10/19 (52.6)	4/6 (66.7)	24/45 (53.3)
Phase II							
Invasive aspergillosis	Micafungin*	58	2/5 (40.0)	7/16 (43.8)	5/18 (27.8)	12/19 (63.2)	26/58 (44.8)
Invasive candidiasis or candidemia	Micafungin	53	19/28 (67.9)	7/11 (63.6)	8/9 (88.9)	4/5 (80.0)	38/53 (71.7)
Phase I							
PK, safety, and tolerability	Micafungin	69	4/5 (80.0)	23/30 (76.7)	13/22 (59.1)	9/12 (75.0)	49/69 (71.0)
*Either alone or in combination.							

[Treatment success rates]

P224

CLINICAL AND MICROBIOLOGICAL FACTORS AFFECTING OUTCOME IN HOSPITALIZED CHILDREN WITH CANDIDEMIA

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Background: Candidemia is a major cause of morbidity and mortality in pediatrics. The purpose of this study was to review the epidemiology and outcome of candidemia at a major pediatric center to identify features related to increased mortality.

Methods: Retrospective chart review of patients hospitalized at our institution between June 1, 2002-December 31 2008 with blood culture positive for Candida spp.

Results: There were 165 candidemic episodes in 151 patients. Most common species were C albicans (58 isolates) and C parapsilosis (57 isolates). Primary gastrointestinal disorder, (41pts; 27%), underlying malignancy (37pts, 24.5%), and neonatal intensive care unit (NICU) stay (34; 22.5%) were common risk factors. Neonates accounted for 41.6% (17/41) of gastrointestinal pathology and had the highest number of candidemic days (mean 6.3d vs 3.9d). All but 9 patients had a central line at time of diagnosis. Death occurred in 23 (13.9%) events, mortality associated with C albicans and C parapsilosis was similar (8/58; 13.8% and 7/57; 12.3%), though less common, C glabrata and C krusei had a higher fatality rate (3/12; 25% and 2/7; 28.6% respectively). Mean days candidemic were 5.7 and 4.45 days in those who died and survived respectively. Mortality was higher in patients candidemic for >72 hours 35% vs 2.4% (OR 14.35; CI 3.24-63.55).

Conclusion: Candidemia remains an important cause of morbidity and mortality in children. Gastrointestinal pathology, malignancy, and NICU stay were risk factors for candidemia. C glabrata and C krusei had high mortality rate. Delayed sterilization of the blood was associated with higher mortality.

P225

SUCCESSFUL TREATMENT IN A CHILD WITH ANAPLASTIC LARGE CELL LYMPHOMA AND COEXISTENCE OF PULMONARY TUBERCULOSIS

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A 13 year old girl was admitted to our department with a history of severe pain of her left axilla and limitation of her left arm active movements. Fever (39^{o}C) with chills developed 3 days later whereas on physical examination a block of lymph nodes in her left axilla, small cervical lymph nodes, diffuse papular rash and red-violet swelling of her supraclavicular and subclavian region were seen. She was initially treated with antibiotics without improvement. Ultrasound and computed tomography investigations revealed left axillar and supraclavicular lymphadenopathy and a small nodular shade in upper lobe of her left lung. Bone marrow aspiration, spinal fluid and bone scanning were negative. A biopsy from an axillary lymph node was performed and the diagnosis of anaplastic large cell lymphoma (LCAL) (LCA, MCHL-1, EMA, CD30 and ALK-1 positive) was established. Moreover DNA of Mycobacterium Tuberculosis was detected in the tissue biopsy. Patient was started on chemotherapy according to current protocols for LCAL and achieved remission of all initially involved fields before maintenance chemotherapy was started. Nevertheless, two nodular lesions (with a diameter of 1cm and 2 cm respectively) were detected in the left lower lobe of the lung. Biopsy from the lesions revealed granulomas and PCR was positive for Mycobacterium Tuberculosis. She received treatment with combination of isoniazide, pyrazinamide and ethambutol and maintenance chemotherapy for her LCAL for one year simultaneously. One year later she is disease free for both mycobacterial infection and lymphoma.

P226

SUBSTANCE AND SEXUAL ABUSE AND HIV AMONG STREET CHILDREN OF KOLKATA, INDIA

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Globally, street children are often seen to struggle for their survival without food, shelter and proper dresses. Apart from poor living conditions and ill health, they appear to be vulnerable to substance and sexual abuses that results blood borne infections including STIs & HIV. A community-based cross-sectional study was conducted among 554 street children (6-18 years) of Kolkata, one of the four major metropolitan cities of India, to understand their substance as well as sexual abuses scenario. Interview was followed by collection of 3-4 ml blood samples to find out HIV, HBV and VDRL status. The study revealed that the overall prevalence of substance abuse was 52% and sexual abuse was 9.2% in them. Commonest abusing substance was 'Dendrite' (43%), cannabis (25%), alcohol (16%), brown sugar (11%), pure heroin (3%) and nitrazepam (2%). Exclusive tobacco smoking was found in 22% children. Similarly, commonest form of sexual abuse was `attempted to have sex against will' (65%), `forceful exposure of genitalia' (61%), `forceful touching of genitalia' (53%), rape (23%) etc. Both substance as well as sexual abuses was associated with factors like orphan children, children having no contact with family and children spending night at public places. Serological test revealed that 1%, 6% and 4% of the studied children were suffering from HIV, HBV and VDRL respectively. It may be interpreted as the beginning of an epidemic in this vulnerable population. An urgent community-based intervention must be targeted that might also include vaccination against hepatitis-B as one of the required measures.

P227

IMMUNIZATION STATUS OF CHILDREN WITH HIV: FAILURE TO PROTECT A VULNERABLE POPULATION

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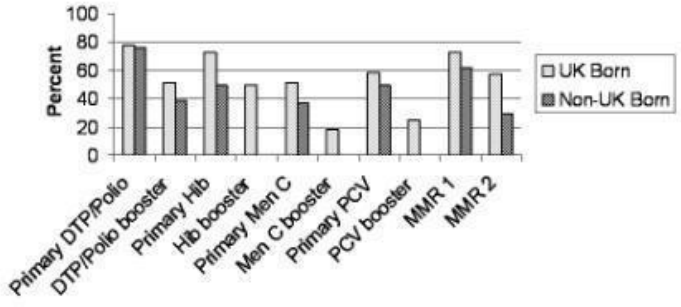
Background and aims: Despite effective treatment with ART, children with HIV are at increased risk of vaccine preventable infections. We aimed to assess immunization status of children with HIV in London.

Methods: Audit of immunization status of children attending four (3 tertiary, 1 secondary care) paediatric HIV clinics. Immunization histories were obtained from clinical records, primary care, and/or parental recall. Each child's status was compared to UK guidelines.

Results: For 75 children: median age 11 years, 55% UK born, median CD4 26%, median viral load 185 copies/mL.

Figure 1 shows the proportion of children known to be fully immunized with each vaccine according to the routine UK schedule, stratified by vaccine course and place of birth. For the additional vaccines recommended for HIV infected children, 32%, 4%, 0% and 28% were fully immunized against influenza, hepatitis B, varicella and pneumococcal polysaccharide respectively.

Figure 1. Proportion of Eligible Children Completing Routine Immunization



Primary vs booster doses p=0.0001, UK born vs Non-UK born p=0.006

DTP, diphtheria, tetanus, pertussis; Hib, Haemophilus influenzae type B; Men C, meningitis C; PCV, pneumococcal conjugate vaccine; MMR, measles, mumps and rubella.

Eligibility for each vaccine based on age and previous immunization history.

[Figure 1]

Conclusions: Immunization of children with HIV is suboptimal in these clinics. Booster doses, recently introduced, and non-routine vaccines are most commonly omitted. Immigrant children are particularly unlikely to be appropriately immunized. As life expectancy and the proportion of immigrant children with HIV increase, appropriate routine and catch-up immunization becomes even more important. Development of evidence-based standards for immunization of children with HIV, improved accessibility of immunization records, and opportunistic immunization in clinic may all improve this situation.

P228

INCIDENCE OF ANEMIA IN HIV INFECTED CHILDREN UNDER TREATMENT AND FELLOWED IN ORAN(ALGERIA)

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Aim: To estimate incidence of anemia in HIV infected children under treatment and fellowed in Oran.

Methodology: Retrospective study of all HIV infected children aged more than 18 months and presenting anemia after receiving antiretroviral drugs and fellowed from 2003 to 2008 in CHU of Oran(Algeria).

Results: 21 children were studied and 07 presented anemia(30%).

4/7 were male.

30% of cases were aged less than 04 years.

03 cases lived in Oran.

50% of cases presented anemia during the month fellowing the onset of antiretroviral drugs.

Anemia was important in 50% of cases.

Blood transfusions were used in 50% of cases.

Antiretroviral drugs were changed in one cases.

Conclusion: 30% of HIV infected children under antiretroviral treatment and fellowed in Oran have presented anemia.

P229

BLOOD ASPERGILLUS PCR RARELY DETECTS INVASIVE ASPERGILLOSIS

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Background & aims: Invasive aspergillosis is an increasing problem in immunocompromised children. PCR may improve the early diagnosis of invasive aspergillosis. Few PCR assays have been tested in body fluids from children with invasive aspergillosis. We audited the use of blood *Aspergillus* PCR in our children's hospital.

Methods: Blood *Aspergillus* PCR assays sent April 2005 - March 2008 were identified from the microbiology database. All *Aspergillus* isolates cultured in the laboratory during the same time period were also identified. Detailed information was obtained for children with positive results.

Results: 251 blood *Aspergillus* PCRs were sent from 53 children. Median number per child was 7 (range 1-14). Four children had proven invasive aspergillosis. Only one of 22(5%) blood *Aspergillus* PCRs sent during invasive aspergillosis were positive.Overall, 6/251 (2.4%) blood *Aspergillus* PCR assays were positive, from 5 children. Positive results did not change clinical management; three children were not given antifungals and had negative PCRs when repeated, one child had disseminated mycobacterial infection and one had CT changes of invasive *Aspergillus* and had already started on antifungal treatment.

Conclusion: Blood *Aspergillus* PCR did not alter clinical management. Most results were negative, even in children with invasive aspergillosis. Positive results were assumed to be false positives or occurred when there were other clinical features suggesting invasive aspergillosis. Blood *Aspergillus* PCR methods require further validation before introduction into routine clinical use in paediatrics.

P230

FAVORABLE OUTCOME OF CHRONIC DISSEMINATED CANDIDIASIS IN FOUR PEDIATRIC PATIENTS WITH HEMATOLOGICAL MALIGNANCY

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Background and aims: Chronic disseminated candidiasis (CDC) is seen mainly in patients with hematological malignancies after recovery of neutrophils. Diagnosis is troublesome due to negative blood cultures for *Candida* species and relies on proper imaging and invasive biopsies to reveal the exact fungal pathogen.

Case-reports: Four children (aged 2 to 4 years) with a hematological malignancy developed CDC during chemotherapy. Time between onset of neutropenic fever and diagnosis of CDC ranged between 20 and 49 days. In all patients, CDC became evident after neutrophil counts had recovered. Three patients developed hepatomegaly. Main reasons for the delayed diagnoses were negative results on imaging (ultrasound 2, CT-abdomen 1) or fever explained by other infections (disseminated varicella zoster infection, catheter-related infection). In two patients, diagnosis was made by liver biopsy, in the other ones the biopsy confirmed the diagnosis after abnormalities were seen on PET-scan and leucocyte-scintigrafy. *C. albicans* was cultured from the liver biopsy in two patients, in one patient yeast cells were observed by direct microscopy. Duration of antifungal therapy ranged from 153 days to 24 months. Chemotherapy was temporary discontinued in 3 patients for respectively 21 days, 7 days and 4 months. All 4 patients survived CDC and all are in hematologic remission.

Conclusion: Common used imaging procedures may fail in the diagnostic process of CDC. Liver biopsy should be considered if fever persists after resolution of neutropenia in children with hematological malignancies without a clear explanation. Outcome in our patients appears favorable compared to mortality reported in the literature.

P231

TINEA CAPITIS IN PRIMARY AND MIDDLE SCHOOL STUDENTS IN SOUTH-EAST OF IRAN

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Introduction and aims: Tinea capitis, is a common infection among schoolchildren and increasing public health importance in developing countries. The present study designed to determine the prevalence of Tinea capitis based on laboratory examination of the causative fungal in primary and middle school students in Iran, 2007.

Methods: During this cross-sectional study, 2060 children from urban and rural primary and middle schools were randomly selected. Specimens were collected from suspicious students by scraping the scalp and removing hair stubs. The collected samples were directly examined microscopically and cultured using Sabouraud's dextrose agar (S), SCC and Slide culture.

Results: The results showed that 56.7% were female. A number of 110 students (5.8%) were suspected to Tinea capitis. Thirty-seven cases of Tinea capitis were confirmed by demonstration of dermatophytes spores or mycelium in direct smears, 25 cases (22.73%) Ectothrix, 8 cases (7.27%) Endothrix and 4 cases (3.63%) were Favus. The isolated dermophytes included 17 anthropophilic, 9 zoophilic and 3 geophilic species.

Conclusions: The results implied that control programs with concern to the sources of infections is of great importance. Health education and development of knowledge among schoolchildren are recommended to be taken into account. It was resulted that all three sources of dermatophytic infections are involved with the incidence of Tinea capitis in children in the studied area, although the anthropophilic and zoophilic reservoirs are predominant.

P232

IMPACT OF TRANSITION TO ADULT SERVICES ON CLINIC ATTENDANCE AND VIROLOGICAL CONTROL IN HIV-INFECTED ADOLESCENTS

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Background and aims: Since introduction of highly active antiretroviral therapy (HAART), more perinatally HIV-infected children survive into adolescence, requiring support for the transition to adult services. We reviewed the impact of transition on engagement with services and disease management.

Method: Notes of perinatally-infected adolescents transitioning from paediatric services to a specialist adolescent service from May 2005 to March 2008 were reviewed retrospectively. Data collected from the 12 months pre- and post-transition included rate of clinic attendance, CD4 count, viral load and details of HAART. Additional data on perceived impact of transition on self-management were collected using a self-report questionnaire.

Results: 17 young people were identified. Age at transition ranged from 15y 6m to 17y 11m. All remained engaged with services at 1 year post-transition. Post-transition, 75% of patients had an increased non-attendance rate (mean rate rose from 21% to 43% ($z=-2.827$, $p < 0.005$)). 8 participants had existing adherence difficulties which persisted post-transition; 1 further patient became non-adherent. No statistical difference was found between mean CD4 count pre- and post-transition ($z=-0.047$, $p=0.962$). The 2 patients with consistently undetectable viral load, and the 6 patients who had viral load < 400 copies/ml during pre-transition year maintained this degree of viral control post-transition.

Conclusion: Adherence and virological control remained consistent post-transition; however, clinic attendance rates declined. This may imply potential long-term negative consequences for disease control, particularly relating to engagement with services, and highlights the need for close and dedicated support as transitioning adolescents take responsibility for independent management of their condition.

P233

HIGH INCIDENCE OF INVASIVE GROUP B STREPTOCOCCAL INFECTIONS IN UNINFECTED INFANTS BORN TO HIV-1-INFECTED MOTHERS

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Background: The occurrence of an unusual number of group B streptococcal (GBS) infections in uninfected infants born to HIV-infected mothers followed in our center prompted this study.

Objective: To describe the incidence and clinical presentation of GBS infections in uninfected HIV-exposed infants born between 2001 and 2008 in comparison to the population of infants not exposed to HIV born in the same hospital.

Methods: The medical charts of all uninfected HIV-exposed infants prospectively followed since birth and the microbiology laboratory records were reviewed to identify GBS infections.

Results: 8 episodes of GBS infection occurred in 7/397 uninfected HIV-exposed infants; 97 % of the mothers were treated with antiretroviral agents during pregnancy, including 6/7 mothers of children with GBS infection. Five episodes occurred > 7 days of life (days 9, 26, 33, 64 and 72). One of the infants had a recurrence 28 days after completion of treatment. Restricting the analysis to the infants born in our centre, GBS infection occurred in 5/322 (15.5/1000) HIV-exposed infants compared to 16/20158 (0.79/1000) infants in the control population (OR=19.6 $p< 0.0001$). In the latter, median age of onset was 1 day.

Conclusion: Between 2001 and 2008 the incidence of GBS infection was significantly higher in uninfected infants born to HIV-infected mothers than in the control population born in our centre. The majority of GBS infections in HIV-exposed infants were late or very late onset and one child had a recurrence; 2 features that were strikingly different than in the general population.

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OFF-LABEL ANTIRETROVIRALS IN PEDIATRICS: USE IN A COHORT OF HIV-INFECTED CHILDREN

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Background: There has been an enormous development on antiretrovirals for HIV. But not all of them have been approved in children mainly because they have not been sufficiently studied in them.

Objective: To determine the extent of off-label antiretrovirals use in a large cohort of HIV-infected children.

Methods: A cross-sectional observational study involving 210 HIV-infected children from the cohort of Madrid, Spain. The instrument used was the data base of this cohort updated to December 2008.

Results: The medium age of the cohort is 13.5 years, 124 (61%) of the patients are girls. The median CD4% is 27 and 121 patients (63%) have < 50 copies/ml. Off-label antiretrovirals are used in 45 (21%) children: 38 (85%) are only on one off-label drug, 4 (9%) are on 2 and 3 (6%) are on more than 2 off-label drugs. The most common ones used are tenofovir (n=16), etravirine (n=9), darunavir (n=8). In the group of children who are receiving off-label drugs, 47% are females versus the 66 % in the group that receives approved drugs, which is statistically significative (p = 0.022). No difference is significant in age, immunological situation and viral load among both groups.

Conclusions: In our study we find that off-label drugs are used in a high proportion of HIV-infected children, this evidences the need of further studies of these drugs in pediatric age. In our cohort there seems to be a trend to use off-label drugs more frecuently in males.

P235

CORRELATION BETWEEN THE TROFILE AND VIROLOGICAL RESPONSE TO A SHORT-TERM MARAVIROC EXPOSURE IN HIV-INFECTED PATIENTS

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Background and aims: Current validated assay to determine tropism of HIV variants is Trofile®, which has multiple limitations. The aim of this work was to correlate the virological response to a short-term maraviroc exposure with the Trofile®.

Methods: Since July 1st up to December 1st 2008, 18 HIV-infected patients with detectable viral load during the last year began a 7-10 days exposure to maraviroc (MRV group); six HIV-infected patients without antiretroviral therapy received no treatment (control group). Plasma viral load was evaluated at days 0, 2, 4-5 and 7-10. Baseline genotype resistance testing and tropism assay were performed. The clinical approach (MCT) was considered positive if viral load was undetectable (< 50 copies/ml) or a reduction > 1 $\log_{10}$ copies/ml was achieved after 7-10 days of maraviroc exposure.

Results: No significant viral load modification was observed in control group patients (figure 1A). In MRV group patients Trofile® and viral load evolution was: in nine patients the Trofile® was informed as R5 and all of them showed a positive MCT (figure 1B); in six cases Trofile® was informed as dual/tropic, but two of them showed a reduction > 1 $\log_{10}$ copies/mL (figure 1C); three patients showed a non-reportable result of the Trofile®, but all of them achieved undetectability after MCT (figure 1D).

Conclusions: A cheaper and faster alternative to Trofile® could be a clinical approach consisting in a short-term exposure to maraviroc. Using this approach, some patients with non-reportable or dual/tropic virus attending to Trofile® could be benefited from maraviroc therapy.

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HLA B5701 PREVALENCE IN A COHORT OF HIV INFECTED CHILDREN

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Introduction: It has been recognized HLA-B57 as a critical factor to develop abacavir hypersensitivity. As international guidelines recommend, abacavir should be more safely used after ruling out the HLA-B*5701 positivity. Due to the lack of data in children, the aim of this study has been to address the prevalence of HLA-B*5701 in the pediatric population.

Methods: An observational, cross-sectional study was performed in 135 HIV-infected children. HLA-B*5701 was determined to 135 HIV-infected children included in the Madrid cohort of HIV-infected children followed at 5 public hospitals in Madrid. In most children HLA-B*5701 was determined long after initiation of abacavir. Hypersensitivity reaction was assessed by clinical evaluation.

Results: One hundred and thirty five patients were screened. Baseline characteristics: Mean age 13,2; range 1-22. Ethnicity: Caucasian 75%, African 9%, Gipsy 9%, Latin American 7%. Fifty children had received abacavir (37%). Of them, there were 40 patients on treatment with abacavir, whereas 10 had been exposed to abacavir, previously. The prevalence of HLA-B*5701 was 3.7% (5/135). None of African children presented HLA-B*5701. Three children HLA-B5701negative developed a hypersensitivity reaction (2,2 %). Another child HLA-B5701+ had been treated with abacavir uneventfully. None of the HLA-B5701+ children was currently on treatment with abacavir.

Conclusions: Similarly to previously reported data in adult cohorts, the prevalence of HLA-B5701 has been 3.7% in this Spanish pediatric cohort. Abacavir hypersensitivity is a serious condition that might be prevented by determining HLA-B*5701 as guidelines recommend.

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CARE OF 108 CHILDREN ON ANTI-RETROVIRAL THERAPY (ART) IN BURKINA FASO: ADHERENCE AND ART-RESPONSE EVALUATION

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Since 2003 Brescia University, carry on a health care project for HIV infected children at S.Camille Hospital (Ouagadougou-Burkina Faso). At May 08, 210 children were enrolled, of which 108 (51.4%) were on ART (42F, 66M). Mean age at first examination was 5yy (0.37-15.7yy, median age 3.43yy). Mean follow-up length was 2.18yy (0.07-5.39yy).

Mean start age of ART varied between 0.24-15.38yy (median age 4.26yy). ART was started after an average of 53 from first examination and mean treatment period was 1.82 yy (0.02-5.4yy).

Compliance was measured by pills count, syrup measurements and caregivers interview. 81.9% assumed >95% of doses, 13.8% 90-95%, 3.2% 80-90% while just one patient < 80%. During follow-up ART adherence didn't vary.

At 6 months the majority of patients on ART switched from immunological-stage IV to lower classes; these modifications were slower in patient with lower compliance. Our statistical analysis demonstrated significant weight-gain ($p< 0.001$) after 6 months of ART, which persisted after 24 months.

At follow-up end, 3.7% of our patients were sent to adult clinic, 1.8% to other centres, 8.3% deceased. Survival Rate (Kaplan-Meier) was 92% after first year of ART and 89% (CI95%:78-95%) after 2yy; beyond this period no deaths were observed.

In regard to age, SR was 93% after 6yy, 91% after 10yy and 87% (CI 95%:75-93%) after 11yy. Deaths were primarily observed during first years of life.

Those high SR has to be ascribed to strict observance to social criteria, accurate clinical/biochemical monitoring, precise therapy-understanding check, qualified personnel and little fixed-dose-combinations use.

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UPTAKE, IMPLEMENTATION AND OUTCOME OF EARLY INFANT DIAGNOSIS OF HIV EXPOSED CHILDREN IN A RURAL AREA IN KENYA

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Each year 50,000 infants become infected with HIV in Kenya. Increased access to PCR has led to the availability of Early Infant Diagnosis (EID) of HIV since 2006 with national guidelines recommending follow-up and testing of HIV-exposed children upto 18 months of age.

A retrospective analysis of routine data collected in the provision of HIV care in a district hospital in rural Kenya was done to describe the uptake, implementation and outcome of EID over a period of two years.

A total of 371 (71.2%) of all HIV-exposed children seen at first contact had a DBS for PCR done. At the end of the study period 170 (45.8%) were still on follow-up and 61 (16.4%) had attended care upto 18 months of age. Five children (1.4%) had transferred care to other facilities while 10 (2.7%) and 125 (33.7%) were reported dead and had dropped out of care respectively.

Although majority of the children dropped out after receiving their PCR results, there was no association between PCR status and completing the EID process (p-value 0.262). However, there was a strong association between mothers who are lost to follow-up with children who dropped out of care (p-value < 0.001).

Despite a good uptake, majority of HIV-exposed children did not complete the EID process as recommended. This was mainly attributed to mothers dropping out of HIV care. To enhance early identification of HIV infected children, involvement and support of other members of the family as well as the community should be encouraged.

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ASPERGILLUS (TELEOMORPH: EMERICELLA) NIDULANS INFECTION IN CHRONIC GRANULOMATOUS DISEASE (CGD): REVIEW OF THE LITERATURE

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Background: Previous reports of our group have shown the difficulties in accurate identification of *Emericella spp* based on morphologic characteristics. There is increasing evidence that the efficacy of antifungal agents is different for the various species underscoring the need for correct identification and in-vitro susceptibility testing. We reviewed the literature to determine the diagnostic yield and management of invasive *A. nidulans* infection in CGD patients.

Methods: Through a systematic search of the PubMed database all reported cases of invasive *A. nidulans* infections in CGD patients were reviewed.

Results: Twenty-four cases were found, 22 were male, with a median age of 8 yrs (range 3-21). Of those whose genetic pattern was reported, 89% were X-linked $gp91^{phox}$.

In only 4 cases details of the microscopic morphology were given on which the strain identification was based.

Lung invasion with direct spread to adjacent chest-wall structures is the main clinical presentation. An unusual mild and localized course of the disease showed to be caused by *A. rugulosa*, originally misidentified as *A. nidulans*.

Extensive and early surgery remains a cornerstone of treatment. All patients received amphotericin B.

Susceptibility testing was performed in only 3 cases. Fifty percent received granulocyte transfusions and 36% were treated by INF-γ additionally. Thirty-five percent died, but follow-up ranged from “still under treatment” to 8 years.

Conclusion: Details regarding strain identification and in-vitro susceptibility testing were scarce in CGD patients with reported invasive *A. nidulans* infections. Correct identification and susceptibility results are needed to guide optimal therapy and improve outcome.

P240

RECURRENT CRYPTOCOCCAL MENINGITIS IN RENAL TRANSPLANT ADOLESCENT ASSOCIATED WITH ENVIRONMENTAL EXPOSURE

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Fungal infection in renal transplant recipients are less common than bacterial but pose significant problem because of immunosuppresion and use of nephrotoxic drugs.We report one adolescent who presented with recurrent cryptococcal meningitis,5 months post transplant.

This 17 years old boy ,with end-stage renal disease secondary to FSGS presented for renal transplant in July,2007.He is a student and stays in a small town where his grandparents rear poultry.CMV status preoperatively was negative.He had cadeveric renal transplant and he received OKT3,mycophenolate mofetil and prednisolone as immunosuppresive agents.

Five months post transplant,he presented with 1 week history of fever and headache.

On examination,he was febrile with no apparent respiratory distress. Neurological examination was normal.His spinal tap showed a positive cryptococcal antigen (titre1:>512) and culture grew cyptococcal neoformans.He was started on conventional amphotericin B (CAB) and after 1 week changed to Fluconazole since his creatinine went off.

Follow-up lumbar puncture was normal except for persistent cyptococcal antigen but in October,2008 his Indian ink became positive again.He was otherwise asymptomatic and was on fluconazole maintenance therapy.He was re-induced with Amphotericin B colloid dispersion and his physical examination showed an otherwise well child with no fever,paronycia of nails and normal neurological examination.His eye examination showed evidence of retinitis but examination of heart,lung and sinuses were normal.

He completed 4 weeks course of amphocil and was started back on fluconazole.

This case showed how in immunocompromised child,serious infection can be asymptomatic and need to have repeated examination and full anti-fungal induction course to eradicate infection.

P241

DIFFERENT PLASMA LEVELS OF INTERLEUKINS AND CHEMOKINES: COMPARISON BETWEEN CHILDREN AND ADULTS WITH AIDS IN CHINA

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Background: The immunological differences between children and adults with AIDS in China are not well documented. This study aimed to identify changes in plasma levels of Th1/Th2 cytokines and chemokines in HIV-1-infected children and adults in China.

Methods: Seventy-five children with AIDS and 35 adult AIDS patients were recruited and clinical datas were collected. $CD4^+$ T lymphocyte counts were measured by flow cytometery and plasma HIV RNA levels were measured by quantitative RT-PCR. Plasma levels of IL-18, IL-10, IL-16, RANTES, MCP-1, SDF-1α and SDF-1β were quantified by enzyme-linked immunosorbent assay(ELISA). The levels of β2-MG and sFas were measured to validate the level of humoral and cellular immune activation.

Results: The mean levels of all cytokines in pediatric and adult AIDS patients were significantly higher than in their healthy controls($P< 0.01$). Mean levels of these cytokines were higher in pediatric patients than in adult patients ($P< 0.05$, except for SDF-1α and β2-MG). Some of the cytokines of patients younger than 6 years old was higher than both older children and adults with AIDS (IL-10, IL-18, SDF-1α, MCP, RANTES and sFas, $P< 0.05$). Levels of IL-18, IL-10, RANTES and β2-MG of pediatric patients increased as the levels of viral load ascending ($P< 0.05$).

Conclusions: Our research demonstrates that abnormal immune activation is highly initiated in pediatric and adult patients with AIDS, and is higher in children patients than in adult patients. The cytokines levels are coincided with disease progression of AIDS, but have no direct relationship with total CD4+ T cell count.

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PREVENTION OF PERINATAL HIV TRANSMISSION IN A GREEK PEDIATRIC COHORT

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Background and aim: Vertical HIV transmission is estimated 14-25%, in the absence of intervention. The aim of the present study is to evaluate the degree of prevention of vertical HIV transmission, in a pediatric patient cohort, during a 3 year period.

Methods: Thirty four neonates (14 days-12 months years old) were assessed for HIV infection. Their mothers were HIV positive: 22/34 had known HIV infection and were under antiretroviral treatment (ART) during pregnancy, 7/34 were found HIV positive at the end of first trimester of pregnancy and began ART, while in 5/34 cases HIV positivity was detected after delivery. HIV virus RNA was detected with real time-polymerase chain reaction, in three subsequent samples.

Results: 30/34 (88%) children were delivered with cesarean section, received prophylaxis with zidovudine (AZT), according to PACTG076 protocol and did not breastfeeding. All of them had negative viral load (< 50 viral copies/mL).

In 1/34 (3%) neonate, delivered with cesarean section, AZT was not administered and did not breastfeeding, HIV viral load was negative.

Positive HIV viral load was detected in 3/34 (9%) children, delivered vaginally, while 2/3 received AZT in the first day of life. In these cases, mothers' HIV positivity was detected after pregnancy.

Conclusions: Although the prompt administration of AZT is important for the prevention of perinatal HIV transmission, there are cases that the implementation of perinatal HIV interventions is insufficient. The detection of mothers' HIV serostatus before pregnancy and the advocacy for perinatal interventions are essential for the reduction of perinatal HIV transmission.

P243

CLINICAL AND ANTHROPOMETRIC FOLLOW UP OF CHILDREN INFECTED BY HIV-1 AND M.TUBERCULOSIS TREATED AT TRAC AND THE HOSPITAL OF KIGALI

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Background and aims: The care and treatment of HIV/TB co-infection is challenging in the children. This study was aimed at evaluating clinical and anthropometrical aspects of children followed during a 9 months period.

Methods: Children under 3 years (or less than 10 kg) co-infected by AIDS and TB were treated in the clinic of TRAC and in the CHU of Kigali (RWANDA). Clinical and anthropometrical parameters were collected before the beginning of the treatments, at 1 month, 3 months, 6 months and 9 months. The side effects and deaths were noted.

Results: From January 2005 to April 2006, 46 children were followed. The average of age was 19 months.The tuberculin test was positive in 5 cases (11%), the microscopy for acid-fast bacilli was positive in 2 cases. Contact with tuberculous adult was reported in 61% of the cases. All the children had anti-TB treatment (RHZ). Further, 69% of them had 2NRTI+2xDose of NVP, 31% had 2NRTI+EFV.The side effects were: 6 cases of anaemia, 3 cases of cutaneous rash, 1 case of pancreatitis, 25 cases of vomiting. Mortality was 41 %. For the survivals, the weight for age Z-scores passed from -4, 28 to -0, 76 (p=0,000) and the height for age Z-scores passed from -4, 14 to -2, 48 (p=0,023) after 9 months of treatment.

Conclusion: The anthropometrical parameters have significantly increased among our patients: in 9 months, weight deficit was corrected but height retardation couldn´t be corrected. Mortality remains high following the delay of diagnosis and beginning the treatments.

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ANALYSIS OF BACTEREMIA IN PEDIATRIC PATIENTS WITH SECONDARY IMMUNODEFICIENCY

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Background and aims: Pediatric patients with secondary immunodeficiency receiving chemotherapy are more vulnerable to bacterial infection. This study is to analyze the pathogens causing bacteremia and their antimicrobial resistance patterns in pediatric patients with secondary immunodeficiency.

Methods: A retrospective medical records review of 188 episodes of bacteremia in 172 pediatric patients with secondary immunodeficiency between January 2001 and January 2008 was conducted at Yonsei University Severence Children's Hospital.

Results: Among the 188 episodes of 172 pediatric patients with secondary immunodeficiency, gram-positive organisms were 52.1%, gram-negative organisms were 37.8% and fungal infections were 8.0%. *Staphylococcus epidermidis* was the most common pathogen and *Pseudomonas spp.* was the most common gram-negative organisms. Gram-positive organisms are resistant to ciprofloxacin 37.8%, erythromycin 75.5% and clindamycin 53.1%. Some of them were resistant to vancomycin but all gram-positive organisms were susceptible to teicoplanin. *E. coli* was resistant to ampicillin 71.4%, *Pseudomonas spp.* was resistant to imipenem 33.3%, ceftazidime 16.7%, and cefepime 25.0%. The patients with central venous catheters showed higher incidence rate of gram-positive organisms and fungus than in them without it (p=0.02). Neutropenia and high C-reactive protein are the risk factors of bacteremia (p=0.003).

Conclusions: Gram positive organisms were more frequent than gram negative as pathogen in immnunocompromised patients, especially in them with central venous catheter. We should carefully choose the antibiotics in case of impending sepsis on the base of patient's conditions including laboratory data such as C-reactive protein, neutropenia, or indwelling catheter and of institutional environment like the specific antimicrobial resistant pattern.

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ANTIRETROVIRAL-RELATED SHORT-TERM TOXICITY IN HEALTHY INFANTS: IMPLICATIONS OF THE NEW NEONATAL 4-WEEK ZIDOVUDINE REGIMEN

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Background and aims: British and Spanish Guidelines on HIV mother-to-child transmission have recently shortened the duration of neonatal zidovudine prophylaxis to 4wk for most infants; whether this regimen leads to a reduction in haematological and mitochondrial short-term toxicity remains unknown.

Methods: Prospective observational study in a cohort of infants born to HIV-infected mothers. Mother-infant pairs demographic, clinical, and laboratory data were collected at birth, 6wk, and 3, 6 and 12 months of age, including full blood count and lactate levels. Infants were compared according to the length of their neonatal zidovudine regimen, either 6wk or 4wk.

Results: As of September 2007, 168 infants had been included (6wk zidovudine regimen, n=137; 4wk, n=31). Mother´s age and use of nevirapine-based HAART regimens were significantly higher in the 4wk group. No other differences were observed in baseline characteristics between groups.

Macrocytosis was observed in both groups up to the age of 3 months: MCV values were higher in infants receiving the 6wk regimen (107fl vs 100fl at 6wk, 86fl vs 82fl at 3 months of life; $p< 0.0001$). No differences were noted in mean haemoglobin and haematocrit levels, platelet, leukocyte, neutrophil or lymphocyte counts at any of the time points assessed. Mild hyperlactatemia up to the age of 3 months was observed, without differences between groups.

Conclusions: Only an incidental decrease in MCV values was noted in infants exposed to the 4wk neonatal zidovudine regimen. This suggests that mitochondrial and haematological toxicity are mainly due to antiretroviral exposure during foetal life.

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PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV IN GEORGIA

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Background and aims: Prevention of mother-to-child transmission (PMTCT) of HIV is one of the strategic priorities as defined by the National Strategic Plan of Action (NSPA) of Georgia in 2006-2010 years. The comprehensive approach to PMTCT is based on existing evidence and includes: provision of prophylactic ART in pregnant and newborn, counseling and support for delivery and infant feeding, including infant PCP prophylaxis by TMP-CTX.

Methods: Testing on HIV/AIDS was based on identification of HIV antibodies b screening method, using Rapid Anti-HIV Test InTec PRODUCTE, INC. Positive result are referred to IDACIRC for confirmation by Western Blot and management that implies: antiretroviral therapy, caesarian section, infant feeding by formula and PCP prophylaxis by TMP-CTX. Data were collected using national HIV/AIDS Data Base.

Results: Throughout the period 1999-2008 total 84 pregnancies were registered at the IDACIRC. Prophylactic strategy was tailored individually according to the national acting guideline, women gestation age, HIV diseases stage, ARV availability. Totally 36 pregnant women received full PMTCT service. In this group no vertical transmission of HIV infection was recorded. 33 pregnant women received partial PMTCT service. The reasons were: late HIV diagnosis, limited access to ARV (from 1999 till 2004), refusal by pregnant women. Number of HIV transmission cases was 3 in this group. As of November, 2008 eight women are still pregnant.

Conclusions: Since 2005 Georgia Ensured comprehensive and sustainable PMTCT service throughout the Country and universal access for all pregnant women. Provision of full package of this service minimized the risk of vertical transmission.

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HIV/AIDS

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Background: India ranks third in the world in absolute burden of HIV. While increasing numbers of Government-sponsored clinics are providing free antiretroviral therapy (ART), its utility is limited by lack of affordability and acceptability and the requirement for lifelong administration. Allopathic practitioners in India are outnumbered by practitioners of traditional Indian medicine and homeopathy (TIMH), which is used by two-thirds of its population in rural areas to help meet its primary health care needs.

Results: Of 160 original articles reviewed, 19 laboratory studies, 17 clinical studies and six previous reviews of the literature were identified that covered at least one system of TIMH, which includes Ayurveda, yoga, naturopathy, Unani medicine, and Siddha medicine and homeopathy. Most studies examined either Ayurvedic or homeopathic treatments.

Conclusions: This review exposes a broad gap between the widespread use of TIMH therapies for HIV/AIDS, and the dearth of high-quality data supporting their effectiveness and safety. In light of the suboptimal effectiveness of vaccines, ART, barrier methods, and behavior change strategies for prevention and cure of HIV infection, it is both important and urgent to develop a rigorous research agenda that uses innovative methodologies to investigate, evaluate and maximize the role of TIMH in managing HIV/AIDS and associated illnesses in India.

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CEREBELLAR DEGENERATION IN PACIENTS WITH HIV CASE PRESENTATION

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Background: The neurologic manifestations in HIV infected long term survivor pacients with HAART determine serious diagnosis and treatment problems.

Objective: We present the case of a 19 years old adolescent with HIV/AIDS, C2 with cerebellar syndrom.

Results: The 19 year old patient was hospitalized with neurologic symptoms consisting of: left deviation of the ocular globes and head, gait ataxia, dysarthria, nystagmus, symptoms that progressively emerged 4 months before. The clinical examination at hospitalization revealed: no fever, good general state, consciousness, dysarthria, nystagmus, gait ataxia. The neurologic examination highlighted: VI oculomotor nerve paralysis, associated with dysarthria, nystagmus, hypermetria, intention tremor, absence of cognitive decline or dementia. Cerebral MRI was performed at this stage, highlighting left cerebellar cortical atrophy, left cerebellar emispehere with oval image area, areas of demielinization of the white substance (fig 1,2 and 3).

At this diagnosis stage, there were the following diagnosis suspicions:

1. Cerebellar Degeneration a novel variant of progressive multifocal leucoencephalopathy (PML)

2. Dementa HIV

3. Cerebral toxoplasmosis

4. Cerebral lymphoma

5. Tuberculosis

6. Meningo encephalitis with CMV

1. It was highlighted the diagnosis of a cerebellar neurologic disorders

2. Limited therapy choices.

3. Slight neurologic improvement.

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NON-TUBERCULOUS MYCOBACTERIAL IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME IN A SEVERELY IMMUNOCOMPROMISED HIV-INFECTED PAEDIATRIC PATIENT

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Background: The use of antiretroviral therapy (ART) in HIV infection is associated with significant reductions in morbidity and mortality by restoring immunity. Non-tuberculous mycobacteria (NTM) infection in severely immunocompromised patients who start HAART can be associated with immune reconstitution inflammatory syndrome (IRIS) with clinical deterioration due to an excessive inflammatory response.

Case report:13-year-old boy admitted with diarrhoea, low grade fever and weight loss. HIV was performed at that point with positive results. Viral load was 47.000 RNA/ml and total CD4 cell count 3/mm^3. Acid-alcohol-resistant bacilli were detected in the bowel biopsy with negative PCR for *Mycobacterium tuberculosis complex*. Therefore diagnosis of NTM infection in an stage C3 HIV infected patient was made. Both ART with abacavir, lamivudine and efavirenz and NTM treatment with azytromicin, rifabutin and etambutol were started at that point. As significant pharmacokinetic interactions have been reported, plasma drug levels were determined and doses adjusted subsequently. Eight weeks later, fever reappeared at the same time that immunological restoration (CD4 cell count was 3.7%) with decreased in HIV viral load (420 RNA/ml) were observed. Abdominal CT scan showed enlarged mesenteric lymphadenopaties and the diagnosis of abdominal NTM-associated Immune reconstitution inflammatory Syndrome (IRIS) was made. A mesenteric node biopsy ruled out lymphoma. Corticosteroids were started with partial response.

Conclusions: IRIS should be suspected in any severely immunocompromised HIV-infected patient starting ART with rapid immunological response and clinical deterioration. Abdominal NTM-associated IRIS is usually difficult to treat and prognosis is often unfavourable.

P250

APOPTOSIS AS MARKER OF EFFECTIVENESS OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPIES AT HIV POSITIVE CHILDREN

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There are still important and difficult questions on its beginning and tactics in case of development of resistency to the preparations of highly active antiretroviral therapy (HAART) in children despite long enough successful experience of application. The aim was to investigate FAS receptor level as additional marker in estimation of efficiency of HAART, FAS-receptor (CD95) a method of REEF with a set of monoclonal antibodies "Status". 47 HIV positive children receiving HAART were examined. 25 were getting combination of two NIOT, and one NNIOT while 22 received two NIOT and one IP. Before HAART, children of both groups had equally high levels of FAS-receptor - 51,35±1,79%. During the observation of these children during 14 months, the decreasing of FAS receptors were noted. In 6 children resistancy to APB preparations developed. In 1-st case progress of resistancy in 1 year from beginning of HAART was connected with low commitment of patient to treatment, in other 5 the commitment was high and made 95-100 %. Nonefficiency of HAART was observed in clinical, immunological and virological aspects. Research of FAS-receptor levels in children resistant to HAART revealed that formation of resistancy at HIV-positive children was accompanied by substantial growth of basic apoptosis marker (FAS-receptor) in blood plasma. In comparison with reference values, CD95 levels increased on the average of 19,8 ±1,3 %. We suggest to use the FAS receptor level as additional prognostical criteria of resistancy formation to HAART.

P251

MORBIDITY AND MORTALITY OF UNINFECTED CHILDREN BORN TO HIV POSITIVE MOTHERS FROM AMATA STUDY

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Background and aims: The choice of infant feeding mode for HIV positive mothers is very difficult in resource-limited countries. The formula feeding (FF) is disputed, whereas breast feeding (BF) remains the main way of HIV mother to the child transmission. The objective of this study is to compare the morbidity and the mortality and to identify the principal reasons of consultation and hospitalization according to the feeding mode.

Methods: In AMATA study, women chose between the FF and exclusive BF for 6 months. The FF group had education sessions on preparation of formula which was provided free of charge. Regular follow-ups were done at D15, D45, M3, M5, M6, M7 and M9 and all diseases events and deaths were recorded.

Results: 525 uninfected children have born, 57.5% were on FF and 42.5% on BF. 173 diseases' events occurred, with an average of 1.5 episode per child in FF group and 1.3 in BF group (p=0.20). Mortality was 6% in FF, against 4% in BF [Relative risque (RR) of 1.4 (CI 95%: 0.6-3.2; p=0.56)]. The main causes of morbidity were: Upper respiratory infections (27%), gastroenteritis (21%) and pneumonia (15%). Pneumonia was more frequent in FF group [RR of 1.6 (CI 95%: 1.1-2.4; p=0,007)], while there was no difference for gastroenteritis and Upper respiratory infections according to feeding mode.

Conclusion: In a context of persistent and regular councils on hygiene and formula preparation, there seems to be no evidence of increased morbidity or mortality related to FF compared to BF.

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CHARACTERIZATION OF THE BIRTHS OF NEWBORNS OF MOTHERS HIV +, IN THE PERIOD 2003 TO 2007, RIBEIRÃO PRETO, BRAZIL

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Background: The epidemic of AIDS is a serious problem of Public Health. The knowledge of the characteristics of the patients is basic for effective action on prevention and assistance. This study aimed to characterize the births of children of mothers HIV+ in the city of Ribeirao Preto, from 2003 to 2007, according to partner-demographic variables.

Methodology: Descriptive study, retrospective, which were analyzed the records of the Program of Child's Health. The data had been analyzed: age and residence of the mother, number of pregnancies, accomplishment of prenatal, sex and birth weight of newborns. The data were organized in tables and then analyzed.

Results: In the period from 2003 to 2007, 37645 children were born. Of these, 196 children whose mothers were HIV + (0.5%). Most mothers were aged 20 to 34 years (75.2%), 81.4% lived on the outskirts of the city, in districts with population of less economic class. As the number of pregnancies, only 17% were in the first pregnancy and 30% had more than 5 children, 6.1% did not have prenatal care. For infants, 50.8% were male, and 18.1% had weight below 2500g.

Conclusions: The results confirm the trend of the epidemic in accentuate in groups with less advantaged social , and with number of children above the brazilian average . The rate of low weight was higher than the average city in this period. It must include all pregnant women in prenatal care, promote the integration of these in programs of counseling, family planning and childcare.

P253

HIV AND HAART-MEDIATED MITOCHONDRIAL DNA DEPLETION COULD BE COMPENSATED AT TRANSCRIPTION LEVEL TO MAINTAIN MITOCHONDRIAL FUNCTION IN CHILDREN

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Background and aims: Both HIV infection and highly-active-antiretroviral therapy (HAART) lead to mitochondrial (mt) dysfunction, a major pathway for some adverse events in HIV-infected adults. Little is known about mt toxicity in the pediatric age. To determine whether there exist alterations in mtDNA and mtRNA content, and mitochondrial respirarory chain (MRC) function in peripheral-blood-mononuclear-cells (PBMCs) from HIV-infected children.

Methods: A cross-sectional study in PBMCs was performed in 64 HIV-infected children (47 HAART-treated and 17 off treatment) and 35 healthy children. We measured mtDNA and mtRNA content by Real-Time PCR. MRC enzymatic activity (complexes IV, II-III, G3PDH, G3PDH-CIII, and CII function) was measured by means of spectrophotometry, and mitochondrial mass was estimated by cytrate synthase activity. Cytochrome-C-oxidase subunits of CIV and mt content were assessed by western-blot analysis.

Results: A reduction in PBMCs mtDNA levels was observed in HIV-infected children compared to healthy controls (4.35±0.25 and 5.82±0.48, respectively; 25%, p=.005), together with similar levels of mtRNA (0.07±0.01 and 0.06±0.01, p=.19), enzymatic activities and protein subunit content. Among HIV-infected children, mtDNA levels didn´t correlate with viral load, CD4 counts or percentages, and lactatemia at the time of assessment. No further differences were observed among treated patients when HAART-related variables (time on treatment, use of ddI or d4T, IP or NNRTI-based regimens) were considered.

Conclusions: The observed depletion in mtDNA content in HIV-infected children did not lead to differences in mtRNA levels or MRC function. Homeostatic compensatory mechanisms at transcription level could explain the lack of correlation between mtDNA depletion and MRC function.

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MONITORING OF ANTIRETROVIRAL THERAPY IN HIV-INFECTED CHILDREN. RESULTS OF A MULTICENTRE STUDY IN SPAIN

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Background and aims: HIV-infected children life expectancy has improved dramatically since highly active antiretroviral therapy began. However, between 20% and 50% of children suffer virological failure during the first year of treatment. One of the factors that limit the success of therapy is suboptimal plasma concentrations of antiretroviral drugs. We present here a study evaluating antiretroviral plasma concentrations in HIV infected children on non-nucleoside reverse transcriptase inhibitors and protease inhibitors based regimen.

Methods: We carried out a multicentre, observational study, including HIV-infected children from five large Hospitals in Madrid, Spain. Clinical, haematological, biochemical and immuno-virological parameters were assessed. Antiretroviral plasma trough concentrations were assessed using a validated high performance liquid chromatography method.

Results: Between April 2006 and April 2008, 134 children were enrolled in the study, with median treatment duration of 41.8 months. 28% of the non-nucleoside reverse transcriptase inhibitors levels were low and 19.4%, high. 25% of the protease inhibitors levels were low and 17.4%, high. Adequate or high levels of antiretrovirals correlated with high CD4 and CD8 percentage and low viral load. Interestingly enough a significant correlation between high lopinavir/ritonavir levels and lipodystrophy was found. Tanner stage 5 was associated with higher plasma levels. Full adherence was reported for all the participants by a questionnaire.

Conclusions: Many HIV-infected children show ARV plasma levels out of the therapeutic range which demand and intensive, child-adjusted approach. However, larger studies are urgently needed in pediatric populations to define optimal reference values.

P255

ASPERGILLOSIS - A CASE REPORT IN A CHILD WITH AIDS

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Background: Aspergillosis is uncommon in HIV-infected individuals (incidence < 10%). Predisposing risk factors include: neutropenia, severe immunodeficiency and prolonged antibiotic use. Pulmonary infection by Aspergillus is the most common, but hepatic involvement has been also documented.

Aim: To present a child with AIDS with suspicion of aspergillosis.

Methods: A case report.

Results: 10-years old girl with newly diagnosed HIV diagnosis (most probably vertical infection) with clinical manifestations of hepatitis was admitted to the Department. She was soon after severe pancreatitis, cholecystitis and had prior history of recurrent pneumoniae (suspicion of mucoviscidosis). HIV diagnosis was established at the AIDS stage with single CD4 cells and HIV RNA VL of 5,7 log. Neutropenia, high aminotransferase level, GGTP and direct bilirubin elevation were observed. PCR DNA Aspergillus from gastric lavage and monoclonal antibody to galactomannan in serum were positive. DNA PCR Candida from gastric lavage was also positive. Other opportunistic infections (TB, MAC, PCP, cryptococcosis) were excluded. With a suspicion of aspergillosis she received treatment with voriconazole for 3 months with rapid clinical improvement. After 10 days she has started combined antiretroviral therapy. After 6 weeks of voriconazole treatment the bilirubin and aminotransferase levels were normal. GGTP remained high. cART resulted in decrease in HIV RNAVL to 2,6 log, but no improvement in CD4 count was observed.

Conclusions: Good response to voriconazole confirmed the diagnosis of invasive aspergillosis with liver involvement.

P256

HIV/AIDS; MODE OF TRANSMISSION, OUTCOME AND OUR EXPERIENCE WITH ANTI RETRO-VIRAL DRUGS IN A POOR RESOURCE SETTING

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Background: Paediatric HIV/AIDS and its management is still poor and of serious concern in poor resource settings.

Aims: To determine the mode of transmission and outcome in children with HIV/AIDS on ARVDs at the Usmanu DanFodiyo University Teaching Hospital (UDUTH), Sokoto, Nigeria.

Methodology: A 5-Year retrospective study of children with HIV/AIDS from January, 2001 to December, 2005. Screening was based on WHO criteria. Confirmation of HIV seropositivity was from a positive ELISA and then a Western Blot assay.

Results: Ten thousand, one hundred and seven (10,107) children were admitted over the 5 year period, 1,359 died giving a mortality rate of 13.5%. Eight hundred and forty (8.3%) of the admitted children had HIV/AIDS and were put on pediatric ARVDs based on WHO clinical criteria, 305 (36.3%) died. Mother to child transmission (MTCT) accounted for the highest mode of transmission, 794(94.5%). There were 44(5.3%) cases of unidentified route of infection and 2(0.2 %) cases of sexual abuse in males aged, 11 and 13 years. Fever (81.3%), diarrhea (75.0%), vomiting (41.4%), difficulty in breathing (39.8%) and refusal of feeds (39.8%) were the commonly encountered clinical features. Septicaemia (49.5%) and acute respiratory tract infections (40.9%) were the major admitting diagnoses and major causes of deaths. Deaths from HIV infection accounted for 22.4% of the total deaths for the study period.

Conclusions: Mother to child transmission of HIV is still high in the area of study and paediatric HIV/AIDS remains a significant cause of childhood morbidity and mortality.

Keywords: Paediatric HIV/AIDS, ARVDs, outcome, Sokoto.

P257

INADVERTENT NEONATAL LOPINAVIR/RITONAVIR OVERDOSE

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Background and aims: The ritonavir boosted protease inhibitor, lopinavir (LPV/r), may be used off label, as part of combination therapy to prevent mother-to-child transmission (MTCT) of Human Immunodeficiency Virus (HIV), when maternal infection is diagnosed at delivery. Parental understanding of the correct administration of the small volumes of antiretrovirals might be hindered by language differences and psychological trauma precipitated by HIV disclosure.

Methods: Despite meticulous education on the correct dose using a 2ml syringe, a Somalian mother with a language barrier inadvertently overdosed her 16 day old twin girls with a tenfold higher dose of zidovudine, lamivudine and LPV/r, by using the 10ml syringe prepacked with zidovudine.

Results: A drastic decrease in the residual volume of LPV/r led to disclosure of the accidental overdose 48 hours after its occurrence. Physical examination revealed two infants who were failing to thrive. Repeated assessments of haematological indices, acid-base balance, liver and renal function, blood glucose and creatine kinase levels were normal. An electrocardiogram and an echocardiogram, performed 7 days later, were unremarkable. Plasma lopinavir levels plotted on the 75th centile.

Conclusions: LPV/r toxicity may be caused by its high alcohol content, but symptoms of overdose are unknown and only one neonatal case of overdose, which resulted in death from cardiogenic shock, has been reported. Although no sequelae were noted in our cases we recommend that only 2ml syringes should be provided to parents administering LPV/r to their newborns. Parental administration of LPV/r should be reassessed again in the community following discharge.

P258

ASSOCIATION BETWEEN MANNOSE-BINDING LECTIN POLYMORPHISMS AND BACTERIAL INFECTIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: With the development of genomic technology there is an increasing interest in determining the genetic predisposition of immunocompromised patients to infections. Mannose-binding lectin (MBL), a protein that recognizes a variety of microorganisms and activates the complement system, is considered to be a potential predictive factor of susceptibility to infections.

Objectives: The aim of this study was to determine whether MBL deficiency influences the frequency and the duration of infections in children with acute lymphoblastic leukemia (ALL) during episodes of febrile neutropenia (FN).

Methods: In a cohort of 30 children with ALL treated at a single pediatric hematology-oncology unit with an almost identical chemotherapy regimen, we studied the relationship between polymorphism of MBL2 gene and the risk of infections during FN episodes retrospectively.

Results: The male/female ratio was 2/1. The mean age was 4.33 years. In 122 FN episodes a total number of 52 infections were microbiologically documented. The predominant Gram-positive microbes were coagulase negative staphylococci (40.3%). The predominant gram-negative bacteria were E. coli (17.3%) followed by Pseudomonas aeruginosa strains (9.62%) and Klebsiella pneumoniae (7.69%). 19 children carried the normal MBL2 gene (A/A) and 11 a mutant allele B (A/O or O/O). A statistical significant difference was found between MBL2 genotype and number of infections (p=0.024), number of FN episodes (p=0.017), duration of first FN episode (p=0.05) and overall duration of FN episodes (p=0,009).

Conclusions: MBL deficiency might predispose children with ALL to more frequent and prolonged febrile episodes during chemotherapy.

P259

INFANT HIV-1 DIAGNOSTIC TESTING AT CLINICAL SITES IN NORTH AMERICA: 2002-2006

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Background and aims: Our objectives were to assess the timing of testing, the types of diagnostic assays used, and the costs associated with the diagnosis of HIV-1 infection among infants born to HIV-1-infected women enrolled in the IMPAACT Protocol 1025 (P1025).

Methods: P1025 is a prospective cohort study of HIV-1-infected women and their infants at multiple clinical sites in the U.S. and Puerto Rico. Enrollment began in 2002 and is ongoing. Follow-up of infants continued for at least six months after delivery/birth. The study population for this analysis comprised all live born infants of known HIV-1 infection status born by December 31, 2006 to women enrolled in P1025.

Results: A total of 5147 HIV-1 diagnostic test results were reported for the 998 infants in the study population. The median number of HIV-1 diagnostic assays performed per infant was 5 (10^{th}, 90^{th} percentiles: 3, 7), and the greatest number of tests reported per infant was 13. The median ages at the time of the first, second, third, and fourth HIV-1 diagnostic assay was 0.1, 2.3, 7.0, and 17.6 weeks, respectively. Nucleic acid amplification assays (NAATs) represented 86.9% of all diagnostic assays. The median cost per infant for HIV-1 diagnostic testing was $1168 (10th, 90th percentiles: $762, $1642).

Conclusions: The great majority of assays reported for HIV-1-exposed infants at clinical sites in the U.S. and Puerto Rico were NAATs. However, the number of HIV-1 diagnostic assays performed per infant, and the cost associated with HIV-1 diagnostic testing per infant, varied greatly.

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NURTURING DIAGNOSIS OF CHILDREN STRICKEN BY MOTHER-TO-CHILD TRANSMISSION OF HIV IN PROGRAM OF NURTURING SUPPORT

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Background: Newly born from mothers HIV+ are under high nutritional risk, once they must not be breastfed. The Brazilian Government praises milk free distribution for these children until they are six months old, to decreasing the risk of malnutrition and vertical transmission. Our purpose is featuring the nurturing status of HIV+ mothers' children, around six months old, who were born in the city of Ribeirão Preto-Brazil, inserted in program of nurturing support.

Methods: Transversal, descriptive study in which the Health Services handbooks of children born out of HIV+ mothers in the first semester of 2006 were analyzed, according to variables: sex, weight at birth and weight at around 6 months old. Data were analyzed as shown on chart NCHS,1977.

Results: Out of 29 children born from HIV+ mothers in 2006, 13 were born in the first six months of the year. With regard to the weight at birth, two showed low weight. The average weight was 2903g. In a final evaluation with 11 children, the average weight was 7186g; about 82% of them showed signs of normal development, whereas 18% were at nutritional risk. Among those at risk, one did not follow the procedures completely. Children showing low weight at birth, at that moment were found having normal development.

Conclusion: Preliminary data show the following up of medical care, as well as milk delivery and mothers' acceptance to the program, all these contribute significantly to the maintenance or recovery of the nurturing status of these children at risk.

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METABOLIC CHANGES ASSOCIATED WITH LPV/R TREATMENT IN A COHORT OF HIV-1 INFECTED CHILDREN

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Background and aims: Highly active antiretroviral therapy (HAART) might lead to the development of toxic effects as dyslipidaemia and lipodystrophy syndrome. Our aim was to evaluate the trend of adipokines and serum lipids in a group of vertically HIV1-infected children treated with lopinavir/ritonavir-based HAART as salvage therapy.

Methods: A multicenter prospective study of 22 PI-experienced children on salvage therapy with LPV/r recruited in 2000-2003. Every 3 months were determined $CD4^+$, $CD8^+$, viral load (VL), cholesterol, triglycerides, lipoproteins and cytokines. Comparisons between children with lipodystrophy (LD) and without lipodystrophy (N-LD) were performed by Fisher exact test, U Mann-Whitney test and Mantel-Haenszel chi-square test.

Results: Median follow-up on LPV/r therapy was 49.0 weeks (IQR: 43.8; 50). We did not find differences in $\%CD4^+$, $\%CD8^+$, $\log_{10}$VL, cholesterol, triglycerides, HDL, LDL, C-peptide, PAI-1, insulin and HOMA at baseline and during follow-up between LD and N-LD groups. We found differences in median leptin levels (pg/mL) at 48 weeks of follow-up (LD vs. N-LD: 754.6 vs. 139.0; P=0.016) and in median adiponectin/leptin ratio (at 36 weeks: LD vs. N-LD: 20,166.1 vs. 158,934.4; P=0.015; at 48 weeks: 25,560.1 vs. 398,444.7; P=0.043).

Conclusions: Increase in leptin concentration in the LD group could be associated to insulin resistance, reflected in the trend of insulin and HOMA that increased steadily during follow-up. Whether this represents a significant increase could be determined in the future with a longer follow-up.

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HOW DO CHILDREN WITH HIV PRESENT IN NORTHWEST ENGLAND?

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Background and aims: Increasing numbers of HIV infected children are being seen in the UK. We wanted to review how children with HIV were diagnosed in the Northwest of England.

Methods: A case note audit was performed of HIV infected children who had been seen in the Northwest Paediatric and Perinatal HIV Network (NWPPHN). Information was obtained on age at diagnosis, year of diagnosis, main reason for HIV testing and who had arranged the test.

Results: 121 HIV infected children had been seen in the NWPPHN between 1993-2008; 48 were born in the UK. Most children were of African origin (n=83). Median age at diagnosis was 4yrs (range 1 month-16yrs). Maternal HIV infection was the main reason for HIV testing (n= 52; 43%). 47 (40%) children were HIV tested because of clinical features; pneumocystis/ CMV pneumonitis (17), recurrent respiratory infections (9), FTT/diarrhoea (5), lymphadenopathy/hepatosplenomegaly (5), parotid swelling (3), raised IgG (2), severe chickenpox (2), TB (1). Children who were diagnosed because of maternal infection were significant older (6yrs vs 1yr; P=0.006), more likely to be diagnosed by an HIV team (62% vs 29%; P=0.0009) and more likely to present after 2003 (60% vs 27% P=0.003).

Conclusion: Children with HIV can present at any age. Half are tested because of their mothers HIV status. Many of these children are asymptomatic; highlighting the importance of testing all children born to HIV infected women. However 40% of HIV infected children present with clinical features suggesting HIV and are often diagnosed by non-HIV specialists.

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LUPUS ERYTHEMATOSUS DUE TO VORICONAZOLE IN AN IMMUNODEFICENCY INNFANT

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Introduction: Voriconazole is now the first therapeutic option for invasive aspergillosis, but is no currently licensed for patients less than two years. A wide variety of dermatologic manifestations adverse effects are described. Eritematous lupus is a rare reaction (0.01-0.1%). We present a patient with chronic granulomatous disease who developed a lupus-like lesions after the start of voriconazole because a thoracic aspergillosis.

Case: An eight-month infant was diagnosed of thoracic aspergillosis, after the development of a thoracic mass appeared two weeks before. MR demonstrated a large thoracic mass envolved thoracic wall. Culture showed Aspergillus nidulans. The oxidative capacity of neutrophils was decreased (52 % of control sample). Intravenous voriconazole was administered at higher dose recommended for these cases (8 mg/kg/12hs) during 39 days, following oral route. After 76 days of therapy, a lupus-like erythema appeared in cheeks and forehead. Biopsy of these lesions confirmed a lupus erythematosus reaction, with depot of IgM and C3 in the basal membrane with the immufluorescence study. Anti-Ro, anti-La and antinuclear antibodies were negatives and the complement was normal. Topic tacrolimus monohydrate, photo-protectors and oral itraconazole were started, and oral voriconazole was stopped. Facial lesions resolved after four weeks, without relapse.

Comentaries: For our knowledge, only a few cases of lupus-like reaction were associated to voriconazole use, but no cases were described in pediatric population. There is no evidence if the immunologic disorder, the short age of our patient or the high dose of voriconazole used predisposed for this rare skin side effect of this drug.

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HIV POSITIVE TEENAGER WITH A MEDIASTINAL MASS

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Background and aims: We present a case with HIV infection which developed a mediastinal mass that we proved to be a tuberculosis lymphadenopathy.

Methods: We are taking the case of a 19 years old female, diagnosed with HIV infection since 2001, admitted in April- May 2008 with family history of cancer.

Results: The patient was admitted for prolonged fever and weight loss. The immunologic profile of HIV infection showed stage B2 with CD4 414/mm^3 and undetectable viral load. Chest radiography showed a mediastinal enlargement in the middle and superior area with a multilobulated outline. CT scan indicated several mediastinal lymphadenopathy masses and an apical opacity in the right superior lobe and also hepatosplenomegaly with perisplenic adenopathy. The serology was positive for chronic infection with EBV, CMV and Toxoplasma gondii. The smears and cultures from sputum were negative for M. tuberculosis. It was performed a surgical biopsy of the mediastinal mass and the histopathology exam showed specific findings for tuberculosis. She started DOTS with isoniazid, pyrazinamide, ethambutol and streptomycin, because she was under treatment with 3TC+AZT and LPV/r, for 2 months, and then 3/7 HZE for 10 months.

Conclusion: The evolution was good. ARV treatment and DOTS led to good results and a new chest x-ray showed that the opacity in the apical area of right superior lobe has been reduced, without mediastinal lymphadenopathy.

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ASPERGILLOSIS PRESENTING AS OSTEOARTHRITIS IN A CHILD TREATED WITH VORICONAZOLE

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Backgrounds and aim: Aspergillosis predominantly occurs as an opportunistic infection in immunocompromised hosts and the lung and the brain are the most common involved areas. Bone involvement and especially articular aspergillosis are exceedingly rare. Due to its rare occurrence, there is no standard treatment for patients with aspergillus osteoarticular infections. Here we report a child with aspergillus osteoarticular infection treated with voriconazole.

Case report: A six-year-old boy presented with painful swelling of the right ankle for one week. Past history revealed that he had been hospitalized 3 years ago due to primary peritonitis. Periton fluid culture had yielded Staphylococcus aureus and the patient had been healed with antibiotic treatment. He also had left posterior cervical lymphadenitis 4 months ago and an abscess was drained. Magnetic resonance imaging (MRI) of the right ankle was consistent with osteomyelitis and artritis. The synovial fluid culture grew Aspergillus fumigatus. Chest X-ray revealed consolidation on the right lung. Although, the phagoburst test could not be performed, the patient was diagnosed chronic granulomatous disease clinically. Voriconazole was given to the patient 4 weeks by intravenous and then by oral route. At the sixth month of the therapy physical examination and chest-X ray findings were normal and repeated MRI of the right ankle revealed a marked regression of the arthritis and osteomyelitis findings.

Conclusions: Aspergillus osteoarthritis can be occure especially in immunologically compromised patients and voriconazole is an effective treatment.

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INTRAVENOUS PALIVIZUMAB FOR THE TREATMENT OF RESPIRATORY SYNCYTIAL VIRUS IN PEDIATRIC HEMATO-ONCOLOGY PATIENS

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Background and aims: Children with cancer are at increased risk for serious complications from Respiratory Syncytial Virus (RSV). Treatment options are limited, with no consensus or guidelines. Palivizumab is approved for prevention of RSV in specific populations, but not for treatment. Few studies demonstrated successful treatment with Palivizumab. We describe our experience with Intravenous (IV) Palivizumab treatment for children infected with RSV, in our pediatric Hemato-oncology department.

Methods: Symptomatic patients are routinely tested for common respiratory viruses. Following a case with severe fatal RSV pneumonia in a 2 years (y) old child with AML, patients were actively screened twice weekly regardless of symptoms. Respiratory samples were tested for RSV using rapid ELISA test, Immunofluorescence or RT- PCR. A single dose of Palivizumab (15 mg/kg) was offered to RSV^+ children ≤3y old.

Results: During a 6 weeks period (1/1/2008-12/2/2008) 12 patients were RSV^+. Seven patients (4 months - 3y) were treated with Palivizumab. Five patients (including index case) had respiratory symptoms, 2 children were asymptomatic. The index case was in respiratory failure when treated and died a month later. No adverse events attributed to palivizumab were recorded. Patients who were treated immediately had no complications attributed to RSV.

Conclusions: Containment of outbreak due to RSV among high risk children is difficult. Active screening with RT-PCR, early recognition of mildly symptomatic or asymptomatic children and use of IV Palivizumab may be effective in preventing complications of RSV infection among high risk patients.

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AN OUTBREAK OF MYCOBACTERIUM MUCOGENICUM BACTEREMIA IN HEMATO-ONCOLOGY UNIT

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Background and aims: Mycobacterium Mucogenicum (MM) is a rapidly growing non-tuberculous mycobacterium (NTM) that is commonly identified in tap water. MM rarely may cause bacteremia. We describe an outbreak of MM bacteremia among pediatric Hemato-oncology patients.

Methods: Charts of children with MM bacteremia were retrospectively reviewed. Demographic data, underlying conditions, Central Venous Catheter (CVC) type, duration of bacteremia, and treatment were retrieved. Epidemiological investigation was conducted during the outbreak including environmental sampling.

Results: During a 6 month period (September 2005-March 2006), 8 patients aged 1.5-17y had MM bacteremia.. Seven patients had underlying malignancy and one with Thalassemia major after Bone Marrow Transplantation. Mean number of positive blood culture was 4.2 (1-11) per patient. Two patients received antibiotic treatment in addition to removal of CVC. One patient had pathological chest Computered Tomography (CT). All patients were cured. Almost 60 environmental samples were obtained from, surfaces, ice and municipal water supply. All were negative and no source was documented. Infection control measures included emphasis on guidelines for prevention of CVC-associated infections. No cases occurred before and after this outbreak.

Conclusions: Mycobacterium mucogenicum is a rare agent of CVC associated bacteremia. Removal of CVC may be sufficient for the management of bacteremia. In the absence of definite source identification, reinforcement of standard infection control measures may be successful in containing outbreaks.

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PREVALENCE OF HIV INFECTION IN PREGNANT WOMEN IN MUMBAI, INDIA

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Prevalence of HIV among pregnant women in India is of great concern especially to prevent HIV in children. Mother to child transmission of HIV is the commonest cause of transmission of HIV in children. Thus estimating prevalence of HIV in pregnant women would aid in developing and prioritizing prevention of parent to child transmission of HIV (PPTCT) programmes. Prevalence of HIV infection in pregnant women in India has ranged from 0.7-1.2%. All pregnant women referred to the antenatal clinic from 1993 onwards were tested for HIV infection by ELISA test after pretest counseling. A woman was diagnosed to be HIV infected if she tested positive on more than 2 HIV ELISA tests. Prevalence of HIV infection in them was calculated and also whether there was an increasing trend was determined. A total of 123439 pregnant women were tested for HIV from 1993 to 2004 of which 1767 women were HIV infected. Prevalence rate was found to be 1.4%. However, this prevalence has not shown an increasing trend (p =0.443) over period of 12 years.

Year	HIV positive	(%)	Total
1993	95	(0.76)	12436
1994	114	(0.92)	12354
1995	111	(0.97)	11557
1996	204	(1.66)	12250
1997	153	(1.4)	11077
1998	287	(2.37)	12065
1999	176	(1.47)	12126
2000	192	(1.74)	11058
2001	183	(2.09)	8767
2002	124	(1.62)	7651
2003	95	(1.47)	6421
2004	33	(0.6)	5677
Total	**1767**	**(1.4%)**	**123439**

Table 1 : Prevalence of HIV in pregnant women over 12 years

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KNOWLEDGE AND RISKY BEHAVIOR OF CHILDREN ACCOMMODATED IN INSTITUTIONS FOR CHILDREN WITHOUT PARENTAL CARE IN SERBIA

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Background and aims: The aim of this study was to analyze difference in knowledge and behavior of children aged 12-14 and 15-19 years, accommodated in institutions for children without parental care, in relation to risk of HIV infection.

Methods: The research was performed in Serbia in period of November to May, 2007. By the use of random sampling procedure in this cross-sectional study were included 483 children 12-19 years old (78% of all children without parents in Serbia) who were accommodated, at least one month before interview, in the 16 of the 22 institutions for children without parental care. Data were gathered from all respondents by a closed-type structured questionnaire. In the statistical analysis chi square test was used.

Results: Among 483 children without parental care 30.6% were less than 14 years. The mean age at first sexual intercourse was 11.8 for children aged 12-14 and 14.9 for children aged 15-19 years. The use of condom at last sexual intercourse with irregular sexual partner was reported by 70.8% of children 15-19 years old during the last year. Only two of younger children had irregular sexual partners in the last year and no one of them used condom. The difference between these two age groups was significant. Correct answers to 5 questions about HIV transmission were significantly more frequent among children 15-19 years old (34.6%) than among younger children (15.5%).

Conclusions: It can be concluded that HIV/AIDS preventive programs are especially necessary for children without parents aged 12 to 14 years.

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PREVALENCE OF HIV INFECTION IN B-THALASSEMIC PATIENTS IN JAHROM, 2008

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Background and aims: Thalassemic patients are high risk group to humanimmunodeficiency virus (HIV) infection due to repeated transfusions. To determine the incidence of HIV infection in thalassemic patients of Jahrom.

Methods: This study was carried out on all 109 thalassemic patients of Jahrom referring to thalassemia center of Jahrom, on May 2007.

Results: No cases of HIV were found. The prevalence of HIV infection in the thalassemic patients of Jahrom was 0%.

Conclusions: It seems that the prevalence of HIV infection in thalassemic patients of Jahrom is lesser than the prevalence of HIV infection in the in thalassemic patients in the most of other cities of IRAN and in other countries.

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MYOSITIS DUE TO MICROSPORIDIUM PLEISTOPHORA HOMINIS IN A HIV-INFECTED CHILD WITH SEVERE IMMUNODEPRESSION

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Introduction: Microsporidia are ubiquitous intracellular protozoa and are important pathogens in HIV-1 infected individuals. Digestive tract is the most frequent organ involved. Myositis was only reported in 3 adults. We report here the first pediatric case of a generalized myositis in a HIV infected child with severe immuno depression.

Case description: A Nigerian 10 year-old boy was admitted in emergency for fever, dyspnea with hypoxemia. Investigations showed an alveolo-interstitial pneumonia due to *pneumocystis Jirovecii* and CMV. HIV-1 testing was positive. HIV viral load was high (5.64 $\log_{10}$ copies/ml) and CD4 cell count was low (15/mm^3).The child was treated with cotrimoxazole, valganciclovir, corticosteroids and triple antiretroviral therapy. Three weeks later, while the pulmonary symptoms improved, the patient experienced polymyalgia in his limbs with muscular nodules, decreased muscular strength, tendinous retractation and elevated serum creatine phosphokinase. Total body MRI concluded to generalized multi-nodular polymyositis. Biopsy showed multiple muscular necrosis lesions containing microsporidian spores. Ultramicroscopic analysis concluded to *Microsporidium Pleistophora hominis*. The patient was treated with albendazole for a month with a rapid clinical response. Three months later, the patient presented an immune reconstitution inflammatory syndrome with *Mycobacterium scrofulaceum* infection and relapsing polymyositis. Albendazole was re-initiated with complete recovery of the symptoms.

Discussion and conclusion: This is the fourth case reported of myositis due to *Microsporidium Pleistophora hominis* in AIDS patients. The *Microsporidium Pleistophora hominis* appears as a microsporidia species preferentially associated with myositis. In AIDS patients who experience polymyositis, muscle biopsy should be performed to rule out atypical or rare microorganisms.

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HUMAN HERPES VIRUS 7 (HHV-7) INFECTION IN A 6 YEAR OLD BOY WITH BURKITT LYMPHOMA

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We present the case of a 6 year old boy diagnosed of Burkitt's lymphoma who underwent treatment according to BFM-NHL 90 protocol. On day 10 after initiation of treatment, the boy presented a macular rash on his back, which spread to the trunk and the inner surface of the thighs. On day 11, the rash became hemorrhagic and pruritic and the patient became febrile. Laboratory testing revealed severe neutropenia, anaemia, thrombocytopenia and increased CRP and ESR values. Blood cultures and serologic tests for viruses and parasites were negative. Antibiotic treatment was immediately initiated. Moreover, he was put on antihistaminic and antifungal treatment. Despite medication, fever and rash persisted. Based on the rash, strong suspicion of a herpes virus infection was aroused and the patient was put on acyclovir treatment. HHV-7 was detected by PCR in blood. Within the next twelve days the patient's condition was improved. He became afebrile and the rash subsided with exfoliation. The boy received acyclovir intravenously for a total of 14 days. Two months later, during a lumbar puncture because of persistent headache, HHV-7 was detected by PCR in CSF. He was administered acyclovir orally for 21 consecutive days.

HHV-7 is a T-lymphotropic virus, infecting CD4+ and CD8+ lymphocytes. Primary HHV-7 infection occurs in early childhood and is generally considered to be a benign and self-limited disease. After primary infection, HHV-7 persists in the host in a latent state, and can act as an opportunistic agent after reactivation during immunosuppression as in our patient.

GASTROINTESTINAL INFECTIONS

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EFFECT OF *HELICOBACTER PYLORI* INFECTION ON STUNTING IN VARIOUS AGE GROUPS OF PAKISTANI CHILDREN

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Background and aims: *Helicobacter pylori* infection leads to gastrointestinal disorders irrespective of age and sex. There have been few prevalence studies of *H. pylori* among Pakistani population and our recent reports revealed an overall incidence of 84.6% among Pakistani adult population manifesting dyspepsia [Ahmad et al. (2009) FEMS Immunol Med Microbiol 55(1):34-38]. As such the major aim of our study was to evaluate *H. pylori* infection-associated stunting in various groups of Pakistani children taking into consideration confounders like socio-economic status and several others.

Methods: A total of 400 children were enrolled from three schools in the suburb of Pakistan capital city Islamabad in accordance with approved protocol from the University Research Board. Upon signing consent/assent forms, each child underwent non-invasive ^{13}C urea breath test to confirm *H. pylori* infection and anthropometric data recorded.

Results: Our analysis revealed that 72.3% of children without gastric symptoms were harboring *H. pylori* bacterium whereas this trend varied in different ages, i.e. 69.3% in 3-6, 71.4% in 7-8, 78.6% in 9-10, 76% in 11-12 and 55% among 13-16 years age groups. A lower occurrence of *H. pylori* in adolescence (13-16 years) is intriguing and needs further longitudinal studies. *H. pylori*-associated stunting was well pronounced in male children when compared with female group (An Odds ratio 3.46 vs. 2.24). We did not see any association between *H. pylori* positivity and wasting in either group.

Conclusions: Based on our data we conclude that a strong association exists between early child growth and *H. pylori* infection.

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ROTAVIRUS INFECTION BURDEN IN CHILDREN IN UKRAINE

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Background and aims: Diarrhea disease in children in Ukraine is one of actual medical problems. It has the 3-rd place in children morbidity. 60-70% of annual hospitalizations of children to infectious departments are connected with diarrhea disease. Our previous data on rotavirus infection surveillance in 2 hospitals since December 2006 till November 2007 showed the high incidence of this infection. In this report we show data on the 2-nd year of observation.

Methods: Hospital-bases sentinel surveillance (Kiev, Odessa) was held since December 2007 till November 2008.

Results: Number of hospitalized children with diarrhea was 1071 in Odessa and 614 in Kiev. Number of children, from whom samples were taken was 911 (85%) and 568 (92.5%) respectively. Proportion of diarrheas caused by rotavirus was 43.8% and 62.2% respectively. Season fluctuations - increased incidence in cold seasons 72% in January in Odessa and 84% in February in Kiev was marked. Vomiting, dehydratation of 2-nd degree and fever were significantly more frequent in rotavirus-positive diarrhea than in rotavirus-negative one.

Conclusions: Rotavirus infection burden in children is still high in Ukraine. Received data might be used for solution of question of application of rotavirus vaccine in Ukraine.

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ROTAVIRUS GENOTYPES DIVERSITY IN DIARRHEAL CHILDREN AT THE FRENCH PEDIATRIC EMERGENCY DEPARTMENTS BETWEEN 2006 AND 2008

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Background and aims: Rotaviruses are the major cause of acute gastroenteritis (AGE) in young children, and require a careful surveillance, especially in the context of vaccine introduction. This study was designed to evaluate the strains circulation and to detect the emergence of potentially epidemic strains in France.

Methods: This prospective study was conducted from 2006 to 2008 in children under 5 years old consulting for acute diarrhea at the pediatric emergency units of 11 University Hospitals across France. Rotaviruses were detected in stools by rapid tests and genotyped by RT-PCR on the basis of their outer capsid proteins VP4 (P type) and VP7 (G type).

Results: The genotyping of 1084 rotaviruses showed that G1 strains (56.8%) were predominant, followed by G9 (28.2%), G2 (6.8%) and G3 (2.5%). Most strains were associated with P[8] (90.8%). Mixed infections, mostly G1/G9 associations, were found in 4.0% of stool samples. The distribution of genotypes was heterogeneous, regional frequencies regarding G1 and G9 ranged from 35.8% to 79.7% and 12.0% to 69.2%, respectively. Finally, 18 atypical reassortant strains were detected of which several G8 and G12 rotaviruses.

Conclusions: The G1P[8] and G9P[8] strains are the main rotaviruses circulating in France and account for 84% of AGE. The surveillance of rotavirus infections should be maintained to document strains distribution and their clinical expression, and to assess the emergence of new reassortants that may be likely to cause severe gastroenteritis and not respond to current rotavirus vaccines.

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NOROVIRUS AND ROTAVIRUS INFECTION IN CHILDREN WITH ACUTE GASTROENTERITIS

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In Northern Italy viruses represent the main cause of acute gastroenteritis in children.

The aim of our study was to evaluate the etiology, number of cases, severity of clinical manifestations, and seasonal distribution of acute gastroenteritis in children over a one period.

Between October 1st 2007 and September 30th 2008, 473 children (225 M, 218 F) between the ages of 16 days and 16 years and 2 months (mean age 3 yrs and 7 months) were recovered in the Pediatric Department of the University Hospital of Parma with acute symptoms which included fever, vomiting and diarrhea. Stool samples were collected from all subjects. Patients with bloody diarrhea or bacteric diarrhea were excluded from the study. Diagnosis was based on standard electronic microscopy and later confirmed through latex agglutination test or polyacrylamide gel electrophoresis (Rotavirus) or Nested RT-PCR (Norovirus).

182 cases:

- 84 (46,2%) Rotavirus
- 77 (42,3%) Norovirus
- 19 (10,4%) Rotavirus-Norovirus coinfection
- 2 (1,1%) Norovirus-Adenovirus coinfection

The peak incidence of Norovirus infection was between November and December (29 cases) and between December and March (71 cases) for Rotavirus infection.

Modified Ruuska and Vesikari clinical score:

- Rotavirus: 3-16; mean score: 11,61
- Norovirus: 0-17; mean score: 9,19

In the province of Parma, Rotavirus and Norovirus infections represent the main cause of hospitalisation for acute gastroenteritis in children.

Modern virological diagnostic technology demonstrates that Noroviruses play an epidemiological role that is similar to that of Rotaviruses.

The duration and severity of clinical manifestations were greater in Rotavirus infections.

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CLINICAL PREDICTIVE FACTORS IN ACUTE BACTERIAL DIARRHEA

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Aim: To determine the clinical predictive factors of bacterial or viral etiology in acute diarrrhea in children.

Methods: 453 children with infectious acute diarrhea, from Arad and Timisoara, Romania, participated in this study. They were divided in two groups: bacterial and viral. The bacterial group included 387 children with diarrhea produced by Shigella, Salmonella, Campylobacter and E. Coli. The viral group included 66 children with Norovirus and Rotavirus infections.

The following parameters were monitored: fever, abdominal pain, vomiting, colic point and stools (frequency, duration, presence of pathologic elements).

The data were introduced in an Excel database and analysed with statistical methods in SPSS 10.

Results: The following results were obtained for the bacterial and the viral group: onset fever (84.2%, respectively 37.3%, p< 0.01), abdominal pain (15.8%/10.6%, p=0.278), vomiting (40.3% / 81.8%, p< 0.01), vomiting preceding diarrhea (12.1%/80.3%, p< 0,01), colic point (37.7%/0%, p< 0,01), watery stools (41.4%/96.5%, p< 0,01), mucus stools (50%/ 0%, p< 0,01), blood stools (98.3% / 1.5%, p< 0,01).

The average number of stools was 5.57±2.69 (p< 0.01) versus 4.65±1.66 (p=0.009) in the first day and 4.59±2.39 versus 3.7±1.66 (p=0.003) in the second day; the duration of stools was 6.39±2.56 and 4.29±1.39, respectively (p< 0.01).

Conclusions: The high fever at onset, the colic point, the stools with mucus and blood, the frequency of stools >5/ day and the prolonged duration of the diarrhea are highly significant for the bacterial etiology.

The vomiting preceding diarrhea and the watery stools are frequently associated with the viral etiology.

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PREVALENCE OF SALMONELLA INFECTION IN CHILDREN AND INFANTS WITH GASTROENTERITIS ADMITTED TO A SECONDARY CARE HOSPITAL

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Background: Diarrheal disease continues to be one of the most common causes of admittance to a children´s hospital.

Salmonella infections are recognized as major causes of childhood diarrheal illness.

In addition to the effect of antibiotic use in animal feeds, the relationship of Salmonella infections to prior antibiotic use among children in the previous month is well recognized.

Materials and methods: The aim of this review was to analyse the prevalence and epidemiologic characteristics of Salmonella.

From January 2005 to July 2008, we analysed the stool samples for Salmonella of 198 children with diarrheal disease admitted in our hospital.

Results: Salmonella was detected in 60 cases, more often during summer months, particularly in children aged between 4 and 9 years.

In majority of cases, the transmission source was unknown. Curiously, our rural population has an exotic habit-drink water of the well.

The two most severe cases had co-morbilities. In 36 cases, children had taken antibiotic six weeks before.

Conclusions: Our review revealed the most typical characteristics of Salmonella infections and a particular transmission source in our population.

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FOLIC ACID, VITAMINB12 AND IRON LEVEL IN THE 6-12 YEARS OLD PATIENTS INFECTED WITH *GIARDIA LAMBLIA* IN SOUTH TEHRAN

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Giardia lamblia is a factor in creating diarrhea for human and other mammaliam through the world. Sometime such unicellular caused transfer diarrhea through food which is circulated too much over developed country and caused extending of infection within a part of world. Contamination of water to *Giardia* cyst is a common reason of existence of that among tourist and passengers. The feature of cyst is in conic form by length in 8-12 and width in 7-10 micron this parasite is a single host and needs not to mediate. Over this research three times faces of 3000 patient aging 6-15 years old referred to healthy and treatment center at south of Tehran considered in view of parasitic infection by two direct method (moisture) then was taken blood from 30 people whom were affected to giardia immunoassay B12 vitamin host and full and by application the ferene method the amount of iron was measured. Based on the obtained conclusion the ratio and Vitamin B12 among the affected people compare to under controlled patient to be reduced while the acid folic rate not change among those people in comparison with under controlled patient.

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GASTROENTERITIS REVIEW AT SHAIKH KHALIFA MEDICAL CITY (SKMC) IN THE UNITED ARAB EMIRATES

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Background: Acute gastroenteritis (AGE) in children carries significant mortality and morbidity. Rotavirus is a leading causative pathogen. Currently there is a vaccine to prevent the severe forms of this infection. Studying the epidemiology of the infection can help in implementing the vaccine.

Objectives: To evaluate the epidemiology and clinical course of AGE cases presented to SKMC. To identify the percentage of AGE caused by rotavirus in young children.

Methods: We conducted a retrospective case review of children < 6 years admitted to SKMC with AGE including both rotavirus positive and negative over the period Jan. 2003- May 2004.

Results: There were 204 cases of AGE, which accounted for 12.93% of total admissions. There was seasonal distribution, more infections occurred in the months Dec.-Feb. The rate of AGE varied among different age groups. In those ≤ 1 year of age there was a total of 39 cases (19.1%), ≤ 18 months a total of 90 cases (44.1%), ≤ 2 years a total of 117 cases (57.4%), and ≤ 3 years a total of 163 cases (79.9%). Rotavirus testing was done in 150 (73.5%) patients; rotavirus was positive in 39.3% and negative in 60.6%. The mean length of hospital stay (LOS) was 2.1 (0.3-16) days.

Conclusion: AGE accounted for significant number of hospital admissions. Rotavirus is a leading causative pathogen. A vaccine implementation will clearly reduce a significant number of hospitalizations. An economic impact analysis is needed to show the efficacy of vaccination.

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THE PARASITIC INFECTIONS. A CASE SERIES

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Background and aims: According to World Health Organization, the helminths infect more than a quarter of the world´s population. The authors emphasize the clinical particularities regarding parasitic infections.

Methods: The authors present 3 cases of children with anemia and growth impairment. The 1st case was suspected by kidney malformation because of repeated urinary tract infections. The 2nd case was admitted for further investigations regarding a chronic allergic conjunctivitis. The 3rd case was admitted in the context of recurrent wheezing episodes.

Results: In the 1st case, the parasitological stool exam was negative but adhesive tape test has identified an infection with Enterobius vermicularis. In the 2nd case has been identified an infection with Hymenolepis nana associated with Giardia intestinalis and in the 3rd case the parasitological exam has shown a massive infection with Ascaris lumbricoides and Trichiuris trichiura. We have reconsidered the diagnosis for all 3 cases and the specific therapy was initiated with good clinical evolution regarding growth impairment and the associated pathologies.

Conclusions:

1. All 3 cases have presented impairment nutritional status and were admitted for different reasons;

2. The combined parasitic infections suggest a poor hygiene;

3. Even though the parasitic infections are frequent, they are generally underdiagnosed because the symptoms could be so variable.

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SEVERE COMPLICATIONS IN HOSPITALIZED CHILDREN WITH GASTROENTERITIS DUE TO ROTAVIRUS VS. GASTROENTERITIS OF OTHER CAUSES

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Introduction: Rotavirus gastroenteritis (RV-GE) affects every child up to school age; hospitalisation rates are high, mortality is high in developing countries. Little is known on morbidity and eventually specific complications of severe RV-GE. Little is known on morbidity and eventually specific complications of severe RV-GE. In the light of 2 available RV vaccines evidence on morbidity for vaccine recommendations is needed.

Material and methods: In 3 large pediatric hospitals files of all hospitalised children ≤6 years from 10/2002 - 5/2008 with any ICD-10 Code for infectious GE (A00-A09) were retrospectively analysed with a predefined protocol.

Results: 7235 cases were included in the study, 55,6% male; children were on average 1,4 years old and spent 6,56 days in hospital, median 4 days.

20,8% of all children had an underlying disease.

In 2178/7235 (30,1%) cases RV was found.

7/7235 children died, one premature newborn with NEC in the context with RV infection.

In 45,5% of RV cases vs 56,3% of other GE cases another diagnosis or complication was present (p=< 0,01). Neurological symptoms and trauma were diagnosed more frequently among children with non-RV GE.

Hypertonic dehydration (sodium >150 mmol/l) occurred in 79 cases, 63,3% cases were RV positive, in 17,7% RV was not searched for, in 19% RV was excluded. In severe hypertonic dehydration (sodium > 160 mmol/l) RV was found in 15/21 cases (all p< 0,01).

Conclusion: Hypertonic dehydration is a complication specific for RV-GE putting children at risk for CNS damage.

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ROTAVIRUS GENOTYPING IN HOSPITALIZED CHILDREN. EXPERIENCE FROM A SINGLE CENTER IN ATHENS, GREECE DURING 2007-2008 REVEALED ABSENCE OF G9 STRAIN

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Background and aims: Paediatric Rotavirus Gastroenteritis (PRG) is the most frequent and severe cause of acute gastroenteritis (AGE) in young children worldwide. Rotavirus genotype distribution varies between seasons and among countries and regions. Studies from European centres report G1P[8], G2P[4], G9P[8] G3P[8] and G4P[8] as their most frequently identified genotypes. In this prospective study the prevalence of rotavirus genotypes in hospitalized children with PRG was evaluated.

Methods: During the 2007-2008 season 385 children were hospitalized for acute gastroenteritis. Rotavirus was detected in stool specimens of 76 (19.7%) children admitted with acute diarrhoea using rapid antigen detection tests. Forty four rotavirus-positive samples were G and P types by RT-PCR.

Results: Genotyping revealed that G2P[4] genotype was the predominant type (30/44, 68.2%) followed by G1P[9] (25%) and G4P[4] (6.8%), and 2 mixed infections were detected . Interestingly we did not identify any G9 strains in the study samples period.

Conclusions: Although the number of children in this study is very limited, our results are in accordance with those reported from other European centres over the 2007-2008 season.

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PREVALENCE OF ROTAVIRUS INFECTION IN CHILDREN AND INFANTS WITH GASTROENTERITIS ADMITTED TO A SECONDARY CARE HOSPITAL

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Background and aims: Since its discovery in 1973 by Bishop, Rotavirus has emerged as the single most important etiologic agent of diarrhea in infants and young children.

Rotavirus and other gastroenteritis viruses not only are major causes of paediatric mortality but also lead to significant morbidity.

The infection typically begins after an incubation period of 48 hour with mild to moderate fever as well as vomiting followed by the onset of frequent, watery stools.

The aim of this review was to determine the prevalence and epidemiological characteristics of rotavirus infection.

Methods: In a 12 month survey (2008) of infants and children with gastroenteritis admitted to our hospital, Rotavirus was detected in stool specimens by enzyme-linked immuno sorbent assays (ELISAs).

Results: Rotavirus was detected in 32 cases - 48.5% (total of gastroenteritis - 66), more often during winter months, particularly in children aged between 6 months and 2 years, with a mean hospital stay of 4.1 days.

Routine bacterial and viral studies revealed that bacterial pathogens and common enteric viruses were associated with relatively few cases of gastroenteritis.

The most frequent clinical manifestations were fever and diarrhea.

The disease was most severe in patients 3-12 months of age.

Only one patient was vaccinated against Rotavirus and in that case the disease was mild.

Conclusions: This study confirmed that Rotavirus is the most important etiologic agent of paediatric acute gastroenteritis in our hospital, although the small sample size.

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EFFECT OF ZINC SUPPLEMENTATION ON CLINICAL COURSE OF ACUTE DIARRHEA

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Introduction: Zinc Sulfate is a medication used in acute diarrhea for reduction of its duration. Recently several studies have conducted in many countries to confirm the value of zinc sulfate in reduction of diarrhea duration and WHO recommended it was a usual treatment for acute diarrhea.

Method and material: We conducted an interventional Study (Clinical trial). In patient who admitted in Ali_Asghar children hospital with one episode of acute diarrhea. The patients was divided in 2 groups (cases= 75 and control=75). In the case group zinc sulfate was added as supplement and in control group no supplement was added to usual treatments. The Zinc prescribed as zinc sulfates syrup; 10 mg for children less than 6 months and 20mg for children greater than 6 months.

Results: Mean duration time of diarrhea in control group without Zinc Sulfate was 5.63 days and for that of case group using zinc sulfate was 3.21 days. Data was analyzed by SPSS-13 software using T-test and Chi-square Test, there was a significant difference between 2 groups in duration of diarrhea (P value=0.001).

Conclusion: In our study prescription of Zinc sulfate in acute diarrhea similar to other studies reduced the duration of acute diarrhea. Therefore Zinc Sulfate has an important role in treatment of acute diarrhea and should be considered as a supplement in all cases of diarrhea.

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CHOLERA AMONG HOSPITALIZED AFGHAN CHILDREN WITH WATERY DIARRHEA

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Background: Cholera continues to be an major public health problem among many poorer communties. A recent outbreak of watery diarrhea occurred in Afghan refugee population in Southeastern Iran. This study was performed to determine the characteristics of 9 Afghan children hospitalized for suspected cholera.

Methods: We evaluated all cholera patients that had an age < 19 years. All patients were admitted to Boo-Ali hospital (Zahedan, Southeastern Iran) in September 2008.The results of the clinical manifestations, demographic and stool cultures. Faecal culture was done in TCBS media and serotyping and antibiogram of bacterial strains was performed.

Results: Among 62 cases with cholera 9 cases had an age less than 19 years and all patients were admitted to our hospital for watery diarrhea. Significant risk factor was drinking from a contaminated water source in the vicinity of the frontier of Iran. The range age of patients was 12-19 years. All patients were male. The cases had watery diarrhea and 2 patients had abdominal pain. Vomiting and nausea was associated with diarrhea in two cases. The results of stool culture were positive for cholera O1 El-Tor biotype with Inaba serotype. Susceptibility to antimicrobial agents revealed that the O1 strians were resistant to ampicillin, co-trimoxazole, nalidixic acid but were sensitive to tetracycline, ciprofloxacine, doxycycline and erythromycine. There was no case fatality.

Conclusion: The priorities for cholera control remain public health interventions through improved water and sanitation, improved surveillance and further development of appropriate vaccines.

Keywords: Children, cholera, watery diarrhea.

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ACUTE ROTAVIRUS GASTROENTERITIS IN CHILDREN IN UKRAINE

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Background and aims: Pediatric rotavirus gastroenteritis is the most frequent cause of acute gastroenteritis in children up to 5 years old worldwide. The aim of this study was to examine rotavirus epidemiology in Ukraine.

Methods: 647 children less than 3 years old with acute gastroenteritis were investigated. None of that child received rotavirus vaccine. The study was conducted between December 2006 - March 2007 at the pediatric infection diseases departments located in 5 Ukrainian cities - Kiev, Odessa, Lviv, Charkiv, and Sumy; the all Ukrainian regions - West, East, South, North and Center were presented. All children had gastroenteritis symptoms during their hospitalizations. Stool specimens were frozen and tested later for rotavirus with enzyme immunoassays. Rotavirus-positive stool specimens were subjected to G typing. All tests were made at the Department of Virology National Medical Academy Postgraduate Education.

Results: The mean rotavirus antigen detection rate was 35,7%, but distribution rotavirus gastroenteritis in different regions was nonuniform. Rotavires was most common cause infant's gastroenteritis in West and East regions, where rotavirus was detected on 44,5% and 45,4%. Several times less rotavirus gastroenteritis were observed in North and East Ukrainian regions (7,1% & 10%). The most prevalent G type among rotavirus isolates in Kiev (Center reg.) was G4, in Odessa (South reg.) was G1. Types G3, G2 ,G9 ,G12 being identified less frequently.

Conclusions: We observed the nonuniform distribution pediatric rotavirus gastroenteritis of Ukraine. In some Ukrainian regions rotavirus is the most commonly encountered viral pathogen.

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ROTAVIRUS GASTROENTERITIS AMONG CHILDREN UNDER FIVE YEARS IN KARAK JORDAN

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Objective: Is to Estimate the incidence and compare clinical presentation between Gastro entireties due to Rota virus and non Rota virus.

Design: Prospective clinical comparative hospital based study.

Setting: Was conducted in paediatric department At Al Karak General teaching hospital for the period 1-5-2007 to 30-4-2008.

Patient and methods: Patient selected with strict inclusion and exclusion criteria Stool samples were taken from all patient(s) matching the selective criteria ELISA method done for all samples.

Results:

- Total no of cases 148

- Mean age 12.41 (±) 11.15 months

- Positive ELISA test for Rota in 59 samples (39.9%)

- Age, seasonal variation and fever were the most significant variables.

Conclusions:

- Rota virus infection is a major cause for diarrhoea hospitalization

- Age is younger in Rota group compared to non Rota group

- Most cases occurred in Autumn followed by summer & spring, the least number occurred in winter

- There is marginal significant association between fever & Rota virus infection but it is significant with the younger age.

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ABDOMINAL TUBERCULOSIS DUE TO MYCOBACTERIUM BOVIS: THREE CASES REPORT

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Background and aims: The pathology of the Mycobcterium Bovis (MB) is rare in our country. However it's more frequent in undeveloped countries where the way to become infected is usually by raw milk consumption.

Methods: We describe the epidemiologic, clinical and therapeutic characteristics of 3 patients with abdominal tuberculosis due to MB.

Results: Three male children emanating from Morocco with ages between 2 and 6 years, all of them had fever, abdominal pain and constitutional syndrome. Two of them used to drink raw goat's milk. One case was diagnosed with major histocompatibility complex class II molecules deficiency. Tuberculin skin test showed 0 mm in all three. One case had intestinal occlusion which needed surgery in his origin hospital and it was appreciated estercoraceus fistula throughout the cicatrix. Later he needed a new surgery and MB in the peritoneal biopsy culture was positive. In the other 2 cases, we decided medical treatment and abdominal lymphadenopathy biopsy with laparoscopy. In both the biopsy revealed PCR positive to MB.Treatment with isoniazid and rifampicin in the 3 cases was indicated and, during first month, 2 cases with streptomycin and one case with amikacin. We kept this medication during 6 months except for the inmunocompromised child. The cases with medical treatment presented bacterial peritonitis and abdominal abscess because of laparoscopy.

Conclusions: The treatment for the abdominal tuberculosis must be medical. Surgery should be used only in serious complications. When we suspect infection due to MB should avoid using pyrazinamide.

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NOROVIRUS AND ROTAVIRUS - TWO MAJOR CAUSATIVE AGENTS OF SPORADIC VIRAL GASTROENTERITIS IN HOSPITALIZED POLISH CHILDREN

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Background and aims: In Poland, the cause of the majority of viral gastroenteritis cases remains undetermined. We aimed to establish the etiologic agents of acute gastroenteritis in children below 5 years of age, hospitalized during spring/summer 2008 and to assess the severity of disease.

Methods: From April to September 2008, fecal specimens were obtained from 181 children (100 males, 81 females) with acute gastroenteritis. Immunochromatographic test for simultaneous detection of rotavirus and adenovirus were performed soon after the fecal specimens were collected. Then samples were frozen and stored for future testing with IDEA Norovirus. Severity of disease was determined by 20-point score system.

Results: A viral agent was detected in 109 of 181 (60.2%) samples tested. Dual viral pathogens (rotavirus and norovirus) were found in 3 of 181 (1.7%) samples. Rotavirus was the most frequent pathogen (86/181; 47.5%), followed by norovirus (19/181; 10.5%) and adenoviruses (3/181; 1.7%). Approximately 60% of gastroenteritis episodes occurring in children less than 5 years of age were accounted for by infection due to rotavirus and norovirus. Rotavirus infections were leading cause of gastroenteritis in spring months whereas norovirus infections during summer time. Norovirus cases were clinically indistinguishable from those of rotavirus origin, in children aged less than 2 years whereas they were slightly milder in older group of patients.

Conclusions: There is a need to apply molecular diagnostic tools to determine the circulating strains of enteric viruses in Poland.

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DIARRHEA IN CHILDREN: EPIDEMIOLOGY AND CLINICAL ASPECTS

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Aim: To determine the etiology of diarrhea in children with an age < 5 years hospitalised for acute enteritis and to evidence the prevalent clinical aspects in correlation of different etiology agents.

Patients and methods: A total of 402 children with acute diarrhea were examined between February 2003 and December 2007 in the Paediatric Department, Hospital of Sondrio. Fecal samples were collected and processed by routine microbiological and biochemical tests. For all patients the clinical signs and symptoms at the admission were evidenced.

Results: The major part of patients (310/402, 77.1%) resulted infected by rotavirus, while among the remain 82 (22.9%) 40 resulted infected by salmonella species and in 42 any bacterial agent was evidenced by microbiological tests. Clinical signs of mild dehydration were observed in 13 children during the hospital stay (all infected by rotavirus), while any case of metabolic acidosis, hypoglycaemia and hypovolemic shock was documented. Elevated serum levels of uric acid were evidenced in 13/302 (4.3%) of patients with rotavirus infection, while only 1/82 (1.2%) children rotavirus negative presented a minimal increase of serum uric acid level.

Conclusion: Our retrospective study confirms the major epidemiological and clinical importance of rotavirus, as the principal etiologic agent in hospitalised children affected by acute diarrhea with an age < 5 years. Also, we have evidenced a possible correlation between rotavirus infection and hyperuricemia, probably connected with dehydration.

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IS THE SERUM PROCALCITONIN LEVEL USEFUL AS INFLAMATORY BOWEL DISEASE ACTIVITY MARKER IN CHILDREN?

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Background and aims: Procalcitonin is known as an important protein in diagnosis, treatment and prognosis in different inflammatory states. Its clinical significance has not been fully established yet. Aim of the study was to determine clinical usefulness of serum procalcitonin measurement as an activity marker in inflammatory bowel diseases in children.Patients and methods. The studied group comprised of 82 children, including 27 girls (32.9%) and 55 boys (67.1%), aged from 1.4 to 18.0 years (mean 13.9 ± 4.1 [SD], mediane 15.4). The patients suffered from inflammatory bowel disease: Crohn's disease and ulcerative colitis, with different disease activity estimated on Pediatric Crohn's Disease Activity Index and Trulove-Witts score, respectively. There were 23 children with mild, 9 with moderate and 2 with severe Crohn's disease activity, and 30 children with mild, 12 with moderate, and 6 with severe ulcerative colitis activity. Serum procalcitonin level was measured by immunoluminometric method using the commercial kit (LIA PCT; BRAHMS). This quantitative assay uses two monoclonal antibodies which captivate procalcitonin molecules. One of them is labeled with luminescent agent and emits light which intensity is proportional to procalcitonin concentration in analyzed probe.

Results: In majority of patients with inflammatory bowel disease procalcitonin level is normal. Only 4 out of 82 ill children from studied group (0.05%) had procalcitonin values elevated (above 0.5 ng/ml). In one of these four it was higher than 5 ng/ml.

Conclusions: Serum procalcitonin measurement seems to have no clinical value as a marker of inflammatory bowel disease activity in children.

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ACUTE GASTROENTERITIS WITH ROTAVIRUS IN CHILDREN UNDER 5 YEARS IN A PAEDIATRIC DEPARTMENT

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Background and aims: Rotavirus (RV) infection is a major cause of infectious gastroenteritis in children worldwide, requiring hospitalization in most of the cases. The aim of the study was the analysis of rotavirus gastroenteritis incidence and clinical characteristics in children aged under 5 years in a Paediatric Department.

Methods: A prospective study of all cases of acute gastroenteritis presenting to Victor Gomoiu Clinical Pediatric Hospital, Bucharest, from January 2008 to December 2008. There were studied: viral etiology, age and sex of children, clinical aspects, biochemical parameters, stool aspects.

Results: During the 12 months of study, a total of 1313 children with acute gastroenteritis were observed in our Emergency Service and 379 (28.8%) were admitted to the Pediatric Department representing 5.2% of all children hospitalisations. Admitted children had median age 13.25 months. All the children had abdominal pain at admittion. Other common symptoms were: fever (90.2%), nausea and vomiting (87.8%) and sings of dehydration (5.8 stool/day, sunken eyes, dry skin, lethargy, decreased urinary output) in 49.4%. Consistency of stools was liquid in 87.5% of cases, with a mean duration of 5-7 days (45%) and 35% presenting more than 7 stools/day. Rotavirus was positive in 114 (30%) cases (Rotastrip). More children had acid-base and metabolic abnormalities, hypoglycemia, urea and creatinine level. The treatments consisted in increased fluid intake (oral rehydration) or intravenous fluid (95%). IV rehydration was given 4.92 days (extremes 1-8 days).

Conclusions: Rotavirus plays an important role in severe viral gastroenteritis in children, causing a large number of hospitalization during winter.

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RANDOM? FLUCTUATION OF NON-G1 ROTAVIRUSES AFTER LAUNCH OF ROTAVIRUS VACCINES IN FINLAND

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Background: Universal mass vaccination since 2006 with human G1 rotavirus (RV) vaccine (Rotarix®, GSK) in Brazil has been associated with emergence of G2 RVs as predominant cause of RV gastroenteritis (GE) (Gurgel RQ, et al. Emerg Infect Dis 2007;13:1571-1573).

Methods: We conducted a prospective survey of RVGE in hospitalized children over 2 RV epidemic seasons from August 2006 to August 2008. RVs were G-typed by RT-PCR. In Finland Rotarix® was launched in May 2006, and its coverage increased up to 25 % of the birth cohort by August 2008. In addition, RotaTeq® (SP-MSD), which was launched in the beginning of 2007, reached coverage of 4% by the same time.

Results: A total of 152 RV positive cases were found in the first RV epidemic season 2006-2007. G1 RVs accounted for 38%, G2 18%, G3 3%, G4 1% and G9 for 41% of the detections. In the second season 2007-2008, of 293 RV positive cases G1 accounted for 77%, G2 only 3%, G3 6%, G4 13% and G9 had virtually disappeared.

Conclusions: While non-G1 RVs were common: 63% in the first and 22% in the second RV season, there was no regularity in the pattern of emergence. G2 RV did not increase to predominance at the coverage level of 25% for Rotarix® and 29 % for all RV vaccination in the birth cohort of Finland.

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A PROSPECTIVE HOSPITAL-BASED SURVEILLANCE TO ESTIMATE DISEASE BURDEN CAUSED BY ROTAVIRUS INFECTIONS AND ITS COMPLICATIONS IN SWEDISH CHILDREN 2007/2008

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Background: The aim of this study was to determine burden of severe rotavirus gastroenteritis (RV GE) leading to hospitalization and describe evolving complications in three geographical regions during a 12-month period. Isolated rotavirus strains were genotyped and signs of systemic disease were evaluated.

Methods: The study population was hospitalized children with RV GE. Symptoms and complications were described in a questionnaire. Rotavirus excretion was verified by a rapid-test (Vikia, BioMerieux) or ELISA (Oxoid) and further confirmed by PCR and genotyping. S-ASAT/S-ALAT were analysed with standard methodology and viremia was quantified by real-time PCR.

Results: In total 592 children were included. The peak of the rotavirus season 2007/2008 was seen in February - April in all regions. The incidence for hospitalization ranged in different regions from 300 to 500/100,000 children < 5 years. The median age of hospitalized children was 15 months. Less than 1% of the children were below two months of age, the recommended age for initiation of vaccination. Complications, such as hypertonic dehydration and seizures were observed in < 5% of all children. Signs of systemic disease, measured as S-ASAT/S-ALAT, were noted in 77% and 29% respectively of RV+ children compared to 29% and 10% in RV- children. Genotyping of rotavirus strains revealed that 78% were G1P[8], 3% G2P[4], 4% G3P[8], 6% G4P[8], 8% G9P[8], and < 1% a mix of genotypes.

Conclusion: The incidence of rotavirus infections leading to hospitalization is high in Sweden and the virus causes a large burden on hospital resources.

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TRENDS IN INCIDENCE AND GENOTYPES OF ROTAVIRUS (RV) ACUTE GASTROENTERIRIS (AGE) IN COIMBRA, CENTRAL REGION OF PORTUGAL

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Background and aims: Since 2006 we have conducted surveillance for RV in children seen at our Emergency Service (ES). RV vaccine was introduced in Portugal in 2006 but it is not included in the Immunisation Program. Coverage in 2007 was estimated to be ~15% and in 2008 ~25%.

Methods: During the epidemic season (January to June), between 2006 to 2008, children < 3 years of age, attending the ES with the diagnosis of AGE had their stools tested for RV and positive samples were genotyped.

Results: A total of 1290 children were included and RV was positive in 36,7%: 261 (45%) in 2006, 170 (36%) in 2007 and 60 (22%) in 2008.

Overall G9P[8] went from being the most frequent type in 2006 (90%), to a significant decrease in 2007 (32.6%) and undetected in 2008, accompanied by a significant increase in the proportion of G3P[8] that was the predominant genotype in 2008 (from 3.8 to 40%). The proportion of G1P[8] increased in 2007 (from 4.3 to 18%) and remained at similar levels in 2008. G2P[4], undetected in 2006, was found in a significant proportion in 2007 (21.3%) and 2008 (31%).

Conclusion: RV is a major cause of AGE, although its incidence significantly decreased in 2008. Different RVs co-circulate in the same geographic region and seasonal variation in the strain distribution is found. Overall, G1-G3 and G9 were associated with the majority of infections, but interestingly, G1P[8] has never been the most common strain, in contrast to many other European countries.

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CONSERVATIVE MANAGEMENT OF ISOLATED SPLENIC ABSCESS IN CHILDREN

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Background and aims: Isolated splenic abscesses (SA) are rare in children. The management modality for SA varies from antibiotic therapy only to percutaneous drainage to splenectomy. We report a single centre experience of SA in children with emphasis on its diagnosis, etiology, treatment and outcome.

Methods: Eighteen pediatric patients with SA were managed over a period of 8 years in a tertiary care institution. Their age ranged from 3-16 years, average 9 years, and male to female15:3.

Results: The presenting symptoms included fever, abdominal pain, and anorexia in all patients. Splenomegaly was present in 12(67%), leucocytosis in 9(50%), and thrombocytosis in 12(67%) patients. Associated diseases were thalassemia -1, tuberculosis -1, and typhoid fever in 9 patients. Imaging diagnosis was done with ultrasonography and computerised tomography. Solitary and multiple SA was seen in equal numbers. Blood culture was positive for Salmonella paratyphi A in 1 case. Splenic aspirate culture was positive in 3 cases (Escherichia coli-1, Salmonella paratyphi A-1, Acinatobactor-1). Widal's serology was positive in 9(50%), however HIV test was negative in all cases. Management included intravenous broad spectrum antibiotics (ceftrioxone, amikacin, metronidazol) in all and percutaneous aspiration in 10(56%) cases where abscess size was >3 cm. Average duration of antibiotic therapy was 3 weeks. All patients responded to conservative treatment and none was subjected to splenectomy. Complete resolution was observed during follow-up ranging from 3-6 months.

Conclusion: Isolated SA in children responds favourably to conservative treatment with intravenous broad spectrum antibiotics and percutaneous drainage which obviates the need for splenectomy.

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ASSOCIATION BETWEEN ANTRAL NODULARITY, GASTRITIS, POSITIVE CYTOTOXIN ASSOCIATED PROTEIN SEROLOGY, AGE, GENDER, ABO BLOOD GROUP AND HELICOBACTER PYLORI IN CHILDREN

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Helicobacter pylori (Hp) causes one of the most widespread infections worldwide.It is known that blood group antigens are related to the development of peptic ulcer and gastric carcinoma.

To investigate the association between virulence factors of Hp, severe gastritis, age, gender and ABO blood group.

25 patients (15 Male; age range 3-18 years) underwent to esophagogastroduodenoscopy with antral biopsy for a suspicious upper gastrointestinal disease. In all of them serum sample were assayed for IgG antibodies to CagA and ABO blood groups were determined by standard techniques.

19 children (76%) were Hp positive by histopathology and urease rapid test. 15 of these 19 (79%) Hp positive patients were positive for CagA serology, too. At endoscopic examination of the 19 infected children, hyperemia and friability of the gastric antrum was observed in 7 (37%) patients and antral nodularity appearance in 12 (63%) children. The histologic examination of all infected patients showed an active microerosive gastritis and chronic gastritis. The children CagA positive presented an endoscopic finding of more intense hyperemia of gastric antrum, associated to an important lymphoplasmacellular infiltrate and vacuolar lesions of gastric epithelium. In non infected children there weren't histologic signs of gastric inflammation. As expected from previous studies, we found that seropositivity for Hp increased with age and the rate of Hp infection was not significantly different in boys and girls. Similarly, Hp serological status was not significantly different between subjects of different ABO blood groups.

We found no association between Hp infection and ABO blood groups.

P299

ROTAVIRUS IN HOSPITALIZED SPANISH CHILDREN

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Background: In Spain, diarrhoea remains as an important cause of morbidity among children. A surveillance study of children less than 5 years old with acute gastroenteritis was initiated in different regions of Spain by Vigess-net, which is the first national rotavirus study collaboration. It includes 15 collaborating hospitals covering a population of 1.500.000 children under 5 years old.

The aim of this study was to conduct a structured surveillance to determine the prevalence of rotavirus in children hospitalized for acute gastroenteritis, as well as to determine the G and P types among infecting rotavirus strains.

Methods: From April 2006 to April 2008, the specimens were collected and sent to the Viral Gastroenteritis Unit at the ISCIII as the reference laboratory. A total of 2208 stool specimens of hospitalized children were tested by Elisa and different PCR and nested PCR protocols used for nucleic acid detection of RV, NoV, adenovirus and HAstV.

Results: Rotavirus was the most frequent (40,6%) etiologic agent followed by norovirus (33.1%) human adenovirus (2.4%), and astrovirus (3.7%). Enteropathogenic bacteria were detected in 0.8% of samples.

The most predominant Rotavirus genotypes were G1 P [8] (56.7%), followed by G9 P[8] (37.2%) and co-circulating with G12, G2, G6, G3, and G4.

Conclusions: Rotavirus was associated with the majority of hospitalizations for acute gastroenteritis in children under 5 years of age.

G1P[8] and G9P[8] were the predominant types co-circulating in Spain. In addition, multiple rotavirus infection was detected in over 12% of the episodes during this period.

P300

CLINICAL PICTURE OF YERSINIOSIS IN CHILDREN

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Background: In the first half of 2008 in Poland there was an increase in incidence of yersiniosis.

Aim: The aim of the report was to present clinical picture of yersiniosis in hospitalized children.

Material & methods: From March to June 2008 36 children (19 boys, 17 girls, age 13 months-17 years) were hospitalized with diagnosis of yersiniosis, confirmed by positive stool culture and/or positive result of serological testing (ELISA).

Results: Fever occured in 80,6% of patients. In 7 cases fever was the only symptom. Symptoms from digestive tract occured in 27/36 (80,6%): diarrhoea (10/36), abdominal pains (12/36), diarrhoea with abdominal pains (7/36). Pharyngitis and rash were relatively common features (each in 16,7%). Increased CRP level and leukocytosis were found in 66,6% and 44,4%, respectively. Bacteriemia was not confirmed in any case. Abdominal sonography revealed abnormalities in 24/26 cases: enlargment of mesenteric lymph nodes and/or thickening of terminal ileum wall. Among patients with those features 11 did not complain of abdominal pain. 26/36 patients required antibioticotherapy. All children recovered completely. In 3 cases serological testing suggested infection with Yersinia enterocolitica O:8, uncommon in Europe.

Conclusion: Clinical picture of yersiniosis is not specific. Yersinia infection should be taken into consideration in differential diagnosis in children hospitalized because of abdominal pains, diarrhoea or fever of unknown origin.

P301

THE BURDEN OF ROTAVIRUS GASTROENTERITIS IN CHILDREN PRESENTING TO THE TERTIARY -CARE HOSPITALS IN ESTONIA

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Background and aims: In most European countries rotaviruses are the major cause of hospitalization for acute gastroenteritis (GE). We aimed to collect detailed data on the burden, management and outcomes of RVGE in hospitalised children aged < 5 years.

Methods: From 01.01.2007 until 30.11.2008 all children aged below 5 years admitted with the laboratory confirmed RVGE into three major paediatric hospitals of Estonia were prospectively enrolled. The severity and duration of clinical symptoms was evaluated using Clark score.

Results: A total of 671 children fulfilled the inclusion criteria and accounted for 5.5% of all admitted patients aged of < 15years. The mean age was 20.5 ± 12.8 months. A total of 30% of patients were of < 1year and 71% of < 2 years. Majority (429/565; 76%) of community acquired RVGE (CA-RVGE) were of moderate severity. Intravenous fluids were given to 93.4% of patients. Nosocomial RVGE accounted for 106 cases (15,8%) with the rate of 37/10,000 hospitalisation. In comparison to CA-RVGE there were lower number of severe cases based on the Clark scale (4.8% vs 16.3%; OR 0.2; 96% CI 0.1-0.6 with the score >16). The mean duration of hospitalisation was 3.2 ± 1.9 days for CA-RVGE. The nosocomial RVGE prolonged duration of hospitalisation by 4.2 ± 2.2 days. No deaths or severe disabilities were recorded.

Conclusions: RVGE is far the most common vaccine preventable disease presenting high burden to hospitalisation and acquisition of nosocomial infections. The data provide additional information of the assessment of rotavirus vaccination programme.

P302

DIAGNOSTIC VALUE OF STOOL ANTIGEN AND ANTIBODY TESTS FOR *HELICOBACTER PYLORI* INFECTION IN CHILDREN WITH UPPER GASTROINTESTINAL COMPLAINTS

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Objective: Several noninvasive methods, such as *H. pylori* stool antigen (HpSA), *H. pylori* antibody test (HpIgG), have been used to diagnosis of *H. pylori* infection in children. The aim of this study; to evaluate the diagnostic value of HpSA and serologic tests before and after eradication therapy for H. pylori in children with upper gastrointestinal complaints (UGC) in our region.

Methods: In this study, 87 children with UGC and 95 children without gastrointestinal complaints were enrolled. *H. pylori* infection was detected by Urea breath test. HpSA and HpIgG tests were applied to all the children. Eradication treatment were given to the 34 *H. pylori* positive children. These children were re-evaluated after treatment with UBT, HpSA and HpIgG tests.

Results: The UBT was positive for 43 of 87 children (49.4%) with UGC. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), false positivity (FP), false negativity (FN) values of the HpSA in children with UGC were 86%, 84.1%, 86%, 15.9% and 14%, respectively, and those for the HpIgG were 76.7%, 90.9%, 89%, 80%, 9.1% and 23.3% respectively. After eradication therapy the overall HpSA test sensitivity, specificity, PPV, NPV, FP and FN values were detected 88.9%, 84%, 66%, 95%, 16% and 11.1%, respectively, and those for the HpIgG were 77.8%, 36%, 30%, 81%, 64% and 22.2%, respectively.

Conclusion: HpSA test is highly sensitive and specific for the diagnosis of *H. pylori* and confirming eradication in children with upper gastrointestinal complaints living in Western Anatolia, Manisa region.

P303

MOLECULAR EPIDEMIOLOGY OF NOROVIRUS INFECTION AMONG CHILDREN WITH ACUTE GASTROENTEROLOGY IN SHANGHAI, CHINA (2001-2005)

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Background and aims: Norovirus is one of the major pathogens leading to sporadic acute gastroenteritis in young children worldwide. Obtaining the local baseline information regarding this virus is important for development and evaluation of vaccination program. The current study was undertaken to understand the age and seasonal distribution and circulating genotypes during a long period.

Methods: Stool specimens were collected from children hospitalized with acute gastroenteritis under 5 years between 2001 and 2005 in Shanghai, China. A total of 484 samples were chosen for molecular epidemiology study of norovirus. Testing for norovirus was carried out using the Mon 431-434 degenerate primers directed at the 3' end of ORF1. The nucleotide sequence of each PCR product was determined on ABI 3730 sequencer. A multiple sequence alignment of nucleotide sequence of 170nt was constructed using Clustal W and Phylogenetic trees were constructed using Mega 4.1 software.

Results: Of all 484 detected samples, 45 samples (9.3%) were identified to be norovirus. Over 75% of children with norovirus diarrhea were less than 2 years of age. The monthly distribution of norovirus infection illustrated a seasonal peak from August to November. Among the 37 identified norovirus strains, 2 were GII-3 and 2 belonged to GII-7 and all the other 33 strains were GII-4 genoclusters.

Conclusions: This study demonstrated the importance and epidemiological features of norovirus in children hospitalized with acute gastroenteritis in Shanghai. Our findings about the prevalence and distribution of strains will be helpful for prevention of norovirus diseases in children.

IMMUNITY AND INFECTIONS

P304

EVALUATION OF INTERLEUKIN-6 FOR EARLY DIAGNOSIS OF NEONATALSEPSIS IN COMPARISON WITH CRP

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Background: Early diagnosis of neonatal sepsis is essential for successful treatment.Blood culture is a gold standard for diagnosis but the final results are not available until 48-72 hours after culture.

Interleukin-6(IL-6) as a marker plays a critical role in the induction of C-reactive protein (CRP) synthesis in the liver.It has been hypothesized that this cytokine could be detected in blood earlier than CRP during the course of neonatal sepsis.

Methods: Blood samples were collected upon admission from 50 neonates with suspected sepsis, and 10 healthy neonates.The patients were assigned to two groups according to bacteriological and laboratory results.Group I consisted of 19 newborns with positive blood cultures and clinical signs of sepsis.Group II included 31 neonates with negative blood cultures,but with two or three clinical signs of sepsis. The control group(group III)included 10 healthy neonates with no clinical or biological data of infection.Serum CRP was determined by nephelometry and IL-6 by ELISA method.

Results: Mean CRP level in the group with proven sepsis was 22.18 mg/l which was higher than in other groups (P=0.005).The sensitivity and specificity of CRP was 57% and 100% respectively.

Mean level of IL-6 was 117.49 pg/ml in group one, which was higher than in other groups (P=0.001), exhibiting a sensitivity of 78% and a specificity of 95%.

Conclusions: Based on our results, measurement of IL-6 is more useful than CRP for early diagnosis of neonatal sepsis; especially within the 24 hours before the onset of sepsis.

P305

INCONTINENTIA PIGMENTI AND CLINICAL MANIFESTATIONS OF IMMUNODEFICIENCY - CASE REPORT

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Introduction: Incontinentia pigmenti (IP) is an ectodermal dysplasia that affects the skin, hair, teeth and nails. It is an uncommon X-linked dominant disorder, mapped to Xq28, lethal in uterus in the majority of affected males and variably expressed in females. These differences in expressivity have been attributed to lyonization in females, resulting in functional mosaicism. In girls, abnormalities of the immune system have been reported.

Case report: The authors report a case of a female patient with the diagnosis of IP.

She was born from healthy non-consanguineous parents, who presented the classical dermatological stages of IP. The skin biopsy confirmed the diagnosis at 3 weeks of age. She was admitted to our Intensive Care Unit hospital because of bilateral pneumonia requiring of mechanical ventilation. It was isolated Pseudomonas aeruginosa from pleural effusion and posteriorly Staphylococcus aureus. The laboratory studies revealed leucocytosis, eosinophilia, lymphopenia with markedly diminished NK cells. She was treated with parenteral antibiotics without clinical improvement. She died after 22 days of internment. DNA extraction was made for molecular diagnosis.

Discussion: Our case describes a female child with IP and clinical manifestations of immunodeficiency. Genetic studies have demonstrated that mutations in the NEMO/IKKg gene result in the IP phenotype. Mutations in NEMO gene in this clinical case were not found. We are waiting for study of gene IKBA (NFKBI) for genetic advisement and prenatal diagnosis.

P306

KAWASAKI DISEASE: ATYPICAL PRESENTATION IN INFANCY

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Kawasaki syndrome is a rare childhood disease of unknown aetiology, mostly described between ages two and five. Diagnosis is made based on major and minor clinical criteria in a child with fever and irritability. Prognosis depends on early administration of gamma globulin which may prevent coronary disease.

We describe the clinical case of a 4 months old baby with high fever and irritability for one day. On analysis, high leukocyte count with neutrophilia, high CPR and normal CSF were evident. He was hospitalised with the diagnosis of occult bacteraemia and ceftriaxone was instituted. On D3 of hospitalisation he was observed by the cardiologist because of persistent tachycardia. No abnormalities were detected. On D4, a diffuse erythematous macular rash appeared which persisted until D7, as well as fever and irritability. The appearance of hands and feet oedema on D7 led to re-evaluation by the cardiologist. No other Kawasaki's clinical criteria were present. This time he had mitral insufficiency, pericardial effusion and coronary artery irregularities. He received gamma globulin with a rapid disappearance of symptoms. Cardiac follow up showed an amelioration of the cardiac lesions.

Acute febrile syndrome in a small infant is usually infectious and is treated accordingly. Whenever the evolution is atypical, the diagnosis should be reviewed and if inflammatory signs persist despite antibiotic administration, Kawasaki disease should be thought.

This case points out the need of a high clinical suspicion index that led to a cardiologic re-evaluation even with a previous normal examination.

P307

THE LEVEL OF POSTVACCINATION IMMUNITY TO SAME INFECTIONS IN MOLDOVA, 1991-2008

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Background: The aim of this study was to estimate the population´s immunity in Republic of Moldova against some vaccine-preventable diseases (tetanus, diphtheria, measles, rubella and mumps) and to compare the results of serological testing with the level of reported vaccination coverage in various periods and in conditions of different vaccination programs in 1991-2008.

Methods: The levels of tetanus (N 19 630), diphtheria (N 19 610), measles (N 12 804), rubella (N 1 025) and mumps (N 924) antibodies were investigated in groups aged 2-60 years from rural and urban territories with ELISA and RPGA.

Results: The level of immunity to diphtheria with titers ≥0,03 IU/ml was in limits of 89,3-98,7%, ≥0,12 IU/ml - 74,9-90,3%, tetanus antitoxin (n = 17.265) ≥0,1 IU/ml was in limits of 94,8-98,9%, ≥0,8 IU/ml - 68,6-94,5%, the immunity to measles 86,4- 92,0%, to rubella and mumps in last three years - 96,9% and 69,3%, respective. The less level of immunity was in preschool children and adults. The difference between the coverage and serological data is more accentuated for measles and mumps until the introduction of the 2nd dose of MMR.

Conclusions: In the condition of immunization program it is necessary to conduct the serological monitoring of population´s immunity to vaccine-preventable diseases. At the other hand, these data may serve the base of individual immunization schedule, because the majority of persons at the time of ordinary revaccination have a high level of antibodies and not need the booster dose, for example, the DT containing vaccine.

P308

EARLY ONSET AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME (ALPS) IN INFANCY- A DIFFERENTIAL DIAGNOSIS TO HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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ALPS is characterized by non-malignant lymphadenopathy, splenomegaly, autoimmune disorders, hypergammaglobulinaemia and lymphocytosis with increased levels of double negative (CD4-/CD8-) T cells (>1% of total lymphocytes). Often a mutation in genes involved in CD95 (*FAS*) mediated apoptosis is found. In various patients a mutation cannot be identified suggesting alternative pathways of disease pathology.

We present an 8-month old girl, born to non-consanguineous parents with no previous family history of haematological disorder, who presented with a 2-week history of temperature, mild lymphadenopathy, a rash and 4cm splenomegaly. Full blood count showed pancytopenia with relative lymphocytosis; Hb 7.2g/l, WCC $5.4x10^9$/l (lymphocytes 4.4, neutrophils 0.4), platelets $52x10^9$/l; normal coagulation profile. Lymphocyte subsets and stimulation were normal; IgG levels high (27g/l). LDH and triglycerides were raised (2140IU/l and 306mg/dl). CRP 90mg/l. An infectious cause was not found (including EBV, CMV, adenovirus, parvovirus and HIV). Imaging confirmed splenomegaly only. She was thought to suffer from HLH; however a BMA showed no signs of haemophagocytosis, expression for perforin was normal and genetic analysis for possible perforin or MUNC deficiency (seen in familiar HLH) as well as SH1D2 deficiency (X-linked lymphoproliferative disease) were normal. Expression of CD95 on T cells was normal, however circulating double negative T-cells were raised on two occasions (12% and 1.2%). Results regarding mutations in CD95/CD95L are pending.

In summary we present an infant who fulfils some criteria for ALPS, illustrating the difficulty to diagnose this heterogenous genetic syndrome. She has not suffered from infections nor required any immune modulatory treatment.

P309

ANTIBODY RESPONSE PATTERNS TO *BORDETELLA PERTUSSIS* ANTIGENS IN VACCINATED (PRIMED) AND UNVACCINATED (UNPRIMED) YOUNG CHILDREN WITH PERTUSSIS

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Background: It is generally thought that antibody response occurs earlier in primed compared with unprimed persons. However this has not been quantitated in regard to pertussis.

Methods: ELISA (EU/ml) antibody values to *B. pertussis* antigens PT, FHA, PRN and FIM-2 were analyzed by time of sera collection after onset of illness in 183 children with pertussis who were vaccine (DTaP with PT, FHA, PRN, FIM-2) failures or were previously unvaccinated.

Results: For sera collected 0-15 days after illness onset, the GMTs for all 4 antigens were significantly lower in the unvaccinated group as compared to DTaP recipients. In the unvaccinated group GMT of PT antibody rose rapidly over time and was similar to that of DTaP recipients at the 16-30 day period and at 50 days was higher than the GMT of the DTaP group. FHA antibody rise was less marked than that of PT in the unvaccinated subjects and its peak was lower than that in DTaP recipients. PRN antibody rise in the unvaccinated was less marked than that in DTaP group and peak titer was >10 fold less. The response to FIM-2 was delayed and minimal in unvaccinated children.

Conclusions: This study does not support the idea that antibody response in primed subjects is quicker than in unprimed. However, the response is more marked in primed subjects and peak titers are lower than in primed subjects. Interestingly the response to PT in the unprimed has a sharp response and final GMT is higher than that in primed children.

P310

OXIDATIVE STRESS MODULATES THE INFLAMMATORY SIGNALING PROGRAM INDUCED BY GROUP B STREPTOCOCCI (GBS) IN PHAGOCYTES

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Background and aims: In invasive group B streptococcal infections, a potent antimicrobial macrophage response and a limited inflammatory response need to be controlled on the signal cell level in order to prevent potentially deleterious hyperinflammation and multi-organ failure. During uptake and endosomal processing of bacteria, the host-pathogen interface rapidly changes through reciprocal modulation of the two cell types. Mechanisms interrelating these processes with the regulation of inflammatory signaling are poorly understood. Here we examined the role of oxidative stress on the endosomal process, the modification of pathogen-associated molecular patterns and associated signal regulation.

Methods: Primary and immortalized mouse macrophages of various genetic backgrounds (e.g. MyD88 ko, iNOS ko, gp91 ko) were analyzed by complementary methods such as confocal microscopy, luminometry, ELISA.

Results: We found that the nitric oxide (NO) response to GBS depended on both bacterial uptake and Toll-like receptor signaling. Subsequently, NO was crucial for proper lysosomal acidification and the degradation of bacterial DNA, a putative microbial pattern recognized by cytoplasmic DNA sensors. Furthermore, NO was essential for the formation of inflammatory cytokines in response to group B streptococcus. In contrast, the NADPH-oxidase-dependent reactive oxygen species downregulated the transcription of inflammatory genes, however did not influence endosomal maturation.

Conclusions: NO and reactive oxygen species control the inflammatory signaling program in phagocytes processing GBS in a distinct fashion.

P311

DEVELOPMENT OF A BIVALENT FACTOR H BINDING PROTEIN VACCINE TO BROADLY PROTECT AGAINST INVASIVE *NEISSERIA MENINGITIDES* SEROGROUP B (MNB) DISEASE

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Background and aims: Invasive meningococcal serogroup B disease (IMDB) though rare is devastating. There is no licensed broadly protective vaccine available. We are conducting clinical trials with a vaccine (rLP2086) composed of two MnB human factor H binding proteins (fHBP). fHBP is a recognized virulence factor associated with immune evasion. Extensive prevalence and sequence analyses of fHBP were conducted on MnB clinical isolates to determine the potential breadth of vaccine coverage.

Methods: fHBP sequence and surface expression levels were determined for IMDB isolates (n=1,830) from surveillance sites in the US and five European countries. Serum bactericidal antibody (SBA) assays for > 100 IMDB isolates were developed and used to assess human immune sera from clinical trials of the fHBP vaccine.

Results: All isolates had *fhbp* and 197 unique sequence variants segregated into 2 distinct subfamilies (A and B) in all countries surveyed. Human immune sera generated by the rLP2086 vaccine were able to kill a high proportion of IMDB isolates in SBA. Bacterial surface expression of fHBP predicted strain susceptibility to immune sera while fHBP variant sequence, PorA and MLST type did not.

Conclusions: A vaccine that includes fHBP from each subfamily (A and B) elicits antibodies that are broadly bactericidal against epidemiologically diverse IMDB isolates. fHBP can be detected by flow cytometry on >98% of IMDB isolates, and therefore broad protection from the rLP2086 vaccine can be expected.

P312

PNEUMOCOCCAL PERICARDITIS WITH HEMOLYTIC UREMIC SYNDROME: DO WE HAVE TO CONSIDER IMMUNODEFICIENCY?

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Streptococcus pneumoniae is the major bacterial cause of otitis media, pneumonia and septicemia in children.

Here, we report on the case of a 20 months old girl, who was transferred to our hospital with hemolytic uremic syndrome (HUS). *S. pneumoniae*, serotype 14, was isolated from blood culture. Extensive workup revealed purulent pericarditis as the only infectious focus. The past medical history was unremarkable. The vaccination status was complete with the exception of pneumococcal vaccine. Despite adequate intravenous antibiotic therapy with vancomycine and cefotaxime, intermittent hemodialysis and pericardial drainage were required. The pneumolysin PCR of pericardial fluid was positive. The further course was uneventful and the outcome was favorable.

This case demonstrates that invasive pneumococcal disease (IPD) can manifest in virtually any organ system. In HUS, IPD has to be suspected even in the absence of respiratory tract infections. Recent discoveries revealed that monogenetic alterations in Toll-like receptor signaling (*e.g.* mutations in MyD88, IRAK-4, NEMO) are associated with some cases of invasive pneumococcal infections. However, the population based contribution to IPD is currently unknown. A targeted immunological workup is proposed in unusual or recurrent pneumococcal infections.

P313

THE CONDITION OF THE IMMUNE STATE IN CHILDREN WITH A RECURRENT RESPIRATORY SYNDROME

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The aim of investigation is to study the condition of the immune state and the state of flora in nasopharynx in children under 7 going to kindergarten with a recurrent respiratory syndrome.

Methods: 33 children aged 3 to 7 with an acute viral respiratory infection which occurred more than 4 times during a year have been under observation. The immune state have been investigated by the method of flow cytometry. All children were taken a swab from nasopharynx.

Results: The state of the pathogenic microflora in nasopharynx: hemophilic bacillus - 28,6%, pneumococcus - 54,3%, adenovirus - 5,7%.

The lymphocytosis towards the survival rates being accompanied by the B-lymphocytes reduction in 58% was marked in most children (63,4%) after examination. Immunoregulatory index - was normal in 45,5% of cases. The prevalence of CD8+ T-suppressor activity was marked in 30% of cases, CD4+ T-helper orientation of the immune response was seen in 24,2% of cases. The granulocytic phagocytosis rates were normal in 70% of children, and were heightened in 30%, on the contrary the monocytic phagocytosis was reduced practically in all examined children (96,9%). Low rate of genes expression on the surface of immunocompetent cells CD HLA DR was revealed in 54,2% of cases.

Conclusion: Low phagocytic activity of monocytes and the imbalance of cell and humoral component of immune system reveals the tensity of immunoregulatory processes and, more over, produces the inadequacy of anti-infectious defence, that can lead to the frequent respiratory infection reccurences.

P314

ACUTE POLIRADICULONEURITIS OF INFECTIOUS ETIOLOGY IN CHILDREN

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Background and aims: Acute inflammatory demyelinating poliradiculoneuropathy (Guillain -Barre syndrome, GBS), is a disease of peripheral nervous system, that affects the nerves roots and Shafts (demyelinating lesions), with ascending evolution. It is considered to be an immune response to a variety of triggers, most frequently a viral infection, hence the specific treatment, (IV immunoglobulin, plasmapheresis),that tries to block the immune response.

Material and methods: We present 3 cases of children admitted in the ICU, diagnosed with GBS of infection etiology (influenza, chiken pox and borrelia). The diagnosis was based on clinical, serological and electomyographic criteria. All patients receved IV immunoglobulin.

Results: The treatment was initiated between 1 and 2 week from the neurological onset of the disease. The outcome was favorable, 2 patients have no neurological symptoms and third patint was significantly improved (after 2 weeks of evolution).

Conclusions: The patients diagnosed with GBS of viral etiology had a favorable outcome. Elecromyography performed early in the course of the disease, confirmed the diagnosis. The administration of IV immunoglobulin (in adequate dose), was efficient, with rapid recovery and no significant side effects.

P315

RESPIRATORY INFECTIONS INVOLVING CHILDREN WITH PRIMARY IMMUNODEFICIENCY DISEASES

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Introduction: Children with primary immunodeficiency diseases (PID) have a particular evolution of infections depending on the PID type and the nature of the infectious aggression.

Objectives: This study proposes an evaluation of pulmonary disease for children with PID.

Methods: A retrospective study has been done involving all the 96 cases with PID(1998-2008). The study groups have been chosen depending on the PID type.

Results: The PID types were: selective IgA deficit (66 cases), variable PID (15), hypogammaglobulinemia with hyper-IgM (2), mixed PID (3), cellular PID (2), neutrophyle anomalies (4). In 86% of cases, the PID diagnostic was determined in the first 3 years of life, time in which children suffered at least 3 episodes of respiratory tract infections. In the first 5 years of evolution, upper respiratory tract infections were dominating (69%). After 5 years of evolution, 3% of children suffered from chronic respiratory insufficiency determined by pulmonary fibrosys, from which 2 patients have died (ataxia teleangiectasia). The 3 cases suffering from mixed PID, died during their first year from multiple organ infections (sepsis). The etiology was determined in 22% of cases (dominated by Gram negative bacteria and associated with CMV and EBV).

Conclusions: In 86% of cases, the recurrent respiratory infection episodes were helpfull in establishing the PID diagnostic in the first 3 years of life.At all cases that were followed on a long term basics, the PID put their mark onto the unfavourable evolution of the respiratory suffering.

P316

DIAGNOSTIC VALUE OF WHOLE BLOODIFNIMMUNOLOGICAL ASSAY(QUANTIFERON) FOR TB INFECTION IN HOUSE HOLD CONTACTS IN BCG VACCINATED POPULATION

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Objective: To detect the agreement between tuberculin skin test and whole-blood IFN- assay in household contact of active pulmonary TB in BCG vaccinated population with intermediate TB burden.

Methods & materials: A cross-sectional analytic study done in 130 household contact of active pulmonary TB (bacteriologically proven) selected by Convenice sampling. QuantiFERON-TB assay and the TST results compared in all cases.

Results: Mean age 26.2±18.7 years; positive QuantiFERON-TB results seen in 15.8% (19 /120) of cases.15% (7/47) of young (< 20 Years) and 16% (12/73) of adult ones (>20 years) had positive QuantiFERON-TB results without significant difference between two groups. (Fisher´s Exact Test=1) the positive PPD results detected in 11.7% (14/119) of cases. TST had not significant difference between young and adult cases.

50 % (7/14)of TST-positive cases had negative QuantiFERON-TB results. 61% (11/ 18) of cases with positive QuantiFERON-TB results had TST negative results. We found Significant difference between two test (fisher test; 95% CI, *P* =0.01). The agreement between TST and QuantiFERON-TB assay in cases was poor (=0.352); PPV for TST =0.32 ;NPP=0.89; Positive Likelihood Ratio+ (LR+=3.2); Negative Likelihood Ratio (LR-=8.5). TST was dependent to age but not for QuantiFERON-TB.

Conclusion: We recommend Quantiferon TB as a basis for the decision on whether to perform subsequent chest X-ray examinations or to start treatment for latent tuberculosis infection.The cost /benefit should be evaluated by Ministry of Health in our country.

P317

THE FEATURES OF NON-CLASSICAL ,NON-CALCAEMIC IMMUNE DOWN REGULATIORY EFFECTS OF COMPLETE CLASSICAL RACHITIC OSTEODYSTROPHY IN A 2 YEAR MALE CHILD

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Background/purpose: Severe childhood rickets is getting more indistinct due to a better comprehension of its aetiopathogenesis/ intervention. Where it exists, it follows dysfunctions of metabolic organs, genetic factors and famine. Unlike in adults its pathobiology in children is still elusive. A unified model is unlikely to espouse the perturbations in its causality.

Case/intervention: A 2 year old male negroid presented with chronic cough, breathing difficulty for six months and progressive weight loss for three months. He had contact with a grandmother who had PTB. He was developmentally delayed. He was severely wasted with widely open AFs and macrocephalic. He had rachitic rosarys,Harrisons sulcation,widening of the epiphysis of the wrist bones, scoliosis, genu varum and features of respiratory difficulties. He was pot-bellied and globally hypotonic ,radiographs of the upper limbs showed cupping, fraying and splaying of the radio/ulnar-carpal joints, with a left radial and right ulnar fractures. The serum ALP was high; the serum calcium/phosphates were low. The blood glucose was normal. His TST was negative. The Chest X-rays features were consistent with a central pneumonia with probable paediatric tuberculosis. He was managed effectively with oral vitamin D, calcium, antibiotics ,anti TB drugs, nutritional support and orthopaedic referral.

Conclusion/importance: The classical calcaemic effect and the non-classical humoural/ Immunomodulatory functions of vitamin D were highlighted.The associated malnutrition with its related T-cell / B-cell immunodysfunctions could have propagated/sustained the vicious cycle in this case.

This was a good teaching case and an illustrative model of its natural history.A holistic intervention will be implied in such cases.

P318

A NOVEL AP3B1 MUTATION IN HERMANSKY PUDLAK SYNDROME TYPE 2

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Background and aims: Hermansky Pudlak syndrome type 2 (HPS2) is a rare autosomal recessive disorder caused by mutations in the gene encoding the beta-3A subunit of the AP3 complex (AP3B1) resulting in defects in intracellular protein trafficking of lysosome related organelles. HPS2 is characterised by oculocutaneous albinism, congenital neutropenia and platelet dysfunction with a tendency for developing pulmonary fibrosis and granulomatous colitis later on in life. An increased risk of infection is associated with the underlying granulocytopenia.

Methods: We describe a 2-year-old girl, born to healthy unrelated Maltese parents, who presented with oculocutaneous albinism at 2-months of age. Subsequent investigations revealed chronic neutropenia, low serum IgM and impaired platelet aggregation. PHA responses were normal but cytotoxic NK-cell function was reduced. The girl suffered from recurrent upper respiratory tract infections but never sustained any episodes of invasive bacterial or fungal sepsis. She was also found to have bilateral hip dysplasia which was corrected by open reduction.

Results: Mutational analysis revealed a novel homozygous deletion of 624 base pairs including part of intron 18 and exon 19 (g.180117-180740 del) in the AP3B1 gene which led to a premature stop codon. Both parents were heterozygous for the mutation.

Conclusion: Management of children with HPS2 is complex and involves repeated visual assessments, prophylactic antimicrobials, and G-CSF and platelet transfusions prior surgery. In view of the potential risk of haemophagocytic lymphohistiocytosis, secondary to the impaired NK-cell function, a matched bone marrow donor should be sought after diagnosis. Early diagnosis should lead to appropriate genetic counselling.

P319

SUBOPTIMAL PROTECTIVE IMMUNITY OF HEALTHCARE STUDENTS AGAINST VACCINE PREVENTABLE DISEASES

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Background and aims: Immunity of healthcare students (HCS) against infectious agents in a hospital setting is important, as it prevents their transmission to patients and acquisition of disease. Aim of this study was to evaluate immunization rates of HCS and their serologic immunity against certain vaccine preventable diseases.

Methods: Medical and nursing students during their pediatric clerkship at our institution, were enrolled. Information including demographics, past history of disease and immunization status was obtained through personal interview and available records. In addition, serum IgG antibodies were determined for measles, mumps, rubella, varicella-zoster virus (VZV), hepatitis B surface antigen (HBs) and hepatitis A virus (HAVAb). Seronegative students and those with incomplete immunizations, were referred to local vaccination clinics and compliance was assessed three months later.

Results: From April to November 2007, a total of 187 students (84 medical, 103 nursing) were recruited; mean age was 24 years; median: 23 years (range: 20-45 years). Only 131 (70%) of them provided complete vaccination records since birth. Adequate immunity against diphtheria and tetanus was documented in 37.5% and 49% of the students. Seropositivity against measles, mumps, rubella, VZV, HBs (≥ 10 IU/l), HAVAb (≤ 0.900 S/CO) was found in 98, 89.5, 97, 92, 84 and 14.6%, respectively. At follow-up, 67% of the nursing and 48% of the medical students had received none of the vaccines indicated.

Conclusions: HCS presented significant immunization gaps, indicating the need of an appropriate prevention strategy. In order to maximize compliance, Faculty has to bear the costs of vaccination.

P320

HIGH MONOCYTE ACTIVATION IN VERY-PRETERM NEONATES AS CAUSE OF THEIR SUSCEPTIBILITY TO INFECTIONS

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Background/aim: Little is known about characteristics of innate immunity that make very-preterm neonates (< 30 g.w.) more susceptible to infections. Monocytes belong to the first line of innate response, acting as antigen-presenting cells and recognizing molecular patterns of bacterial components (LPS) through Toll-like receptors. Our aim was to describe the differences of the innate immune response between neonates of different gestation age.

Methods: Cross-sectional study in umbilical-cord-blood monocytes of 64 healthy neonates divided into 3 groups: very-preterm (25-30 weeks), preterm (31-36), full-term (37-41). CD14+ monocytes were isolated by an immunomagnetic-technique and cultured with LPS/LPS+IFNγ. Monocyte-population analysis was performed by flow-cytometry and cytokines quantified in culture supernatants. CD14/TLR4-mRNA expression was measured by qPCR.

Results: We found HLA-DR lower values for very-preterm neonates in unstimulated and LPS-stimulated cells. No differences for CD40+-cell percentages were found. We observed a CD80-percentage increase and a CD86-percentage decrease within each group when stimulated with LPS/LPS+IFNγ. CD69+CD40+ and CD69+HLA-DR+ cells showed lower percentages in preterm and full-term groups. We found higher CD69- and CD25-percentages in very-preterm newborns in unstimulated cells and they increased when cells were LPS-/LPS+IFNγ-stimulated. We found higher production of IL-1β, IL-6, IL-8 and TNFα cytokines and higher expression of CD14/ TLR4 mRNA for unstimulated monocytes in the very-preterm neonates.

Conclusion: Monocytes from very-preterm neonates have a diminished function and a higher basal activation seen at both cellular and molecular levels as compared with preterm or full-term neonates. This could explain the susceptibility of very-preterm neonates to bacterial infections because of an uncontrolled proinflammatory microenvironment.

P321

CHANGING OF SERUM DEFENSINE CONCENTRATION IN ACUTE PERIOD OF TICK-BORNE NEUROINFECTIONS IN CHILDREN

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Researching of clinical peculiarities of tick-borne infections - tick-borne encephalitis (TBE), borreliosis (TBB), ehrlichiosis, anaplasmosis) showed the possibility of CNS damage. TBE can be developing as mixed infection. The mechanisms for the different clinical forms and outcome of TBE infection are unclear.

For detecting diagnostic meaning of defensine changing 46 cases of serologically confirmed tick-borne neuroinfections in children (1-15 years of age) were analysed. The sera were tested for TBE virus-IgM and -IgG using ELISA, for B.burgdorferi, E.chafeensis and A.phagocitophila -IgM and -IgG using ELISA. For defensine testing commercial ELISA test systems were used. Among researched clinical cases in 28.2% - TBE, in 6.5 %- TBB, in 65.3% - mixed infection were diagnosed. The results show that the serum defensine concentration in patients with meningeal form of TBE was 80±5.5 ng/ml, in patients with meningeal form of TBB - 65±9.3 ng/ml, in mixed infection - 110±6.3 ng/ml. During the regress of clinical manifestations the lowering of defensine concentration to normal data (62±8.3 ng/ml in TBE patients and 50±6.8 ng/ml in mixed infection patients) was detected. The serum defensine concentration in patients with TBE meningoecephalitis was 135±7.4 ng/ml, in mixed infection - 189±7.4 ng/ml ($p < 0.05$). The changing of defensine concentration in serum is unspecific in different etiological variants of tick-borne diseases, more manifested in mixed infections and reflects the functional activity of leukocytes in inflammatory reactions. The prolonged high level of defensine concentration in serum during meningitis and meningoencephalitis observed in severe cases can be considered as unfavorable sign.

P322

ROLE OF INNATE IMMUNITY IN MOTHER-TO-CHILD TRANSMISSION OF HIV-1

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Background and aims: Innate immunity may contribute to host-viral interactions and impact the risk of mother-to-child transmission (MTCT) of HIV-1. Defensins and toll-like receptors (TLRs) play a crucial role in the host´s innate immune response. This study focused on evaluating the influence of single nucleotide polymorphisms (SNPs) in the beta-defensin-1 (DEFB1) gene and in the TLR9 gene.

Methods: The study was conducted in 300 children (118 HIV-1-infected and 182 HIV-1-uninfected) born to HIV-1-infected mothers, and in 84 available maternal samples. Genomic DNA was evaluated for -44C/G(rs1800972) and -52G/A(rs1799946) SNPs of the DEFB1 gene and 1635A/G(rs352140) and 1174G/A(rs352139) SNPs of the TLR9 gene by TaqMan allelic discrimination assay. Statistical analysis was performed using SNPStats and Haploview programs.

Results: -52GG genotype and the -44G/-52G haplotype of DEFB1 in children were strongly associated with a low risk of HIV-1 infection (odds ratio (OR)=0.52, 95% confidence interval (CI) 0.31-0.86, p=0.03, and OR=0.50, 95%CI 0.31-0.83, p=0.01, respectively). Similarly, the -52GG genotype and the -44G/-52G haplotype of DEFB1 in mothers were associated with a low risk of HIV-1 transmission (OR=0.23, 95%CI 0.06-0.85, p=0.042, and OR=0.23, 95%CI 0.08-0.66, p=0.012, respectively). SNPs of TLR9 were not significantly associated with a risk of HIV-1 infection and transmission. However, the 1174A/1635G haplotype was strongly associated with a low risk of MTCT of HIV-1 (OR=0.15, 95%CI 0.05-0.48, p=0.0012).

Conclusions: Our results demonstrate a significant correlation between genetic variants of DEFB1 and TLR9 genes and risk of MTCT of HIV-1, thus confirming the role of innate immunity in perinatal HIV-1 infection.

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DIFFERENCES IN THE IMMUNE RESPONSE TO *MYCOBACTERIUM BOVIS* BACILLE CALMETTE-GUÉRIN IMMUNISATION BETWEEN CHILDREN AND ADULTS

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BCG vaccine is the most commonly administered vaccine worldwide. It has proven efficacy in preventing severe and disseminated forms of TB in children. In contrast, the reported efficacy of the vaccine for preventing TB in adults is variable. Data comparing the immune response following BCG immunisation in children and adults are scarce. Investigating differences in the immune response to BCG immunisation between children and adults is important to understand differences in protective efficacy.

Healthy, BCG-unimmunised children and adults were administered BCG after exclusion of previous TB exposure. Blood was collected prior to BCG immunisation and at 6 and/or 10 weeks after. Proportions of antigen-specific Th1 cytokine-producing CD4 and CD8 cells were compared in a 12-hour intracellular cytokine assay using multicolour flow cytometry.

Results were available for 13 children (median (range) age 0.9 (0.1 - 2.0) years) and 16 medical students (median (range) age 24.0 (20.9 - 32.4) years). A significant increase in the proportion of cytokine-producing CD4 and CD8 cells was seen in both children and adults. Following immunisation, compared to adults, children had smaller increases in the proportions of INF-γ-producing CD4 and CD8 cells, but greater increases in IL-2- and TNF-producing CD4 cells. In contrast to adults, children had significant increases in all double positive (INF-γ+IL-2+; INF-γ+TNF+; IL-2+TNF+) and triple positive (INF-γ+IL-2+TNF+) CD4 cell populations.

The immune response to BCG immunisation in children and adults differs both quantitatively and qualitatively. Antigen-specific T cells capable of producing multiple Th1 cytokines are more effectively induced by immunisation in childhood.

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INVASIVE PNEUMOCOCCAL INFECTION IN A VACCINATED CHILD REVEALING COMPLEMENT DEFICIENCY

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Background: *Streptococcus pneumoniae* causes a wide spectrum of diseases such as upper respiratory tract infections, meningitis, bacteremia and pneumonia. The primary risk factor of invasive infections is related to age and deficiency of protective antibodies.

Methods: We present a case of meningitis caused by a vaccine serotype of *S. pneumoniae* in a child previously vaccinated with PCV7.

Results: In November 2007 a 3 year-old boy was diagnosed with meningitis causing general seizures. His medical history was marked by recurrent upper respiratory tract infections. He had received immunizations consistent with the recommended childhood immunization schedule and received two doses of PCV7 at the age of 14 months and 18 months and additionally one dose of varicella vaccine. Culture of the cerebrospinal fluid grew *S. pneumoniae* and the isolate was serotyped as 18 C, a strain included in PCV7. Results of immunoglobulins, lymphocyte subsets, neutrophil count and neutrophil oxidative burst were normal but the total complement function (CH50) values were 21-34% (nl 80-120%) and C2 concentrations were undetectable. Specific IgG response to polysaccharide vaccination against *S.pneumoniae* was normal. Upon treatment the child recovered and remained seizure free, but suffered from hearing loss. Prophylactic antibiotics were administered.

Conclusions: Although complement C2 deficiency has been detected in asymptomatic individuals, patients usually present with either autoimmune disease or recurrent pyogenic infection, particularly due to encapsulated bacteria. Evaluation for immunodeficiency was indicated in this vaccinated patient with an *S.pneumoniae* infection due to a vaccine strain.

P325

KAWASAKI DESEASE: EVEN MORE ATYPICAL

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Background and aims: Kawasaki disease (KD) is an acute systemic vasculitis that preferentially affects coronary arteries and is the most common cause of aquired cardiopathy in children in developed countries. Clinical presentation may occur with atypical and incomplete patterns.

Methods: incidence and presentation patterns of atypical/incomplete KD cases admitted at our hospital were registered during the last five years (2003-2008).

Results: 12 cases of KD were diagnosed; 4/12 (33%) can be considered atypical or incomplete.In the first case a 4-years old patient showed Rotavirus gastroenteritis and then developed anasharcatic status with edema of face, hands and feet, ascitis, bilateral pleural and pericardial effusion. In the second case a 4 months-old infant began with chicken-pox and persistent fever lasting over 5 days and associated with right hip-pain without arthritis. In both cases, notwithstanding intravenous immunoglobulins (IGIV 2gr/Kg) and aspirin (ASA 100 mg/Kg) treatment, coronaropathy appeared.Two further cases of incomplete KD occurred in 2 infants. Both started with persistent fever lasting over 5 days. In one child (4 months of age) fever was concomitant to sepsis (serum EBV-CMV IgM positive) and severe anaemia (Hb 6.6 g/dL); in the other infant (3 months of age) fever was accompanied by a skin rash. Both cases were refractory to IGIV infusions, but no coronaropathy was observed at follow-up.

Discussion: Incidence of atypical KD cases in our Paediatric Clinic was high, presented with unusual signs such as anasharca, never described before in literature as a sign of KD, and often were refractory to IGIV theraphy.

P326

EVALUATION OF IMMUNE RESPONSE TO PNEUMOCOCCAL VACCINE IN VACCINATED SPLENECTOMIZED B-THALASSEMIC CHILDREN

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Background and aims: Splenectomy is accompanied by a life-long risk of overwhelming postsplenectomy infection, mainly caused by polysaccharide (PS) encapsulated bacteria such as Streptococcus pneumoniae. The mortality rate in those infected patients remains high. Therefore pneumococcal polysaccharide vaccine has been recommended. To obtain information on the immunity levels of pneumococcal antibody, in splenectomised beta-thalassemic patients in Jahrom.

Methods: This descriptive and cross sectional study was carried out on all splenectomised beta-thalassemic patients in Jahrom, Nov. 2007 - March 2008. Total anti-pneumococcal vaccine antibody concentrations were measured by the enzyme-linked immunosorbent assay method. The parients were divided to two groups based on antibody concentrations: Group 1: Immune patients or good responder with 1.0 µg/ml antibody concentrations and group 2: Non-immune patients or poor responder with less than 1.0 µg/ml antibody concentrations.

Results: The results showed that 57.10% and 42.90% of the patients were immune and non-immune to pneumococcal infections, respectively. There was a negative significant between Immunity level with the period after pneumococcal vaccination ($r=-0.573$, $P< 0.001$).

Conclusions: These results suggest that high percentage splenectomised beta-thalassemic patients are poor responders to pneumococcal vaccination. Therefore evaluations immunity levels to pneumococcal vaccine are recommended in these patients.

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DETERMINATION OF ANTI-HEPATITIS B SURFACE ANTIBODY TITER IN HBV VACCINATED B-THALASSEMIC CHILDREN

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Background and aims: Thalassemia patients are more susceptible to hepatitis than the normal population due to the frequent blood transfusions. To determine the immune response of children with major ك-thalassemia, by measuring anti-hepatitis B surface antibody (anti-HBs Ab) following the last HBV vaccine injection.

Methods: This study was carried out on all (110) thalassemic patients of Jahrom 15.34 ± 5.99 year, who received three standard intramuscular recombinant HBV vaccines- 2006. Based on the serum levels of anti-HBs antibody, subjects were categorized as: good responders (anti-HBs >100 IU/Lit), low responders (anti-HBs 10-100 IU/Lit) and non-responders (anti-HBs < 10 IU/Lit).

Results: In females, the mean antibody level was 133.69 ± 107.647 and in males it was 158.02 ± 109.640 IU/Lit (P=0.243). Out of 110 thalassemic patients of Jahrom 66 (60%) were good responders, 21 (19.1%) low responders and 23 (20.9%) non-responders.

Conclusions: Standard HBV vaccination in thalassemic patients results in an immune response in about 60% of the subjects. Therefore, annually assessment of anti-HBs antibody level, after the last vaccination (booster), is recommended.

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COMPARISON OF CYTOKINE GENE POLYMORPHISMS AMONG GREEK PATIENTS WITH MENINGOCOCCAL OR VIRAL MENINGITIS

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Background and aims: Inflammatory responses play a significant role in the pathogenesis of viral and meningococcal meningitis (VM and MM); white blood cells in cerebrospinal fluid differ, neutrophils predominantly with MM and lymphocytes with VM. We compared single nucleotide polymorphisms (SNPs) in pro- and anti-inflammatory cytokine genes among patients with VM or MM, particularly interleukin-8, a powerful attractant for neutrophils.

Methods: Ethical permission was obtained from Hunter New England Research Ethics Committee. Patient DNA samples were prepared by the National Meningitis Reference Laboratory in Athens: MM=98; VM=53. Results were compared with data published for healthy Greek control data.SNPs were assessed by real-time PCR. *IL6* G-174C, IL1B C-511T, IL1RN T+2018C, *IL10* G-1082A, *IL8* A-251T and *TNF* G-308A were assessed. Fisher's exact test was used for analysis.

Results: Compared with controls (31%), the genotype for high IL-6 was predominant among MM (51%, p=0.0008) and VM (74.5%, p< 0.0001). The genotype associated with high TNFα was 5% among controls, lower for MM (1.1%, p=0.0014) and VM (0%, p=0.052). There was no difference between distribution of IL-8 SNPs between controls and MM (p=0.162), but was significant for VM (p=0.0025). Distribution of IL-6 and IL-8 SNPs between MM and VM groups differed, IL-6=0.024, IL-8=0.00004.

Conclusions: Reports on associations between the IL-8 SNP and cytokine responses differ. Because of its role in neutrophil attraction, differences in the frequency of the IL-8 SNP between the MM and VM groups require further investigation.

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SERUM BACTERICIDAL ACTIVITY IN CHILDHOOD AND ADOLESCENCE 3-6 YEARS AFTER VACCINATION WITH SEROGROUP C MENINGOCOCCAL CONJUGATE VACCINE

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Background and aims: Serogroup C meningococcal conjugate vaccines were introduced in Greece since 2001 and contributed to the decrease in disease incidence in the following years. Although no cases of serogroup C disease were recorded in 2004, a steady increase was observed since 2005. This study aimed to examine the duration of protective immune responses to the vaccine in children immunized at different ages.

Methods: Serum bactericidal activity (with rabbit complement) and geometric mean titers of specific IgG antibody (with ELISA method) were assessed in 269 children and adolescents (135 males) immunized with a single vaccine dose (at ≥12 months of age) at a mean time of about 5 years after vaccination.

Results: In total 79/269 (29.4%) children had serum bactericidal antibody titres ≥ 1:8. Non-protective antibody titers were observed in most children vaccinated at age < 6 years (85.9%), followed by those between 6 and 10 years (62.2%), while this percentage was considerably lower in adolescents vaccinated at an age > 10 years (37.8%) ($p < 0.01$). Geometric mean titres of serum IgG antibodies against serogroup C showed a similar variation.

Conclusion: These results indicate that serum bactericidal antibody titers significantly correlate with age of vaccination; most children do not have protective antibody titers few years after immunization in infancy and childhood whereas most adolescents maintain sustained protection. A booster dose of conjugate vaccine in adolescents may provide further protection to them as well as indirect protection to younger children.

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CIRCULATING B CELL MEMORY AFTER MEASLES AND MUMPS VACCINATION

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Background and aims: To evaluate the presence of circulating measles- and mumps-specific memory B-cells using a Human-PBL-SCID-mouse model in which PBMC were transferred of donors with either low or high antibody titers against measles and mumps.

Methods: PBMC's of 6 donors (3 subjects with low and 3 with high antibody titers against measles and mumps) were injected in the spleen of conditioned NOD-SCID-mice (3 per subject). In vivo production of human antibodies against measles and mumps was evaluated in mouse plasma on days 7, 10 and 13 with a commercial ELISA (Enzygnost measles and mumps, Behring).

Results: For mumps, 3 donors had undetectable antibody titers and 3 had very high antibody titers, whereas for measles 2 donors had undetectable antibodies, 1 donor had a very low antibody titer and 3 donors had high antibody titers. None of the mice injected with PBMC from subjects with undetectable antibody titers for measles and mumps developed detectable human antibody titers for either virus. All mice injected with PBMC from subjects with high(er) antibody titers against mumps and/or measles, also showed detectable antibody titers for measles and/or mumps in the animal plasma.

Conclusions: In vaccinees without detectable serum antibodies against mumps and/or measles viruses, no or a very limited number of circulating memory B-cells against these viruses could be detected. These findings further add to the existing evidence suggesting that individuals without circulating antibodies are at risk of developing either measles or mumps disease upon encounter with wild-type virus.

P331

SEVERE GROUP A STREPTOCOCCAL INFECTIONS IN THE PAEDIATRIC INTENSIVE CARE UNIT - CASE SERIES AND ROLE OF INTRAVENOUS IMMUNOGLOBULIN

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Background and aims: We have experienced a significant increase in severe Group A streptococcal infection (GAS) presenting to paediatric intensive care (PICU). Our aim is to describe our experience in the management of these patients. Our secondary aim is to review the current literature regarding the use of intravenous immunoglobulin (IVIG) in severe GAS infections.

Setting: Tertiary paediatric intensive care unit.

Patients: Children < 18 years of age presenting over a one year period to 2008.

Methods: Retrospective case note review. Data extracted from computerised information system database. Accompanying Medline literature review to 2008.

Results: 11 children were included. Mean age: 5.04 years (range 0.16-12.32). 3 had co-morbid pathology. Duration of admission range: 8-257 hours (mean 103). Nine children required ventilation, range 57-186 hours (mean 87). Six patients required inotropes. One child required VA ECMO for cardiorespiratory failure. GAS was isolated from the following: Pleural fluid 3; Throat swab 4; Bronchoalveolar lavage 2; Joint aspirate & Blood Culture 1; Skin lesion 1.All patients received antibiotics (cefotaxime, clindamycin). Two patients fulfilling STSS criteria received IVIG. Ten of eleven children survived to PICU discharge. One patient died of cardiorespiratory failure. Literature review reveals 2 conflicting randomised controlled trials in the use of IVIG. One Cochrane meta-analysis was inconclusive. Current guidelines suggest that IVIG may be useful.

Conclusions: Serious GAS infection frequently requires PICU intervention. Cardiorespiratory failure is common although usually responds to conventional intensive care therapy. Mortality is low. Evidence supporting the use of IVIG is inconclusive.

P332

INTRANASAL IMMUNIZATION WITH GBS SURFACE PROTEIN SIP AND SCPB INDUCES SPECIFIC MUCOSAL AND SYSTEMIC IMMUNE RESPONSES IN MICE

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Sip and ScpB are highly conserved among all strains of Group B streptococcus (GBS). Thus, the two proteins are attractive antigens for inclusion in a vaccine against GBS. In this study, we constructed and expressed the two proteins, investigated their specific mucosal immune responses against GBS induced by intranasal immunization with cholera toxin (CT) and CpG-ODN as adjuvant. Intranasal immunization with different doses of recombinant Sip and ScpB all elicited specific antibodies in serum and [ct1] vagina of mice. A mixture of rSip and rScpB with either CT or CpG-ODN elicited specific antibodies in serum and vagina. Sera from the mice group intranasally immunized with rSip +CT, rScpB +CT, and a mixture of rSip+rScpB +CT also showed bactericidal activity compared with the serum of the control group; the serum of rSip+rScpB mixture group had the highest phagocytic index. The current findings suggested that

(1) rSip and rScpB would be useful antigens as the components of the vaccine to induce protective immune responses against GBS, and

(2) CpG-ODN could be used as a very effective mucosal adjuvant in inducing a good mucosal immune response.

The use of an intranasal vaccine composed of the different surface protein antigens is an attractive strategy for the development of a vaccine against GBS.

Keywords: Group B streptococcus; surface protein; rSip; rScpB; intranasal immunization.

P333

HUMORAL IMMUNITY TO HEPATITIS A IN BONE MARROW TRANSPLANTED PATIENTS

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Background and aims: Bone marrow transplant (BMT) recipients lose immune memory of exposure to infectious agents accumulated through a lifetime and therefore need to be revaccinated. We conducted a prospective study to evaluate the

hepatitis A seroprevalence in pre-bone marrow transplant cases and the loss of anti-hepatitis A virus (anti-HAV) immunoglobulin-G antibodies following BMT, in intermediate endemic region, Turkey.

Methods: Between 2002 and 2007, candidates for BMT at our institution were tested for anti-HAV IgG prior to transplantation. Seropositive patients were retested at 12 months of BMT, then once or twice yearly until they became seronegative.

Results: Bone marrow transplanted ninety one patients whose age range was 2-57 years old were evaluated. Sixty eight of them (74.7 % in overall group, 61.1% in children, 94.6% in adults) were seropositive before BMT. There was no history of hepatitis A virus vaccination before BMT reflecting natural infection. Loss of anti-HAV IgG was observed at a mean of 46.9 mo after transplantation with survival analysis.

Conclusions: BMT recipients should have serological screening before hepatitis A virus vaccination.

P334

IMMUNOLOGICAL DERANGEMENT AGAINST CAUSATIVE PATHOGENS IN OTITIS-PRONE CHILDREN

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Otitis media is the most common disease seen in childhood. *Streptcoccous pneumoniae*(SP), nontypeable *Haemophilus influenzae*(NTHI), and *Moraxella catarrhalis*(MC) are the most frequent pathogens and are isolated 35-40%, 30-35%, and 10-15%, respectively, in all episodes. Protection against the disease due to these pathogens may depend on pathogen-specific antibody. The pathogen-specific antibodies may be directed against surface protein antigens.

In this study, we studied the causative pathogen specific immune responses among otitis-prone children. We evaluated specific IgG levels against pneumococcal surface protein A (PspA) for SP, outer membrane protein P4 and P6 for NTHI, and ubiquitous surface protein (UspA) for MC in sera of both otitis-prone children and healthy children. Antibody levels to PspA, P4, P6, and UspA in otitis-prone children was measured and specific IgG antibodies against these proteins were defined if the concentration was lower than 2 SD below the mean of age in healthy children. Against SP, 46.1 to 57.1% of otitis-prone children showed subnormal levels of anti-PspA IgG. Against NTHI, 45.0% and 54.0% of otitis-prone children showed subnormal levels of anti-P4 and P6 IgG, respectively. Against MC, 18.1% to 45.5% of otitis-prone children showed subnormal levels of anti-UspA IgG. These results strongly suggested that selective immunologic derangements in otitis-prone children might be wider than previously believed. Moreover, the results raise the possibility that otitis-prone children may not respond adequately to immunization with these protein-based vaccines. Effective active immunoprophylaxis against otitis media will be possible only when the mechanism of immunologic defects in otitis-prone children is understood.

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DIFFERENTIAL EXPRESSION OF TOLL-LIKE RECEPTOR SIGNALING GENES IN LEUKOCYTES: NEWBORN COMPARED TO ADULT IN RESPONSE TO LIPOPOLYSACCHARIDE STIMULATION IN VITRO

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Background and aims: Compared with adults, newborn infants have developmentally immature immune systems and increased susceptibility to invasive microbial infections. Toll-like receptors (TLRs) are critical components of innate immunity. This study was designed to evaluate differential expression of genes for TLR signaling pathway in leukocytes from cord blood compared with those from adult peripheral blood in response to lipopolysaccharide stimulation in vitro.

Methods: Blood samples were obtained from three health term newborns and three health adult donors. Whole blood cells culture in vitro and lipopolysaccharide was added. After 2, 4, 6, 8, 12, 24 hours of cultured, leukocytes were isolated and total RNA was extracted. The Oligo GEArray Human TLR Signaling Pathway Microarrays, representing 117 genes, were used in this study. Gene expression levels were determined using ScanAlyze and GEArray Analyzer software.

Results: A total 101 differential express (more than twofold) genes were found. Among them 40 genes, mostly associated with positive accommodation of TLR signaling, were down-regulated, and 11 genes, mostly associated with negative accommodation of TLR signaling, were up-regulated in the cord blood leukocytes compared with those in the adult leukocytes at all time points of cell cultured with lipopolysaccharide. The other 50 genes were up or down regulated trade-offs between newborn and adult at different time points of lipopolysaccharide stimulation.

Conclusions: The suppressed TLR response to bacterial endotoxin appear to be part of the functional immaturity of the neonatal immune system and might predispose them to bacterial infection.

P336

INCIDENCE AND ETIOLOGY OF INFECTIOUS COMPLICATIONS DURING TREATMENT FOR HEMATO-ONCOLOGIC DISORDERS AT HIGH RISK FOR INVASIVE INFECTIONS

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Introduction: Prolonged neutropaenia in patients with severe aplastic anaemia (SAA), myelodysplastic syndrome (MDS), acute myeloid leukaemia (AML), relapsed acute lymphoblastic leukaemia (rALL) and after bone marrow transplantation (BMT), is a well-known risk factor for infectious complications. Few data are available about the incidence and etiology of infections during the total treatment period associated with a decreased T-cell function, in children diagnosed with these conditions.

Methods: Paediatric patients diagnosed with SAA, MDS, AML, rALL and post-BMT between 1 January 2000 and 31 December 2005 in our centre were included in our study. A retrospective review of medical, laboratory, microbiology, and pathology records was performed to describe the incidence and etiology of the infectious complications and the associated morbidity and mortality.

Results: We included 138 patients in our study. 68% of 180 microbiological proven infections were diagnosed during neutropaenia; 83% bacterial (98% blood stream infections), 6% fungal and 11% viral infections. 54% occurred in patients with AML, 37% after BMT. In the period without neutropaenia, 58 (32%) microbiological proven infections were diagnosed; 37% bacterial (85% bloodstream infections), 3% fungal and 60% viral. 86% of micro-biological proven infections occurred in patients after BMT. Infection related mortality was 4.3%. Four patients died during neutropaenia (fungal infections), two patients in the period without neutropaenia (systemic adenovirus infection).

Conclusion: Bacterial infections were most frequently seen during neutropaenia, especially in AML patients. Fungal infections are associated with a high mortality. Viral infections were most frequently seen in the period without neutropaenia, mainly in post BMT-patients.

INFECTION CONTROL IN HOSPITAL AND IN THE COMMUNITY

P337

MRSA INFECTION AND COLONIZATION - A NEW CHALLENGE IN PEDIATRICS

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Introduction: Colonization and infection by MRSA has increased in adult patients throughout the years in Germany. As well in pediatric institutions cases have been reported.

Patients and methods: We have seen 8 patients with positive results for MRSA within 18 month. All patients were isolated and treated by standardized hygienic protocol. All patients were treated for eradication.

Results: Mostly colonization with MRSA was seen at different localizations (nose, perineum, gastro stoma). In 3 cases an infection was found. 5 patients were chronically ill. 1 premature infant, 1 term born and 1 older infant were found positive for MRSA during time of hospitalization. 4 parents were as well found positive for MRSA. In 7 patients MRSA could be eradicated. 3 chronically ill patients were later on again positive for MRSA. MRSA elimination has not been possible at all parents' homes.

Discussion: Chronically ill patients (living in care facility, multiple hospitalizations) have to be seen as risk patients for acquiring MRSA even at young age. At each time of hospital admission (readmission or known MRSA in history) these patients should be isolated until negative results for MRSA are found. Eradication of MRSA is required. For family members with close contact there is no obligation for treatment by law at the moment.

Conclusion: Within the next years an increasing number of MRSA colonization has to be faced. Medical employees should therefore familiarize with this problem and protective care and eradication should start at an early stage including maternity clinics and pediatric wards.

P338

EPIDEMIOLOGY AND MANAGEMENT OF A NOSOCOMIAL NOROVIRUS OUTBREAK IN A PEDIATRIC HOSPITAL

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Background and aims: Norovirus are a frequent cause of gastroenteritis worldwide. Nosocomial outbreaks by norovirus are well documented, being difficult to control because of their stability in the environment and efficient transmission. We describe a norovirus outbreak and its control in a paediatric tertiary hospital in Spain during October-November 2008.

Methods: Hospital Vall d'Hebron is a 1396-bed tertiary hospital in Barcelona. Paediatric area is an independent 364-bed center. Patients and HCWs met the case definition if they had new onset of vomiting and/or diarrhea after 24 hours from admission and during the outbreak period. Selected stool samples were tested for norovirus by RT-PCR.

Results: We identified 32 cases that affected 17 patients and 15 HCWs that were clustered in two general paediatric wards. Laboratory confirmation was available in 4 patients and 2 HCWS. Attack rates were 7,6% (17/224) for patients and 16,7% (15/90) for HCWs. No hospitalizations were required for HCWs. Epidemiological investigation revealed that the index case was a child admitted for an acute gastroenteritis whose mother also was affected. Aggressive infection-control measures, including contact precautions isolation of patients with symptoms, cohorting patients and HCWs, intensive environment disinfection and instructing HCW not to go to work if they suffer for suspected symptoms, were required to terminate the outbreak.

Conclusions: The significant disruption of patient care of this single nosocomial outbreak, as it occurs in other similar outbreaks, support aggressive efforts to prevent transmission of norovirus in health care setting.

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COMPARISON OF NOSOCOMIAL INFECTION IN A NEONATAL INTENSIVE CARE UNIT BEFORE AND AFTER MOVING INTO A NEW BUILDING

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Introduction: The purpose of this comparative study was to investigate changes in nosocomial infection rates, infection sites, bacterial species, and discussed the related factors in a Neonatal Intensive Care Unit (ICU) before and after moving into a new building at a medical center in central Taiwan.

Method: Data were collected on 30 premature infants who matched inclusion criteria (including spending time in the old ICU) and 31 infants who spent time in the new facility. Nosocomial infection rates, infection sites and changes in bacterial species were included in a descriptive analysis.

Result: Data were collected 6 months before moving and 6 months after moving. We moved from old building into a new building on 5 July 2003.The results show that the nosocomial infection rate decreased from 12.99 ‰ to 8.81‰ (statistically significant at $p < .05$). The lower respiratory tract was the most common infection site in both buildings, and Methicillin-resistant Staphylococcus aureus was the most common infection species in both buildings. We analyzed the potential effects of several related factors, including changes in environment; encouraged staff members to wash hands more frequently, and the use of higher quality isolation facilities.

Conclusion: The findings suggest that change in environment and convenient hand washing facilities can promote hand washing rate of health care workers, in the other word, it may reduce nosocomial infection rate.

P340

A VANCOMYCIN-RESISTANT *ENTEROCOCCUS* (VRE) OUTBREAK IN A NEONATAL UNIT (NU): CONTROL THROUGH SURVEILLANCE AND INTERVENTION

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Background and aims: VRE has become an important cause of nosocomial infections. Detection and control of VRE colonization is important to prevent patient-to-patient transmission and subsequent development of infection. The aim of this study was to use both active surveillance and enhanced infection control measures to combat high incidence of VRE colonization.

Methods: In a 44-bed NU (15-bed NICU), an active surveillance study of VRE colonization was conducted, after a VRE ventriculoperitoneal shunt infection occurred. During a 12-wk period stool samples were collected weekly from all neonates that were hospitalized ≥5 d. Enterococci were isolated on selective media and tested for susceptibility to vancomycin. *Van* resistance genes were detected by PCR. Other interventions included daily written reporting of VRE colonization status and enhanced infection control measures.

Results: A total of 319 stool cultures were obtained. Among 151 neonates screened, 59 (39%) were colonized with VRE. Active surveillance during the first 4 wks yielded a maximum of 85% daily prevalence of VRE colonization and a rate of 10-14 new cases weekly. During the following wks prevalence of VRE colonization significantly decreased to 32% (8th wk) and finally to 13% (12th wk), $p < 0.05$. In the last 3 wks there were no new cases of VRE colonization. Besides, there was no case of VRE infection during active surveillance. All VRE isolates tested were *Enterococcus faecium* harbouring *Van*A gene.

Conclusion: Both active surveillance cultures and enhanced infection control measures are important to combat high incidence of VRE colonization in the NU setting.

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MEASURES TO CONTROL A VANCOMYCIN-RESISTANT *ENTEROCOCCUS* (VRE) OUTBREAK IN A PEDIATRIC ONCOLOGY DEPARTMENT (PONCO)

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Background and aims: VRE can cause serious and treatment-refractory infections in immunocompromised children. Detection and control of VRE colonization is important to prevent patient-to-patient transmission. The aim of this study was to evaluate the role of active surveillance and infection control measures to combat an outbreak of VRE colonization in PONCO.

Methods: In a 16-bed PONCO, an active surveillance of VRE colonization was conducted after two VRE bloodstream infections occurred. During a 12-wk period stool cultures were taken every 14d from all inpatients. Enterococci were isolated using selective media and tested for susceptibility to vancomycin. *Van* resistance genes were detected by PCR. Other interventions included enhanced infection control measures and closure of the unit to all new admissions for 3 mos.

Results: A total of 26 patients (median age 6 yrs, 13 patients with leukemia) were screened during the study period. Eleven (42%) patients were colonized with VRE based on the first screening during the 1st mo of the study. Among the remaining 15 patients, in whom the first culture did not detect VRE, 7 patients acquired VRE before the end of the 2nd mo. During the 3rd mo there were no new VRE acquisitions. Daily prevalence of VRE colonization among inpatients ranged from 40 to 75%. There were no other cases of VRE infection during the study period. All VRE isolates tested were *Enterococcus faecium* carrying *Van*A gene.

Conclusion: Active surveillance cultures and strict adherence to infection control policies are needed to eliminate transmission of VRE among PONCO patients.

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RISK FACTORS FOR HOSPITAL INFECTIONS FOLLOWING CARDIAC SURGERY IN CHILDREN

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Background and aims: Hospital infections are a major cause of morbidity and mortality. The aim of our study was to determine the main risk factors for hospital infections following cardiac surgery.

Methods: We studied 427 patients. The age of the patients varied from 1 day to 15 years.

Results: Postoperative infections occurred in 15,7%. The rate of hospital infection following primary operations was 12,1%, after the reoperations - 33,3%. After the planned operations hospital infections were developed in 14,0% and after the emergency operations in 32,5%. From patients with cardiopulmonary bypass time ≤ 120 min, the rate of hospital infection was 9,3%, whereas from patients with cardiopulmonary bypass time >120 min 31,7% cases were complicated with hospital infection. From patients with aortic cross clamp time ≤60 min hospital infection developed in 10,8%, whereas from patients with aortic cross clamp time >60 min in 30,5% cases. Patients developing hospital infection had longer duration of surgery - 4,12±0,26 h, compared to patients without infection - 3,18±0,19h. Similarly the duration of hospitalization before surgery was longer among infected patients - 6,74±1,25 day, compared to patients without infection - 4,32±0,25 days. The rate of hospital infections were more in patients under 1 year.

Conclusions: The main risk factors for hospital infections were: age, emergency operation, reoperation, longer duration of cardiopulmonary bypass, aortic cross clamp time, prolonged hospitalization before surgery, longer duration of surgery.

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SCREENING FOR METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) IN A DISTRICT HOSPITAL

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Background and aims: MRSA is now endemic in many hospitals. Colonization with this organism is a risk factor for eventual MRSA clinical infection which is associated with poor clinical outcomes, prolonged hospital stay and high cost. There is conflicting evidence on universal screening to reduce the risk for clinically important MRSA. In our unit, screening for MRSA was carried out in all paediatric elective and urgent admissions over a 9 month period. The main aims were to quantify the burden of MRSA colonisation in our setting, to identify carriers and offer decolonisation treatment.

Methods: Swabs were taken from all children admitted to the paediatric wards within 24 hours of admission during March-Dec 2008. Swabs were taken from the nose, groin and any areas with accessible medical devices (e.g. gastrostomy, tracheostomy, central venous line site) Children who had positive results were offered decolonisation treatment via either their general practitioner or the paediatric team for those who were still in the ward when results were available.

Results: Approximately 4000 children were admitted to the wards and 11 grew MRSA (median age 66m). 9 represented colonisation (nose 5, groin 8, and perineum 1) and 2 represented skin infections. Risk factors included recent antibiotic treatment, recent contact with healthcare facility and admission to hospice.

Conclusion: MRSA colonisation and infection is rare in children admitted to a district hospital with acute illness or electively admitted for minor surgical procedures.

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THE BURDEN OF POLYPARASITISM AMONG PRIMARY SCHOOLCHILDREN IN RURAL AND FARMING AREAS IN ZIMBABWE

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A cross-sectional study was conducted in Zimbabwe among 1303 primary schoolchildren from a rural (53.3%) and a commercial farming area (46.7%) to determine the prevalence of co-infection by helminths and *Plasmodium falciparum.* Urine was examined on three successive days using the filtration method. Two stool specimens were processed using the Kato-Katz method and a third specimen was processed using the sedimentation method. *Plasmodium falciparum* was diagnosed from thick blood films. The prevalence of *Schistosoma haematobium* in the rural and farming areas was 66.8% and 52.3%, respectively, and for *S. mansoni* the prevalence was 12.4% and 22.7%, respectively. *Plasmodium falciparum*, hookworms, *Ascaris lumbricoides* and *Trichuris trichiura* occurred only in the farming area, with a prevalence of 27.9%, 23.7%, 2.1%, 2.3%, respectively. Co-infection and triple infection with schistosomes, *P. falciparum* and soil-transmitted helminths occurred in the commercial farming area only. Hookworm and *S. mansoni* infections were associated with *P. falciparum* malaria ($P < 0.001$, OR = 2.48, 95% CI 1.56-3.93 and $P = 0.005$, OR = 1.85, 95% CI 1.20-2.87, respectively). Overlap of helminths with malaria is a concern among primary schoolchildren and incorporating helminth control in programmes aiming to control malaria will improve funding and increase the efficiency of control for neglected tropical diseases in identified co-endemic settings.

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10 YEARS EXPERIENCE OF MRSA IN CHILDREN: INFORMING A SCREENING PROGRAMME

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Background and aims: Screening of hospital admissions, with decolonisation of carriers, is increasingly advocated. In England paediatric guidance is ambiguous. We report using 10 years experience of MRSA to inform a screening programme.

Methods: Analysis of prospective data on 405 consecutive in-patients with MRSA between April 1998 and March 2008.

Results: 210 patients presented with infection; 195 had asymptomatic colonisation. Surgical, Cardiac and PICU specialties accounted for 80.5% of colonised and 79.0% of infected patients. 62 MRSA bacteraemias occurred in 53 patients. 22 (41.5%) and 27 (50.9%) of first bacteraemias presented within three and seven days of MRSA being first detected.

	No. (%) patients with MRSA at diagnosis with:		
Specialty	Asymptomatic colonisation	Infection	No. (%) episodes of MRSA bacteraemia
Surgical specialties	67 (34.4)	76 (35.5)	13 (21.0)
Cardiac services	49 (25.1)	47 (22.4)	4 (6.5)
PICU	41 (21.0)	43 (20.5)	22 (35.5)
Paediatric specialties	25 (12.8)	25 (11.9)	8 (12.9)
Liver Unit	9 (4.6)	6 (2.9)	6 (9.7)
Nephrology	2 (1.0)	7 (3.3)	2 (3.2)
Haematology & Oncology	2 (1.0)	6 (2.9)	7 (11.3)
Totals	195 (100)	210 (100)	62 (100)

Conclusions: Most in-patients with MRSA were unrecognised before developing infection. Half of bacteraemias presented before conventional culture could have detected colonisation. Screening of three high-risk specialties would have identified 80% of colonised children, but rapid molecular methods would have been required to to prevent infections in these patients.

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EVALUATING PCR FOR DETECTION OF MRSA FROM NASAL SWABS IN A PAEDIATRIC ICU

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Background and aim: To evaluate PCR for detection of MRSA in paediatric ICU patients.

Methods: A pair of nasal swabs was collected at the time of admission. The first swab was used for PCR (GeneXpert, Cepheid). The second swab was cultured using MRSA selective medium and enrichment broth. The accuracy of PCR was determined by comparing PCR results with direct and enrichment culture or any other clinical specimen growing MRSA at the same time. PCR was also used to investigate contacts of a hospital acquired MRSA case.

Results: Over a 15-week-period, 286 nasal swabs were processed from 249 patients. Ten out of 249 patients (4%) were MRSA positive by culture. Fifteen of 286 swabs were found to be positive by either PCR or culture. The sensitivity, specificity, PPV, NPV and accuracy of PCR when compared with culture results of nasal or other clinical specimens was 91%, 98.5%, 71.4%, 99.6% and 98.3%, respectively. We reviewed four PCR positive and culture negative cases. Two were admitted to PICU from home with no known risk factors for MRSA. The other two were long-term in-patients who were found to be positive when investigating a hospital acquired culture confirmed MRSA case on the unit.

Conclusion: Our preliminary data suggest that PCR may be more sensitive than culture. Further work is required to fully evaluate the usefulness of PCR as a rapid and specific detection method for MRSA in PICU setting.

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OUTBREAK OF *ENTEROBACTER CLOACAE* ISOLATES OVERPRODUCING AMPC B-LACTAMASE IN A NEONATAL INTENSIVE CARE UNIT

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E. cloacae is a growing problem in Neonatal Intensive Care Unit (NICU). Indeed, many outbreaks by cross-transmission via health-care workers and material have been reported. Here we report the investigation of an outbreak of *E. cloacae* isolates overproducing AmpC b-lactamase (ECOAC) in a NICU in a French teaching hospital.

At the end of October, 4 ECOAC strains were isolated from three 3-weeks old babies (twins sisters and a boy), 3 from anus and 1 from bronchial aspirate. Another *E. cloacae* strain was isolated from the twin mother's milk but this strain did not overproduced the AmpC b-lactamase. All these five strains were analyzed by pulsed-field gel electrophoresis (PFGE) and belonged to a same pattern, suggesting that a same clone has spread in the NICU. The twins were treated by antibiotics (amoxicillin, cefotaxime and gentamicin) since their birth. We thus suggest that this treatment has selected the mutant ECOAC from the susceptible milk strain. The ECOAC strain could have been transferred to the boy by hands or environment. Two weeks later, a fourth case was detected in the NICU, an ECOAC strain being isolated from an anus sample from a girl at birth. Surface and material samples were carried out in the unit. ECOAC was found on a glove box and on the thermometer used for the fourth case. The PFGE analysis of the last strain showed that it belonged to the same clone.

We concluded to a contamination involving mother's milk, use of antibiotics and care practices.

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DEVELOPING A PAEDIATRIC DEFINED DAILY DOSE (DDD) METHODOLOGY TO ALLOW COMPARISON OF ANTIBIOTIC EXPOSURE BETWEEN EUROPEAN COUNTRIES

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Background and aims: At a European level DDD is used for adult antimicrobial comparative data, but there are few prospective studies in children. Aim of this pilot study was to evaluate the daily dose variability for the antibiotics prescribed in both paediatric wards and Neonatal Intensive Care Unit (NICU) of a large hospital in London.

Methods: In a 5 day prospective observational study, 73 children were exposed to 19 antibiotics in a 154 prescriptions. The data shown is for the three main drugs prescribed: amoxicillin+clavulanate (24 prescriptions/21 patients, only paediatric wards), benzylpenicillin (21 prescriptions/18 patients, both paediatric wards and NICU) and amikacin (18 prescriptions/18 patients, only NICU).

Results: The mean amoxicillin+clavulanate oral daily dose was 896.6 mg (220 - 1875 mg), and the mean intravenous dose was 1711 mg (525 - 4000 mg). The mean iv benzylpenicillin daily dose for paediatric wards was 2155.4 mg (174 - 5300 mg), while in NICU it was 414 mg (178 - 1000 mg). For intravenous amikacin, the mean total daily dose was 30 mg (7.8 - 60 mg). The adults WHO DDDs are respectively 1 g for oral and 3 g for parenteral amoxicillin+clavulanate, 3.6 g for parenteral benzylpenicillin and 1 g for parenteral amikacin.

Conclusions: There are difficulties with the current adult based DDD system to analyze paediatric antimicrobial consumption because of the wide dose variability and the weight and age dependence of paediatric daily doses. A proposed new method is discussed to compare antimicrobial exposure between paediatric units in Europe.

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NOSOCOMIAL INFECTIONS IN HIGH-RISK NEWBORNS

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Background and aims: Nosocomial infections (NI) result in considerable mortality and morbility. Newborns in neonatal intensive care units (NICU) are at high risk due to their immature immune system and the need for invasive procedures and treatment.

We evaluated the frequency, characteristics and risk factors for NI in a NICU of a tertiary care hospital, using data from our National NICU nosocomial infection surveillance system. We used German NEO-KISS protocol definition of NI.

Results: We included 408 newborns admitted from January to December 2008, corresponding to 5819 days of stay. Average birth weight (BW) was 2433g (6,6% with BW< 1000g) and average gestational-age was 35 weeks (range:24-41 weeks).

A total of 31 NI were diagnosed in 23 newborns, corresponding to 5,3 NI per 1000 patient-days. Newborns with BW< 1000g were most affected (11,2NI/1000patient-days). The most frequent location was septicaemia(80,6%) and coagulase-negative *Staphylococci* were the most commonly isolated pathogens(47%) followed by *Enterobacteriaceae*(31,5%).

Invasive-ventilation utilization ratios for all BW groups were below percentile(p)10 according to NNIS system-report 2004 (0,21 days-of-invasive-ventilation/days-of-stay in BW< 1000g). The central-venous-catheter utilization ratio was below p50 for BW< 1000g (0,39 catheter-days/1000 days-of-stay), but in P75-90 in other BW groups.

Conclusions: The epidemiology of NI is characteristic of a NICU. NI rates are acceptable and similar to national rates. Greatly contributing to this were the institution of proper hand-washing-policies, compliance with catheter care guidelines and low invasive-ventilation rates in our unit. It is important to reduce central venous catheters indwelling times especially in higher BW group newborns.

P350

EUROPEAN GUIDANCE ON EXCLUSION OF CHILDREN WITH COMMUNICABLE DISEASES FROM SCHOOLS AND DAY CARE CENTRES: AN EVIDENCE-BASED APPROACH

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Background and aims: International recommendations on exclusion from schools for communicable diseases vary widely and are often not evidence based. A new collaborative project was set up, funded by the European Centre for Disease Prevention and Control (ECDC) which aimed to update previously published evidence-based guidelines (Richardson *et al* ,2001), and to make recommendations which would be applicable to the whole of Europe.

Methods: The following primary parameters were studied for 39 communicable diseases: mode of transmission, incubation period, risk of transmission, period of infectivity, duration of shedding and serial interval. For each of these variables, the best available evidence was obtained by systematic searches of the medical literature . The evidence was critically reviewed and categorised into high, moderate or low quality and was then peer reviewed by experts. A UK steering group and a European expert panel considered the evidence as well as other relevant factors including public health importance of the disease and effectiveness of exclusion. Consensus recommendations were made for each disease which were categorised into 'strong' or 'weak'.

Results: High quality evidence was not available for many of the diseases.The final guidance for 39 diseases was presented to the ECDC scientific advisory forum. European consensus was achieved on all diseases except typhoid fever and will be presented.

Conclusion: The best available evidence for the relevant epidemiologic parameters of 39 communicable diseases was collected and European guidance for school exclusion policies were produced based on the same.

P351

MANAGEMENT OF A CRYPTOSPORIDIOSIS OUTBREAK IN A DAY-CARE CENTER

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Background and aims: *Cryptosporidium* outbreaks in day cares centres (DCC) are commonly occurring. Controlling spread of infection in these settings is difficult however and data about effectiveness of different control strategies are sparse.

In this study, a cryptosporidium outbreak in a large DCC is described with evaluation of hygienic and therapeutic interventions.

Methods and results: In a 3 week period in a 130 - children DCC located in Brussels, 43 developed enteric symptoms. From 120/130 children stools were examined for microbial pathogens, with in 34/120 *Cryptosporidium* oocysts being diagnosed. Twenty eight of them were symptomatic (82%), 6 asymptomatic. Strict hygienic measurements were installed in the first week after the start of outbreak. After 4 weeks, 27/34 children (79%) were still symptomatic and cryptosporidium positive. Because of fear of further spread of infection and symptomatology, all 27 children were treated with paromomycin. Two weeks afterwards, 6 weeks after the start of outbreak, 18/27 children were asymptomatic and negative for cryptosporidium. The remaining 9 children, still symptomatic and cryptosporidium positive were treated with nitazoxanide. Three weeks afterwards, week 9 after the start of outbreak, all 34 children involved in the outbreak were asymptomatic and cryptosporidium negative. No other children developed cryptosporidiosis after the three weeks after start of the outbreak.

Conclusion: Our study underscores the need to exclude *Cryptosporidium* aetiology in cases of diarrhoeal outbreak in a DCC. Regarding to our results, direct instalment of specific hygienic measurements most likely halted spread of infection, possibly with some additional effect of specific treatment.

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8 CASES OF PAEDIATRIC TB IN ONE FAMILY FOLLOWING AN ADULT PULMONARY TB DIAGNOSIS- THE IMPORTANCE OF TIMELY CONTACT TRACING

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Case history: 10 children from 2 related Somalian families presented to TB clinic in September 2008. Their maternal Aunt had been diagnosed with smear positive pulmonary TB in June 2008. In the preceding months, she had lived with her two sisters, sometimes sharing a room with their children. Three months following her diagnosis, her 15 year old niece presented with respiratory symptoms and a diagnosis of culture positive TB was made. Subsequent contact tracing of her siblings and cousins revealed that all had enlarged TST responses (>15mm). 8 children were commenced on 6 months treatment for active TB, including 4 year old twins. 2 were treated for Latent TB infection.

Discussion: It is well recognised that children contract TB infection from household contacts. They are more susceptible to TB infection and more likely to develop primary and disseminated TB/TB meningitis than adults. Diagnosis is also a challenge due to the paucibacillary nature of paediatric TB. Early diagnosis and immediate initiation of treatment are essential for an effective TB control program, but even more important in the paediatric population. Becerra described the TB prevalence detected through combined active and passive case finding was 0.91%, much higher than with passive case finding alone (0.18%). 21% of TB cases in London occur in Somalian patients. This case series highlights the importance of early, effective contact tracing following adult TB diagnosis. This is more difficult with mobile large families, and with a language barrier. These issues need to be addressed for effective case finding.

NEONATAL INFECTIONS

P353

IL-6-174, IL-10-1082 GENETIC POLYMORPHISMS AND OUTCOME OF FULL-TERM NEONATES WITH BLOOD STREAM INFECTIONS

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Background: Genetically determined variation in the magnitude of inflammatory response may play a role in determining the risk of developing neonatal sepsis, as well as its outcome.

Objective: To test the hypothesis that IL-6 -174, IL-10 -1082 genetic polymorphisms are associated with the risk of sepsis and clinical outcomes in full-term neonates with blood stream infections.

Methods: A total of 54 full-term neonates with blood stream infections and 70 matched controls were included in this case/control study. DNA amplification using PCR with sequence- specific primers was done for detection of promotor single nucleotide polymorphism of IL-6 -174 G/C, IL-10 -1082 G/A genes in blood samples from all infants enrolled in the study.

Results: The IL-6 -174 and IL-10-1082 genotypes were not significantly different in neonates with blood stream infections compared to controls. Whereas; IL-6-174CC and IL-10-1082GG genotypes were associated with increased risk for mortality [Odds ratio (95% confidence intervals): 6.17 (1.34-28.41), p= 0.02 and 12.19 (0.26-228.34), p=0.01, respectively]. Moreover, IL-6 174CC and IL-10-1082GG genotypes were significantly higher in neonates who required inotropic support and those who developed disseminated intravascular coagulopathy.

Conclusion: The IL-6 -174 CC and IL-10 -1082 GG genotypes were associated with increased risk for mortality, need for inotropic support and development of disseminated intravascular coagulopathy in full-term neonates with blood stream infections. These findings suggest that the genetic composition of the IL-6 and IL-10 promoter areas play a significant role in the pathogenesis of neonatal sepsis.

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PROCALCITONIN AS A USEFUL MARKER FOR DIAGNOSING OF NEONATAL SEPSIS

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Neonatal sepsis cause significant neonatal mortality and morbidity in spite of appropriate antibiotic therapy. Therefore Early diagnosis of neonatal sepsis is essential for the successful treatment . Blood culture is a gold standard but the final result is not available until up to 48-72 hours after collection. Since Procalcitonin concentration is raised in the serum of patients with infection diseases, we attempt to measurment procalcitonin as an early marker of neonatal sepsis.

Methods: Blood samples were collected at admission from 69 neonates with suspected sepsis. Patients were included in 2 different groups according to bacteriological and laboratory results: Group 1 consisted of 20 newborns with positive blood cultures . Group II, 49 neonates with negative blood cultures but had two or three of clinical signs of sepsis. The control group (group 3) included 18 healthy neonates with no clinical and biological data of sepsis.PCT measured by Immunoluminometric assay.

Results: Mean levels of PCT were 5.7 ng/ml in proved sepsis group which was higher than those other two groups (P value< 0.05). Sensitivity, specificity and negative predictive value of PCT were 70% and 80% and 75% respectively.

Discussion: Procalcitonin is a useful additional tool for the diagnosis of bacterial disease in neonates and children.

Keywords: Procalcitonin, C Reactive Protein, Neonatal sepsis.

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AN 11 YEAR STUDY OF CAUSES OF NEONATAL BACTERIAL MENINGITIS IN EMAM KHOMAINI HOSPITAL IN AHVAZ, IRAN (1997- 2007)

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Introduction: Bacterial meningitis is a devastating infection with high mortality rate especially in neonates. The aim of this study was to recognize the etiological agents of the bacterial meningitis in Khuzestan province (south west region) of Iran.

Methods: A descriptive cross-sectional study was carried out between 1997 and 2007 at the neonatal ward of A university teaching hospital in Ahvaz, South West region of Iran. All infants less than 29 days who suffered from meningitis were included; laboratory tests included Gram stain and culture. Cases were defined as meningitis if the cerebral spinal fluid (CSF) was positive by aerobic bacterial culture.

Results: Based on cerebrospinal fluid (CSF) cultures, 31 cases were identified as bacterial meningitis, of which 11(35.5%) were *Klebsiella pneumoniae,* 9(29%) *Enterobacter spp*, 3(9.6%) *E.coli*, 3(9.6%) *Entercoccus,* 2(6.4*%) Acinetobacter,* and *Staphylococcus aureus*. *Pseudomonas aeroginosa*, and *nontypeble Haemophilus influenzae* each were seen in one cases (3.2%). The male: female ratio was 2/1 (67.7% / female). Birth weights of 20 (64.5%) cases were under 2500 grand 11(35.4 %) cases had normal birth weight. Considering the type of the infection, 13(42%) were in early onset and 18(58%) in late onset. More than r half of the cases (54.8%) had acquired the infection from hospital. Blood cultures were positive in 18(58%) of the patients. Thirty two percent of cases were died in spite treatment.

Conclusion: The *Klebsiella* and *Enterobacter* were two main etiological agents of neonatal bacterial meningitis, and nosocomial meningitis was the most common type.

Keywords: Enterobacter, Klebsiella, Newborn, Nosocomial meningitis.

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TREAT OR NOT TO TREAT (CONGENITAL CYTOMEGALOVIRUS INFECTION) CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Cytomegalovirus is a ubiquitous virus that commonly infects people across the spectrum of all ages, races, and ethnic groups, and those from a variety of socioeconomic, cultural, and geographic backgrounds. Although most CMV infections are asymptomatic or cause mild disease, the virus can cause serious disease in newborns and immunocompromised children. All treated infants reported in literature presented with symptomatic CMV infection and only one RCT showed clinically meaningful beneficial effect of ganciclovir on hearing deterioration. Potential harms include haematological abnormalities, central line related problems and animal experiments with high doses of ganciclovir showed that short term exposure Induces testicular damage, affect sperm variables and may have carcinogenic effects.

Case: We report a case of neonatal CMV, a premature infant born with emergency C/S for fetal distress and in poor condition at birth, head US scan on D1 showed intracranial calcification, full septic screen done on D1, CSF protein was1.8gm/d, CXR showed right sided consolidation and was shown to have positive urine, blood and CSF CMV. After consultation with infectious disease specialists, she was started on intravenous ganciclovir. The central line problems especially had a major negative impact on the mother's emotional wellbeing. Treatment, alongside the trauma of diagnosis and possible outcomes, has caused considerable distress to all the family.The dilemma is, taking into consideration all factors, do you treat or not?

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UNUSUAL ORGANISMS IN NEONATAL CONJUNCTIVITIS: LESSONS FROM A CASE SERIES

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Background and aims: Infection with unusual organisms can complicate the clinical picture in neonatal conjunctivitis and might lead to treatment failure. We aimed to identify the prevalence of these organisms in a large geographical area in the United Kingdom (UK) and discuss the management issues raised.

Methods: A large case series on neonatal conjunctivitis previously reported from the UK was reanalysed for unusual or uncommon organisms. For the purpose of this study 'uncommon' was defined as organisms accounting for less than 1 in 100 of all positive eye swabs.

Results: Of 255 positive swabs in a five year period, the following organisms were identified as 'uncommon': Serratia marcescens, Acinetobacter, Morganella morgagni, Neissiria meningitidis and Haemophilus parainfluenzae. The clinical and microbiologic features were reviewed.

Although the baby who grew Serratia made an uneventful recovery, infection control measures were considered in view of the risk of nosocomial spread. Acinetobacter although known to be a commensal, has occasionally caused serious infections. Morganella species has never been reported before as a cause of neonatal conjunctivitis although it has been implicated in sepsis. Neisseria meningitidis was associated with carriage in nose and throat. This necessitated systemic therapy for decolonisation and prophylaxis for all contacts including all staff. Interestingly, all the organisms were sensitive to chloramphenicol.

Conclusions: All the 'uncommon' organisms were gram negative species. They posed interesting management dilemmas. Chloramphenicol proved to be effective against all the isolates. Clinicians encountering unusual organisms should consider the wider implications and seek specialist advice.

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NEONATAL SEPSIS WITH UNUSUAL PATHOGENS IN THE NEONATAL UNIT AT NORTH MIDDLESEX HOSPITAL IN THE YEAR 2008

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Background and aims: With the widespread use of antibiotics in neonatal units there has been an emergence of unusual and resistant organisms. Our aim was to analyse the factors associated with infection with unusual organisms.

Methods:

- Retrospective analysis of all positive blood cultures in year 2008 in the neonatal unit at the North Middlesex Hospital
- List of all positive blood cultures was obtained from the Microbiology department.
- Case notes for the neonates with unusual organisms were reviewed to gather information regarding the factors associated with infection with unusual organisms.

Results: 36 positive blood cultures were obtained.

Most common organism isolated were coagulase negative Staphylococcus. Other organisms included GBS, Micrococcus.

The unusual organisms causing sepsis were:

E. coli gentamicin resistant: 2

MRSA 1

Staph aureus 1

Staph haemolyticus 1

Enterococcus 1

Lactococcus 2

Diptheroids 1

Retrospective analysis of the notes of these 9 babies revealed:

9 out of 9 babies were premature.

6 out of 9 babies were one of twins/triplets

6 out of 9 babies were born by C. section

Mortality was 2 out of 9 babies.

Conclusion: Our study shows that prematurity, prior treatment with antibiotics, invasive procedures and a long stay in the neonatal unit predisposes to infection with unusual organisms.

We recommend hand washing, strict aseptic precautions while carrying out procedures and judicious use of antibiotics.

Further larger studies are needed to study the increased risk of infections with unusual organisms in babies born by C-section and multiple pregnancies.

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IDENTIFICATION OF FACTORS AFFECTING INCIDENCE AND OUTCOME OF CANDIDEMIA IN A NEONATAL INTENSIVE CARE UNIT FOR DEVELOPING PROPHYLAXIS STRATEGIES

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Background: Candidemia is a major cause of morbidity and mortality in premature infants. Epidemiological, clinical and outcome data will help us identify better target sub-populations for antifungal prophylaxis.

Methods: Retrospective chart review of all neonates hospitalized at our neonatal intensive care unit (NICU) between June 1, 2002-December 31 2008 with blood culture positive for Candida spp.

Results: We identified 34 subjects (5.2% of NICU admissions); 21 (61.8%) < 1000g birth weight (BW). Mean day of life at infection was 44.8 days (range 6-145), 73.5% occurring in the first 6 weeks of life. History of gastrointestinal (GI) pathology, including necrotizing enterocolitis (NEC) was present in 17 subjects (50%). Complications included endovasculitis and meningitis (4 and 2 patients respectively). Candida albicans (15) and C parapsilosis (15) were equally represented. There were 5 deaths (3 albicans, 2 parapsilosis), all in < 1000g BW, 4 (80%) of deaths had history of NEC. The average age at time of death was 32 days (median 13; range 6-93days). One patient died within 24 hours of infection, 4 deaths occurred > 7 days from infection (mean 12.25d, median 11.5d). Mortality in infants < 1000g BW that survived >72hours of life, was higher in candidemic patients (5/21; 23.8% Vs 45/377; 11.9%; OR 2.31; CI 0.8057-6.5976).

Conclusion: Candidemia in our NICU occurred most often in the first 6 weeks of life. BW < 1000g and those with history of GI pathology are at higher risk for candidemia and mortality. These groups may be appropriate targets for fungal prophylaxis.

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COMMUNITY-AQUIRIED STAPHYLOCOCCUS AUREUS INFECTION IN PREVIOUSLY HEALTHY NEONATES

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Community-Aquired *S aureus* (CA-*Sa*) resistance are changing in the last ten years inArgentina, increasing methicillin-resistant *S aureus* (MRSA) strains. First case in ourneonatal unit was diagnosed in 2006.

Objectives: Identify clinical features, risk factors, sensibility and outcome of neonate withCA-*Sa* infection.

Material and methods: Prospective observational study . We included previously healthypatients ≤ 30 days of age admitted to the neonatal unit with CA-*Sa* infection from 2006 to2008. We defined CA-*Sa* infection based on CDC guidelines.

Results: We included 7 healthy newborn with CA-*Sa* infection.The labor was vaginal delivery in 6/7 . Mean gestational age 39 weeks, weight 3197grs, and < 3 birth hospital days. Of 7 *S aureus* infections, 4 (57%) were MRSA .Six of 7 were male. Median age at symptoms onset was 11days (r:9-18).All infection involved skin and soft tissue (7/7) with pustulosis, omphalitis, mastitis, chest , facial/neck , and goin abscesses. Invasive manifestations were sepsis, ostheoarticular infection, orbital cellulitis and necrothizing pneumonia. Culture positive were form softt tissue in 6, and 3 from blood cultures. All recived sistemic antibiotics. Three of 4 and 2/ 3 MRSA and MSSA infections respectively required surgical drainage. One patient died because of sepsisMaternal skin/soft tissue infection history occured with 3/ 4 MRSA versus none of MSSA infections.

Conclusion: Epidemiology of CA-*Sa* infection is changing even in the newborn period,with increasing MRSA strains. Male neonates 9-18 days of life were affected more often,Maternal infection has a strong association with MRSA.

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RISK OF SERIOUS BACTERIAL INFECTIONS IN HOSPITALIZED INFANTS ≤3 MONTHS WITH FEVER BY HISTORY ONLY VERSUS DOCUMENTED FEVER

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Objective: To assess the risk of serious bacterial infections (SBI) in hospitalized infants with fever by history only and to compare it to infants with documented fever.

Patients and methods: The study group consisted of all infants ≤3 months hospitalized at our center for fever evaluation from September 2006 to December 2008. Data were collected prospectively regarding the presence of fever during hospitalization and diagnosis of SBI.

Results: A total of 1229 infants met the inclusion criteria, 229 (18.6%) had fever by history only and 1000 (81.4%) had documented fever. SBI was detected in 23 of the 229 infants with fever by history only (10%) (UTI in 20, bacteremia in 1, pneumonia in 1 and enteritis in one) compared to 108 of 1000 infants with documented fever (10.8%) (UTI in 79, urosepsis in 6, bacteremia in 8, bacterial meningitis in 1, pneumonia in 12 and enteritis in two). This difference was not statistically significant (p=0.813).

Conclusion: The risk of SBI in hospitalized infants≤3 months with fever by history only does not differ from infants with documented fever. Thus, we believe similar sepsis evaluation is warranted regardless documentation of fever in this age group.

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PRELIMINARY STUDY OF PRO-VASOACTIVE PEPTIDE FOR EARLY DIAGNOSIS IN SEVERE NEONATAL INFECTION

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The purpose is to assay the concentration of proadrenomedullin (pro-ADM), pro-atrial natriuretic peptide (pro-ANP), pro-endothelin1 (pro-ET) and copeptin in neonates,and explore the correlation between the level of pro-vasoactive peptide and the gestational age, birth weight, age and the severity of infection; the diagnostic efficiency of pro-vasoactive peptide in the neonate with severe infection; the correlation between the level of pro-vasoactive peptide and the severity and the prognosis of the neonates. Three hundred fifty six neonates (169 preterm,187 full-term infants) were divided into three groups: non-infection group (160), mild infection group (114) and severe infection group (82).The severe infection group were subdivided into two groups: critical group and non-critical group. Serum level of pro-ADM, pro-ANP, pro-ET and pro-AVP were determined.

The infection is the independent influencing factor for the variation of the level of pro-ADM, pro-ANP and pro-ET. There were positive correlation between the level of pro-ADM, pro-ANP and pro-ET and the severity of infection ($P< 0.0001$). There was no correlation between the level of copeptin and infection.The pro-ET, pro-ADM and pro-ANP had good diagnostic efficiency for neonatal infection. Among them pro-ADM had highest diagnostic efficiency and the sensitivity and specificity was 82.65% and 61.25% respectively.The positive predictive value and negative predictive value were 68.08% and 77.93%, respectively.The level of pro-ADM in critical patient (2.498±1.140 nmol/L) was significantly higher than that of non-critical patient (1.810±1.162 nmol/L) ($P< 0.05$).The concentration of pro-ANP was significantly higher in non-survivors (1680.93±712.88 pmol/L) than that of survivors (1185.85±767.09 pmol/L) ($P< 0.05$).

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A PROSPECTIVE STUDY OF NOSOCOMIAL INFECTIONS IN A CHINESE NEONATAL INTENSIVE CARE UNIT

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This study aimed to determine the epidemiologic profile of NIs, including rates, main infection sites, common microorganisms and risk factors, in a Chinese NICU.

A prospective study was conducted during 1 year from February 2006 to February 2007 in the NICU at a university hospital. The National Nosocomial Infection Surveillance (NNIS) definitions of Centers for Disease Control and Prevention for NIs were applied with modifications to neonate.

During the study period a total of 1159 patients were admitted, and 135 patients had a total of 169 NIs. The cumulative incidence rate for NIs was 14.58%. The incidence of NIs was 19.52 per 1000 patient-days. Respiratory infection (54.44%), conjunctivitis (21.89%), bloodstream infection (14.20%) and gastrointestinal infection(7.10%) were the most frequent NIs observed.

The ventilator-associated pneumonia (VAP) rate was 29.56 per 1000 mechanical ventilation days. Major microorganisms isolated for VAP were Gram-negative rods, including Acinetobacter species (56.52%) and Klebsiella species (23.91%). Coagulase-negative staphylococci (40%) and Escherichia coli (30%) were the most common organisms isolated for bloodstream infection. The durations of hospitalization for patients with and without infection were 12 and 5 days, respectively ($P < 0.001$). The stepwise logistic regression analysis showed that risk factors associated with NIs was birth-weight less than 1500g, low Apgar score at birth, delayed oral feeding and treatment of ibuprofen.

P364

ROLE FOR EYE PROPHYLAXIS IN NEONATAL CONJUNCTIVITIS

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Background and aims: The effectiveness of prophylaxis for bacterial conjunctivitis is a matter of debate. A study was designed to compare topical oxitetraciclin versus no prophylaxis, followed by a surveillance period.

Methods: In our hospital, a randomized clinical trial was designed, divided in Phase I (08/2006-07/2007) which included all newborn, randomized in two groups: group A with prophylaxis (oxitetraciclin) and group B without. Newborn were controlled up to their 28th day postnatal age. During phase II (02/2008-01/2009), prophylaxis was discontinued, but newborn were still controlled as in phase I. Data was compared after completion of phase I and at the end of phase II.

Results: We included 2181 newborns in phase I. Demographic data, delivery, postconceptional age and infectious risk were without statistical difference between both phase I groups. About 108 developed conjunctivitis, 27 with identifiable germen. In the 108 newborns with conjunctivitis, 51 had done previous eye prophylaxis; from the 81 without identifiable germen 33% had prophylaxis and in the 27 with identified germen 55% had previous prophylaxis. There was no statistical significance in the outcome (conjunctivitis) between phase I groups.During phase II, from a total of 2292 births, 105 newborn were reported with conjunctivitis. A germen was identified in 33: S. aureus (14); E. coli (8); S epidermidis (3); other (8).

Conclusions: In our study, prophylaxis with oxitetraciclin did not prove superior to no prophylaxis in phase I. Phase II surveillance confirmed this assumption.

P365

BIOFILM-FORMING CAPACITY OF *CANDIDA* BLOODSTREAM ISOLATES FROM NEONATES WITH CANDIDEMIA

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Backround: *Candida* species constitute an important nosocomial pathogen in the NICU. Little is known about the capacity of *Candida* species to produce biofilm (BF) in neonates with candidemia. Our aim was to investigate and quantify BF production of bloodstream *Candida* isolates from NICU patients.

Methods: 5x10^5 planktonic cells/mL from each of bloodstream *Candida* isolates were grown in YNB medium. For BF formation, 10^6 cells/mL were grown on silicone disks placed in 96-well plates with RPMI-1640 under shaking. BF production was evaluated by XTT metabolic assay, safranin staining and light microscopy (LM). Documented BF producer isolates were used as positive controls. Isolates that a) showed XTT conversion ≥80% of positive controls, b) stained with safranin and c) produced a microscopically visible fungal network were considered high-BF producers. Isolates with XTT conversion of < 80% were considered non-BF producers, whereas those with conversion ≥80% but inconsistent safranin staining and LM findings were considered low-BF producers.

Results: Among 45 neonates (21 male) with candidemia an equal number of *Candida* strains was isolated; 51% were *Candida albicans*, 29% *Candida parapsilosis*, 4% each *Candida lusitaniae* and *Candida guilliermondii* and 12% other non-albicans *Candida* species. 18/23(78%) of *C.albicans* were BF-producers vs. 9/22(41%) of non-albicans *Candida* isolates ($p < 0.05$). However, while all 9 BF-producing non-albicans *Candida* isolates were high-BF producers, only 11/18(61%) of BF-producing *C.albicans* isolates were high-BF producers ($p=0.059$).

Conclusions: BF-forming capacity is a frequent characteristic among neonatal bloodstream *Candida* isolates, especially *C.albicans*. High-BF production tended to be observed more frequently among non-albicans *Candida* BF-producing isolates.

P366

CLINICAL SPECTRUM OF "NEONATAL" PICORNAVIRUS CNS-INFECTIONS

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Methods: Between July 2001 and October 2008 we treated 23 infants below the age of 3 months, out of these 11 were neonates, who suffered from a clinically severe picornavirus infection not infrequently.

Results: In 13 cases we succeeded to prove the virus by the PCR, 10 times the cell culture was positive (Coxsackievirus N=4; Echovirus N=6, among these twice type 6 and 30 respectively, and once type 13 and type 25 resp.). In 15 cases the agent was found in the CSF, in 8 cases in the throat swab, in the tracheal secretions and / or in the faeces. The infections occurred nearly all over the year with the exception of January and May. Clinically some infants appeared to be **septic**; others were **comatose** with **central respiratory insufficiency**, resembling an **intoxication**. In 3 infants ventilation was necessary. In some cases CSF findings were suggestive of a **bacterial infection** (i.e. leucocytes > 1000/µl and interleukin 6 > 1000 pg/ml).

Conclusions: After detection of the virus by the PCR the antibiotic and antiviral herpes-therapy usually was discontinued, however in single cases double infections were also observed (concomitant bacterial sepsis). Infections with picornavirus are not rare illnesses in neonates and young infants. The proof of the virus allows the diagnosis of **initially unclear illnesses** and mostly also a shortening of the antibiotic therapy. In addition a surveillance is necessary to exclude a poliovirus infection.

P367

PAEDIATRIC GROUP B STREPTOCOCCAL INFECTION IN NORTH COUNTY DUBLIN - A FIVE YEAR RETROSPECTIVE REVIEW

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Background: We undertook a chart review of cases of invasive Group B Streptococcus (GBS) infection, to audit rates of GBS disease, treatment and outcomes.

Methods: Neonates and infants in whom GBS had been isolated from blood culture, and/or cerebrospinal fluid (CSF) were identified from the laboratory computer systems in both hospitals. There were no isolates of GBS from other sterile sites in infants. The clinical notes of each identified infant were reviewed.

Results: 29 patients were identified as having GBS disease during the five years reviewed.

Early onset disease (presenting within the first 7 days of life)

15/29 (51.7%) of cases were early onset disease, EOD rate 0.38/1,000 live births. Blood cultures were positive in all cases. A lumbar puncture performed in all cases; none were positive. All infants received >10 days antibiotic therapy. In 2 cases the mother was a known GBS carrier and prophylactic intrapartum antibiotics had been given. One neonate (26 week gestation) died of GBS sepsis following preterm delivery secondary to GBS chorioamnionitis.

Late onset disease (> 7 days of age)

14/29 (48.2%) of cases were late onset disease (age range 10 days - 7 weeks). 12/14 had positive blood cultures on presentation, 4 also had positive CSF. GBS was isolated from CSF only in 2/14. The 6 infants with meningitis were treated for a minimum of 21 days. All 14 survived.

Conclusions: EOD with GBS remains uncommon. The GBS mortality rate is low.

P368

LISTERIA INFECTION IN AN IRISH OBSTETRIC HOSPITAL - A TWO YEAR REVIEW

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Background: *Listeria monocytogenes* is an uncommon pathogen in the Irish population but can cause serious infections in patients in the extremes of life, pregnancy, and in the immunosuppressed. In our institution an increase in laboratory-diagnosed listeriosis occurred during 2007 and 2008.

Methods: Patients with laboratory confirmed listeriosis were identified from the LIS and their medical records were reviewed.

Results: There were 5 maternal and 1 neonatal infections (c. 17,455 live births/ 2 year period). In 2 cases, IUD occurred prior to presentation and *L. monocytogenes* was isolated from the fetus. Two women had peripartum listeria bacteraemia; the liveborn infant of the 1st woman had fatal congenital listeriosis. Listeria was isolated from the placenta of the 2nd woman; the infant was treated for presumptive listeriosis and recovered fully. The remaining woman presented in the second trimester with flu-like symptoms, and had an uncomplicated course after appropriate treatment. All 5 women were non-Irish born. 4/5 had poor spoken English and reported purchasing food in ethnic shops. None of the patients were aware of food handling/consumption risks during pregnancy. Epidemiological typing revealed four different listeria types. Environmental/ public health investigations did not identify contaminated foodstuff.

Conclusion: All cases of maternal *Listeria monocytogenes* infection occurred in the non-Irish born population and 4 had very poor English. This population are targets for education regarding safe eating in pregnancy. A leaflet highlighting ways of minimising risk during pregnancy has been produced by the Food Safety Authority, and has been translated into several languages.

P369

EVALUATION OF THE XPERT GBS® ASSAY FOR RAPID *PER PARTUM* DETECTION OF GROUP B STREPTOCOCCI

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Background and aims: Early onset neonatal sepsis due to Group B streptococci (GBS) is responsible for severe morbidity and mortality in newborns. In this context, a routine screening is regularly performed between the 35th and the 37th weeks of pregnancy. However, for approximately 17% of pregnant women, GBS carriage status can change until delivery. Real time PCR (Xpert® GBS, Cepheid) was thus evaluated versus current routine assays, optic immuno enzymatic assay (OIA) and culture for pregnant women in *per partum* and babies whom mothers had displayed higher risks of GBS transmission during delivery.

Methods: From 09/01/2008 to 11/30/2008, 286 mothers and 20 babies were enrolled. Vaginal swabs were taken from mothers at the very beginning of the labor while ear, pharyngeal and rectal swabs were taken from newborns. PCR (Xpert® GBS, Cepheid), OIA (Quick pack One StrepB test®, BMD) and culture were thus performed on all samples.

Results: The prevalence of GBS was relatively low, 7,3%, in the 286 pregnant women. OIA was negative for 7,4% of patients while Xpert GBS and culture were positive. Furthermore, negative predictive value (NPV) for Xpert GBS was 98,8%. All babies were screened negative (PCR and culture), however 4 OIA were positive.

Conclusion: Real time PCR allowed an earlier detection of GBS for a 7,4% of the mothers. NPV of PCR can be considered as a relevant parameter with a 98,8%. The cohort of babies is too small for now but displays encouraging results that could be involved in *per partum* monitoring.

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NEONATAL CROSS INFECTION DUE TO *LISTERIA MONOCYTOGENES* - CASE REPORT AND REVIEW OF THE LITERATURE

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This report heightens awareness of Listeria in the UK perinatal population and reinforce the need for universal infection control precautions and isolation of infected cases. It adds to the world literature of nosocomial acquired Listeria in neonates.

The bacterium Listeria monocytogenes is an opportunistic pathogen which most often affects the immunocompromised, the elderly, pregnant woman, the unborn and newborn (McLauchlin 2006). Until the mid 1980s, 34% of all cases in the UK were associated with pregnancy (McLauchlin 1987), however this has now reduced to less that 15% (10-35 cases per year, HPA 2008). Although the infection is predominantly food-borne, other routes of transmission occur, including cross-infection between newborn infants. A series of 10 instances of neonatal cross-infection occurring in the UK between 1967 and 1984 was previously described (McLauchlin et al., 1985). These showed a common pattern of two neonatal cases occurring in the same hospital within a short period of time. The index case was a congenitally infected newborn which resulted in a single late onset secondary case (8-12 days post partum) following a contact shortly after delivery. Since describing this series, we are aware of a further 22 instances in the UK and Ireland reported between 1985 and 2007, together with a further 30 instances reported in the world literature between 1936 and 2003.

The purpose of this paper is to describe an outbreak in England in 2007 and review data from all 62 episodes.

P371

EFFICACY AND SAFETY OF TEICOPLANIN IN SEVERE GRAM- POSITIVE NEONATAL INFECTIONS

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Background: Information on the efficacy and safety of teicoplanin administration in neonatal infections is limited.

Objectives: We present a case series of 4 neonates treated with teicoplanin monotherapy for severe Gram positive infections that were followed up for its safety.

Patients and method: Series of 4 male neonates (mean age 3 weeks) who received teicoplanin as single antibiotic for severe infections due to Staphylococcus aureus.

Results: One neonate had septicemia, two twin brothers had pneumothorax and pleural empyema associated to pneumonia, one cervical abcess. The two twins were 6 weeks old and the other two boys were 3 weeks old.

Mean birth weight was 2,27 kg and mean admission weight was 3,32 kg. Mean WBC count was 10,870 ± 2,830 at initiation of treatment and 7,573 ± 2,010 at its completion. Mean ESR and CRP values at diagnoses were 34,16 ± 3,14mm/h and 10,44 ± 1,93 mg/dl respectively. Mean SGOT and SGPT at diagnoses were 29,5mg/dl and 37,5 mg/dl respectively and 24 mg/dl and 31,16 mg/dl at completion of treatment. Bilirubin levels were in normal range. Renal function was in normal range at the start and end of treatment measured by urea, creatinin and uric acid levels. Blood cultures were positive for Staphylococcus aureus and the boy with cervical abcess was MRSA positive. We administered teicoplanin for 7 days continued with a 14 days course of Ceftriaxone.

Conclusion: Teicoplanin is an efficacious and safe treatment option for neonates with severe Gram positive infections.

P372

CLINICAL PRESENTATION OF GROUP B STREPTOCOCCUS IN NEONATES

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Background and aims: Neonatal Infection is a significant cause of morbidity and mortality. Group B streptococcal (GBS) infection is the commonest cause of early onset (EO) neonatal sepsis. The aim of this study is to describe the clinical presentation of neonates with EO GBS sepsis, diagnosed by a combination of blood culture and PCR.

Methods: Subjects were recruited from two UK neonatal units. Neonates undergoing a septic screen in the first 72 hours of life were eligible and clinical details were collected. Septic screen included blood culture and PCR analysis.

Results: Over 12 months 99 subjects' data were analysed; 37 (37.3%) were < 37 weeks; median gestational age 38 weeks (range 23-43), median birth weight 3.08kg (range 0.575-4.84). 65 (65.7%) presented with ≥1 clinical features consistent with sepsis. 6 (6.1%) subjects had positive blood cultures; 5 (7.7% of babies with clinical sepsis) with GBS (3 culture, 4 PCR). Of the GBS group, 2 presented with fever alone, 1 presented with respiratory distress alone, 1 presented with fever, convulsions, hypoglycaemia, and respiratory distress, and 1 presented with fever, convulsions, and poor feeding. Babies with GBS were more likely to have fever or convulsions than culture/PCR negative babies with clinical sepsis ($p< 0.01$, $p< 0.01$ respectively), but no other clinical differences were apparent.

Conclusions: These preliminary findings suggest that PCR methodology may be of value in determining the cause of EO clinical sepsis and that babies presenting with GBS sepsis may have different clinical features to other babies presenting with clinical sepsis.

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MONOCYTE HLA-DR EXPRESSION AS PREDICTOR OF POOR OUTCOME IN NEONATES WITH SEPSIS

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HLA-DR molecules are expressed on monocytes and reflect the activation state of these cells. Down regulation of HLA-DR expression has been reported in adult sepsis. The aim of this study is, first to evaluate the diagnostic value of monocyte HLA-DR expression for the early diagnosis of neonatal infection and second to investigate the prognostic value of monocyte HLA-DR expression on admission for the final outcome.

Peripheral blood samples were taken from neonates, who were classified into three groups: neonatal sepsis (n=39); noninfective disorder (n=24) and healthy newborn with physiologic hyperbilirubinemia (n=22). Monocyte expression of HLA-DR was determined by flow cytometry and presented as MFI and percentage of cells showing expression of the assessed adhesion molecules.

The percentage of monocytes expressing HLA-DR and the density of HLA-DR, expressed as MFI were lower in neonates with sepsis than those in non-infective disorder and in control groups, but this difference did not achieve statistical significance. Of the 39 septic patients enrolled in the study, 32 survived, while 7 died. The percentage of HLA-DR expressing monocytes was significantly lower in the non-survivor sepsis group (19.2±17.5%) compared with that in survivor sepsis group (47.3+20.6%) ($p< 0.05$). MFI of HLA-DR was also significantly lower in septic non-survived patients than in survived patients (3.3+0.7and 4.5+1.1, respectively, $p< 0.05$). The optimal cutoff value of HLA-DR for predicting mortality was 30% with 85% sensitivity and 81% specificity.

According to our findings, monocyte HLA-DR expression seems to be an early predictive marker for the prognosis of outcome in neonatal sepsis.

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NEONATAL SEPSIS IN NICU. AETIOLOGY AND ANTIMICROBIAL SUSCEPTIBILITIES

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Background and aims: This study aimed at evaluating the incidence and aetiology of nosocomial sepsis (NS) and antimicrobial susceptibilities of causative agents isolated in blood cultures of newborns admitted to our NICU.

Methods: We performed a retrospective chart review of newborns with NS admitted during 2008. Data on gestational age (GA), birth weight (BW), central venous catheter (CVC) usage, hospital stay length, blood proven NS aetiology and its antimicrobial susceptibilities were collected.

Results: During the study period, 336 newborns were admitted. The incidence of NS was 18.7% (n=63). Of these newborns (median GA of 33.1 weeks and median BW of 2015g), 53.9% needed CVC. Positive blood cultures (n=134; 7.5% from CVC) were evaluated and the most commonly isolated micro-organisms were coagulase-negative staphylococci(74.6%), Klebsiella pneumoniae(9.5%), Acinetobacter(7.9%), Candida spp(7.8%), Enterobacter cloacae(3.1%), Pseudomonas aeroginosa(3.1%), Klebsiella oxytoca(1.5%), Enterococcus faecalis(1.5%) and Staphylococcus aureus(1.5%). All gram-positive micro-organisms were sensitive to vancomycin. Gram-negatives had no resistance to polymyxin and medium resistance to b-lactams, quinolones and aminoglycosides. The length of hospital stay was 18.2±13.03 days. Nine newborns died from gram-negatives -44.4% Klebsiella pneumoniae, 22.2% Acinetobacter and Enterobacter cloacae and 11.2% Pseudomonas aeroginosa-.

Conclusions: The incidence of NS in our NICU was not very high, considering the severity of comorbidities of the newborns admitted. The majority of causative agents identified are common skin and fluids contaminants, though a continuous effort in aseptic manoeuvres must be emphasized. The knowledge of the microbial spectrum and its resistance pattern in each centre plays the most important role in the establishment of therapy.

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CLINICAL CHARACTERISTICS OF ROTAVIRAL ACUTE GASTROENTERITIS IN NEONATAL CARE UNIT IN SINGLE CENTER

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Background and aims: About one third of neonates in neonatal unit who are transferred from the regional OB clinics and the private facilities where mother and her baby are stayed for a while. We had experienced a lot of neonates with acquired infections that presumed to be affected neonates from these facilities. This study was to know the differences between out-born and in-born rota viral gastroenteritis in the neonatal ward.

Methods: Total of 1,530 neonates who were hospitalized at our neonatal care unit from June to August 2008. Group I is out-born, admitted to neonatal unit with positive rotaviral tests. Group II is in-born who were previously negative for rotaviral antigen test and developed positive results later, and then sharing their hospital periods with Group I neonates.

Results: Among 1,530 neonates, 535 out-born admitted, and 62 out of 535 (11.6%) were positive for rotaviral antigen test (Group I). Of 995 neonates, 87 (8.7%) developed positive test while staying in neonatal unit (Group II).

There was no seasonal difference in out-born. However, the incidence of acquirement infection in Group II was 2.5 times higher from March through May. There were no differences in body weights, geographic regions, and feeding patterns between with or without infections in in-born.

Conclusions: We found that our neonatal unit and the isolation room have locative, structural and functional problems in controlling infections. Further studies on these points and the epidemiologic characteristics, and some efforts to control out-born including transferred-in patients with asymptomatic infections are needed.

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TRANSIENT OCULOMOTOR NERVE PALSY AS A COMPLICATION OF LATE ONSET NEONATAL GROUP B STREPTOCOCCAL MENINGITIS

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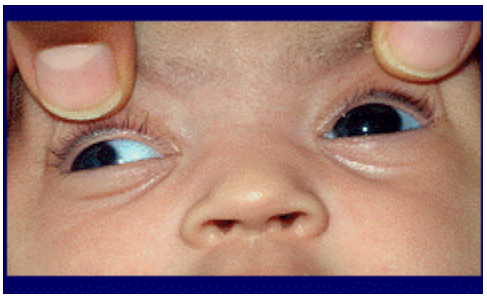
A 3 week-old female term infant presented with 3 days history of fever and poor feeding. Lumbar puncture confirmed Group B Streptococcus (GBS) meningitis. On day 8, she developed incomplete R oculomotor nerve palsy and marked thrombocytosis with a platelet count of 1167 $x10^9$ /L. She received 16 days of aspirin and 4 weeks tapering course of prednisolone. The oculomotor nerve palsy completely resolved on day 49.

Paediatric oculomotor nerve palsies are rare lesions and the aetiology in children is much different from adult counterparts which normally caused by diabetes and posterior communicating artery aneurysm. In children, the commonest cause is congenital followed by trauma. Oculomotorl nerve involvement was reported mainly with TB and pneumococcal meningitis. GBS meningitis causing oculomotornerve palsy is extremely rare. Only one case had been reported in literature. The mechanism of transient oculomotor crainal nerve palsy may be related to a vasculitic process or mild cerebral oedema or both. The oculomotor nerve is in close proximity with blood vessels of the circle of willis. Any Inflammation of the blood vessels can impinge on the nerve. There is no conclusive data looking at the effectiveness of steroids or aspirin in the management of cranial nerve palsy associated with meningitis.



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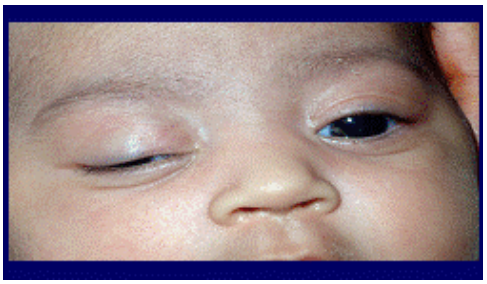

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NOSOCOMIAL INFECTIONS (LATE ONSET SEPSIS) IN THE NEONATAL INTENSIVE CARE UNIT (NICU)

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Background and aims: Neonates admitted to NICU are at high risk of developing nosocomial infections. Ongoing infectious disease surveillance is essential to minimize the occurrence of nosocomial infections. To determine the incidence of nosocomial infections, distribution of pathogens, associated risk factors and outcomes, we evaluated a cohort of 263 neonates who were admitted in NICU between May 2005 to May 2007.

Methods: The SGH neonatal database was tapped into to obtain information on all nosocomial infections that occured during the review period. Detailed data on epidemiology of infections, results of blood and cerebral spinal fluid culture were collected; associated risk factors and outcomes were evaluated.

Results: Out of 255 neonates who were analyzed, 20 infants (7.8%) developed nosocomial infections. The vast majority of infections (85%) were caused by gram positive organisms with coaugulase - negative staphylococci accounting for 55% of infections. Birth weight and gestational age were inversely related to rate of infections (13% of very low birth weight [VLBW] infants versus 4.1% for non-VLBW infants). Among VLBW infants prolonged mechanical ventilation, central line insertion and chest tube insertion were associated with increased rate of late onset sepsis. Neonates with late onset sepsis had a significantly prolonged hospital stay (mean length of stay 85 versus 54; P = 0.001]). The mortality rate for nosocomial sepsis was 5%.

Conclusions: This study documents the high prevalence of nosocomial infections in neonates admitted to NICU particularly VLBW infants. Effective strategies to reduce late onset sepsis needs to be addressed urgently.

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DIAGNOSTIC OF BACTERIAL MENINGITIS IN TERM AND PRETERM NEWBORNS

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Background and aims: Meningitis is a great problem in neonatology, because of its high mortality. In survived patients there is mentioned breaking of physician, motoric, cognitium, social- emotional sphere's development.

Methods: There was open prospective research, agreed with clinical bioethical commission of the hospital. There were studied 77 patients at whom developed meningitis. There were divided 2 groups. In the 1st group there were 50 term newborns, and in the 2nd group -27 preterm newborns. There was stated C-reactive protein(CRP) by latex-agglutination method, Procalcitonin (PCT)-by immunoluminometric method. Diagnostic of meningitis was established by abnormal formula of liquor. Identification of bacteria was made by PCR and by routine culture method. Research was statistically reliable

Results: In the 1st group during meningitis, the level of CRP was increased, but peak was in 36 hours; the level of PCT increased In 3 hours after infection; In the 2nd group during meningitis the level of CRP was normal, the level of PCT increased in 3 hours after infection. The culture of blood and were the same. Bacteriological view was: B Streptococcus-10, Serratia marcesens-12, Pseudomonas auroginosa-9, Proteus mirabilis-8, Klebsiella pneumoniae-12, Escherihia coli-20, Acinetobacter-6.

Conclusion:

1. In term newborns PCT and CRP are reliable diagnostic markers of bacterial meningitis, but PCT is more informative, quick, then CRP.

2. In preterm newborns PCT is reliable diagnostic markers of bacterial meningitis, but CRP is not reliable and informative.

3. Gram-negative bacteria is characterized with tropism towards brain tissue, more then B Streptococcus.

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CONTRIBUTION OF UMBILICAL CORD BLOOD PROCALCITONIN CONCENTRATION TO MATERNO-FETAL INFECTION DIAGNOSIS IN NEONATES

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Background and aims: Bacterial materno-foetal infection is one of the most frequent causes of neonatal morbidity and mortality. Its prognosis is closely related to early diagnosis and treatment. The aim of our work was to evaluate the value of procalcitonin (PCT) dosage in umbilical cord as an early and specific marker of perinatal bacterial sepsis.

Methods: We retrospectively studied serum procalcitonin concentrations in umbilical cord blood in a cohort of newborns with infectious risk factors. According to clinical, biological and bacterial course, three groups (infected, probably infected and non infected) were defined by experts unaware of the value of the PCT.

Results: 2181 patients were included (infected n =2, probably infected n =24 and non infected n=2155). There were 818 preterms and 1363 term newborns. According to the Receiver Operating Characteristic curve, a PCT value of 0.6 ng/ml was considered as a significative cut-off. PCT was positive in 24/26 infected or probably infected patients and in 60/2155 non infected patients. The sensitivity, specificity values were respectively 92% (95% CI: 0.75-0.97) and 97% (95% CI:0.95-0.96). Positive and negative likelihood ratios were respectively 33.15 (95% CI: 25.23-43.56) and 0.07 (95% CI:0.02-0.3), corresponding to positive post-test probability of 26% and negative post test probability of < 0.1%. The results were not different between premature and term newborns.

Conclusions: We demonstrated on a large cohort of newborns that procalcitonin concentration in umbilical cord blood is a discriminant and early marker of materno-fetal infection. The low negative post-test probability should limit unnecessary probabilist antibiotherapy.

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MANAGEMENT OF LOW RISK NEONATE BORN FROM INSUFFICIENTLY TREATED STREPTOCOCCUS B (GBS) POSITIVE MOTHERS

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Early onset GBS infection remains an important threat with high morbidity and mortality rates. In order to avoid treatment delay, the Hygiene High Commission (Recommandations du Conseil Supérieur d'Hygiène Bruxelles, 2003, n° 7721) recommends to perform a limited evaluation (complete blood count and CRP at 12h and 24h of life) on all children born from a GBS positive mother not, or insufficiently, treated during labour. In our service we try to evaluate the burden of this protocol.

From October 1st to December 31st 2008 we had 343 deliveries, with 63 GBS positive mothers and 12 unknown ones. Out of those 75 babies, 38 were not completely treated and 35 underwent a “limited evaluation”. None required antibiotic treatment even if some CRP levels were lightly positive; all babies remained asymptomatic (even the 3 non assessed ones).

We performed skin swabs (33/38 neonate) to estimate the colonization, only 3 babies were positive: 2 mothers were treated with clindamycin due to penicillin allergy and 1 was not treated.

During the same period, we had 1 case of early onset GBS infection (blood culture positive) on a term neonate born from a GBS negative mother.

Most of the insufficiently treated neonates were born at term, after an uneventful pregnancy and spontaneous labour, and none required any special treatment. Isn't a minimum of 2 blood samples in the first 24 hours too extensive? Shouldn't one try to establish some risk factors in order to target the susceptible babies in this low risk cohort?

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PREVENTION OF STREPTOCOCCUS B NEONATAL INFECTION - IMPROVING PROCEDDINGS

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Introduction: Group B streptococcus (GBS) is a leading agent of perinatal infection, being maternal colonization a major risk factor. Since not all obstetricians follow CDC 2002 guidelines, the recommendations are uncompleted followed. The objective of this study was to identify difficulties in guidelines application and promoting better practices.

Methods: During one year we investigated: GBS colonization status of pregnant women at HCD through culture screening of vagina, urine and rectum; antibiotic prophylaxis practice; provenience of obstetricians (Hospital staff or external ones). In the first 4 months (group 1) 482 inquiries were done, accompanied by an individual intervention towards promoting full application of CDC guidelines. Six months later the same inquiries were applied to 462 pregnant women (group 2) without any intervention.

Results: In group 1, rectal exudates were done more often by hospital staff than by outside obstetricians: 70,1% vs 37% ($p< 0,001$).GBS screening in vaginal exudates and urine were done with similar frequency by staff doctors (respectively, 92,1% and 92,5%) and the others (86,2% and 87,0%). Prophylaxis was correctly instituted in 45,3% .

In group 2, there was an improvement in overall screening, particularly in rectal exudates from pregnant women from external obstetricians (52,7% vs 76,6%), ($p< 0,001$). There was a 20% increasing in correctly GBS antibiotic prophylaxis from group 1 to group 2($p< 0,001$).

Conclusion: This study revealed that abnormalities regarding GBS screening and prophylaxis during pregnancy can be ameliorated by specific training directed to this issue. At HCD the overall improvement was 20%.

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SCREENING GROUP B STREPTOCOCCAL DISEASE WITH URINARY ANTIGEN DETECTION

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Background and aims: Group B streptococcus (GBS) is still the leading pathogen causing neonatal infection. The gold standard for its diagnosis remains a positive blood and/or cerebrospinal fluid (CSF) culture.

The aim of this study was to evaluate the sensitivity, specificity, positive and negative predictive values of urinary GBS antigen latex agglutination (LA) test in diagnosing GBS infection.

Methods: GBS infection was defined as clinical evidence of disease in a colonized infant with GBS and/or a positive blood culture. The Slidex® méningite Strepto B was used in detecting urinary GBS antigen.

Results: From 2000 to 2008, 2073 tests were enrolled in this study, almost half of them performed in the last 3 years. They were identified 46 infants with GBS infection, of whom 28 had positive blood cultures. There were 4 positive CSF cultures. The LA test had a sensitivity of 81% and a specificity of 98%. The positive predictive value was 63% (41% if the test took place in the first 24 hours of life and 67% if performed after) and the negative predictive value was 99%.

Conclusions: The low sensitivity of this test makes it inadequate as a screening test, although its high specificity may be of use in infants with clinical evidence of disease and a negative blood culture. A negative result in urinary GBS LA test is also a very useful tool in excluding GBS disease.

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CITROBACTER KOSERI MENINGITIS: A REPORT OF THREE NEONATAL CASES

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Background: Citrobacter species are responsible for sporadic and epidemic clusters of neonatal meningitis and C. koseri is associated with brain abscesses resulting in high rate of neurological sequels. We report 3 term babies admitted within their 2 first weeks of life in our institution.

Clinical cases: Our first patient developed fever at twelve days of life. Meningitis was confirmed and culture yielded C. Koseri. Imaging showed multifocal abnormalities of the white matter with stroke of the left sylvian artery territory. Antibiotherapy using cefotaxime, amikacin and metronidazole was given for 21, 14 and 7 days, respectively. The child developed West syndrome and hemiplegia. The two other patients were diagnosed with C. Koseri meningitis within their first week of life. Patient #2 developed an apneic syndrome. Brain US showed a focal lesion in the left parieto-occipital lobe. He received cefotaxime for 6 weeks. After 6 weeks, he developed hydrocephaly requiring ventriculo-peritoneal shunt. Patient #3 developed seizures rapidly controlled by anticonvulsivant. Brain US showed multifocal lesions with signs of liquefaction. Antibiotherapy including cefotaxime and ciprofloxacin was given for 6 weeks. His neurological outcome is uncertain. Lumbar puncture was controlled after 4 days of treatment in patient #2 and #3 and CSF was sterile.

Conclusion: Our three cases illustrate the severity of C. Koseri meningitis with different types of brain injury. The best choice for antibiotherapy is still undetermined, as well as its influence on the clinical outcome.

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CANDIDA COLONIZATION AT BIRTH IN NEONATAL INTENSIVE CARE UNIT (NICU) PATIENTS: EPIDEMIOLOGY, RISK FACTORS AND OUTCOME

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Background and aims: Candida dermatitis and candidemia due to progression of a preexisting colonization is a major problem in NICU patients. The purpose of this study was to determine risk factors of perinatal Candida colonization and its association with subsequent Candida infections in NICU patients.

Methods: This 10 year retrospective case-control study was conducted in one NICU. Surveillance cultures of the skin and meconium were routinely performed at admission in the NICU. Each case of perinatal Candida colonisation was compared with 3 non-colonized controls. Maternal and neonatal risk factors for perinatal Candida colonization were determined by multivariate analysis.

Results: Thirty-nine out of 3219 (1.2%) NICU patients acquired Candida colonization at birth. The severity of colonization was: skin only (24%), gastrointestinal tract only (45%) and at both sites (31%). Both vaginal delivery (OR 3.54) and degree of prematurity (OR=3.74) were independently associated with Candida colonization at birth ($P < 0.010$). Rates of CI were significantly higher in colonized neonates than in controls; Candida dermatitis (46.2% versus 3.4 %, $P < 0.05$), candidemia (20.5 % vs. 0%, $P < 0.05$). Severity of Candida colonization at birth was an independent risk factor for both Candida dermatitis (OR=8.33, $P < 0.05$) and candidemia (OR=5.9, $P< 0.05$).

Conclusions: After correction for prematurity, vaginal delivery is associated with perinatal Candida colonization and the severity of the latter contributes to nosocomial CI in NICU patients.

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FACTORS PREDICTING FAILURE OF CONVENTIONAL EMPIRICAL ANTIBACTERIAL THERAPY IN EARLY ONSET NEONATAL SEPSIS (EOS)

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Background: About 10-15% of neonates requiring AB treatment for suspected EOS fail on presently recommended regimens of AMP or PEN with gentamicin. We aimed to identify perinatal and neonatal factors predicting failure of empirical AB regimen in neonates with suspected EOS.

Methods: Database including 283 neonates treated in two 3rd level NICUs from August, 2006 to November, 2007 for suspected EOS with AMP or PEN and gentamicin, was analyzed by univariate logistic regression to identify risk factors of treatment failure, defined as need for change of empirical AB regimen within 72 h and/or death within 7 days. To ensure earliest possible recognition of infants at risk factors available by 24 h of age and significant by univariate logistic regression analysis were entered into CART analysis.

Results: 40 neonates fulfilled criteria of treatment failure: 20 required change of AB regimen; 24 died within 7 days. The primary cause of early neonatal death was EOS (13/24). Univariate logistic regression analysis identified a variety of perinatal and neonatal factors to be predictive of treatment failure.

In CART analysis need for vasoactive treatment, abnormal blood glucose level and intolerance of enteral feeds allowed prediction of treatment failure with a sensitivity of 77% and a specificity of 80% at 24 h of age. Addition of CRP, WBC and platelet count did not improve accuracy.

Conclusions: Within the first 24 h of life characteristics reflecting the severity of disease rather than those specific for infection help to identify neonates at risk of empirical AB treatment failure.

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COMPARISON OF AMPICILLIN WITH PENICILLIN IN EMPIRIC THERAPY OF EARLY ONSET SEPSIS (EOS) IN EXTREMELY LOW BIRTH WEIGHT (ELBW) BABIES

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Background: AMP and PEN combinations with GEN are used in empirical treatment of EOS but have never been compared head to head. In a prospective, two center cluster randomized study we compared the clinical effectiveness of AMP and PEN combined with GEN and conducted a subgroup analysis of ELBW neonates.

Methods: Within 16 months all neonates admitted to 3rd level NICUs in the first 72 hours of life needing antibiotic (AB) treatment were included if different regimen had not been administered for more than 24 hours and was not considered necessary on admission. AMP was used in one and PEN in another unit. After recruiting half of pre-calculated sample size AB regimens were switched. Clinical effectiveness was evaluated by composite end-point of need for change of AB regimen within 72 hours and/or 7 day all cause mortality.

Results: All ELBW neonates fulfilled the inclusion criteria. Among AMP (n=36) or PEN (n=39) receiving patients the change of AB regimen (4 vs 3; OR 1.5; 95% CI 0.3-7.2), 7 day mortality (8 vs 14; OR 0.5; 95% CI 0.2-1.4) and composite endpoint (11 vs 16; OR 0.6; 95% CI 0.2-1.6), occurred at similar rates. Bacteriologically proven EOS occurred in 5 subjects in PEN and none in AMP group. NICU mortality of infants born before 26th week of gestation was lower in AMP vs PEN group (6/24 vs 13/21 OR 0.2; 95% CI 0.06-0.7).

Conclusions: In the empiric treatment of EOS in ELBW neonates GEN combined with AMP may be superior to PEN.

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GROUP B STREPTOCOCCAL DISEASE - A RETROSPECTIVE REVIEW IN THE ERA OF MATERNAL SCREENING

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Background: Streptococcus aggalactiae infections are a leading cause of neonatal infection. With the widespread implementation of intrapartum antibiotic prophylaxis, early neonatal disease incidence has decreased dramatically, but late onset has maintained stable.

Objective: To determine the incidence and clinical features of early and late onset Group B Streptococcal (GBS) disease since the introduction of intrapartum antibiotic prophylaxis (IAP).

Methods: Retrospective review of all cases of culture proven GBS at Fernando Fonseca Hospital from 2004 to 2008.

Results: Among 20854 live births, 15 cases of invasive disease were observed (0,71 per 1000 live births). Of the 7 infants with early onset disease, 2 were preterm babies; 3 out of 5 mothers with antenatal screening were GBS colonized. All women undergone vaginal delivery, IAP was not administered (precipitous labor). The diagnoses were sepsis (7), pleural effusion (1) and meningitis (1). One baby died (preterm).

Within the 8 infants with late onset disease, all women had antenatal screening, three tested positive for GBS and no IAP was administered due to planned ceasarian section delivery. Other risk factors for GBS disease were unknown or not found. The diagnoses were sepsis (8), meningitis (5), urosepsis (1). One baby died (meningitis and sepsis).

Conclusions: The incidence of invasive disease was higher then expected. Some early infections were still observed because of negative screening or missed opportunity for prevention. Late GBS disease has increased in our hospital and represented more serious disease. It's important to maintain clinical suspicion of late GBS infection and start early antibiotic treatment.

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MICROBIOLOGICAL SCREENING OF NEONATAL UNIT (NNU) ADMISSIONS

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Background & aims: Admission screening of multiple sites is widely used in NNUs. As well as predicting the causes of early-onset sepsis swabs can identify infection control risks, e.g. MRSA. We reviewed NNU admission screens to investigate types of microorganism, and the sensitivities of different sites.

Methods: Retrospective review of screens from 828 NNU admissions, 01.11.2007 and 31.10.2008. Microorganisms were categorised as of possible (α-haemolytic streptococci, anaerobes) or unequivocal (GBS, S. aureus, Enterobacteriaceae) significance.

Results: 564 were admitted directly from labour ward; 264 were admitted indirectly from another ward/hospital. There were differences in colonisation patterns between direct and indirect admissions. Unequivocally significant microorganisms were isolated more frequently, and from a wider range of sites, in indirect admissions. A deep ear swab alone was a sensitive indicator of colonisation in direct admissions. Only two babies (0.2%) had MRSA: both indirect admissions positive at only one site.

	No. of samples from 564 direct admissions yielding:			No. of samples from 264 indirect admissions yielding:		
Sample type	No significant groth	Microorganisms of possible significance	Microorganisms of unequivocal significance	No significant growth	Microorganisms of possible significance	Microorganisms of unequivocal significance
Ear	470	32	36	194	4	18
Umbilicus	456	25	32	121	1	33
Nose	478	25	30	189	1	39
Gastric aspirate	223	26	22	39	0	3
Other	25	1	3	101	3	11

Conclusions: An ear swab suffices for screening newborns admitted directly to NNU. In older babies triple swabs are required. There was no benefit from gastric aspirates, or swabs from other superficial sites.

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BLOOD CULTURE ISOLATES AND ANTIMICROBIAL SENSITIVITIES FROM 3875 CRITICALLY ILL NEONATES

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Background and aim: The study was undertaken to determine the profile and antibiotic sensitivity patterns from blood cultures of 3875 neonates hospitalized at Dr. Behcet Uz Children's Hospital Izmir, Turkey.

Methods: Over a period of one year (January 2008 to December 2008) 4991 samples of culture from blood, urine, CSF material from 3875 neonates were taken. Among these 3565 blood culture samples were investigated for microbial etiology and the isolates obtained were tested for their susceptibility to the commonly used antibiotics.

Results: Among 4991 samples 15% (706/4991) were culture positive. The positivity of blood culture was 13% (464/3565). Gram positive bacteria were the predominant isolates (89.7%) commonest being coagulase negative staphylococci (77.5 %). Methicilline resistance rate of coagulase negative staphylococci was 78.8%. Gram negative organisms were isolated in 5.8% and candida sps in 4.5%.

Conclusion: Coagulase negative staphylococcus is the most common organism causing neonatal sepsis and there is high degree of resistance to methicilline.

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ACTIVIN-A IS INCREASED DURING NEONATAL INFECTIONS AND HAS AN ANTI-INFLAMMATORY ROLE DURING ACTIVATION OF NEONATAL LEUKOCYTES *IN VITRO*

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Activin-A is a cytokine involved in immune responses and its expression has been associated with inflammatory processes. The aims of our study were to investigate the expression of activin-A in:

a) neonates with nosocomial infection and

b) neonatal monocytes and lymphocytes following stimulation *in vitro*.

Furthermore, we examined the role of activin-A during inflammatory responses mediated by neonatal peripheral blood leukocytes.

Methods: 37 infected neonates were studied: 27 preterm and 10 fullterm. 37 healthy neonates were used as controls. Serum samples were obtained on the 1^{st}, 3^{rd} and 5^{th} days following infection and activin-A levels were measured by ELISA. Purified monocytes and lymphocytes from healthy term neonates were stimulated with LPS and PHA, respectively, and activin-A was measured in supernatants. In identical cultures, cells were stimulated with recombinant activin-A and cytokine levels were measured in supernatants.

Results: Preterm neonates had significantly increased activin-A levels on the 1^{st}, 3^{rd} and 5^{th} days. Neonatal lymphocytes and monocytes produced significantly increased activin-A following stimulation. Activin-A treatment significantly decreased the release of the pro-inflammatory cytokines IL-6, IL-1β and IL-8 from LPS-stimulated monocytes, while it increased anti-inflammatory IL-10. Activin-A significantly decreased IL-8 release by PHA-stimulated lymphocytes.

Conclusion: Activin-A is increased in neonatal serum during nosocomial infection. Lymphocytes and monocytes produce activin-A following stimulation, pointing to these cells as the main source of activin-A in neonatal blood. Activin-A suppresses pro-inflammatory cytokine release, while enhancing the expression of anti-inflammatory ones. Our data reveal an anti-inflammatory role for activin-A critical for prevention of excessive inflammatory responses in neonates.

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MONOZYGOTIC TWINS WITH FATAL ENTEROVIRUS MYOCARDITIS

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Background: We report a twins who presented with a fatal enterovirus myocarditis.

Methods: Retrospective data collection from notes, virology laboratory.

Study and results: Monochorionic diamniotic twins were born at 30+2 weeks gestation by caesarean section because of foetal bradycardia. Mother is 23 yrs old with no antenatal problems.

Twin 1 was born in good condition. She was ventilated on day one for 24 hours. She became unwell on day 11 with pallor, poor perfusion and decreased urine output. ECHO showed severe left ventricular dysfunction and ECG showed ST segment changes. Troponin 1 levels were raised. She was commenced on ventilation, antibiotics, inotropes . Repeat ECHO showed dilated hypokinetic left ventricle and dilated left atrium. Her condition deteriorated leading to shock, lactic acidosis and she died. Enterovirus and echo type 22 virus DNA was detected in serum by PCR.

On post mortem study, macroscopically left ventricular wall was thin and mottled in colour. Histology showed myocardial fibre necrosis, inflammatory infiltrate.

Twin 2 was ventilated soon after birth for 2 days for RDS of prematurity. On day 5 of life, she became unwell, pale, mottled. She progressed to develop recurrent apnoeas, deranged clotting, pulmonary haemorrhage and hypotension. She was supported on HFOV and inhaled nitric oxide, inotropes, antibiotics and blood products. Echocardiogram showed poor LV function. Her condition deteriorated and intensive care was withdrawn on day 9.

Post-mortem report was similar to twin's findings.

Conclusions: Our case report highlights perinatal enterovirus can affect twins and can be fatal.

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PREVENTIVE STRATEGY FOR GROUP B STREPTOCOCCAL EARLY-ONSET DISEASE: EFFECT ON NEONATAL OUTCOME IN AN ITALIAN COUNTRY

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Background and aims: In the USA the rate of early onset disease (EOD) by Group B Streptococcus (GBS) decreased markedly after use of CDC's guidelines and of antibiotic prophylaxis (IAP).The best strategy in our countries is still a matter of debate because data about GBS maternal colonization and GBS-EOD are lacking. Aim of this study was to evaluate the compliance with CDC's guidelines and the effects on neonatal management.

Methods: From 2003 in the Imola Hospital we adopted the revised CDC's 2002 guidelines. In order to improve compliance, we performed a risk factors' checklist added to medical record, filled in and undersigned by obstetricians at the beginning of labour. In asymptomatic newborns from mothers with incomplete antibiotic therapy (IIAP), was started if there were risk factors (RF) or neutrophilia and/or C-reactive protein (C-RP) increase (2 evaluations within 24 hours after birth).

Results: From January 2003 to December 2007 we enrolled 5382 consecutive pregnant women and their 5437 live-born children: 4796 rectovaginal screens were performed. The prevalence of GBS vagino-rectal colonized mothers was 18.6%; 74% received complete IAP. 60 out of 224 asymptomatic infants born from mothers with IIAP (27 were preterm) were treated with antibiotic therapy (40 with RF, 20 with C-RP increase). Ampicillin empiric therapy was administered for 36-96 hours, pending cultures and laboratory results. Any GBS-EOD was detected.

Conclusions: We registered good compliance to GBS-EOD prevention policy, but we think that efforts should be made to reduce the inappropriate use of laboratory tests and antibiotics in newborns.

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LIVER ABSCESS IN A NEWBORN LEADING TO PORTAL VEIN THROMBOSIS

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Liver abscess is a rare condition in neonates. Portal vein thrombosis and cavernoma formation are even rarer complications following neonatal liver abscess.

Case report: A 20 day neonate presented with fever and discharge from umbilicus with excessive crying. On examination, he had pus discharging from umbilicus and tender hepatomegaly. Investigations showed leucocytosis with normal liver function tests except hypoalbuminemia. Blood culture was negative. Ultrasound of abdomen showed liver abscess with minimal free fluid in abdomen. CT abdomen showed infective multiloculated right liver abscess. The child was treated with IV antibiotics for 1 month and surgical drainage of abscess was done. However a repeat ultrasound of abdomen after 16 days of treatment showed complete thrombosis of portal vein with cavernous formation and decrease in the size of liver abscess. A follow up ultrasound after 1 month of therapy showed partial canalization of right portal vein and main portal vein with multiple collaterals and splenomegaly suggestive of portal hypertension. The liver abscess had completely resolved. Now the child is 2½ years of age. He does not have any variceal bleed and is otherwise asymptomatic with normal liver function tests but has a splenomegaly with portal collaterals.

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BACTERIAL ETIOLOGY OF EARLY-LATE ONSET NEONATAL SEPSIS AND ANTIBIOTIC SENSITIVITY PATTERNS IN SOUTHERN IRAN

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Objectives: Neonatal sepsis is a major cause of mortality and morbidity especially in developing countries. The aim was to determine the bacterial etiology and antibiotic sensitivity patterns of neonatal sepsis.

Methods: This prospective study was conducted on 208 neonates with clinically suspected sepsis admitted to the neonatal units over a 30-month period, from October 2003 to March 2006, southern Iran, Shiraz. Sepsis was divided into early-onset and late-onset sepsis (EOS&LOS) including both proven (culture positive ± abnormal markers) and suspected (culture negative + abnormal markers). Blood culture was performed using Bactec 9240 system.

Results: Of 208 cases, 90 (43.3%) had neonatal sepsis consisting of 38 (26 proven) presented as EOS and 52 (42 proven) as LOS. In the EOS, *Escherichia coli* (E.coli) was the commonest organism followed by *staphylococcus aureu* (S.aureus) and *klebsiella spp*. As for LOS, *Coagulase negative staphylococci* (CONS) was the most commen organism followed by *Enterococcus spp*, *S.aureus*. The antibiogram on the isolated *E.coli* and *klebsiella spp* revealed a greater combined sensitivity to cefotaxime. Gram-positive pathogens were most sensitive to vancomycin and had a high degree of resistance to ampicillin.

Conclusion: Considering the results of the study, E.coli and CONS were the most common organisms causing EOS and LOS, respectively. Since the sensitivity patterns of these organisms to conventional antibiotic therapy is changed, it seems we need to conduct bacterial etiology and determine antibiotic sensitivity patterns once every few years in order to make the empirical therapy more effective and efficient.

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RECURRENT E.COLI SEPSIS/ MENINGITIS IN NON IDENTICAL TWINS DUE TO MANNOSE BINDING LECTIN (MBL) DEFICIENCY

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Mannose binding lectin (MBL) is a pattern recognition molecule of the innate immune system recognizing carbohydrate structures on the surface of microorganisms. MBL can mediate phagocytosis and activate the complement pathway in an antibody and C1 independent manner.

Circulating MBL concentrations are correlated with genetic variations in the structural and promoter regions of the *MBL-2* gene. MBL deficiency is common, affecting 30% of the population. Severe deficiency (< 400 ng/ml) occurs in about 10% of the population. Individuals, deficient in MBL are more susceptible to infections, particularly in the context of another “immune defect” such as children undergoing chemotherapy or preterm neonates with physiological “transient immunodeficiency” (1).

We present a term twin-1 neonate who suffered from vertical transmitted ampicillin resistant E.coli sepsis/meningitis on day 1 post partum. Antibiotic therapy was administered for 21 days; however 2 more episodes of phenotypically the same strain on day 42 and day 60 post partum occurred. Treatment was reinitiated with good clinical and laboratory response. An anatomic defect and a possible collection as source of infection was ruled out. Immunology studies revealed severe MBL deficiency (100ng/ml). Antibiotic prophylaxis was initiated and no further episodes occurred. Female twin-2, also suffered from ampicillin resistant E.coli sepsis/meningitis on day 1 post partum, corresponding MBL levels were 120ng/ml. There were no further episodes after treatment possibly due to a lower bacterial inoculate.

Screening for MBL deficiency should be considered in neonates with recurrent infections; recombinant MBL may be a useful adjuvant in these patients.

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BIOCHEMICAL MARKERS OF CEREBROSPINAL FLUID AND C-REACTIVE PROTEIN TO EXCLUDE NEONATAL MENINGITIS IN PRETERM NEONATES

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Background and aim: Acute bacterial meningitis (ABM) remains an important cause of morbidity and mortality in neonates and a positive cerebrospinal fluid (CSF) culture is the gold standard for its diagnosis. We aimed to determine if other CSF and/or other blood markers can reliably exclude the presence of ABM in preterm neonates.

Methods: In a retrospective study of 518 neonates, admitted to our tertiary neonatal intensive care unit over a 6-year period, we evaluated data from 249 preterm neonates (gestational age < 34 weeks) who underwent lumbar puncture. We analysed culture (CSF and blood) data to calculate predictive values for white blood cell count, total protein concentration and Gram stain in CSF and C-reactive protein in serum.

Results: ABM was confirmed by culture in 13 of 249 (5.5%) preterm neonates. Positive predictive values of the analysed biochemical markers and gram stain were extremely low, as shown in table 1.

Table 1 Test parameters biochemical markers and gram stain in neonates <34 weeks

Variable	Sensitivity (%)	Specificity (%)	PPV[a] (%)	NPV[b] (%)
White blood cell count in CSF[c]	45.4	77.8	10.0	96.3
Total protein concentration in CSF	90.9	13.5	5.3	96.6
Gram stain in CSF	0	99.6	0	94.8
C-reactive protein in serum	69.2	47.9	7.4	96.3

[a]positive predictive value, [b]negative predictive value, [c]cerebrospinal fluid

[Table 1]

Conclusions: No single biochemical marker can reliably exclude acute bacterial meningitis in preterm neonates.

P397

PCR FOR THE RAPID AND ACCURATE DETECTION OF GROUP B STREPTOCOCCUS IN NEONATAL SEPSIS

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Background and aims: This study aimed to prospectively evaluate PCR as a diagnostic tool in the detection of early onset neonatal Group B Streptococcus (GBS) infection. It was hypothesised that PCR would more frequently detect GBS in neonates than conventional culture techniques.

Methods: Subjects were recruited, with ethical approval, from two UK level 3 neonatal units. All babies undergoing a septic screen in the first 72 hours of life were eligible for inclusion. In addition to routine screening, a deep ear swab was stored in serum tryptone glucose glycerol broth at -20C for PCR analysis. An additional aliquot of blood was stored in a sterile EDTA eppendorph prior to DNA extraction and analysis. Primers targeted the cylB gene, described in our related abstract, which encodes a haemolysin specific to group B streptococcus.

Results: 100 babies were recruited. Four babies had PCR positive blood for GBS; all had overt clinical signs of sepsis, only 2 had positive blood cultures. Fifteen ear swabs were positive for GBS on PCR, but only 5 had positive culture results. All 4 blood PCR positive babies had PCR positive ear swabs.

Conclusions: More babies were identified by PCR to have group B streptococcus in their blood and ear canal than were identified by culture. The sensitivity and specificity of PCR in this setting appears superior to culture based techniques. This molecular approach may limit inappropriate antibiotic use, identify those who should be considered for treatment, and improve our understanding of the true burden of neonatal disease.

P398

ETNICITY IS HIGLY CORRELATED WITH POSTNATALLY ACQUIRED CMV INFECTION IN PRETERM INFANTS ADMITTED TO A NICU IN THE NETHERLANDS

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Background: Breast milk of CMV seropositive women is the most important source of postnatally acquired CMV infection among preterm infants. Ethnicity is an important determinant of CMV seroprevalence in Dutch women; it is higher in non-native mothers.

Aims: To study the incidence of postnatally acquired CMV infection in preterm infants in relation to their feeding and demographic characteristics.

Methods: All preterm infants born < 32 wk treated in our NICU between 1 April 2007 and 1 October 2008 were included. All postnatally infected preterm infants were diagnosed at term by positive CMV RT PCR in urine. Congenital infection was excluded by examination of urine which was collected shortly after birth or Guthrie cards. Differences between the infected and not infected infants were statistically analyzed. Statistical significance was assumed for $p < 0.05$.

Results: In total 202 preterm infants were included. Thirty seven (18%) of these infants were born from non-native Dutch mothers. In 13% (27/202) of infants postnatally acquired CMV infection was diagnosed. Ninety six % of infected infants received breast milk compared to 77% of non-infected infants ($p = 0.024$). Sixteen (59%) of infected infants had a non-native mother. Forty two % (16/38) of infants from non-native mothers became infected compared to 7% (11/164) of infants from native mothers ($p = 0.000$).

Conclusion: The incidence of postnatal CMV infection among preterm infants was 13%. Preterm infants born from non-native Dutch mothers, and fed with breast milk were at higher risk of developing postnatal CMV infection compared to preterm infants from native mothers.

P399

ANTIBIOTIC PROPHYLAXIS DOSE IMPROVES UREAPLASMA AND OXYGEN INDUCED NEONATAL LUNG DISEASE

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Background: Ureaplasma infection increases lung disease in high-risk neonates. Recently we reported: >74% of Ureaplasma in the perinatal period is resistant to erythromycin; a neonatal mouse model of ureaplasma+oxygen induced lung disease; appropriate antibiotic prophylaxis improved survival, morbidity, and decreased lung inflammation in this model.

Aim: In our ureaplasma+oxygen induced lung disease mouse model, determine:

1) if survival due to antibiotic prophylaxis is dose related,

2) the optimum antibiotic prophylaxis dose of several selected,

3) if survival correlates with serum and lung tissue antibiotic levels.

Methods: Littermate FVB mouse pups randomly received intraperitoneal prophylaxis with either 1 of 3 azithromycin schedules or normal saline daily from birth. All pups received: 0.8 inspired oxygen concentration (FiO_2) till 14 days of age (dams rotated every 24 hrs between 0.8-0.21 FiO_2); clinical ureaplasma strain (serotype 14, azithromycin sensitive) subcutaneously daily for first 3 days of life. In pharmacokinetic studies, pups had blood and lung tissue collected one, six and 24 hrs after each dose for azithromycin levels performed by bioassay.

Results: Increasing azithromycin dose improved survival. Survival was: 74% (n=89) with 25 mg/kg/day for 5 days; 60% (n=85) with 12 mg/kg/day for 5 days; 56% (n=89) with 12 mg/kg/day for 3 days; 45% (n=80) with normal saline. All azithromycin treatment groups were significantly better then placebo. Survival correlated with blood and lung tissue levels (R>0.6).

Conclusions: In a neonatal mouse model of ureaplasma+oxygen induced lung disease, azithromycin prophylaxis improves survival directly related to blood and tissue levels.

PNEUMOCOCCAL INFECTIONS

P400

STREPTOCOCCUS PNEUMONIAE BLOOD STREAM INFECTIONS (BSI) IN HOSPITALIZED CHILDREN AFTER BROAD UTILIZATION OF HEPTAVALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV-7)

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Background: PCV-7 has decrease the incidence of S pneumoniae BSI in the US and Europe. Several reports suggest a switch to non-PCV-7 serotypes. The epidemiology, outcome and pattern of resistance of these isolates need to be delineated.

Methods: Retrospective cohort study of all patients with a positive blood culture for S pneumoniae from 1 Jul 05 - 31 Dec 08. Records were reviewed for epidemiological, clinical and microbiologic data.

Results: We identified 58 events in 56 patients (mean age = 4y10m); 59 isolates were recovered; 32(55%) subjects had an underlying medical diagnosis, 23 (39.6%; mean age 5y8m) with immunodeficiency (25 events). Lumbar puncture was done in 18 patients, 6 (10.3%) had meningitis; 21 had pneumonia, 9 with empyema. One patient died. Serotype was available for 41 isolates, 5 were PCV-7; 3 were recovered from patients with immunodeficiency; 16 isolates (39%) were 19A. MIC 50/90 and % sensitive were 0.06/2; 91.2% for penicillin; ≤0.06/> 0.5; 87.7% for erythromycin; ≤0.25/1; 96.5% for ceftriaxone; 0.5/0.5; 100% for vancomycin and 1/1; 100% for levofloxacin. Mean WBC, band count and CRP were 15,814/mm^3, 3,951/mm^3 and 14.47mg/dl respectively. Average length of stay was 8.2 days, 36 patients were discharged to home with oral antibiotics.

Conclusions: Though reports indicate decreased incidence, S pneumoniae BSI in hospitalized children is still a serious infection, more frequently seen now in older subjects with underlying medical diagnoses. Meningitis and pneumonia are common; penicillin resistance is common, ceftriaxone, levofloxacin and vancomycin retain excellent activity. 19A has become the most common serotype.

P401

PNEUMOCOCCUS SEROTYPES COLONIZATION AND VACCINE IN PREGNANCY

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Background and aims: Pneumococcal (Pnc) carriage is associated with pneumococcal diseases. Breast feeding and maternal vaccination may be an useful approach to prevent pneumococcal infection in young infants. This study addresses the risk of Pnc carriage by infants at 6 months of age after pneumococcal polysacharide in pregnant woman.

Methods: We selected 139 pregnant woman and their newborns. Those woman were randomized, to receive 23 valent polysacharide vaccine during the pregnancy (Group V) or to not receive any vaccine or receive the vaccine after the pregnancy (Group NV). Nasopharyngeal swabs were collected from the infants at 3 and 6 months of age.

Results: From the Group V we included 45 cases and Group NV we included 94 cases. From those patients 38 were colonized by Pnc at 3 or 6 months (13 from group V and 25 from group NV). From those strains 34 were serotyped. The most important serotypes were 6B (N=6), 19F (N=6), 11 (N=5) and 15 (N=5). Comparing the groups, the colonization rate was similar 28% in tne group V and 26% in the group NV. There were differences in the serotypes colonizing. The group group V was less colonized than the group NV by serotype 6B and more colonized by serotype 19F ($p < 0.5$).

Conclusions: Young infants (3 months old) are already susceptible to pneumococcal carriage. Vaccination in pregnancy with a polysacharide vaccine did not decreases Pnc colonization rate but decrease colonization of serotype 6 B.

P402

PREVALENCE OF STREPTOCOCCUS PNEUMONIAE NASAL CARRIAGE AMONG CHILDREN WITH COMMUNITY ACQUIRED RESPIRATORY TRACT INFECTIONS

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Background: Nasopharingeal carriage of respiratory pathogens has been considered to be the first step towards development of respiratory diseases as well as invasive diseases associated with bacterial spread.

Objectives: To determine nasal carriage of common pathogens emphasizing on the *Streptococcus pneumoniae* position.

Materials and methods: We conducted a retrospective study consulting the medical files of all children who were recommended nasal swabs over a 10 month period (January - October 2008) at a primary health care clinic in Bucharest.

Results: There were 488 nasal swabs collected from 398 children aged 2 month to 14 years. *Streptococcus pneumoniae* was isolated from 128 nasal swabs - 26.22 % of all the nasal swabs collected. 106 children aged 6 month to 6 years, representing 26.63% of all examined children were identified as *Streptococcus pneumoniae* carriers.

Nasal swabs were collected mainly in children presenting with upper respiratory tract infection - 36.71% of cases, persistent upper respiratory tract infections such as adenoid vegetations and chronic rhinitis - 28.12% of cases, acute otitis media (AOM's) - 8.59% of cases and lower respiratory tract infections such as bronchitis and pneumonia - 8.59% cases.

The sensitivity spectrum of Streptococcus pneumoniae revealed a high pecentage of intermediate sensitivity to penicilins and cephalosporins (70.59-74.8%) and resistance to Azytromycin, Erythromycin and Clindamicin (52.94-82.35%).

Conclusions: This study aimed to prove that an important percentage of toddlers carried *Streptococcus pneumoniae* in the nasopharynx thus justifing further studies on serotypes as well as more efforts to vaccinate children.

P403

EARLY COMPLICATIONS OF PNEUMOCOCCAL PNEUMONIA AND ITS RELATIONSHIP WITH ANTIBIOTIC TREATMENT

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Background and aims: Empirical antibiotic therapy for children hospitalised with moderate o severe pneumococcal pneumonia includes penicillin/ampicillin or cephalosporins as cefuroxime, cefotaxime or ceftriaxone. Data about the outcomes with both regimens are scanty. Our aim was to determine whether the risk of complications with penicillin/ampicillin is greater than with cefuroxime or cefotaxime.

Methods: Retrospective investigation that included hospitalized children, from Jan/2001 to Dec/2008, with pneumococcal pneumonia. The etiology was confirmed by *S. pneumoniae* (SP) isolation or suspected by clinical, hematological and radiological criteria.

Results: 153 patients were included. The median age was 2,9 years. In 20 (13%), SP was isolated (18 from blood, 2 from pleural fluid). *In vitro* susceptibility was obtained (17 MIC ≤ 0,06 mcg/ml, 2 MIC 0,12-1 and 1 MIC ≥ 2). Eighty children (52%) were treated with ampicillin, 58 (38%) with cefuroxime, 11 (7%) with cefotaxime, 4 with other antibiotics. On admission, 31 children (20%) had pleural effusion. After admission, 10 (7%) developed pleural effusion. Two cases (12%) of 17 penicillin-susceptible SP developed pleural effusion after admission. Fifteen (10%) were referred to intensive care. No statistically significant association was found between treatment with ampicillin/penicillin *versus* cefuroxime/cefotaxime and development of pleural effusion, thoracocentesis or being referred to intensive care.

Conclusions: We found no relationship between the antibiotic treatment and the frequency of early complications. Penicillin/ampicillin treatment is not relationed with a worse outcome of hospitalised children and probably remain the drugs of choice for the treatment in areas where the MIC does not exceed 2 mcg/ml.

P404

NON-RESPONSIVE ACUTE OTITIS MEDIA (NR-AOM): PREDICTION OF POST-PCV7 BACTERIOLOGY BASED ON A PROSPECTIVE 5-YEAR PRE-PCV7 STUDY

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Background: Most data on bacteriology of AOM derive from NR-AOM. Recent post-PCV7 data on NR-AOM have suggested replacement disease. We determined the pre-PCV7 era NR-AOM bacteriology as a basis for predicting PCV7-effect in Israel.

Methods: The setting, population and methodology were previously described (Dagan, PIDJ 2008;27:200-6). NR-AOM was defined as AOM occurring during antibiotic treatment.

Results: During 2003-2007, we studied 5728 AOM episodes (3871 culture-positive, 889/3781 NR-AOM with 1074 organisms. The distribution of NR-AOM pathogens and pneumococcal serotypes in relationship to antibiogram is presented in the Table.

	NR-AOM organisms (n=1074) in the pre-PCV7 era							
	M. catarrhalis	*S. pyogenes*	*H. influenzae* (NTHi)		*S. pneumoniae* (Pnc)			
			β-lactamase (+)	β-lactamase (-)	7VT	6A	19A	Others
n	63	33	177	388	237	29	56	91
%	6	3	16	36	22	3	5	9

	Antibiotic-resistance in Pnc serotypes in NR-AOM in the pre-PCV7 era							
	Penicillin-resistant *S. pneumoniae* (PRSP) (MIC ≥ 1.0 µg/ml)					Multidrug-resistant *S. pneumoniae* (MDRSP)		
	7VT	6A	19A	Others		7VT	6A	19A	Others
n	190	25	55	35	n	90	7	15	10
%	62	8	18	12	%	74	6	12	8

[Distribution of NR-AOM pathogens and antibiogram]

PCV7 introduction to the US, resulted in the near-disappearance of 7VT and >50% serotype 6A reduction. Assuming similar effect in Israel and no replacement disease, we predicted that in the post-PCV7 era, the distribution of NR-AOM pathogens will include NTHi, 69%; Pnc, 20%; beta-lactamase-positive isolates, 29%. Serotypes 6A and 19A will constitute 9% and 35%, 12% and 55%; and 11% and 54% of all Pnc, PRSP and MDRSP, respectively.

Conclusion: NTHi and Pnc serotype 19A will be the most important pathogens in NR-AOM in the post PCV7 era, with high antibiotic-resistance rates. This will occur even if replacement does not play an important role.

P405

FIRST TWO YEARS OF EXPERIENCE WITH PNEUMOCOCCAL CONJUGATE VACCINE IMPLEMENTATION IN THE NETHERLANDS

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Background and aims: The 7-valent pneumococcal conjugate vaccine (PCV-7) was implemented in the Dutch national immunization protocol (NIP) in June 2006.

This study aims to assess the impact of PCV-7 vaccination on the incidence and clinical manifestation of invasive pneumococcal disease (IPD) in the Netherlands from June 2004- June 2008.

Methods: Isolates received by the Netherlands Reference Laboratory for Bacterial.

Meningitis were serotyped. Isolates from meningitis cases (all ages) had nationwide coverage and other IPD (all ages) covered 9 sentinel laboratories, representing 25% of the Dutch population. Clinical manifestation and outcome of IPD patients was derived from hospital records.

Results: Among children eligible for vaccination, the number of IPD cases caused by vaccine type pneumococci was reduced by ± 98%. A reduction of 80% was observed for meningitis in children < 2 years of age. However, in this age-group the number of cases of IPD due non-vaccine types increased. Serotypes that had increased in post-vaccination period were 1, 7F, 19A, 33F. None of the 19A strains were penicillin resistant. In other age groups no significant effect of vaccination was observed.

Conclusion: Two years after the introduction of PCV-7 a reduction of vaccine-type IPD was observed in vaccinated cohorts. Increase of cases of IPD due to pneumococci with non-vaccine types among children eligible for vaccination partly abolished the effect of vaccination. Until now no herd-immunity effect has been observed.

P406

PHYSICIAN CLAIMS FOR OTITIS MEDIA AFTER IMPLEMENTATION OF PNEUMOCOCCAL CONJUGATE VACCINE PROGRAM IN THE PROVINCE OF QUEBEC, CANADA

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Background: Pneumococcal conjugate vaccine (PCV) was licensed in 2001, and free vaccination of children aged < 5 years was offered in December 2004, in the province of Quebec. The objective was to describe the monthly frequency of physician claims for otitis media (OM) in relation to PCV-7 coverage during the period 1996-2007.

Methodology: OM claims in the population aged < 10 years was obtained from the provincial health insurance board. Time series in different age-categories were analyzed using structural models with unobserved components, including seasonality, linear trends, level changes and outliers. The explanatory variable was PCV uptake rate in the population aged < 5 years in the Quebec City area.

Results: PCV program implementation was followed by a marked increase in uptake and by the end of 2007, > 90% of children had received ³ 1 dose. Seasonality was a major determinant of OM frequency rates and there were statistically significant downward trends, as well as downward level breaks and outliers. PCV coverage was a significant predictor in children 6 months to 2 years. The effect was of lesser magnitude in the group 2-4 years, and absent in the group 5-9 years. Since PCV licensure, an estimated 100,000 visits were averted in children < 5 years, and OM claim frequency reduction attributable to PCV-7 was 13.2% by the end of the study period.

Conclusion: PCV implementation was associated with a reduction in the frequency of OM in the target population. There was no indication of herd protection in older children.

P407

MODELLING THE IMPACT OF A NEW VACCINE ON PNEUMOCOCCAL AND NON-TYPEABLE HAEMOPHILUS INFLUENZA DISEASES: RESULTS FROM A SIMULATION MODEL

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Background: Currently, two pneumococcal conjugate vaccines are available. PCV-7 is used in many countries. The new PHiD-CV contains three additional S. pneumoniae serotypes and is expected to provide protection against non-typeable H. influenzae infection. A new age-compartmental and steady-state population model was designed to assess the impact of PHiD-CV as compared with PCV-7 using epidemiologic data from the UK.

Methods: Scenarios included 3+1 and 2+1 routine schedules. Vaccination induced direct and herd protection, as well as bacterial replacement. Vaccine effectiveness was estimated from clinical trials and post-marketing studies in the US and Canada for invasive pneumococcal disease, pneumonia, otitis media and ventilation tube insertion. The input of a board of international experts was required for some parameters.

Results: Estimations produced by the model showed that introducing any form of program has a striking impact upon the incidence of all outcomes. It is estimated that the PHiD-CV will have a greater impact than PCV-7 on all forms of health burden analysed, regardless of vaccination schedule although the impact of PHiD-CV will be most noticeable in terms of prevention of otitis media. The main uncertainties in the model are the level of replacement that could partially offset programme benefits, and the relative effectiveness of 3- vs 4-dose schedules.

Conclusions: Modelling the marginal benefits of different vaccines, programme schedules and coverage is increasingly complex. At price-parity per course, the implementation of PHiD-CV was predicted to be cost-saving compared with PCV-7 in the UK.

P408

EFFECTIVENESS OF PNEUMOCOCCAL CONJUGATE VACCINE (PCV) AGAINST INVASIVE PNEUMOCOCCAL DISEASE (IPD): RESULTS OF A CASE-CONTROL STUDY IN QUÉBEC, CANADA

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Background: In Québec, universal immunization with a 3-dose schedule (given at 2, 4, 12 months) of PCV was implemented in 2004. A case-control study on vaccine effectiveness (VE) against IPD was conducted from January 2005 to December 2007.

Methods: IPD cases in children 2m-4y notified to public health authorities and the provincial reference laboratory were identified, and controls were randomly selected in the provincial health insurance registry. Parents were interviewed and immunizations records were reviewed. VE was estimated using logistic regression, weighting for sampling fractions and adjusting for potential confounders. VE in specific age-windows was estimated by an exact method adjusting for age and calendar year only.

Results: Full information was available for 180 cases (60% of 298 notified cases) and 897 controls. Risk factors for IPD included age, season, high risk medical condition, day care attendance and low family income. VE (≥ 1 dose) against vaccine-serotypes was 92% (95% CI: 83% to 96%), 43% (95% CI: -59% to 80%) against 19A and was 60% (95% CI: 38% to 75%) against any IPD. No VE against vaccine-serotypes in children aged 2-4 mo vaccinated with 1 dose could be demonstrated. VE was 99% (92% to 100%) at age 5-12 mo following 2 doses, and was 100% (82% to 100%) following a third booster dose given at ≥ 12 mo.

Conclusion: The recommended 2+1 PCV schedule showed high level of protection against IPD caused by vaccine serotypes, in line with results of previous studies in the US.

P409

PERICARDITIS WITH CARDIAC TAMPONADE DUE TO STREPTOCOCCUS PNEUMONIAE (PNC)

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Background: *S. pneumoniae* is the most common cause of pneumonia in children under the age of 5 years. Pericarditis due to Pnc is a rare but serious complication.

Aim: To describe 3 cases of cardiac tamponade due to Pnc in children and literature review.

Patient and method: Short series of 3 children that had cardiac tamponade due to Pnc.

Results: 3 cases, two girls: 20m, 7m and a 10y old boy. All had: fever, pallor, temperature, shortness of breath, were tachycardic, had hepatomegaly. Chest X-ray shows enlarged heart silhouette, echocardiography pericardial effusion. Analysis of the pericardial fluid of the 20m old girl showed white cell count (WBC) of 72810/ mm3, with 77% segmented cells, total protein 5g/dl, glucose 2mg/dl and LDH 4,752 U/l, Pnc serotype 6A. C-reactive protein was 4.63mg/dl, WBC 16,500 leucocytes, with left shift. The 10y old boy had ESR of 95mm/h, WBC 20,300 71% of granulocytes, pericardial fluid culture was positive for Pnc. Patients was discharged after 10 days of antibiotic treatment. The 7m old girl deteriorated after admission had cardiorespiratory arrest WBC of 37,700/mm3, 47% granulocytes, CRP was 32.3 mg/dl pericardial effusion Pnc serotype 23F. Patient was discharged after 34 days in good conditionSince 1980 fewer than 20 cases of Pnc were described. Only 4 cases were serotyped, 2 cases of serotype 14, 1 case of 6A, 1 of 23F.

Conclusion: Pnc purulent pericarditis in children is a life threatening disease but when treatment is started early its outcome is favorable.

P410

HIGH INCIDENCE OF INVASIVE PNEUMOCOCCAL DISEASE (IPD) IN BARCELONA, SPAIN

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Background and aims: During the last years we have observed a significant increase in the rate of IPD caused by virulent non-PCV7 serotypes in Barcelona, Spain.The aims of this study are to determine the incidence of IPD among children aged < 5 years in our area during 2007 and to analyse the clinical presentation and serotype distribution of IPD.

Methods: Prospective study comprising all children < 5 years with IPD who were admitted to Sant Joan de Deu Hospital in the southern area of Barcelona, between January 2007 and June 2008. IPD was defined as the presence of clinical findings of infection together with isolation or detection of DNA of *S. pneumoniae* in a sterile fluid sample. We collected clinical and microbiological data.

Results: We included 87 patients (50,6% female). The mean age was 2,3 years (SD 1,4 years). The rate of IPD among children aged < 5 years in 2007 was 35,3 cases per 100.000 population taking into account only the diagnosis by culture. The rate increases to 80,2 episodes per 100.000 population if we also consider the Polimerase Chain Reaction. The distibution of clinical presentation was:empyema (50,6%,n:44), pneumonia (16,1%,n:14), meningitis (16,1%,n:14) and bacteriemia (12,6%,n:11). 37 patients(42,5%) had received at least 1 dose of PCV7. We could identify the serotype in 62 cases,54 (87%) of them were non-PCV7 serotypes. 61% of identified serotypes were serotype 1,19A and 3.

Conclusions: The rate of IPD among children aged < 5 years in our area is 80 cases/100.000 population. The main clinical presentation is empyema (50,6%). The non-PCV7 serotypes are responsible for 87% of the IPD cases. The predominant serotypes are 1,19A and 3.

P411

STREPTOCOCCUS PNEUMONIAE GROWTH RATE VARIES BY SEROTYPE IN AN *IN VITRO* ASSAY

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Background and aims: Epidemiological studies suggest that individual pneumococcal serotypes differ in disease causing potential and carriage rates. The aim of this study investigates whether the growth rate of different serotypes explain epidemiological patterns of S. pneumoniae.

Methods: Isolates of S. pneumoniae were obtained via the ongoing invasive pneumococcal surveillance project in the Thames Valley region, UK. Serotypes (n=15 of each) were grown for 24 hours in Brain Heart infusion broth (tryptic soy and Todd-Hewitt broth were done in duplicate). Growth was determined by OD_{600} readings collected hourly using a PowerWave™ Microplate spectrophotometer. Growth curves were analysed using Gen5 software.

Results: Data on 8 serotypes (1, 4, 8, 18C, 19A, 6A, 6B and 7F) were obtained. There was a difference in growth variance between serotypes under the conditions used in these experiments. We found that serotype 1 and 6B show a significantly ($p < 0.01$) lower growth rate whilst serotypes 4 and 19A had a significantly higher growth ($p < 0.001$) rate compared to the medium serotype. The growth variance within each serotype was consistent.

Conclusions: There was growth rate variance between the serotypes. Any correlation between this variance and host-serotype interactions, e.g. disease causing potential, will be investigated. Similarity, growth rate differences in growth rate could impact on the ability of the pneumococcus to compete within the nasopharynx and establish colonisation in vivo. There are implications for determining carriage rates in nasopharyngeal samples that potentially have mixed colonisation.

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PNEUMOCOCCAL NASAL COLONIZATION HAS SYSTEMIC EFFECTS IN INFANTS IN LOW RESOURCE REGIONS

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Background: Many infants are colonized with pneumococcus (Spn) in low resource regions. In a population of low-income families in urban southern India, we prospectively evaluated the acquisition and duration of Spn colonization, and its association with infant growth patterns.

Design/methods: 200 infants were followed from birth to 1 year of age with home visits every 3 weeks. At each visit, infants were weighed, data on interim illnesses were collected, and nasal swabs were obtained for culture of Spn.

Results: The infants were mildly malnourished with declining mean Z values during the first year of life [-1.18 weight-for-age Z-score (WAZ) at enrollment and -1.92 at 12 months], a common pattern in this region. There were an average of 2 Spn colonization episodes per infant. The mean age of first nasal Spn was 8 weeks, and average duration of colonization episodes was 11 weeks. Using duration of Spn colonization data, we classified each infant as short (< 5.6 mo.), medium or long (>7.9 mo.) duration. The measurements of the 51 infants with short duration were substantially greater at 6 mo. and at 1 year for weight [+400gm], and length [+1.2cm], compared to 51 infants with long duration colonization. A multivariable analysis showed independently significant factors in the final weight included initial enrollment WAZ score ($p < 0.0001$), female sex ($p=0.0004$), and duration of colonization ($p=0.03$).

Conclusion: These data suggest a substantial effect of pneumococcal nasal colonization without disease on infant weight and length in this Asian setting, and require elucidation of mechanisms.

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SEROTYPE DISTRIBUTION OF INVASIVE PNEUMOCOCCAL ISOLATES IN SPAIN (SAUCE-4 PROJECT)

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Background and aims: The 7-valent pneumococcal conjugate vaccine was licensed in Spain in June 2001. Initial uptake was low but 2006-2007 estimated coverage was ~ 50-60%. Serotype distribution of Streptococcus pneumoniae associated with invasive pneumococcal disease in children in Spain is presented.

Methods: A prospective, multicenter (34 hospitals) antimicrobial surveillance study was carried out between June-2006 and May-2007. A total of 2,559 pneumococcal isolates from patients with community-acquired respiratory tract infections were collected and forwarded to a central laboratory. Of these, 130 strains were recovered from a normally sterile body site (123 from blood and 17 from pleural fluid) from paediatric patients (< 14 years). Serotyping was performed by the Standard capsular reaction test using the chessboard system and specific sera (Statens Serum Institute, Copenhagen).

Results: The most common serotypes isolated were serotype 1 (11.5%), serotype 7F (8.5%) and serotype 14 (7.7%), followed by 3 and 19A (3.8%, each). The rest of isolates belonged to other different serotypes or were non-typeable or non-capsulated strains. No serotype 5 was identified. Of the serotypes isolated in this study, only 11.6% are included in the currently available 7-valent vaccine. Up to 31.5% of the strains are present in the new GSK 10-valent pneumococcal conjugate vaccine.

Conclusions: The most frequently isolated serotypes (1 and 7F), comprising up to 20% of all cases, are not covered by the 7-valent vaccine. By contrast, both serotypes are included in the new GSK 10-valent vaccine. Continuous surveillance is needed to monitor the effects of vaccine use.

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EFFECT OF A REDUCED DOSE INFANT SCHEDULE OF THE 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7) ON NASOPHARYNGEAL PNEUMOCOCCAL CARRIAGE (NP-PNC-CARR)

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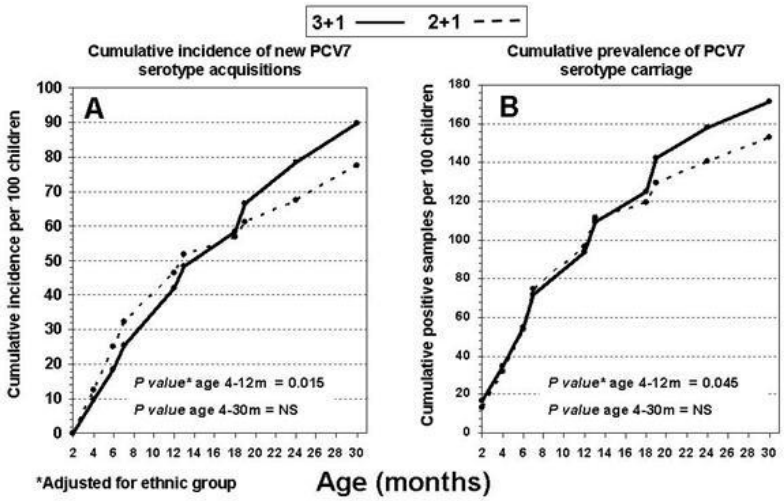
Background: Although PCV7 is licensed in infants for 3 doses + booster (3+1), several countries adopted a reduced 2-dose schedule (2+1). However, the effect of the 2+1 vs. 3+1 on NP-Pnc-CARR was not studied. This study compares NP-Pnc-Carr between 3+1 and 2+1.

Methods: In this open-label study, two groups were randomized: 3+1 (primary 2, 4, 6m [n=353]; booster 12m [n=163]); and 2+1 (primary 4, 6m [n=188]; booster 12m [n=169]). Nasopharyngeal cultures were obtained at 2, 4, 6, 7, 12, 13, 18, 19, 24, 30m (total=3798). Serum serotype-specific IgG ELISA was obtained at 2, 7, 13, 19m.

Results: At 7m, antibody concentrations and % ≥0.35µg/ml were significantly lower in the 2+1 vs. 3+1 groups, mainly for serotypes 6B and 23F; this persisted after booster (age=12m). The prevalence and new acquisitions cumulative incidence of PCV7-serotypes carriage appear in the Figure.



[Cumulative incidence & prevalence, PCV7 serotypes]

After ≥1 PCV7 dose, during 1st year, PCV7-serotype carriage was significantly higher in the 2+1 groups, mainly due to 6B and 6A carriage. However, this was reversed after booster, and thus for the entire period of 4-30m, no significant difference between the groups was observed.

Conclusion: The effect of the 2+1 reduced-dose regimen on NP-Pnc-Carr was similar to that of the 3+1. This suggests that 2+1 PCV7 regimen in national immunization plans may provide extensive indirect protection.

P415

S. PNEUMONIAE IN INVASIVE DISEASE IN CHILDREN IN THE PAST 10 YEARS: EVOLUTION OF RESISTANCE AND CHANGE IN SEROTYPES

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Background and aims: *Streptococcus pneumoniae* (SP) is an important cause of invasive bacterial infection in children. A change in SP serotypes and antibiotic resistance has been observed coinciding with the introduction of heptavalent pneumococcal vaccine.

Methods: Retrospective study in children aged 0 to 16 years with invasive pneumococcal disease (IPD) defined by the isolation of SP from sterile fluids, from 1998 to 2008. We analyzed three study periods: 1998 to 2000 (P1), pre-vaccine period; 2001 to 2006 (P2), with 40% vaccination coverage; and 2006-2007 (P3), with vaccine in the immunization schedule.

Results: We report 155 patients diagnosed with IPD: 44 in P1, 74 in P2 and 36 in P3. A trend to less meningitis and pneumonia and a significant increase in bacteremia was seen between P1 to P3. There was a significant decrease in vaccine serotypes (VS) from P1 to P3 (48% vs 17%), and a significant increase in non-vaccine serotypes (NVS) 5 (0% vs 17%) and 19A (1% vs 28%), with no changes in serotype 1. We observed a decrease in penicillin resistance in P2 vs P1, with further increase in P3 (57% vs 26% vs 36%), probably related to a significant increase in NVS resistance (8% vs 30%).

Conclusions: Our study shows a VS decline and a NVS increase causing IPD. We observed an initial decline in penicillin resistance with further increase, which may be related to a NSV emerging as etiology of IPD. We should continue epidemiological surveillance and evaluate the utility of vaccines with additional serotypes.

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EFFECTIVENESS OF PNEUMOCOCCAL CONJUGATE VACCINATION ON INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN AFTER ITS INTRODUCTION IN THE DANISH CHILDHOOD VACCINATION PROGRAMME

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Objective: On 1 October 2007, the heptavalent pneumococcal conjugate vaccine (PCV7) was introduced in the Danish childhood vaccination program in a 2+1 schedule, plus a two-dose catch-up program for children between 12-17 mo. Before PCV7s' introduction, the estimated serotype coverage was approx. 64% for PCV7 and between 80-90% for PCVs containing 10-13 serotypes. We evaluated the effectiveness of PCV7 on invasive pneumococcal disease (IPD) one year after its introduction.

Methods: Prospective cohort study including nation-wide laboratory surveillance data on IPD and data on PCV7 coverage from the Danish Childhood Vaccination Registry. The effectiveness of PCV7 in children < 5 years was estimated for 2008 based on IPD data from 1 January -31 December 2008. PCV7 coverage was estimated per 1 June 2008.

Results: In 2008, 54 IPD cases were registered vs. an annual average of approx. 90 cases in the pre-PCV7 period. 80% were bacteraemia cases. In children < 2 years the mean incidence declined significantly from 54 to 23 per 100.000 in the pre- and post-PCV7 period ($p < 0.005$). By far, the most prevalent serotype in the post-PCV7 period was 7F, which caused nearly one third of all cases. PCV7 serotype coverage was 37% after PCV7 introduction. PCVs containing 10 and 13 serotypes would cover between 70-80% of all cases in the post-PCV7 period.

Conclusion: After the universal introduction of PCV7 in Denmark we have observed a significant decline in the incidence of IPD in young children. Serotype 7F was the dominant serotype in the post-PCV7 period.

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IMMUNOLOGICAL EVALUATION OF 53 CHILDREN WITH RECURRENT INVASIVE PNEUMOCOCCAL DISEASE

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Background: Recurrent invasive pneumococcal disease (rIPD) is a rare event and often occurs in immunocompromised individuals.

This is a retrospective population-based follow up study of pediatric rIPD in Denmark, where pediatric HIV has a very low prevalence and where routine pneumococcal vaccination was first introduced in 2007.

The immune system of all patients was thoroughly evaluated.

Aim: To study humoral immunity in children with rIPD.

Method: Laboratory confirmed IPD cases in children aged 0-15 in the period jan 1980 to dec 2008 was identified from the National Centre of Reference and Research on Pneumococci, Statens Serum Institut. Recurrent episodes were defined as isolation of Streptococcus Pneumoniae from any normally sterile site ≥ 30 days after initial positive culture or ≤ 30 days if the recurrent infection was with a new pneumococcal serotype.

Clinical data was obtained from hospitals and The National Diagnosis Register.

Children without an apparent underlying condition was followed up by having a bloodsample taken, which was thoroughly analyzed for abnormalities in the immune system.

Results: 2085 children were diagnosed with IPD over the 29 years with 67 recurrent episodes in 53 children.Children in the age 0-5 years accounted for 73% of rIPDcases.

8 patients had a primary immune deficiency (PID), most frequently was Complement2 deficiency. 26 children had an underlying condition where the most frequent cause was transplantation.

Conclusion: In our study ...of the children had a PID.

48% had another underlying condition.

Preliminary results data on all patients will be presented at the conference.

P418

INVASIVE PNEUMOCOCCAL DISEASE - CASE REPORT

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Background: Pneumococcal infections are very important health problem in children causing many outpatient visits and hospitalizations. Invasive pneumococcal disease in children can have severe clinical course and may result in numerous complications and death. It can be prevented by prophylactic vaccinations.

Case report: We present the clinical case of 7 year-old male, healthy before, who was admitted to hospital due to severe abdominal pain and fever of few hours duration He presented in severe distress with dyspnoea, clinical signs and symptoms of pneumonia, tenderness of left epigatrium and middle abdominal area, herpetic lesions on his face. Accessory investigations showed increased levels of inflammatory markers. Streptococcus pneumoniae serotype 10A was found in blood culture. The diagnosis of bacteriemia Streptococcus pneumoniae, lobar pneumonia and skin herpes was made. The patient was treated for 14 days with ceftriaxone and for 5 days with acyclovir intravenously with rapid improvement of his condition.

Conclusions: Pneumococcal disease is found by WHO of highest priority in diseases which can be prevented by vaccinations. Serotype 10A is included in 23-valent pneumoccoccal nonconjugate vaccine, but it is not an ingredient of new conjugate vaccines.

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INVASIVE PNEUMOCOCCAL DISEASE (IPD) IN ENGLAND & WALES AFTER 7-VALENT CONJUGATE VACCINE (PCV7); POTENTIAL IMPACT OF 10 AND 13-VALENT VACCINES

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Background and aims: The introduction of PCV7 in September 2006 reduced vaccine-type IPD in children < 5 years old and other age groups. Surveillance data were analysed to estimate the likely impact of introducing PCV10 and PCV13 vaccines.

Methods: Changes in non-vaccine type IPD incidence age after the introduction of PCV7 were analysed and the QALYs potentially gained from higher valency vaccines estimated, based on one England & Wales birth cohort over 5 years.

Results: From July 2005 to June 2006, 797 cases of IPD in children < 5years of age were reported to the HPA Centre for Infections. This number dropped by 41% to 470 by 2007/8. There was no significant reduction in cases in ≥ 5 years olds (Table). Percentages of IPD caused by serotypes covered by PCV7, PCV10 and PCV13 are shown in the table.

Year	< 5 yrs (n)	< 5 yrs (n)	<5 yrs PCV7	<5 yrs PCV10	<5 yrs PCV13>=	≥ 5 yrs (n)	≥ 5 yrs PCV7	≥ 5 yrs PCV10
2005/2006	797	70%	81%	92%	5514	42%	62%	75%
2007/2008	470	24%	53%	74%	5496	28%	49%	67%

Estimating the reduction in IPD due to the extra serotypes, assuming herd immunity and serotype replacement effects balance and ignoring non IPD disease endpoints, with estimated 90% coverage and 86% vaccine effectiveness, the QALYs gained from the extra serotypes in the higher valency vaccines were 454 for PCV10 and 815 for PCV13.

Conclusions: Of the IPD remaining in England and Wales an extra 29% is potentially preventable in children by switching to PCV10 and an extra 50% by switching to PCV13.

P420

AIR POLLUTION (PM_{10}) IS ASSOCIATED WITH PNEUMOCOCCAL CARRIAGE IN INFANCY. THE GENERATION R STUDY

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Background: Pneumococcal diseases are preceded by asymptomatic colonization of the nasopharynx. Risk factors for pneumococcal carriage are widely studied. It has been shown that concentrated ambient particles cause a functional impairment of the antibacterial capacities of murine macrophages and diminish bacterial clearance in the lungs of mice. In humans the association between air pollution and pneumococcal carriage is not studied. We investigated the association between particulate matter (PM_{10}) and pneumococcal carriage in young children.

Methods: In a prospective population based cohort of 1244 children, pneumococcal carriage was assessed at the age of 14 months. PM_{10} concentrations were measured at a monitoring station situated in the study area. Associations of average PM_{10}, during different periods of time, with pneumococcal carriage were assessed by odds ratios adjusted for gender, educational level of mother, season, temperature and relative humidity (aOR).

Results: An association of PM_{10} exposure in the preceding week with pneumococcal carriage was found (aOR 1.32, 95% CI 1.12-1.52, p< 0.001), representing an increase in risk for pneumococcal carriage of approximately 30% with every 10 $\mu g/m^3$ rise in average PM_{10}. Further analyses showed a significant aOR for pneumococcal carriage at day three and day four prior to carriage assessment of 1.16 (95% CI, 1.04-1.30, p< 0.01) and 1.23*** (95% CI, 1.09-1.40, p< 0.001), respectively.

Conclusion: Our data demonstrate an association between pneumococcal carriage and PM_{10} concentration. Further research is warranted to disclose the underlying mechanisms and the implications for respiratory diseases in children.

P421

INVASIVE PNEUMOCOCCAL DISEASES (IPD) IN CHILDREN IN THE CZECH REPUBLIC: CLINICAL SYNDROMES, SEROTYPES, ANTIBIOTIC SUSCEPTIBILITY AND PRESENCE OF UNDERLYING CONDITIONS

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Background: Vaccination with PCV-7 in the Czech Republic is available for patients at high risk of developing IPD and for private sector. The main objective of this study was to collect data on serotypes, antibiotic susceptibility and to describe clinical syndromes associated with IPD in children before PCV-7 national introduction.

Methods: Retrospective hospital-based clinical and epidemiological study included children hospitalized with IPD in four university centres (Prague and Western-Bohemian Region) in 2000 - 2008. Clinical and microbiological data were obtained from hospital records and databases of laboratories of National Health Institute.

Results: A total of 87 IPD cases (56 boys and 31 girls) with defined serotype were enrolled to the study. The median of age of patients was 3 years. 66 children were younger than 6 years. The commonest clinical manifestation was invasive pneumonia, followed by meningitis. Osteomyelitis and primary peritonitis were also observed. The leading serotype was 1 (13 cases), followed by serotypes 14 (11) and 6B (9). But in children younger than 6 years the most frequent serotypes were 14 (10), 6B (9) and 23F (6) and potential vaccine coverage with PCV7, 10 and 13 was 62%, 73% and 83%. Susceptibility testing according CLSI guidelines showed very good sensitivity to beta-lactams.

Conclusions: Pre-vaccination data on disease severity and outcome of IPD are important to determine the impact of vaccination strategies. Serotypes distribution change with age and geographical location, therefore there is a need for improvement of active surveillance of IPD.

Study was supported by grant IGA-MZCR-NR/8770-3.

P422

THE HUMAN ANTI-PNEUMOCOCCAL CAPSULAR POLYSACCHARIDE IGG ANTIBODY RESPONSE IS GENERATED BY THE CD5(-)CD19(+)B CELL SUBSET

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Background: The delay in antibody formation to capsular polysaccharides (caps-PS) renders children younger than 2 years of age highly susceptible to infections with encapsulated bacteria, such as *Streptococcus pneumoniae*. Children with a persisting defect in the production of antibodies specific for pneumococcal caps-PS after this age have the so-called ´specific antibody deficiency with normal immunoglobulins´ (SPAD). It has been suggested that the predominance of CD5(+)CD19(+)B cells observed in patients with SPAD may in part explain the impaired anti-caps-PS responses (Antall et al. 1999).

The aim of this study was to test whether CD5(-)CD19(+)B cells are involved in the human anti-caps-PS-IgG antibody response.

Methods: Anti-Natural Killer cell treated *SCID/SCID* mice were reconstituted with human peripheral mononuclear cells (PBMC) or PBMC subsets after cell separation. The human anti-caps-PS-IgG antibody response to Pneumo23®, a 23-valent caps-PS vaccine, was measured with ELISA.

Results: Preliminary data revealed that the anti-caps-PS-IgG antibody response (serotype 1, 3 and 4) of HU-SCID mice reconstituted with CD5(-)CD19(+)B cell subset, T cells and monocytes was comparable to the response observed in HU-SCID mice reconstituted with PBMC. On the other hand, HU-SCID mice reconstituted with CD5(+)CD19(+)B cell subset, T cells and monocytes were unable to generate an anti-capsular polysaccharide IgG antibody response after immunization with Pneumo23®.

Conclusion: Our data demonstrate an association between the presence of CD5(-)CD19(+)B cells and the generation of human anti-caps-PS-IgG antibody response to Pneumo23®.

P423

ROLE OF STREPTOCOCCUS PNEUMONIAE CO-INFECTIONS IN CHILDHOOD PULMONARY TUBERCULOSIS (PTB) DETERMINED THROUGH A PNEUMOCOCCAL CONJUGATE VACCINE (PCV)-PROBE STUDY DESIGN

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Introduction: PTB frequently presents with severe respiratory symptoms that resolve following empiric antibiotic therapy for bacterial community-acquired pneumonia (CAP) in African children. Experimental studies suggest *Mycobacterium tuberculosis* (MTB) infection predisposes to *S. pneumoniae* infection, which is difficult to confirm clinically due to diagnostic limitations.

Aim: To probe the role of *S. pneumoniae* co-infection in children with PTB using a vaccine-probe design.

Methods: Retrospective analysis of PTB occurring among 39 836 participants in a phase 3 DBRCT of 9-valent PCV in South Africa. PTB occurring during the 5.3 years of follow-up of the cohort were identified and categorized as definite-PTB (MTB cultured) or probable/possible-PTB (attributed where bacteriological confirmation was lacking but clinical/radiological investigations were suggestive). The incidence of first-episode of PTB was compared between PCV Vaccinees and placebo recipients.

Results: Overall, definite-PTB was 43.7% (95%CI 12.5; 63.7) less likely among Vaccinees (n=31) compared to placebo recipients (n=55; incidence: 2.76 per 1 000 children). Similarly, in HIV+ children, definite-PTB was 47.4% (95%CI 10.1; 69.0) less likely among Vaccinees (N=20) compared to placebo recipients (n=38; incidence: 29.5 per 1 000). HIV-uninfected Vaccinees (n=11) were 35.3% (95%CI -38.1; 69.7) less likely to present with definite-PTB than placebo recipients (n=17; incidence 0.91 per 1 000), P=0.26. The incidence of possible/probable PTB did not differ by vaccination status.

Conclusion: A high proportion of definite-PTB in African children, in settings of high incidence of TB, is associated with pneumococcal infection. African children successfully treated initially for bacterial CAP in such settings should be followed-up for underlying TB.

P424

SURVEILLANCE OF INVASIVE PNEUMOCOCCAL DISEASE IN THE CZECH REPUBLIC

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Background and aims: To better estimate the incidence of invasive pneumococcal disease (IPD) and the distribution of serotypes causing IPD, laboratory surveillance of IPD was established in 2000. Nation wide enhanced surveillance of IPD started in 2008.

Methods: The incidence of IPD in the Czech Republic was analysed using two sources of data: laboratory based data and enhanced surveillance data. An IPD case was defined by the isolation of *S. pneumoniae* from blood, cerebrospinal fluid, or other normally sterile sites. Each isolate was identified by standard methods and *S. pneumoniae* isolates were serotyped by the Quellung reaction using serotype specific antisera.

Results: Based on laboratory surveillance data, the IPD incidence rates varied from 2.3 to 4.3 per 100 000 population between 1997 and 2007 and in 2008 the rate based on enhanced surveillance data was 3.0 per 100 000 population. The annual IPD incidence remained stable during the study period. The age specific IPD incidence rate was highest in the < 1 year age group, reaching 15.7 per 100 000 from laboratory-based surveillance data and 16.6 per 100 000 from enhanced surveillance data. The coverage by 7-valent pneumococcal conjugate vaccine was 66.0% in the under 1 year olds and 65.1% in 1 - 4 year olds.

Conclusions: The incidence of IPD in the Czech Republic is comparable to the pre-vaccination data reported in other European countries. It is recommended to include pneumococcal conjugate vaccine in the routine vaccination scheme of infants in the Czech Republic.

P425

DIVERSE PROFILE OF INVASIVE S.PNEUMONIAE IN JAPAN

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Background: S.pneumoniae is one of the main causes of pediatric infection in Japan, but its disease burden and serotype profile is not clear enough. After Hib vaccine was finally introduced in Dec 2008, S.pneumoniae infection remains the next important vaccine preventable invasive disease for children. PCV7 is expected to become available by 2011 in Japan.

Method: Population-based surveillance of meningitis, bacteremia and pneumonia has been conducted in eastern Hokkaido (north-end of Japan, sub-arctic climate) and whole Okinawa (south-end of Japan, sub-tropical climate) prefecture. This is a part of the interim data of this continuing surveillance.

Result: We collected 13 specimens from Hokkaido (0 meningitis: 13 bacteremia) and 53 specimens (2 meningitis: 51 bacteremia) from Okinawa in the 2008.1-6. PCV7 serotype coverage for Hokkaido was 22% (excluded 4 specimens died during transport) and for Okinawa 75%. PCV13 coverage for Hokkaido was 67%, for Okinawa 90% respectively. Details of serotype distribution and antibiotic resistance are shown in the following figures.

Summary		
	Okinawa+ Hokkaido	%
serotype6A	9	16.98
serotype 6B	17	32.08
serotype 14	10	18.87
serotype 4	6	11.32
serotype 15A	1	1.89
serotype23A	1	1.89
serotype 23F	6	11.32
serotype19A	4	7.55
serotype 19F	1	1.89
serotype 9A	4	7.55
serotype 9V	1	1.89
serotype28F	1	1.89
serotype 28A	1	1.89
total tested	62	

[PCV coverage of the S pneumoniae isolates]

n=64		%	
Antibiotic name	S	I	R
Penicillin G	45.31	50.00	4.69
Ampicillin	93.75	6.25	0.00
Amox/Clavulanate	98.44	1.56	0.00
Cefuroxime	25.00	9.38	65.63
Cefotaxime	96.88	1.56	1.56
Ceftriaxone	96.88	3.13	0.00
Cefepime	98.44	1.56	0.00
Erythromycin	18.75	3.13	78.13
Azithromycin	23.44	0.00	76.56
Clarithromycin	26.56	0.00	73.44
Clindamycin	29.69	6.25	64.06
Tetracyclin	26.56	0.00	73.44
Minocyclin	100.00	0.00	0.00
Chloramphenicol	40.63	0.00	62.50
TMP-SMX	6.25	0.00	93.75
Ofloxacin	100.00	0.00	0.00
Vancomycin	100.00	0.00	0.00
Meropenem	45.31	43.75	10.94
Imipenem	65.63	32.81	1.56
Panipenem	100.00	0.00	0.00

[Resistance profile of the 64 S pneumoniae isolates]

Conclusion: PCV coverage is relatively high in Japan, but circulating serotypes vary by region and by year. Continuous surveillance is important to best illustrate the usefulness and impact of PCV.

P426

A PILOT PROSPECTIVE STUDY: THE IMPACT OF VIRAL AND BACTERIAL CO-DETECTION IN THE PNEUMONIA SEVERITY IN HOSPITALIZED CHILDREN

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Background and aims: Pneumonia is the major cause of mortality in children. Causative microorganisms may be bacterial or viral. The aim of this study is to identify by molecular tests the presence of viruses and bacteria in pleural effusions and nasopharyngeal aspirates in order to determine if co-infections are an aggravating factor in hospitalized children with severe pneumonia.

Methods: Twenty nine children between 4 months to 15 years old hospitalized with severe pneumonia were selected in two groups according to pneumonia severity i.e. the absence (n=12) or presence of pleural effusions (n=17). Bacterial presence in blood and pleural effusions was first analyzed by classical bacteriological methods; in parallel, the identification of respiratory viruses and bacteria in nasopharyngeal aspirates and pleural effusions were performed using molecular assays.

Results: Using quantitative real-time PCR and antigen detection, *Streptococcus pneumoniae* was identified in 85% (11 out 13 tested) and *Staphycoloccus aureus* (8%) in pleural effusions. Viral detection, in pleural effusions, showed the presence of Parainfluenza and Bocavirus in 40% of specimens. In nasopharyngeal aspirates, Bocavirus, Enterovirus, Rhinovirus, hMPV, Parainfluenza 1-3, Influenza-B and RSV were detected in both populations; however, the percentage of viral co-detection was higher in nasopharyngeal aspirates from patients with pleural effusions (35%) compared with those without (17%).

Conclusions: Viral co-detection was observed mainly in patients with more severe pneumonia. In our knowledge, this is the first time that the presence of Parainfluenza viruses, Bocavirus associated with bacteria in pleural effusions is demonstrated. Molecular biology assays improved the pathogens detection in pneumonia.

P427

IMPACT OF PCV-7 AT 24 MONTHS AS DELAYED BOOSTER OR AS PRIMARY VACCINATION

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Background: Several countries have implemented a PCV-7 vaccination schedule with a reduced number of primary immunizations, and with different timing of the booster dose in the second year of life. Delaying the booster dose possibly induces higher and prolonged antibody levels.

Methods: This study was conducted as subset of the Dutch trial studying the impact of reduced PCV-7 schedules (ISRCNTN25571720). PCV-7 vaccination at the age of 24 months was given to children who already received PCV-7 at 2 and 4 months (2 dose); PCV-7 at age of 2, 4 and 11 months (2+1 dose) or no PCV-7 (controls). Serum was obtained one month after vaccination. IgG antipneumococcal antibody levels were determined by double absorption ELISA.

Results: After a delayed PCV-7 booster at 24 months of age, children having received 2 primary doses achieved equal or even significantly higher (serotypes 4 and 9V) serum IgG levels for all vaccine serotypes compared to children having received 2+1 PCV-7 doses. Children who received a first PCV-7 vaccination at 24 months of age also showed protective antibody levels, except for the serotypes 6B and 23F.

Conclusion: Delaying the booster dose can have positive consequences for long term protection. For a proportion of children one PCV-7 vaccination at 24 months seems less immunogenic for the serotypes 6B and 23F.

Table
Antibody levels post PCV-7 vaccination at 24 months IgG GMC (µg/ml) in the different pre-vaccinated groups

	GMC µg/ml (95% CI)			Percentage infants with GMC >0.35 µg/ml		
Serotype	2 primary dose (n = 82)	2+1 dose (n = 80)	Controls (n = 81)	2 primary dose (n = 82)	2+1 dose (n = 80)	Controls (n = 81)
4	5,91 (4.99-7.01)	3,85 (3.23-4.60)[#]	2,44 (2.01-2.96)[a,b]	100,0%	100,0%	97,6%
6B	6,73 (4.97-9.11)	8.54 (6.47-11.29)	0,55 (0.42-0.70)[a,b]	96,3%	97,4%	63,1%[a,b]
9V	4,29 (3.70-4.99)	3,16 (2.69-3.71)[#]	1,70 (1.42-2.03)[a,b]	100,0%	100,0%	96,4%
14	14,01 (11.25-17.43)	11,64 (9.50-14.25)	2,49 (1.87-3.30)[a,b]	100,0%	100,0%	95,2%
18C	3,32 (2.86-3.86)	3,03 (2.34-3.91)	2,58 (2.15-3.08)[a]	100,0%	98,7%	98,8%
19F	6,01 (4.86-7.43)	5,84 (4.86-7.11)	1,91 (1.61-2.28)[a,b]	100,0%	100,0%	98,8%
23F	4,93 (3.91-6.22)	5,14 (4.16-6.33)	0,70 (0.52-0.94)[a,b]	98.8%	100,0%	61,9%[a,b]

[#] p-Value < 0.05. PCV-7 at 24 months after 2 primary dose vs 2+1 dose
[b] p-Value < 0.05. PCV-7 at 24 months after 2 primary dose vs controls
[°] p-Value < 0.05. PCV-7 at 24 months after 2+1 dose vs controls

[Table]

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COMPARABILITY OF ANTIBODY RESPONSES AFTER A 2+1 OR 3+1 PCV-7 SCHEDULE IN INFANTS AT 12 MONTHS OF AGE

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Background: Immunogenicity studies comparing 2 and 3 primary dose schedules with the 7-valent pneumococcal conjugate vaccine (PCV-7) in infants are lacking. Therefore, we compared infant pre- and post-booster IgG antibody levels after PCV-7 vaccination at 2, 4 and 11 months, and 2, 3, 4 and 11 months of age.

Methods: Infants receiving the 2+1 dose schedule participated in the Dutch trial studying the impact of reduced PCV-7 schedules (ISRCNTN25571720). Infants receiving the 3+1-dose schedule, participated in a vaccination study on DaKTP (ISRCTN97785537). Serum IgG antibody levels to pneumococcal polysaccharides as covered by PCV-7 were measured by double absorption.

Results: Pre- and post-booster antibody levels of the 2+1 and 3+1 dose schedule were comparable. Exceptions were observed for serotypes 6B and 19F where lower antibody levels were seen after a 2+1 compared to a 3+1 PCV-7 schedule. For serotype 6B, both schedules showed comparable proportions of infants reaching 0.35 µg/ml post-booster, however significant differences were seen for the thresholds 1.0 and 5.0 µg/ml.

Conclusions: The clinical significance of reduced 6B and 19F antibody levels after a 2+1 PCV-7 schedule compared to a 3+1 schedule in prevention of respiratory or invasive pneumococcal disease remains to be evaluated.

Table
Pre- and post-booster serotype specific antibody response in infants receiving a 2+1 and 3+1 PCV-7 schedule with early primary vaccinations at 2, 3 and 4 months or 2 and 4 months of age

	Pre-booster GMC µg/ml (95% CI)		Post-booster GMC µg/ml (95% CI)		Post-booster % of infants	
Serotype	2 primary dose (n = 80)	3 primary dose (n= 98)	2+1 dose (n = 72)	3+1 dose (n= 90)	2+1 dose >0.35 / 1.00 µg/ml	3+1 dose >0.35 / 1.00 µg/ml
4	0.28 (0.23-0.34)	0.30 (0.26-0.34)	2.66 (2.26-3.12)	3.05 (2.57-3.61)	100.0 / 93.1 %	100.0 / 92.2 %
6B	0.23 (0.19-0.30)	0.40 (0.31-0.49)[a]	2.26 (1.64-3.12)	4.73 (3.62-6.17)[b]	88.9 / 73.6 %	95.6 / 88.9 %[c]
9V	0.27 (0.22 0.33)	0.31 (0.27-0.36)	2.21 (1.90-2.58)	2.36 (2.00-2.78)	100.0 / 84.7 %	98.9 / 85.6 %
14	1.76 (1.39-2.24)	1.56 (1.23-1.81)	9.43 (7.76-11.46)	10.32 (8.62-12.34)	100.0 / 100.0 %	100.0 / 98.9 %
18C	0.19 (0.16-0.23)	0.22 (0.18-0.25)	1.97 (1.66-2.34	1.91 (1.61-2.27)	100.0 / 81.9 %	98.9 / 77.8 %
19F	0.94 (0.76-1.16)	0.96 (0.74-1.24)	3.43 (2.85-4.12)	4.80 (4.01-5.76)[b]	100.0 / 95.8 %	100.0 / 97.8 %
23F	0.21 (0.16-0.27)	0.22 (0.18-0.26)	2.61 (2.12-3.21)	3.15 (2.54-3.92)	98.6 / 88.9 %	100.0 / 85.6 %

[a] Pre-booster 2 vs. 3 primary dose. *p*-Value < 0.05; Calculated using log transformed unpaired t test
[b] Post-booster 2+1 vs 3+1 dose. *p*-Value < 0.05; Calculated using log transformed unpaired t test
[c] Post-booster 2+1 vs 3+1 dose; percentage of infants > 1.00 µg/ml. *p*-Value < 0.05; Calculated using Fisher's exact test

[Table]

P429

A REVIEW OF COLONIZATION BY *STREPTOCOCCUS PNEUMONIAE* IN CHILDREN: IMPLICATIONS FOR DISEASE BURDEN ESTIMATION AND DISEASE CONTROL

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Background and aims: Because pneumococcal colonization can lead to invasive disease, characteristics of colonized patients and the geographic distribution of *Streptococcus pneumoniae* (SP) serotypes are important considerations for vaccination. This paper reviews nasopharyngeal (NP) colonization by SP and changes in colonization experienced with pneumococcal conjugate vaccination.

Methods: A MEDLINE (1950 to March 23, 2007) and EMBASE (1988 to 2007 Week 12) search, with search terms "Prevnar/Prevenar/PCV7/pneumococcal conjugate vaccine" and "*Streptococcus pneumoniae* carriage/colonization/serotype distribution" or "nasopharyngeal carriage/pneumococcal carriage", and "*Streptococcus pneumoniae*" and "carriage" was conducted (results were limited to studies published in English).

Results: Colonization in children depends on age, number of siblings, day care attendance, and season whereas serotype distribution among NP carriage isolates may vary by age, geography, and cohort studied. In addition to young age (less than 2 years), other host factors for pneumococcal colonization include ethnicity, crowding, environmental conditions, and socioeconomic factors. The most invasive serotypes were the least commonly carried while the most commonly carried were the least likely to cause invasive disease. Introduction of the heptavalent pneumococcal conjugate vaccine (PCV7) has decreased vaccine-serotype pneumococcal colonization and replacement by non-vaccine serotypes has been observed.

Conclusion: Surveillance programs that include monitoring of pneumococcal colonization will capture important information to understand the impact of pneumococcal conjugate vaccines.

P430

DEVELOPMENT OF A MURINE NON-INVASIVE INFECTION MODEL TO STUDY *STREPTOCOCCUS PNEUMONIAE* ACUTE OTITIS MEDIA

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Introduction: Acute Otitis Media (AOM) is one of the most frequent diseases in childhood, and *Streptococcus pneumoniae* is among the main causative bacterial agents. Since there is a lack of adequate animal models to study the bacterial pathogenesis of AOM, we developed a non-invasive murine AOM model. We used this model to investigate the contribution of two surface-associated pneumococcal proteins, the streptococcal lipoprotein rotamase A (SlrA) and the putative proteinase maturation protein A (PpmA) to pneumococcal virulence during experimental AOM.

Materials and methods: A pressure cabin was used to translocate pneumococci from the nasopharyngeal cavity into the middle ears of the mouse. The course of infection was monitored using health scores, otomicroscopy, bacterial culture, cytokine analysis and histopathology. The contribution of SlrA and PpmA to virulence during OM was studied using knock-out mutants.

Results: A pressure increase of 40kPa was adequate to transfer pneumococci from the nasopharynx into the middle ear cavity. Maximum bacterial load was seen 96 hours after infection. Inflammation of the middle ear was confirmed by IL-1β and TNF-α cytokine levels and histopathology at 96 and 144 hours post infection. Pneumococci lacking the genes encoding SlrA, PpmA or both, were significantly reduced in virulence.

Conclusion: We developed a non-invasive murine OM model for pneumococcal infection, very suitable to study pneumococcal pathogenesis and virulence *in vivo*. The importance of SlrA and PpmA in the pathogenesis of pneumococcal AOM was demonstrated. The usefulness of our model to study the effectiveness of pneumococcal vaccines against AOM is currently under investigation.

P431

LIMITED ROLE OF *STREPTOCOCCUS PNEUMONIAE* INFECTIONS IN CHILDREN WITH RECURRENT ACUTE OTITIS MEDIA AND CHRONIC OTITIS MEDIA WITH EFFUSION

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Introduction: Otitis Media (OM) is one of the most frequent diseases in childhood. Although often self-limiting, in some cases recurrent (rAOM) and chronic (COME) episodes of OM result in significant morbidity. In contrast to the major burden on public health, the pathogenic mechanisms of OM remain largely unclear. A prospective cohort study was designed to investigate the patient characteristics and the role of bacterial and viral pathogens were studied.

Materials and methods: Children < 5 years of age, suffering from rAOM or COME and scheduled for surgery were enrolled. Middle ear fluid (MEF) and a nasopharyngeal swab were collected during surgery for bacterial culture and virus-specific multiplex-PCR.

Results: From April to December 2008, 101 patients were enrolled. rAOM was mostly diagnosed at younger age heading towards COME with increasing age. *H. influenzae* was the most frequently detected pathogen in the nasopharynx (71%) and the MEF (16%). Although it is known that the prevalence of *H. influenzae* exceeds the *S. pneumoniae* prevalence in COME, only 2% of the MEF samples and 43% of the nasopharyngeal swabs contained *S. pneumoniae*. *M. catarrhalis* was detected in 31% in the nasopharynx and 5% in MEF. Rhinovirus was the most frequently detected viral pathogen in MEF (60%).

Conclusion: Our data suggest that the presence of *S. pneumoniae* in both rAOM and COME is limited, presumably as a result of the introduction of the Prevnar vaccine in the national vaccine program in 2006. The role of rhinovirus in the pathogenesis of OM needs to be elucidated.

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BIOFILM FORMATION OF *STREPTOCOCCUS PNEUMONIAE* ISOLATES FROM PEDIATRIC PATIENTS

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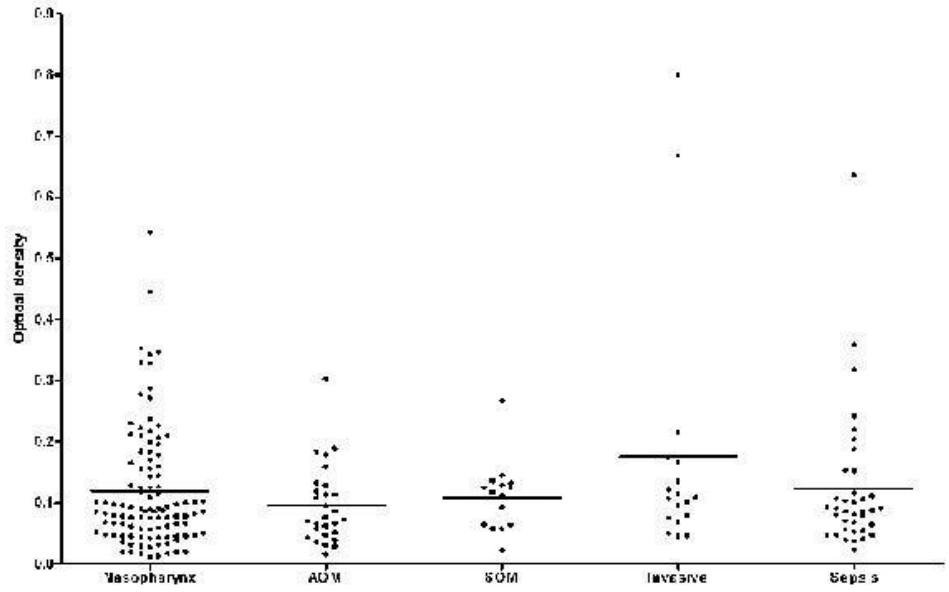
Background and aims: Clinical data on pneumococcal biofilms are limited. Pneumococcal biofilm formation may play a role in maintaining chronic middle ear effusion. We hypothesized that the differences in the ability of pneumococcal strains to form biofilm *in vitro* account for diverse clinical outcomes of pneumococcal diseases.

Methods: We assessed the biofilm formation *in vitro* of 298 clinical pneumococcal isolates from nasopharynx or middle ear effusions of children and from blood cultures in our hospital in 2000-2008. Optical density (OD) values of biofilm plaques after 18 hours of incubation in microtitre plates and crystal violet stain were used to measure the biofilm formation.

Results: The biofilm formation of pneumococcal isolates *in vitro* did not differ in respect to the clinical diagnosis (P=0.45) (Figure 1. Each dot presents OD of each isolate studied as a mean and the bar indicates the mean of each diagnostic group). Two highest OD values in the whole data were obtained from a child with meningitis (serotype 14) and a child with preseptal cellulitis (serotype 14).

Conclusions: Even though there was marked variation between the strains, the clinical presentation did not differ in respect to biofilm formation *in vitro* which was common among all pneumococcal strains studied.



[Figure]

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MICROBIOLOGY OF ACUTE OTITIS MEDIA AFTER THE INTRODUCTION OF HEPTAVALENT PNEUMOCOCCAL CONJUGATE VACCINE

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Background and aims: The heptavalent pneumococcal conjugate vaccine (PCV7) has a considerable impact on the epidemiology of invasive pneumococcal disease and respiratory infections. The PCV7 was introduced in our settings late in 2004. The aim of this study was to examine the microbiology of acute otitis media (AOM) after the introduction of pneumococcal immunization.

Methods: All positive middle ear fluid cultures obtained from children < 5 years of age were prospectively recorded during a three-year period (2006-2008). Serotyping of pneumococcal strains was performed with the Pneumotest- latex and with the capsular sweling method.

Results: Among the 846 recorded cultures *Haemophilus influenzae* was the most common pathogen (301/846, 35.6%), followed by *Streptococcus pneumoniae* (268/846, 31.7%) and *Streptococcus pyogenes* (259/846, 30.6%) while *Moraxella catarrhalis* was found only in 2% (18/846). Nonvaccine serotypes (NVTs) accounted for 60/114 (53%) of the pneumococcal strains that were serotyped (51%, 45%, 61%, each year respectively, p=0.414) compared to 30% (16/75) before the introduction of immunization (p.001). A progressive increase was noted in the rate of serotype 19A among the NVTs during the three study years: 1/23, 5/15, 7/22 (p< 0.001). 25% of pneumococcal strains were intermediate resistant to PNC and 16% resistant. There was a significant difference with the two-year period before the introduction of immunization when these rates were 41% and 5%, respectively (p< 0.001).

Conclusion: The current microbiology of AOM is characterized by the predominance of *H. influenzae*. Nonvaccine types are increasingly more common and 19A is predominant. Antibiotic resistance rates remain high.

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LOSS OF PNEUMOCOCCAL SPECIFIC B-CELL MEMORY IN HIV INFECTED MALAWIAN CHILDREN

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Invasive pneumococcal disease is an important HIV-associated problem in sub-Saharan African children. In order to test the hypothesis that high prevalence of invasive pneumococcal disease in HIV^+ children is associated with loss of humoral immune memory, we assessed B-cell phenotype and memory B-cell responses to the pneumococcus. We recruited 64 HIV^+ children and 30 HIV^- controls. B-cell subsets (CD27, IgD) were phenotyped by flow cytometry. Peripheral blood mononuclear cells were stimulated with pokeweed mitogen, pansorbin and CpG DNA, to expand memory B-cell populations, and immune memory to a pneumococcal protein antigen (CbpA) was assessed by cultured B-cell ELISpot assay. B-cells represented a lower proportion of total lymphocytes ($p=0.003$) in HIV^+ children than controls. Interestingly, a loss of marginal zone memory B-cell ($CD19^+$, $CD27^+$, IgD^+) and naïve/transitional B-cell ($CD19^+$,$CD27^-$) numbers was seen in HIV^+ children ($p=0.0002$ & 0.0004 respectively), however HIV^+ and HIV^- children had similar numbers of germinal-centre memory B-cells. Nonetheless, CbpA-specific memory B-cell numbers were lower in HIV^+ children (median 7.9, IQR 2.5-20.8) than in controls (median 17.5, IQR 5-44.2) ($p=0.0036$). These data suggest that even though similar numbers of germinal centre memory B-cells was observed in both groups, HIV^+ children had impaired ability to mount pneumococcal antigen-specific B-cell memory response. Whether immune stimulation through nasopharyngeal carriage of *S. pneumoniae* preserves this immunity or accelerates this process of immune attrition, and whether this depletion of the antigen-specific memory B cell pool is the basis of the increased susceptibility of HIV^+ individuals to invasive pneumococcal infection is currently under investigation.

P435

A CASE OF MONDINI DYSPLASIA WITH RECURRENT *STREPTOCOCCUS PNEUMONIAE* MENINGITIS

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Recurrent meningitis are rarely seen, but when they occur, an detalied search for the pathogenesis underlying the recurrent episodes must be pursued. Underlying pathology may either be a communication between the subarachnoid space and the base of the skull or an immunological disorder. The most common predisposing condition is anatomic defects. Mondini´s dysplasia is a developmental anomaly of the middle ear characterized by cochlear malformation with dilation of the vestibular aquaduct, vestibule and ampullar ends of the semicircular canals. These deformities may result in a connection between subarachnoid space and the middle ear resulting in recurrent episodes of meningitis. Additionally, it is commonly associated with hearing impairment. We describe here a boy with recurrent meningitis and unilateral sensorineural hearing loss. Mondini dysplasia was demonstrated with high resolution computed tomographic (HRCT) scans of the temporal bones in the search for pathogenesis of recurrent meningitis. Surgical closure of the defect was carried out successfully. Although rare, Mondini dysplasia must be included as a possible diagnosis when faced with a patient with recurrent bacterial meningitis and sensorineural hearing loss. Early recognition and successful repair of the cerebrospinal fluid leak is important to avoid the sequelae or repeated episodes of meningitis. Therefor, we recommend sensitive imaging studies, especially HRCT, in children with recurrent meningitis and hearing loss.

RESPIRATORY TRACT INFECTIONS

P436

EFFECT OF OMEGA-3 FATTY ACIDS SUPPLEMENTATION IN ASTHMATIC CHILDREN

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Objectives: Asthma is a chronic inflammatory airways disease. Nutritional intervention is an important tool to decrease the severity of many chronic inflammatory diseases including asthma. The aim of this study is to evaluate the role of omega-3 fatty acids in children with persistent asthma.

Methods: Placebo-self-controlled 35 children with moderate persistent asthma completed the study, were subjected to alternating phases of supplementation with omega-3 fatty acids. pulmonary function tests and sputum inflammatory markers were evaluated at the beginning of the study and at the end of each therapeutic phase.

Results: There was a significant improvement in pulmonary function tests and sputum inflammatory markers with diet supplementation with omega-3 fatty acids, ($p < 0.001$).

Conclusion: Diet supplementation with omega-3 fatty significantly improved pulmonary function tests and pulmonary inflammatory markers in children with moderately persistent bronchial asthma.

P437

CLINICAL PREDICTION FOR STREPTOCOCCAL ACUTE PHARYNGITIS IN CHILDREN

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Background: Acute pharyngitis is a common illness in children. Most of the cases are viral but group A β- hemolytic *Streptococcus* (GABHS) causes 15-30% of paediatric cases of acute pharyngitis.

Appropriate diagnosis and treatment of GABHS pharyngitis is important for avoiding complications and inadequate use of antimicrobials.

Objective: To correlate the prediction value of a clinical score and laboratory test results.

Methods: We performed a retrospective review of 310 cases admitted in an ambulatory clinic during 8 months. The patients were divided in 2 groups: 160 cases of acute pharyngitis (group A) and 150 cases of upper respiratory tract infections (group B), other than pharyngitis.

For the clinical score we used 5 parameters: history of exposure, fever (>38 C°), swollen cervical lymph nodes, tonsillar exsudate, absence of cough/coryza/ conjunctivitis. High prediction was considered for score 4-5, moderate for 2-3 and low for 0-1.

For laboratory confirmation we used throat culture and rapid antigen detection test.

Results: We found a pretest probability of 27% in group A ; posttest probability was 17% for low score cases, 34% for moderate score and 35% for high score . For all cases pretest probability was 17% and posttest probability 10% for low score, 28% for moderate score and 26% for high score. In group B only 9 cases were positive (6%).

Conclusions: The clinical score was useful in predicting GABHS pharyngitis and it could be helpful in avoiding excessive use of antimicrobials especially when laboratory tests are not available.

P438

GENDER, CLINICAL RICKETS, AND VITAMIN D DEFICIENCY: ASSOCIATION WITH THE OUTCOMES OF CHILDHOOD VERY SEVERE PNEUMONIA: A PROSPECTIVE COHORT STUDY

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Background: The association of vitamin D deficiency with pneumonia is well established but not with its outcomes.

Objectives: To investigate whether rickets and vitamin D deficiency affect the outcomes in very severe pneumonia (VSP) and whether the effect is different for girls and boys.

Methods: The study was a prospective cohort. A total of 152 children aged 2-59 months hospitalized with WHO-defined VSP were enrolled, managed, and followed for 30 days. Treatment outcome was either successful or failure (antibiotic modification for clinical worsening, death, relapse after 10-day antibiotics, or development of complications). Serum vitamin D (25OHD) was measured in 79 cases.

Main outcome measures: Association of rickets and vitamin D deficiency, according to gender, with treatment failure and the circulating neutrophils, respectively.

Results: Treatment failure occurred in 24 (15.8%), all aged 2-12 months, and 21(87.5%) were rachitic. Of the 79 subset, 29 had vitamin D deficiency of which 23(79.3%) had rickets. Treatment failure was significantly higher in the rachitic compared to non-rachitic [20.6% (21/102) vs 6% (3/50); OR 1.38 (95% CI 1.13-1.69),P=0.031]. In multivariate regression, it was significantly higher in rachitic girls than boys [31.7% (13/41) vs [13.1% (8//61); Adjusted OR 3.2(95% CI 1.2-9.14); P=0.031]. In girls, 25OHD was significantly associated with the mean neutrophils [mean% (SD) for non-deficient 49.2(19.3) and deficient 32.6(14.3), Adjusted OR 1.11(95% CI 1.02-1.21); P=0.023).], but not for boys.

Conclusions: In VSP, rickets and vitamin D deficiency were significant risk factors for treatment failure and reduced circulating neutrophils, respectively in girls but not in boys.

P439

HUMAN METAPNEUMOVIRUS INFECTIONS - BIANNUAL EPIDEMICS AND CLINICAL FINDINGS IN CHILDREN IN THE REGION OF BASEL, SWITZERLAND

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Background: Human metapneumovirus (hMPV) epidemics vary in time and severity.

Methods: PCR for hMPV and respiratory syncytial virus (RSV) was performed on nasopharyngeal aspirates (NPA) of hospitalized and outpatient children with respiratory tract infections between October 2004 and April 2008 at our institution.

Results: A total of 3934 NPAs were tested for hMPV and 3859 for RSV. Of these 198 (5%) were hMPV positive and 869 (23%) were RSV positive. Median age was 17 months and 9 monthsfor hMPV and RSV, respectively. 59% of hMPV and 58% of RSV patients were hospitalized. Proportions of hMPV positive samples for the four winter seasons were 0.4%, 11%, 0.2% and 14%. For RSV, they were 28%, 15%, 28% and 28%.

Conclusions: HMPV epidemics follow a biannual variation in our area. Major epidemics were observed in winter seasons starting in odd years (2005/06 and 2007/08), minor epidemics in those starting in even years (2004/05 and 2006/07). RSV epidemics usually follow a reciprocal biannual pattern, leading to annually alternating major RSV and hMPV epidemics.

P440

TRANSCRIPTOME ANALYSES OF BLOOD LEUKOCYTES AND NASOPHARYNGEAL SAMPLES IN CHILDREN WITH RSV INFECTIONS REVEAL DISTINCT SIGNATURES CORRELATING WITH DISEASE SEVERITY

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Background: The course of respiratory syncytial virus (RSV) infection in young healthy children is often unpredictable. While some develop mild rhinitis, others suffer from severe pulmonary insufficiency requiring mechanical ventilation. More insight into host-virus interactions is needed for the development of new intervention and prevention strategies. We hypothesized that leukocytes and nasopharyngeal cells from RSV infected children with different clinical severity might have discriminative transcriptional signatures that can lead to the identification of diagnostic and prognostic biomarkers.

Methods: Gene expression profiles of different blood leukocyte subpopulations and nasopharyngeal cells from 11 children suffering from severe RSV infection who required mechanical ventilation were compared to 9 children with mild symptoms. RNA isolated from peripheral blood mononuclear cells (PBMCs), granulocytes, nasopharyngeal cells and PBMC subpopulations (CD4 and CD 8 T lymphocytes, B lymphocytes and monocytes) was used to perform Affymetrix microarray gene expression analyses.

Results: Gene expression profiles of PBMCs, granulocytes and nasopharyngeal cells were clearly different between the mild and severe group. The differential expressed genes were involved in immunological pathways, and pathways involved in cell signaling and apoptosis. Transcriptome analyses of CD4 and CD8 T lymphocytes, B lymphocytes and monocytes provided more insight in cell specific immune responses.

Conclusions: Our findings suggest that severity of disease in children suffering from RSV infections is reflected in distinct gene expression profiles. Exploring genes that allow discrimination between patients with different clinical manifestations is expected to lead to the identification of biomarkers for the prediction of severity of disease in an early stage.

P441

MULTIPLE VIRAL INFECTIONS IN ASSOCIATION WITH CLINICAL DISEASE SEVERITY IN CHILDREN WITH VIRAL LOWER RESPIRATORY TRACT INFECTIONS

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Background: Both host and viral factors contribute to the clinical course of viral lower respiratory tract infections (LRTI). Although some studies suggest that infection with multiple viral pathogens leads to a more severe course of disease, the role of such multiple infections in clinical disease severity remains unclear. We investigated the association between mono- and multiple viral infections and disease severity.

Methods: Children < 6 years of age with clinical symptoms of viral LRTI were prospectively included during three consecutive winter seasons. Nasopharyngeal samples were collected and multiplex polymerase chain reaction (PCR) of 14 respiratory viral pathogens was performed. Patients were categorized in 3 patient groups based on disease severity; mild (no supportive treatment), moderate (supplemental oxygen and/or nasogastric feeding) and severe (mechanical ventilation).

Results: At least one virus was detected in 94 from 105 included children (90%). Multiple infections were detected in 31 (33%) of these 94 children. Respiratory syncytial virus was the most frequently detected virus (68%), followed by rhinovirus (34%). Multiple viral pathogens were detected in 6.9% of the mechanically ventilated patients, compared to 41.4 and 36.2% respectively in the patient groups with a moderate and mild course of disease (χ^2-test , p=0.010 and p=0.025 respectively).

Conclusion: In this study, no positive association between multiple infections and a more severe course of disease was found. We suggest that other factors, such as host immune response or viral loads, contribute to a larger extent to disease severity during viral lower respiratory tract infections.

P442

ACUTE OTITIS MEDIA (AOM) CAUSED BY *MORAXELLA CATARRHALIS* (MC): EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS

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Background: Information on epidemiological and clinical characteristics of MC-AOM is limited.

Objectives: To describe epidemiological, microbiological and clinical features of MC-AOM and compare them with AOM caused by other bacterial pathogens.

Patients and methods: AOM patients < 5 years with a middle ear fluid specimen obtained during 1999-2006, were enrolled. MC, *Streptococcus pneumoniae* (SP)*, Haemophilus influenzae* (HI) and group A *Streptococcus* (GAS) were considered true pathogens. Information collected included demographic characteristics, clinical history, signs and symptoms.

Results: 12799 AOM episodes were studied; 8198 (64%) were culture positive, with isolation of 10,382 pathogens: 4982 (47.9 %) HI*,* 4450 (42.8%) SP*,* 501 (5%) MC and 449 (4.3%) GAS. Unlike all other pathogens, MC-AOM was mostly a mixed-pathogen AOM (67% in MC vs. 38%, 42% and 39% of HI, SP and GAS-AOM; P< 0.001). In single-pathogen AOM, spontaneous perforation of tympanic membrane occurred less frequently in patients with MC (7%) *vs*. those with other pathogens (15%, 18% and 42% for HI, SP and GAS, respectively, *P*< 0.001). In multivariate analysis (adjusted for age, previous AOM history/treatment and clinical/otological presentation), MC-AOM occurred more commonly in first AOM and in mixed infections and was associated with less spontaneous perforation and less concomitant pneumonia than the other 3 pathogens. None of MC-AOM episodes was associated with mastoiditis (*vs*. 12 and 6 cases caused by SP and GAS, respectively, *P*< 0.02)**.**

Conclusions: Compared with AOM caused by other pathogens**,** MC-AOM is mostly part of a mixed-infection AOM, and is less often associated with spontaneous perforation and mastoiditis.

P443

COINFECTION OF MYCOPLASMA PNEUMONIAE IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA

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Background: Coinfection of Mycoplasma pneumoniae is not uncommon in children with respiratory syndromes. We try to investigate the role of M. pneumoniae in childhood community-acquired pneumonia (CAP) with mixed infection and to further define the manifestations and outcomes in such instances.

Methods: A prospective study of the etiology of CAP was conducted on 209 hospitalized children referred to Chang Gung Children's Hospital and children with acute mycoplasmal infection were enrolled into our study.

Results: A total of 59 children were enrolled and stratified into 3 groups: M. pneumoniae infection alone (n = 31), M. pneumoniae with Streptococcus pneumoniae coinfection (n = 9), and M. pneumoniae with virus coinfection (n = 19). As compared with children infected with M. pneumoniae alone, children coinfected with S. pneumoniae were more likely to occur under five years of age with a longer duration of fever and hospital stay. Furthermore, total leukocyte count and serum C-reactive protein level were also significantly higher in these children ($P < 0.01$). However, no significant difference of clinical characteristics, complications and outcomes was observed between the patients infected with either M. pneumoniae alone or with virus coinfection.

Conclusions: In children with CAP, the influence on the clinical outcomes of M. pneumoniae infection may be heavily dependent on the coinfected pathogen. It is important for clinicians to realize that a potential coexistence of M. pneumoniae infection should be considered in children with features suggesting typical bacterial pneumonia.

P444

LIVE IMAGING: REAL-TIME, NON-INVASIVE ASSESSMENT OF TB DISEASE IN ANIMAL MODELS

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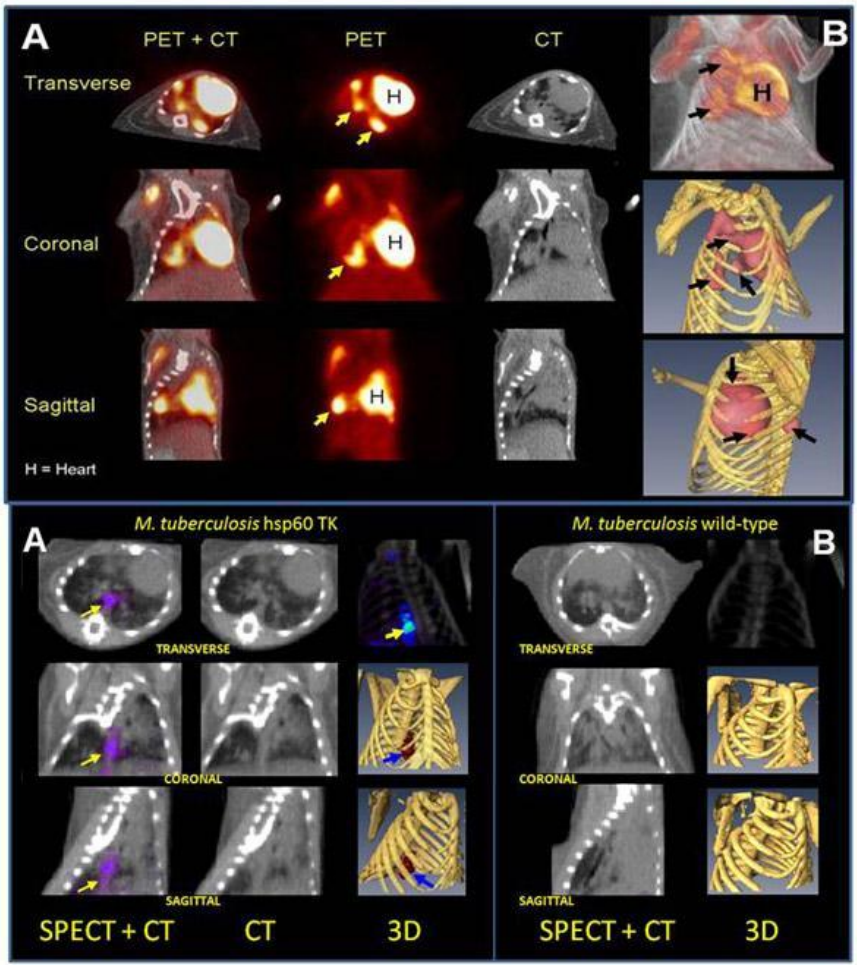
Background: Pre-clinical studies for tuberculosis (TB) are cumbersome. Non-invasive imaging technologies [positron emission tomography (PET), single photon emission computed tomography (SPECT)] that allow the *same* live experimentally-infected animals to be monitored serially can revolutionize pre-clinical studies.

Methods: We used standard (BALB/c) or the caseating TB granuloma (C3HeB/FeJ) mouse models of TB. [^{18}F]FDG-PET/CT or [^{64}Cu]ATSM-PET/CT were used to monitor TB-induced inflammation and hypoxia. [^{125}I]FIAU, a substrate for bacterial thymidine kinase (TK), can be used to selectively image bacteria in experimentally-infected animals. Mycobacteria lack TK and we therefore engineered *Mycobacterium tuberculosis* (*Mtb*) expressing bacterial TK. This strain was evaluated both *in vitro* and *in vivo* as a biomarker for bacteria.

Results: [^{18}F]FDG and [^{64}Cu]ATSM localized to granulomas and could monitor TB-induced lung inflammation and hypoxia respectively. Moreover, serial [^{18}F]FDG-PET/CT could be used to monitor response to anti-TB therapy. *Mtb* TK strain had no *in vivo* growth defect, was stable *in vivo* and susceptible to common anti-TB drugs. Using [^{125}I]FIAU-SPECT, activity from *Mtb* TK was clearly visualized in the lungs of infected mice.



[Figure 1]

Conclusions: We have developed novel biomarkers for non-invasive assessment of TB disease in live animals. These biomarkers will significantly simplify pre-clinical studies. Moreover, mycobacterial pathogenesis will be powerfully augmented by real-time observational capabilities of these biomarkers. In the future these biomarkers will also be used to evaluate human TB.

P445

MICROBIOLOGICAL RESULTS IN BELGIAN CHILDREN WITH NON-RESPONDING OR RECURRENT COMMUNITY ACQUIRED LOWER RESPIRATORY TRACT INFECTION (CA-LRTI)

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Background and aims: Non-responding and recurrent CA-LRTI are frequent in children and known causes of high morbidity. Documentation of etiology is difficult but important for prevention and treatment strategies. We aimed to document the possibly responsible pathogens.

Methods: Retrospective analyses of bronchoalveolar lavage fluid (BAL) (aerobe and viral culture, viral PCR), nasopharyngeal aspirate (viral PCR and culture) and blood culture, for all (otherwise healthy) children, who underwent a flexible bronchoscopy with BAL, for CA-LRTI, from 2005- 2007.

Results: 384 children (128 acute non-responding (broncho)-pneumonia, 123 recurrent (broncho)-pneumonia, 92 persistent X-ray abnormalities and 41 persistent wheezers) were included. The median age was 33.1m (range: 1.0-171.6m) and female:male ratio was 1:1.2. 143/384 (37.2%) patients received antibiotics with certainty before BAL. Bacterial cultures were negative in 156/384 (40.6%) patients. BAL-cultures were positive in 227/384 (59.1%) patients and blood cultures in 3/384 (all S. pneumoniae). In BAL, Haemophilus influenzae, Moraxella catarrhalis and Streptococcus pneumoniae were most often isolated, in respectively 164, 55 and 33 patients. 148/164 (90.2%) H. influenzae strains were not typable, 2 belonged to serotype e and 1 to serotype b. Biotypes 2 and 3 were predominant and 42/164 (25.6%) were β-lactamase producers. SGT´s 23, 19 and 6 were the predominant pneumoccoccal serotypes. In 96/380 (25.2%) patients viral PCR and/or cultures were positive: RSV, parainfluenzavirus type 3 and human metapneumovirus being most isolated. Mixed bacterial/viral infections were found in 62/380 (16.3%) patients.

Conclusions: Non-typable H. influenzae was the most isolated pathogen, possibly responsible for the non-responding or recurrent character of the CA-LRTI.

P446

THE ROLE OF TEMPERATURE IN THE DEVELOPMENT OF ACUTE RESPIRATORY INFECTIONS

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Background and aims: Little is known about the reasons of seasonality of influenza and RSV in temperate climates. Recently we found significant associations between these viruses and outdoor temperature, which could be an explanation for seasonality. For RSV even prediction was possible based on continuous measures of outdoor temperature. The question was whether our results are in agreement with the international literature.

Methods: In a comprehensive review of scientific articles which are concerned with the association between meteorological factors and acute respiratory infections (ARI) in Pubmed we used keywords like “chilliness” or “coldness” for low temperature and “respiratory infection” or “common cold” for ARI. No limits were set for time of publication, geographical region or study design.

Results: Whereas the majority of observational studies in temperate climates were in agreement with our findings the association between outdoor temperature and ARI in tropical regions seems to be less pronounced. Some studies found associations between ARI incidence and rainy days only or not any association to meteorological factors. In experimental studies on volunteers low temperature alone without an infectious pathogen was not sufficient to cause a respiratory infection. In agreement with our finding there was an association between temperature and influenza and RSV respectively, but not for hRV and adenovirus.

Conclusions: In the international literature there were comparable findings of the association between temperature and influenza or RSV. Low temperature may trigger the interaction between host and certain seasonal pathogens. This could be a plausible explanation for the seasonality of these pathogens.

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NOSOCOMIAL INFECTION BY HUMAN BOCAVIRUS

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Background and aims: Human bocavirus (HBoV) is a new respiratory pathogen that affects mostly children under 2 years of age.

We aim to describe nosocomial infection in young children by HBoV.

Methods: Nasopharyngeal aspirates (NPA) from children under 2 years of age, hospitalized that were with lower respiratory tract (LRT) symptoms were collected during February 2008 to November 2008, in Brazil. Detection of the following respiratory virus, HBoV, adenovirus, respiratory syncycitial virus (RSV), human metapneumovirus (HMPV), parainfluenza 1, 2 and 3 (P1, P2, P3) and influenza A and B (IA, IB) were performed by genescan RT-PCR.

Results: During the study period 474 NPA were collected for viral detection, with 51 positive samples for HBoV (10,7%). Seven were confirmed and 2 were possible nosocomial HBoV infections. Four of these 9 children with HBoV were in the neonatal intensive care unit (ICU) since birth. The other 5 patients, 4 were in the pediatric ICU and 3 of them had previous samples from the same hospital stay negative for HBoV. Two patients possibly were infected inside the hospital since the detection of HBoV was in samples collected after 17 and 29 days of admission. All patients had respiratory symptoms at time of detection. HBoV was the sole virus found in all but one of the nine patients who had coinfection with adenovirus.

Conclusions: HBoV is a cause of LRT infection in children and can be acquired inside the hospital. Diagnosis and prophylactic measures are crucial to avoid nosocomial infection, especially in ICU.

P448

OBSTRUCTIVE SLEEP APNEA (OSA) IS A RISK FACTOR FOR COMMUNITY ACQUIRED ALVEOLAR PNEUMONIA (CAAP) IN CHILDREN

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Background and aims: Children with OSA have significantly higher rates of both lower and upper respiratory infections during early childhood. Our aim was to assess prospectively whether OSA is more frequent in children with CAAP than in healthy controls.

Methods: A prospective nested case-control study assessing children < 5y with CAAP presenting to a Pediatric Emergency Room from 2006 to 2008. CAAP was diagnosed based on chest x-ray according to the WHO Pneumonia Vaccine Trialists Radiology Working Group (WHO/V&B/01.35, 2001). Controls were healthy children visiting community clinics for routine vaccination and children admitted for elective surgery. Symptoms of OSA were documented using a structured questionnaire**.** Data were also obtained from the hospital sleep lab database.

Results: 1546 children with CAAP (58% male) and 441 controls (54% male) were enrolled. Frequent snoring (≥2 nights/week) was reported in 18.6% CAAP *vs.* 2.9% controls, p< 0.0001. Respective figures for movements during sleep were 21.6% *vs*. 5.3%, p< 0.0001; respiratory problems during sleep 5% vs. 1.4%, p< 0.0001; daytime abnormal behavior 6.4% vs. 0.2%, p< 0.001; chronic rhinorrhea 12.9% vs. 1.8%, p< 0.0001. 79/1546 (5%) children with CAAP vs. 6/441 (1.3%) controls had OSA diagnosed by a previous polysomnographic evaluation; p< 0.0001, and 50 (3.3%) children with CAAP vs. 3 (0.7%) controls had already undergone adenoidectomy; p< 0.0001. Odds ratio for OSA in CAAP patients vs. controls was 3.7 (1.6-10.0).

Conclusion: OSA is a predisposing risk factor for CAAP in children younger < 5y. The underlying mechanism for this observation needs to be explored.

P449

AN EXAMINATION OF HOUSEHOLD ENVIRONMENTAL FACTORS ASSOCIATED WITH ACUTE RESPIRATORY INFECTION IN CHILDREN UNDER FIVE YEARS IN EAST NUSA TENGGARA

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The household environmental factors that were included in the study are ventilation, natural light, crowding, type of wall, roof, ceiling, floor and cooking fuel, while the symptoms of ARI investigated are cough, runny nose and rapid breathing.The study used a cross sectional design.Sample is the children under five years in East Nusa Tenggara based on data from the National Socio-Economic Survey 2001.An analysis using chi-square and logistic regression was then undertaken to see whether there is an association between the prevalence of ARI symptoms and the household environmental factors.It was found that kitchen´s natural light and monthly expenditure are the variables with the strongest association with the prevalence of ARI symptoms. However, the response of natural light is based on the perception of respondents without any accurate measurements which are possibility in bias.It is recommended that the construction of houses be changed by adding some windows and ventilation to improve the natural light in the kitchen is the mandatory. More attention should be given to large more of people with a low level income in East Nusa Tenggara.The health promotion and health education program that target the essential household environmental factors that influence the prevalence of ARI should be encourage.Detailed information on health and measurements and observations of some household environmental factors such as ventilation, natural light, floor area, and some types of household constructions are very important and should be highlighted in the national survey and would be useful to be included in the national survey of this kind.

P450

THE DIFFERENCES OF CLINICAL MANIFESTATIONS OF ACUTE LOWER RESPIRATORY TRACT INFECTIONS BETWEEN WITH AND WITHOUT MYCOPLASMA PNEUMONIAE INFECTION

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Background: *Mycoplasma pneumoniae* (Mp) has been known as a major pathogen causing acute lower respiratory tract infections (ALTIs) and aggravating asthma. We studied what influence and differences Mp infections could make in the acute lower respiratory tract infections in Korean children and the genetic diversity of 16 S rDNA with sequencing.

Methods: Among 129 ALRTI children admitted between September 2003 and March 2004 in Cheju National University Hospital in South Korea, M pn infections were diagnosed by seorology and 16S rDNA nested PCR.

Results: There were forty patients with Mp infections and eighty nine without Mp infections. Mean age was 4.2 years with Mp infections and 2.8 years without Mp infections. There were 8 atopic patients in each group which means two times more in the group with Mp infections than without Mp infections. Mean time interval from the symptom onset of ALRTIs until admission was 8.7 days for with Mp infections and 4.9 days for without Mp infections. Coinfection of Streptococcus pneumoniae were found in 7 among with Mp infection and 4 among without Mp infections. Sequencing 102 bp of nested PCR for 16 S rDNA showed no point mutations and variability.

Conclusions: There was 45% of M pn infections among children admitted with ALRTIs between September 2003 and March 2004 in Cheju National University Hospital in South Korea. ALRTIs patients with Mp infections had more prolonged disease course, coinfection with *S.pneumoniae* and underlying atopic diseases. The 102 bp sequences of GPO probed 16S r DNA were preserved well.

P451

RISK AND OUTCOME OF *CHLAMYDIA TRACHOMATIS* INFECTION IN INFANTS WITH UPPER AND LOWER RESPIRATORY TRACT DISORDERS

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Background: *Chlamydia trachomatis* infection is associated with a wide range of clinical manifestations in infants going from mild to severe upper and lower respiratory tract disorders(RTD), such as nasal stuffiness, rhinitis, pneumonia and apnea.

Aims: To determine the clinical characteristics and outcomes of *C.trachomatis* RTD in infants.

Methods: From 1997 to 2008, infants with feeding difficulties and respiratory distress consulting at the Children's Hospital Acosta Ñu, the Maternity Hospital and the Children's Institute in Asuncion, Paraguay, were prospectively subjected to pharyngeal swabs for direct fluorescent antibody assays against *C. trachomatis*. Infants with a positive result received antibiotic treatment and were followed-up until one year of age(OYA). Clinical data were also recorded. The variables considered were: mother's age (MA), type of delivery, gestational age (GA), sex, symptoms of RTD, need for hospitalization, ICU stay, and recurrent episodes of obstructive bronchial syndrome (OBS) until OYA**.**

Results: Fifty-one infants were positive for *C.trachomatis*. Average MA was 28±4 years and cesarean deliveries were performed in 70.6%. GA was 38±1 weeks.52.9% were female. The mean age at onset of the symptoms was 12±8 days. Rhinitis was observed in 56.9%, apnea in 7.8%, obstructive bronchitis in 11.8%, bronchiolitisin 9.8% and newborn transient tachypnea in 2%. Hospitalization was necessary in 45,1 %, and 23,5% in ICU. Recurrent OBS was observed in 47,1% at OYA.

Conclusion: An important morbidity was observed in infants with*C. trachomatis* infection, resulting in a high percentage of ICU admission and recurrent OBS episodes.

Acknowledgement: To Prof. Alain Gervaix for his help reviewing the abstract.

P452

A CASE WITH RECURRENT PNEUMONIA - DIFFICULTIES OF DIAGNOSIS

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Background and aims: The authors present the particularities of an infant diagnosed during the 3rd admittance with congenital hiatal hernia.

Methods: The 1st admittance (6 months age) was triggered by paroxistic cough and cyanosis. The clinical exam revealed malnutrition and the radiological diagnosis was right pneumonia. The 2nd admittance (10 months age) was due to high fever and respiratory failure. We've considered right pneumonia according to chest X ray exam. The clinical evolution was good after antibiotic therapy although the repeated X ray image was unchanged. At 11 months of age the infant was admitted for hematemesis and clinical exam has revealed cachexia (-3 SD) and cyanosis. The sweat test and haemostasis function were normal. During the 3rd day, an episode of cyanosis and cough was induced by feeding. Specific intestinal bruits were identified on chest auscultation and the chest X ray image was almost similar as compare to previous ones. We didn't find the stomach air bubble.

Results: The clinical signs induced by feeding correlated with an abnormal chest X ray image have led to the contrast examination of gastro-intestinal tract. A hiatal hernia due to a shortened esophagus has been found and the patient was transferred in surgical department.

Conclusions: This case was diagnosed incidentally after to 2 life-threatening pneumonia episodes in the context of malnutrition. The contrast examination of GI tract was mandatory for the diagnosis. The absence of bubble air in gastric fundus could be a precocious radiological sign for congenital hiatal hernia diagnosis.

P453

PRESCHOOL ASTHMA AFTER BRONCHIOLITIS IN EARLY INFANCY

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Bronchiolitis, usually caused by respiratory syncytial virus (RSV), leads often to subsequent wheezing and even to asthma. The outcome of bronchiolitis in early infancy is poorly studied.

This pilot study was aimed to evaluate the occurrence of asthma at preschool age after hospitalization for bronchiolitis at < 6 months.

Eighty-one infants aged < 6 months were hospitalized for bronchiolitis during 6 months in 2001-2002. Sixty-eight (84%) attended a follow-up in 2008, at a mean age of 6.78 (SD 0,42) years. RSV had caused bronchiolitis in 50(73.5%) cases. Atopic dermatitis or food allergy at < 12 months was present in 25(36.8%) children.

Data on wheezing and asthma were collected for the preceding 12 months by interviewing the parents. Doctor-diagnosed asthma, and the age when asthma was diagnosed, were registered. Fisher`s exact test was used in statistical analyses.

Wheezing during the last 12 months was reported in 17 (25%) children (11 in the RSV+ (p=0.357) and 7 in the atopy+ (p=0.663) group). Doctor-diagnosed asthma was present in 7(10.3%) children aged 1-2 (atopy+ 6/7, p=0.006), in 9(13.2%) children aged 2-3, in 5(7.4%) children aged 3-4, in 6(8.8%) children aged 4-5 and in 7(10.3%) children aged 5-6 years. The figure was 8(11.8%) for 12 months preceding the study (RSV- 5/8 vs. RSV+ 3/8, p=0.026).

The prevalence of asthma at preschool age was only 12% after hospitalization for bronchiolitis at < 6 months of age. Early-life atopy predicted wheezing at < 24 months and non-RSV etiology predicted asthma at >5 years of age.

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THERAPEUTIC AND DIAGNOSTIC DIFFICULTIES OF RESPIRATORY SYSTEM DISEASES IN CHILDREN WITH NEUROLOGICAL DISORDERS IN ASPECT OF CLINICAL PICTURE AND TREATMENT

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Background and aims: Severe clinical course of acute respiratory tract diseases is very frequent in children with neurological disorders. Pneumonia often can be lethal in this group of patients.The aim of this study was to create the diagnostic and therapeutic procedures giving the best results in this group of children.

Methods: The symptoms, clinical picture, diagnostics and treatment of acute respiratory system diseases in children with neurological disorders, who were hospitalized in the Pulmonological Ward in the years 2007-2008 were analyzed.The patients, according to the type of neurological dysfunction, were divided into 4 groups:

- cerebral palsy

- neuromuscular diseases

- chromosome aberrations

- progressive encephalopaties.

Among increasing risk factors of respiratory tract diseases we estimated:

- Anamnesis - mainly in the aspect of inborn pneumonia, BPD syndrome, respiratory insufficiency in the neonatal period and the number of bronchopulmonary exacerbations

- Muscular hypotonia - due to underlying disease and also as the side effect of the treatment(eg antiepileptic drugs, baclofen)

- Conditioned by neurological disorder abnormal chest anatomy leading to bronchial secretion retention

- Primary and secondary immunodeficiences

- Pathogenic flora colonization of the airway

- Coexistence of gastroesophageal reflux.

Results: The biggest groups of patients were children with cerebral palsy and with progressive encephalopaties. Those patients required target, broad-spectrum antibiotic therapy, intensive chest physiotherapy, energetic and metabolic deficits supplementation, using prokinetics and careful administration of mucolitics.

Conclusions: In the treatment of acute respiratory tract diseases in children with neurological disorders cooperation of pulmonologist, neurologist, gastrologist and physioterapeutist is necessary.

P455

SENSITIVITY AND SPECIFICITY OF GROUP A STREPTOCOCCI AND PNEUMOCOCCUS TESTS IN A NEW RAPID MULTIANALYTE RESPIRATORY INFECTION TEST SYSTEM

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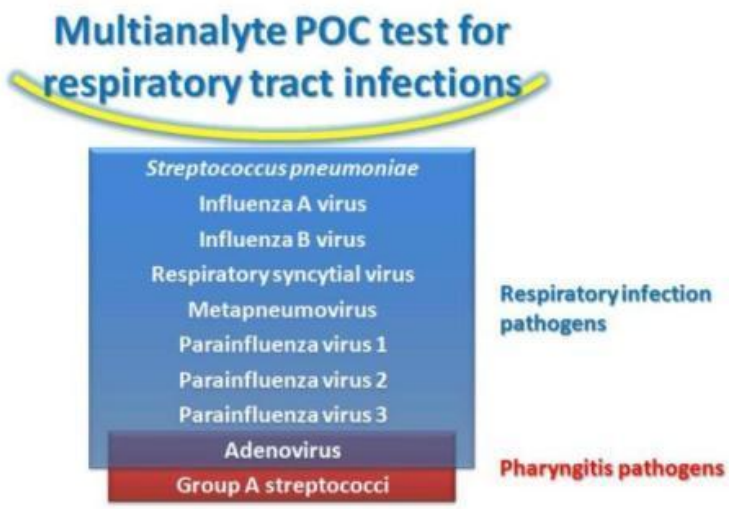
Background and aims: A novel automated multianalyte methodology has been developed for rapid point-of-care testing of respiratory infections. The methodology would be a valuable tool in pathogen-specific diagnosing and treatment of respiratory infections. For a test, swab samples from the nose or from the throat are dissolved in sample buffer and subjected to quantitative immunoassay testing on a fluorescent one-step ArcDia TPX platform. Positive results are reported electronically in 20 minutes. The results for low positive and negative samples are reported within two hours. Currently the test system covers ten common respiratory pathogens (figure).

Methods: Analytical sensitivity and specificity of the bacterial methods were studied by using cultured standard bacterial strains (N=22), purified virus preparations (N=8), and clinical samples (N=200). Commercial lateral flow tests were used as reference.

Results: The detection sensitivities of the methods for Group A streptococci and *Streptococcus pneumoniae* were 2 and 4 CFU (100 and 200 CFU/ml), respectively. The high sensitivity was also demonstrated in a dilution study against the commercial methods, which indicated equal or higher analytical sensitivities. No cross-reactions were found.

Conclusions: The results demonstrate that the new multianalyte methodology enables rapid testing of serious respiratory bacteria with extremely high analytical sensitivity and specificity. High sensitivity might enable giving up from back-up culturing which is often used in context to bacterial rapid tests.



[figure]

P456

EPIDEMIOLOGY AND CLINICAL PRESENTATIONS OF HUMAN CORONAVIRUS NL63 IN HONG KONG CHILDREN

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Background: Human coronavirus NL63 (HCoV-NL63) has been found in children presented with upper and lower respiratory tract infections (RTIs). However, the epidemiology and clinical course of this newly identified virus has not been fully elucidated. This study investigated the epidemiology, seasonality and clinical features of HCoV-NL63 in Hong Kong children.

Methods: This study consisted of two cohorts of children hospitalized in a university-affiliated teaching hospital. In the 12-month retrospective part, low-stringent reverse transcription-polymerase chain reaction (RT-PCR) was used to detect HCoVs in nasopharyngeal aspirates (NPAs). Positive samples were sequenced to confirm its identity and to determine the phylogenetic relationship with HCoV-NL63 found elsewhere. The second part covered a subsequent 12-month period in which patients were prospectively recruited.

Results: Altogether, 1981 and 1001 NPAs were studied in 2005/2006 and 2006/2007, respectively. Seventy-four (2.5%) HCoVs were identified, which consisted of 17 (0.6%) HCoV-NL63, 37 (1.2%) HCoV-OC43, 14 (0.5%) HCoV-HKU1 and 6 (0.2%) HCoV-229E. The peak season for HCoV-NL63 infection was in September-October, which was earlier than the peak for HCoV-OC43 infections (December-January). HCoV-NL63-infected patients were younger, and more likely to have croup, febrile convulsion and acute gastroenteritis. Majority of local HCoV-NL63 isolates were phylogenetically closely related to those found in Belgium and the Netherlands.

Conclusions: HCoV-NL63 is important yet uncommon among our hospitalized children with acute RTIs. Such infection peaks in autumn, and this is more likely to have croup, febrile convulsion and gastroenteritis compared to those infected with other viruses.

Funding: Research Fund for the Control of Infectious Diseases (04050372), HKSAR.

P457

ABSOLUTE NUMBERS OF MYELOID AND PLASMACYTOID DENDRITIC CELLS IN PERPHERAL BLOOD OF INFANTS WITH ACUTE BRONCHIOLITIS

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Background and aim: Dendritic cells (DCs) constitute a link between innate and adaptive immune responses and are critical in the process of control of viral infections. The role of DCs in respiratory tract infections such as bronchiolitis is under study. RSV bronchiolitis has been characterized by increased numbers of myeloid (mDCs) and plasmacytoid (pDCs) DCs in the nasal mucosa and by a significant decrease of pDCs in peripheral blood. The purpose of this study is to evaluate the number of mDCs and pDCs in peripheral blood of infants at a first episode of acute bronchiolitis.

Methods: Blood samples were taken from 20 infants with a first episode of acute bronchiolitis and from 19 age and sex matched healthy controls which had blood testing prior to elective surgery. The percentages of mDCs (CD 11+) and pDCs (CD 123+) were determined using three-colour flow cytometry.

Results: The absolute numbers (cells/μl) of mDCs as well as those of pDCs in infants with acute bronchiolitis were found significantly lower compared to those in controls. The mean number±SEM of mDCs in bronchiolitis was 8,339±1,067 whereas in controls it was 19,27±2,640 (p=0,0005). pDCs mean number±SEM in bronchiolitis was 13,58±1,752 whereas in controls it was 26,20±3,898 (p=0,0047). There were no differences within the control group, between healthy children and children with non-respiratory infections.

Conclusion: Decreased numbers of DCs subsets in peripheral blood of patients with acute bronchiolitis may be due to their migration to the respiratory epithelium.

P458

SIX MONTHS FOLLOWING THE FIRST EPISODE OF BRONCHIOLITIS: RECURRENT WHEEZING IS MORE FREQUENT AFTER RHINOVIRUS RATHER THAN RSV INFECTION

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Background and aim: Virus-induced bronchiolitis in infancy often precedes the development of recurrent wheeze or asthma. However, the impact of the specific viral etiology of these episodes on relapses and future asthma development is still under scrutiny. This study aims to examine possible relationship between specific viral agents and early childhood asthma development.

Methods: Infants hospitalized for their first episode of bronchiolitis were recruited. Nasopharyngeal washes were collected and the viral etiology of bronchiolitis was assessed using reverse-transcriptase polymerase chain reaction (RT-PCR). Parents were asked to complete a weekly diary with symptoms and therapy. All parents were contacted by phone at the end of follow up (6 months).

Results: A total of 50 infants (median 3.6 months old) were included. So far 35 infants have completed a six month follow up. Viral etiologies were identified in the majority of patients with bronchiolitis (46/50); RSV in 24 (48%), Rhinovirus (RV) in 22 (44%), adenovirus in 10 (20%), Parainfluenza virus in 9 (17%), influenza A/B in 4 (8%) and human corona virus in 1 patient. Double infections were detected in 11/50 infants. During follow up RV(+) infants had a significantly higher incidence of relapse compared to RSV (10/11 versus 6/12, $p< 0.0043$).

Etiology	Incidence	Follow-up	Recurrent wheezing
RSV	24/50	12/24	6/12
RV	22/50	11/22	10/11
adenovirus	10/50	9/10	5/9
PIV(1-3)	9/50	6/9	2/6
Influenza A/B	4/50	4/4	1/4
HCov	1/50	1/1	1/1

Conclusions: RV-induced bronchiolitis in infancy seems to be associated with a higher incidence of wheezing episodes within the next 6 months, than RSV-bronchiolitis. The cohort is ongoing with a planned assessment of wheezing persistence at the age of 3 years.

P459

USE OF COMPLEMENTARY AND ALTERNATIVE THERAPY IN CHILDREN WITH RECURRENT ACUTE OTITIS MEDIA

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Background and aim: Control of environmental factors, chemoprophylaxis, immunoprophylaxis and surgery are considered acceptable preventive options of recurrent acute otitis media (RAOM). No data are available concerning the use of complementary and alternative medicine (CAM) as prevention in children with RAOM. We evaluated the preventive use of CAM (homeopathy and/or herbal medicine) in Italian children with a history of RAOM.

Methods: A survey in 2008 of 840 children, aged 1 to 7 years, with RAOM (≥ 3 episodes in 6 months), using a face-to-face questionnaire and exploring prevalence, determinants, reasons, cost, perceived safety and efficacy of CAM.

Results: About one-half (46.5%) of children used CAM, significantly more than immunoprophylaxis (influenza vaccine 15%, PCV-7 34%) and chemioprophylaxis (2%). A CAM using family, a highly educated mother, day-care attendance, smoking exposure, having no siblings were the main determinants. Perceived inefficacy and fear of side effects of traditional treatments were the main reasons for use (62%). CAM was perceived as safe and effective in most patients (95.7% and 68.6% respectively). CAM prescribers were pediatricians in 50.7%, other specialists in 15.9%, pharmacists in 9.9%; self-initiation was reported in 23.9%. Cost for CAM was ≥ 25 €/month in 27.6% and ≥ 50 €/month in 16.3%.

Conclusions: Children with RAOM should be included among the categories of subjects at risk for using CAM. This finding and the role of pediatrician as main prescriber are worrying, considering the actual lack of evidence regarding efficacy, safety and cost effectiveness of CAM for the prevention of otitis media.

P460

UNDERUSE OF INFLUENZA VACCINE IN SCHOOLCHILDREN WITH CHRONIC RESPIRATORY DISEASES IN CURITIBA (BRAZIL), 2008

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Background and aims: The influenza vaccination reduces the number of medical appointments, hospitalizations and use of medications in asthmatics. The vaccine is available in Brazil with no charge, for children over 6 months of age with chronic respiratory diseases (CRD) and asthma, but there is few information about the use of this vaccine for risk groups . The aim of this study was to describe the influenza vaccine coverage in schoolchildren with asthma or other CRD attended in private elementary schools in Curitiba, in 2008, and to analyze the arguments for non immunize these children.

Methods: Parents/guardians of 415 schoolchildren (median, 6 years) attended in private schools, were interviewed in order to fill out a standard form with information about their children and the registers of vaccination was checked.

Results: The prevalence of CRD and asthma were 17.6% (n=73) and 5.5% (n=23), respectively, according to the parents' reports. In the last year, the influenza vaccine coverage was 4% (CI95%:0-12) in the CRD-group and 9% (CI95%:0-25) in the asthmatic group. The main reasons for not vaccinating the children were: non-indication by the pediatrician 35% (CI95%: 26-43), vaccine cost 21% (CI95%: 15-26) and unawareness of the influenza vaccine 15% (CI95%: 10-21).

Conclusions: Despite of the fact that access to medical services in Curitiba is 100% and influenza is offered free of charge to risk groups, this vaccine was underused. Physicians and patients should be informed about the recommendations and benefits of influenza vaccine for children with chronic respiratory diseases.

P461

ETIOLOGY OF ACUTE RESPIRATORY INFECTIONS IN CHILDREN IN KINSHASA (DEMOCRATIC REPUBLIC OF CONGO)

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Background and aim: Very few etiological studies of acute respiratory infections (ARI) in children have been documented in Africa and especially in central Africa. The aim of our study was to look at the prevalence of four common respiratory viruses, namely RSV, adenovirus, influenza A and influenza B in the infancy population in Kinshasa, Democratic Repulic of Congo (DRC), over a 3-months period.

Methods: We analyzed 451 samples from patients with ARI aged 0 to >11months using three rapid tests for detection of viruses in respiratory specimens: Adeno Respi-Strip, RSV Respi-Strip and Influ-A&B Respi-Strip (Coris BioConcept, Gembloux, Belgium). Results were analyzed according to viral infections or co-infection types and by age distribution for each virus type.

Results: Among the 451 analyzed samples, 151 were shown to be positive for at least one virus (overall prevalence of 33,4%), adenoviral infection accounting for more than 58% of positive cases followed by RSV (15,9%), Influenza B (11,9%) and Influenza A (6,6%) the remaining 11 cases (7,3%) being co-infections. Most of Influenza A or B infections were found in older infants (>11 months), Adenovirus infections were equally distributed through all age groups, while RSV infections were more present in younger infants (< 5 months).

Conclusions: Prevalence of respiratory viruses in ARI paediatric patients from Kinshasa was high during the evaluated period, Adenovirus being peculiarly the most prevalent virus. Co-infection are not uncommon and RSV is more prevalent in younger population, similarly to what is found in other well-documented infant populations.

P462

PROCALCITONIN IS USEFUL IN DISTINGUISHING BACTEREMIC FROM NONBACTEREMIC, VIRAL, AND ATYPICAL BACTERIAL PNEUMONIAS IN CHILDREN

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Background and aims: Empiric antibiotic use is a worldwide practice in managing children with Community-Acquired Pneumonia(CAP). We aimed to assess the usefulness of procalcitonin(PCT) and alpha-interferon(IFN-alpha) measurements in differentiating viral from bacterial childhood pneumonias.

Methods: In a 22-month period, CAP was diagnosed among 159 hospitalized children based on respiratory complaints or fever plus presence of pulmonary infiltrate read by an independent pediatric radiologist. Etiology was investigated for 9 viruses, 4 atypical and 3 typical bacteria. Blood culture had been performed before treatment in 149 cases. PCT and IFN-alpha were measured in the serum sample collected on admission.

Results: Etiology was bacterial in 28(18%), viral in 57(36%), viral-bacterial in 40(25%) and unknown in 34(21%). Among the patients with bacterial infection, 8, 38 and 20 had bacteremic, nonbacteremic and atypical bacterial pneumonia, respectively. The median(25^{th}-75^{th}percentile) PCT(ng/ml) was 0.72(0.13-3.04). IFN-alpha(IU/ml) was detectable in 20(13%) cases. The difference of median PCTs of the bacteremic (4.22;1.56-7.56), nonbacteremic (1.47;0.24-4.07), atypical bacterial (0.18;0.06-1.03) and only viral (0.65;0.11-2.22) subgroups was significant(p=0.02). PCT was $\geq$2ng/ml in 52(33%) cases. Presence of IFN-alpha was associated with PCT< 2 ng/ml (90% *vs* 64%,p=0.02). The Negative Predictive Value (95%CI) of PCT $\geq$2ng/ml was 95% (89%-100%), 89% (78%-101%), 93% (85%-100%) for differentiation of bacteremic from viral, atypical bacterial or nonbacteremic bacterial pneumonia, respectively, and 58% (49%-68%) for differentiation of bacterial and viral infection.

Conclusions: PCT is useful in identifying bacteremic infections among children hospitalized with CAP. Although detectable IFN-alpha was associated with PCT< 2ng/ml, the presence of IFN-alpha was uncommon.

P463

RESPIRATORY RATE IN FEBRILE CHILDREN: DERIVATION OF AGE-SPECIFIC CENTILE CHARTS

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Background and aims: As both body-temperature and respiratory disease may affect respiratory rate in febrile children, we aimed to derive age specific reference values for respiratory rate.

Methods: We recruited all children visiting the paediatric emergency department of the Erasmus-MC Sophia children's hospital in 2006, with recorded values of temperature and respiratory rate. Children with significant co-morbidity or a diagnosis interfering with respiratory rate (asthma-exacerbation, metabolic derangement or febrile seizure) were excluded. With multivariate regression analysis we explored the relationship between respiratory rate, age, and temperature. Median and upper centiles of respiratory rate at a given temperature were calculated and centile charts were derived using LmsChartMaker Pro.

Results: Preliminary results are based on 1255 children, aged 1 month - 16 years, 722 (58%) boys. Overall we found an increase of 2.2 breaths per minute (bpm) per degree Celsius body-temperature (CI: 1.7 - 2.8). In stratified analysis age-specific slopes ranged from 1.7 to 3.7 bpm per degree Celsius with linear association in all age-groups except for the 1 - 2 years old group. Temperature and age-dependent centile charts show specific thresholds for respiratory rate.

Conclusions: Age-specific charts for respiratory rates expected at different temperatures allow paediatricians to determine if an observed respiratory rate is higher than expected at a given level of fever. This may improve the interpretation of the significance of respiratory rate in children attending emergency departments. Further work is needed to determine the predictive value of respiratory rates that are above the upper centiles for age and temperature.

P464

PROBIT ESTIMATES OF CHEST INFECTIONS IN CHILDHOOD NEUROPSYCHOPATHOLOGY USING INCIDENTAL CHEST RADIOGRAPHY COULD DIRECT A MODIFIED SUBSET APPROPRIATE IMMUNIZATION/ANTIMICROBIAL POLICY

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Background/purpose: Chest infections are common in childhood neuropsychopathology, due to pseudobulbar palsy, aspiration, gastro-esophageal reflux, poor cough reflexes, immobility, scoliosis, pickwickian effect, associated immunodeficiencies/cardio-pulmonary anomalies, use of anxiolytics, muscle relaxants, anticonvulsants, immobility. Anaerobic chest infections/abscesses are commoner because of aspiration. Febrile responses to infections/radiologic features could be blunted or paradoxical. Chest infections could predispose to meningo-encephalitis/cerebral abscesses, acute on remote convulsive seizures and compromised aerodynamics. Resulting anoxia of variable degrees of severity will have negative effects on an already compromised neurological status, making an accurate/timely diagnosis imperative. Recommendations directing immunization/antibiograms were consensus based/generic.Specific figures on accurate incidence estimates will yield data for modified setting/subset specific appropriate immunization/prophylactic/therapeutic antimicrobial guides.

Cases: A prospective review of the clinical, laboratory/chest radiographic data of 521 cases of childhood neuropsychopathology seen at a tropical referral child´s neurology clinic. The spectra of neuropsychopathology in rank order were Idiopathic seizures, symptomatic cryptogenic seizures, cerebral palsy, neurodevelopmental delays, dysmorphologies/chromosomal disorders, acute hemiplegias, neurocutaneous syndromes.

Related features were feeding difficulties, drooling , vomiting, growth failures, failure to thrive, leucocytosis, leucopaenia/ anaemia.

Significant radiologic features evaluated,interpreted,validated/reported in a standardized manner by the radiologist/neurologists relative to recognized aetiological patterns, in rank order were perihilar infiltrates, central pneumonia´s, variable degrees of consolidations/laterality , air bronchograms and pleural effusions.

Interventions: Antibiotics,supplemental oxygen, small frequent feeds, chest physiotherapy, airway suctions, rinatidine, antipyretics and anticonvulsants.

Conclusion/importance: Incidence of chest infections were related to chronological/developmental ages. Incidence of chest infections were related to chronological/developmental ages.I ncidence was more common in cerebral palsy than in dysmorphology/chromosomal disorders and cryptogenic symptomatic seizures. It was least common in idiopathic seizures and unclassified paroxysmal events. Chest infections are more common/non-specific in neuropyschopathology and should be searched for. A lower threshold for the application of antimicrobials/ modified differential immunization schedule should be recommended in this subset with variance.

P465

USE OF A MULTIPLEX MOLECULAR ASSAY IN THE RAPID DIAGNOSIS OF RESPIRATORY VIRAL INFECTIONS IN FEBRILE NEUTROPENIC CHILDREN

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Background and aims: Studies in febrile neutropenic children using Direct Fluorescence Antibody techniques (DFA) on nasopharyngeal washes (NPW) indicate that up to 37% of patients have a respiratory virus infection. In this study, we evaluated the use a novel multiplex molecular diagnostic technique (Resplex, Qiagen Inc) to detect respiratory virus infections during a winter season.

Methods: This prospective study included all febrile neutropenic episodes at British Columbia Children's Hospital for a period of 6 months (01/10/2007-01/04/2008). NPW's for virus detection were routinely obtained in children presenting with respiratory symptoms. Specimens were analysed by DFA for 8 common viruses and by multiplex PCR using the Resplex assays, detecting up to 21 viral and bacterial respiratory pathogens.

Results: 126 episodes of febrile neutropenia in 67 patients were recorded. In 37 episodes (29%), the patient presented with respiratory symptoms. 33 NPW aspirates were tested both by DFA and Resplex. DFA was positive for a respiratory virus in 8/33 episodes (24%) and the Resplex assay in 20/33 (60%). The pathogens isolated were: Enterovirus/Rhinovirus group (8), Influenza (5), Metapneumovirus (3), Parainfluenza (2) and RSV (2). No dual viral respiratory infections were identified. In 4 episodes there was evidence for the presence of a bacterial co-pathogen.

Conclusion: This study demonstrates superiority of a multiplex molecular assay compared with DFA in identifying viral respiratory pathogens in pediatric patients with febrile neutropaenia and respiratory symptoms. Evidence of a viral respiratory pathogen was found in 60% of those patients during a winter season.

P466

ACUTE BRONCHIOLITIS IN A PAEDIATRIC DEPARTMENT: RESULTS OF SIX MONTHS OF RESEARCH

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Background and aims: Acute viral bronchiolitis is an important cause of severe low respiratory tract infection in infants worldwide, occuring in winter epidemics. Respiratory syncitial virus is the most common cause.The aim of the study was the analysis of acute bronchiolitis incidence and clinical characteristics in a Paediatric Department.

Methods: A prospective study of all cases of acute bronchiolitis presenting to Victor Gomoiu Clinical Pediatric Hospital, Bucharest, from June 2008 to December 2008. There were studied: age, sex, risk factors, seasonal variation, clinical aspects, duration of hospitalization, treatment.

Results: During the 6 months of study, a total of 237 children with acute bronchiolitis were examined at our Emergency Service and 183 (77.21%) were admitted to the Pediatric Department. In hospitalized children 75% were younger then age 12 months and among those, infants between 3 and 6 month (33.5%) were more often affected. 64.55% of the children were of males. Risk factors were: prematurity, pre-existing heart or lung diseases, parental smoking, low socioeconomic conditions. All children had moderate to severe respiratory symptoms (wheezing, expiratory dyspnea, cough), poor feeding and 15% had evidence of respiratory distress at admittion. The mean duration of the hospitalization was 5.3 days. Controversial therapy was discussed (bronchodilators, corticotherapy inhaller/general route, antileukotriens).

Conclusions: Acute viral bronchiolitis is an important cause of hospitalization in children. Viral etiology is most common. All hospitalized children had favourable outcome.

P467

AI-LIKE ILLNESS TREND PRIOR TO HUMAN AI CASE IN INDONESIA

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Background: The first epidemic avian influenza (H5N1) infection among domestic poultry in Indonesia was declared officially in the beginning of 2004, while the first human case of AI was identified in July 2005. A retrospective study was conducted to investigate the AI-like illness (hospital based review) prior to the emerging human AI case in Indonesia.

Objective: To describe the prior situation of AI-like illness (acute respiratory tract infection/ARTI) in pediatric patients (0-16 year old) who were hospitalized (2002-2005), by medical record review.

Results: Data were retrieved from medical record of ARTI (AI-like illness) cases hospitalized in 27 reference hospitals in 17 provinces divided into 3 zones (high, moderate, low risk for human AI infection spread) based on the presence of human AI cases at those areas since 2005. Eight provinces had human AI cases previously, 7 provinces had poultry AI cases, and two other provinces had no AI case yet (in human nor poultry). There were 1720 infants (44.6%) out of 3859 pediatric patients hospitalized within four year period. The number of cases tends to increase gradually by year and most cases found in the first trimester (January-March) yearly. The admission diagnosis of 52.3% cases were lower respiratory tract infection and the fatal cases were 236 (6.1% of all cases).

Conclusion: The AI-like illnesses tends to increase by year and the number of cases in 2005 more than 3 fold compared to 2002 and further investigation is needed.

P468

COST OF RSV INFECTIONS IN ADULT OUTPATIENTS IN GERMANY

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Background: The direct and indirect medical costs of adult outpatient RSV infections are not known.

Methods: Between 2001 and 2004, a total of 946 patients with prolonged (≥ 7 days) coughing were recruited in a sentinel from general practitioners and internists. Diagnostics for RSV infections and other agents of upper respiratory infections (Adenovirus, Bordetella pertussis/parapertussis, influenza virus A and B, Mycoplasma pneumoniae, parainfluenzavirus 1-3) were performed. Medical records from 39 patients with laboratory confirmed RSV infections were screened individually. Resource use data as well as occupation and contact history were extracted. Direct medical and work loss costs (indirect costs) per RSV episode were estimated by applying unit costs developed from published sources to abstracted resource use profiles.

Results: On a population based estimate, RSV infections occurred at an incidence of ~300/100,000 population per year. During the course of the infection, RSV patients averaged 4.3 physician visits (median 3.0), 49% were sent to a specialist, 92% received antibiotics and 28% received corticosteroids. The estimated average direct medical cost per RSV episode as 103 €, average indirect medical cost was 84 € per case.

Conclusions: RSV infections presenting as long lasting coughs in adults occur frequently in this German population, are mostly treated with antibiotics, and have a relevant medical resource use.

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PARAMETERS TO AID IN THE DECISION TO PERFORM A MICROBIOLOGIC ANALYSIS IN CHILDREN AT RISK OF HAVING TUBERCULOSIS DISEASE

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Background and aim: Tuberculosis is difficult to manage and to obtain a definitive diagnosis may be complicated. Children with positive gastric aspirate culture for Mycobacteria (MTB) were compared with those with negative results (NMTB).

Methods: We reviewed charts of children with gastric aspirates obtained for culture between 2003-2008, and compared MTB with NMTB. We analyzed demographics, family evaluation, clinical and radiological presentation, PPD and microbiological results.

Results: Thirty-two children belonged to MTB whereas 194 children were in the NMTB. Among NMTB we randomly chose 45 children and compared them with MTB. There were no differences between MTB and NMTB related to age, gender, symptoms, and PPD in relatives. We observed a significant difference in: immigrant origin (56% vs 29%), existence of index case (67% vs 33%), positive PPD (73% vs 46%) and its size (14 vs 5 mm). We found no significant differences in the percentage of children with normal chest-x-ray (46% vs 67%; p=0.095) and normal chest-x-ray without symptoms (19% vs 42%; p=0.055) in MTB vs NMTB, respectively.

Children studied because of contact with TB and normal chest-x-ray without symptoms had a risk of having a positive culture of 5.6% (8.9% when positive PPD vs 1.6% when negative PPD).

Conclusions: Among the risk factors to isolate M. tuberculosis in children at risk, having a positive PPD was one of the most relevant. A microbiological study may be indicated in non-symptomatic children with normal chest-x-ray but positive PPD given the percentage of M. tuberculosis found in these children.

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SEVERE PNEUMONIA IN A CHILD WITH COMPLETE INFΓR1 DEFICIENCY: RHODOCOCCUS EQUI AS PROBABLE OPPORTUNISTIC PATHOGEN

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Background and aims: Rhodococcus equi, a recognized pathogen in horses, is emerging as a human pathogen in immunocompromised host. Recently it has been demonstrated that newborn foals, that show an increased vulnerability to Rhodococcus equi, exhibit a marked inability to express the INFγ gene and produce INFγ protein.

Methods: We describe a probable Rhodococcus equi pneumonia in a child with complete INFγ receptor 1 (INFγR1) deficiency.

Results: A 5 year-old boy affected by complete INFγR1 deficiency was admitted to the hospital with a 3-day history of fever, productive cough and tachypnea. A chest radiograph showed consolidation of the left lower lobe. The C reactive protein concentration was 430 mg/L. Clarithromycin, ceftriaxone and teicoplanin were administered. Because of persistence of fever, worsening of radiologic findings that were suggestive of necrotizing pneumonia, respiratory distress and hypoxia a bronchoscopy with bronchoalveolar lavage (BAL) was performed. The antibiotic therapy was changed to meropenem, ciprofloxacin, amikacin and clarithromycin. The child was discharged after 4 weeks of intravenous therapy and oral antibiotic treatment was prescribed for a further 3 weeks. On BAL sample rare gram-positive coccobacilli were demonstrated. During a subsequent interview with the parents it was learned that ten days before admission the child visited a riding track that is located near to his home. Intriguingly PCR performed on BAL sample was positive for Clavibacter michiganensis, a plant pathogen that is related to other plant pathogens as Rhodococcus.

Conclusion: Rhodococcus equi might be considered as opportunistic pathogen in children with INFγR1 deficiency and severe pneumonia.

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NASOPHARYNGEAL MICROBIOTA DURING UPPER RESPIRATORY INFECTION, COMPARISON BETWEEN CHILDREN WITH AND WITHOUT ACUTE OTITIS MEDIA

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Background and aims: Nasopharynx is gateway to microbes that cause respiratory infections. Nasopharyngeal microbiota consists of both bacteria and viruses, this complex ecosystem is inadequately characterized. The aim is to compare nasopharyngeal microbiota during upper respiratory infection (URI) between children with and without acute otitis media (AOM).

Methods: Nasopharyngeal specimens were taken from 319 children with AOM and 238 children with uncomplicated URI (all aged 6-35 mo). Bacteriota was analysed by semi-quantitative culture and respiratory viruses by PCR and antigen detection.

Results: In 82% of the samples in both groups respiratory viruses were detected in the descending order: rhinovirus, human bocavirus, respiratory syncytial virus, enterovirus, human metapneumovirus, influenza A virus, parainfluenza virus 3, influenza B virus, and adenovirus. Human metapneumovirus was significantly more frequent in AOM than in URI group (6% vs. 2%; P=0,012). At least one typical bacterial pathogen of AOM (*S. pneumoniae, H. influenzae, M. catarrhalis*) was found in 295 (92%) AOM patients but only in 180 (76%) URI cases (P< 0.001). *S. pneumoniae, H. influenzae*, and *M. catarrhalis* were found in 61%, 25%, and 74% of AOM patients and in 42%, 14%, and 61% in URI patients. AOM group had less often non-pneumococcal streptococcal species than URI group (32% vs. 48%; P< 0.001). The same applied to corynebacterial species and other non-pathogenic bacteria (43% in AOM vs. 56% in URI; P=0.004).

Conclusion: Respiratory viruses were detected equally often regardless of ear status. However, AOM group had more pathogenic bacteria and less non-pneumococcal streptococci and other non-pathogenic bacteria.

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SYMPTOMS OF CHILDREN HAVING UPPER RESPIRATORY TRACT INFECTION WITH OR WITHOUT ACUTE OTITIS MEDIA

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Background and aims: Most of the symptoms of children having acute otitis media (AOM) are nonspecific. Still the symptoms are used in parental suspicion of AOM; diagnostics of AOM; AOM severity scaling; and measuring outcome. The aim was to find out whether the symptoms differ in children having upper respiratory tract infection (URI) with or without AOM.

Methods: 378 children aged 6-35 months (mean age 15 months; boys 53%; mean number of previous AOM 1,9; mean duration of URI symptoms 7,5 days; no difference between AOM and URI group) came for an outpatient visit with URI and parental suspicion of AOM. Before ear examination we asked the severity and duration of symptoms using a structured questionnaire.

Results: 160 children had AOM and 218 URI without AOM. Children with AOM had fever more often (AOM 43% vs. URI 33%; P=0,056), but the mean duration of fever (2,5 vs. 2 days) and mean temperature (38,5 vs. 38,4 ^{o}C) were not different. The mean durations of earache (1,6 vs. 1,4 days) and irritability including night restlessness (4,0 vs. 3,8 days) were not statistically different between AOM and URI groups. By parental evaluation, earache was severe significantly more often in AOM than in URI group (23% vs. 12%; P=0,032).

Conclusions: Our study further confirms that the symptoms of children having URI with or without AOM do not differ remarkably. The focal role of the symptoms in the diagnostics and classification of AOM severity should be reconsidered.

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CLEARANCE OF CHLAMYDOPHILA PNEUMONIAE FROM THE AIRWAYS FOLLOWING ANTIBIOTIC THERAPY WITH ROXITHROMYCIN IN CHILDREN WITH BRONCHITIS OR PNEUMONIA

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Chlamydophila(C.) pneumoiae is an intracellular slowly growing bacterium causing respiratory tract diseases and the potential to cause persistent infection. Therefore, persistent or recurrent respiratory tract symptoms might be the consequence of persistent infection.

Over a period of two and a half years all inpatient children with bronchitis or pneumonia were screened for C. pneumoniae - infection by means of polymerase chain rection with enzyme-immunoassay-detection (PCR-EIA) in a throat swab. Roxithromycin was given one or two times a day for four weeks. Throat swabs were controlled for C. pneumoniae infection after 3-5, 9-12, and 28 days (end of antibiotic therapy) as well as 56 days (four weeks after antibiotic therapy).

The study was approved by the local ethical committee.

C. pneumoniae was detected in 124 of 1085 (11.4%) children. Parents of one hundred children gave informed consent. Fifty children were randomised for one or two doses of roxithromycin per day, respectively. Ninety seven children completed the study.

After 3-5 days C. pneumoniae was detected in two of fifty children (roxithromycin given once a day) and five of fifty children (roxithromycin given twice; p=0.4), respectively. Afterwards it could not be detected in any child independent of the doses given.

C. pneumoniae is not reliably eradicated from the airways prior to 9-12 days. Therefore, antibiotic therapy has to be given for at least 9-12 days. There is no persistent or re-infection. In case of persistent or recurring symptoms, this is not the consequence of actual C. pneumoniae - infection.

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PATTERN AND PREDICTORS OF ANTIBIOTIC PRESCRIBING IN PAEDIATRIC UPPER RESPIRATORY TRACT INFECTIONS

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Objective: To evaluate the pattern of antibiotic prescriptions for paediatric upper respiratory tract infections (URTI) and determine the associated predictors for such antibiotic use in the Kingdom of Bahrain.

Methods: From March 2005-March 2006, demographic data, clinical presentation, investigations and antibiotic prescription for children diagnosed with URTI (n=184) at the Bahrain Defence Force Hospital was recorded. To assess the factors influencing physician antibiotic prescription for URTI, a cross-sectional survey of doctors was carried out using a pre-tested questionnaire administered to paediatricians, general practitioners (GPs) and emergency room physicians.

Results: Antibiotics was prescribed to 51.6% (95/184) of patients mainly children < 3years (40/95). Significant association was demonstrated for antibiotic prescription, age and diagnosis of tonsillitis or acute otitis media ($p < 0.05$). Amoxicillin (37/95) was the most frequently prescribed followed by beta-lactam/beta lactamase combination and second generation cephalosporins. Fever, younger age, sorethroat and presence of earache increased the likelihood of antibiotic prescription. Data from the cross-sectional survey of doctors revealed that lack of national guidelines, parental pressure and diagnostic uncertainty contributed to antibiotic overuse.

Conclusion: Antibiotic over-use for the treatment of paediatric URTI remains a problem in our setting. The development of national guidelines integrated with structured continuing medical education, public awareness campaigns and introduction of rapid streptococcal antigen tests in outpatient clinics is recommended.

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THE ROLE OF EX-TB PATIENTS AS TREATMENT SUPPORTERS IN TB CARE AND MANAGEMENT

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Background: Non-adherence to TB treatment is receiving considerable attention among HIV/AIDS implementers. Kamwokya Christian Caring Community (KCCC) provides HIV/TB treatment in Kampala District. Whereas the Ministry of Health developed different strategies to ensure adherence to TB treatment, including TB DOTS, and increased availability of drugs, there is lack of network systems among patients, their families, and health institutions so as to tackle other challenges that impact on adherence. Most health centers dispense and do not link up with the community. KCCC experience demonstrated that the absence of treatment supporters and linkage between families and service providers has increased non adherence to TB medication, yet co-infection of HIV/TB is on the increase.

Methodology: The time period studied in includes 2003- 2007. Two major research strategies were employed: quantitative analysis of clinical data and two case stories Data has been extracted from T.B register, and project reports, and analyzed using SPSS version 12.0.

Results: Between 2006 and 2007, 360 patients were treated for TB and overall, 73 % adhered to the treatment. During the same period, 238 patients were co-infected with HV/TB. By the end of 2005, default rates averaged at 25%. This reduced to 11% in 2007 among patients visited by Ex-TB supporters. Treatment supporters have reached a total of 120 TB patients in their homes.

Conclusions: The success of TB treatment depended on the linkages between the clinic, communities, families, and ex-TB supporters. TB treatment should look beyond the DOTS approach, to more sustainable methods, like expert treatment supporters.

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VIRAL CO-INFECTIONS AND SEVERE LOWER RESPIRATORY INFECTION (LRI), IN FILIPINO INFANTS

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Backround: In the context of an 11 valent pneumococcal vaccine (11 PCV) trial, in the Philippines, we examined the role of multiple viral infections in the causation of severe LRI.

Methods: 12 194 Filipino infants, enrolled in a randomized controlled trial, received 3 doses of 11-PCV or placebo , at 6, 10 and 14 weeks. Nasal wash specimens, clinical, laboratory and radiographic data were collected from 1 in 3 outpatient or all inpatient subjects admitted with LRI to the Government hospital serving the population. Viral culture and multiplex PCR (Eragen™) were done on the nasal wash specimens. We attempted to determine if co-infections with multiple viral agents were more severe than single infections with respiratory syncytial virus (RSV), parainfluenza viruses (PIV), Influenza A or B (Flu A, Flu B), human rhinovirus (hRV), adenoviruses or coronaviruses.

Results: 2086 specimens obtained from subjects with LRI that were tested for viruses, 1086 were from infants1.5-11 mo, 698 were from children 12-23 months and 304 from children 2-5 years of age. Co-infections with FluB and coronaviruses may have resulted in significantly more WHO defined severe pneumonia, while hRV appeared to be protective!

Indicator of Severity	RSV	PIV	Flu A	Flu B	hMPV	hRV	Adeno viruses	Coronaviruses
Number of Infections	*642 (30.8%)*	*217 (10.4%)*	*122 (5.8%)*	*39 (1.9%)*	*97 (4.6%)*	*598 (28.6%)*	*92 (4.4%)*	*87 (4.2%)*
Hospital Admissions	0.1965	0.3385	0.0777	0.4982	0.1266	0.4061	0.8121	0.8548
Severe Pneumonia	0.2435	0.1649	0.6403	0.0411	0.3984	0.5193	0.3779	0.0401
Very Severe Pneumonia	0.1403	0.7356	1.0	.	0.2917	*0.0003*	0.5483*	1.0
Hypoxemia	0.8025	0.3089	1.0	.	0.4403	0.0499	.	.
Radiographic Pneumonia	0.9871	0.1610	0.1792	0.6665	0.1960	0.8646	1.0	.

[Viral Infections and Co-Infections]

Conclusions: Most viral co-infections with multiple viruses don't appear to cause more severe respiratory disease. Simultaneous infection with hRV may protect children against the very severe effects of other viral co-infections.

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EPIDEMIOLOGIC STUDY ON THE ACUTE RESPIRATORY INFECTIONS IN THE HOSPITALIZED INFANTS

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Material and method: We carried out an epidemiologic study on the acute respiratory infections (ARI) in the infants admitted in the 2nd Pediatric Clinic of the Emergency County Hospital in Craiova, over a period of two years (01.01.2006 - 31.12.2007).

Results: The study group was made up of 1,192 admitted infants with various ARI, representing 80.9% out of the total admitted infants (1,473). The group structure: according to sex M 678 (56.9%), F 514 (43.1%); according to environment U 604 (50.7%), R 575 (48.2%), placement centers 13 (1.1%); age groups (months): 0-1/ 98 (8.2%), 1-3/ 306 (25.7%), 3-6/ 346 (29%), 6-12/ 442 (37.1%). Among the 1,192 infants, 422 (35.4%) had acute upper respiratory tract infections: 210 (49.8%) acute rhinopharyngitis, 119 (28.2%) acute rhinoadenoiditis, 50 (11.8%) acute otitis media [31 (62%) congestive; 19 (38%) festering], 43 (10.2%) acute laryngitis; 770 (64.6%) had acute lower respiratory tract infections: 208 (27%) acute bronchiolitis, 428 (55.6%) viral acute pneumonias and 134 (17.4%) pneumonias/ bronchopneumonias. Anemia was registered in 398 (33.4%) infants, rickets in 285 (23.9%) and dystrophy in 158 (13.3%). Among the 1,192 infants with ARI 10 (0.84%) died of bronchopneumonia, sometimes presenting other associated pathology. The average period of hospitalization was 6.87±3.45 days (1-24).

Conclusions: 80.9% of the admitted infants presented ARI. They prevailed in the male infants (56.9%) and in the 6-12 months age group (37.1%). The acute lower respiratory tract infections represented about 2/3 out of the total of the ARI. The most frequent ARI was acute viral pneumonia.

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SOCIAL DETERMINANTS OF SEVERITY OF PNEUMONIA IN A NORTH INDIAN PEDIATRIC POPULATION

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Purpose: To assess the relationship between Pneumonia severity, antibiotic use, gender and socioeconomic status (SES) in children (< 5 years) in north India.

Methods: Retrospective review of 600 cases of pneumonia diagnosed clinically and on Chest X-Ray admitted to Children Hospital in Punjab, India from 2004-2006. Subjects were divided into low-SES (Group A) and middle to high SES (Group B). Treatment protocol was either a Ampicillin (100-200mg/kg/24-hours) & Gentamicin (5-7.5mg/kg/24-hours) or Benzyl-penicillin (50,000-150,000 units/kg/24-hours) & Kanamycin (15-30mg/kg/24-hours). Carbenicillin (250-300mg/kg/24-hours divided in 4 equal doses) was added if there was no improvement in 72-120 hours.

Results: Length of hospital stay (HS), in-hospital-mortality and carbenicillin use was significantly higher in Group A ($p< 0.001$). Malnutrition and in-hospital-mortality was higher in females ($p=0.001$). Greater males (86.1%) were breast-fed compared to females (58.3%) ($p=0.01$). SES was a significant predictor of HS ($p< 0.0001$). The odds of staying > 5 days in the hospital among Group A was 3.08 (95% CI 2.21, 4.30) compared Group B. After adjusting for gender, this relationship persisted with the odds of longer HS among children of low SES being 3.07 (95% CI 2.20, 4.29). Malnutrition, maternal anemia, hospital-delivery and being breast-fed as an infant were also significant predictors of HS ($p< 0.0001$). SES was a significant predictor of Carbenicillin use ($p< 0.0001$) after failure of initial antibiotics.

Conclusions: There was a significant increase in severity of Pneumonia among lower SES children. Although malnutrition and in-hospital mortality were higher in females gender did not significantly predict the severity of Pneumonia.

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SEQUENCE VARIATIONS IN REPMP2/3 AND REPMP4 ELEMENTS REVEAL INTRAGENOMIC HOMOLOGOUS DNA RECOMBINATION EVENTS IN *MYCOPLASMA PNEUMONIAE*

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The gene encoding major adhesion protein P1 of *Mycoplasma pneumoniae*, MPN141, contains two DNA sequence stretches, designated RepMP2/3 and RepMP4, which display variation among strains. This variation allows strains to be differentiated in two major P1 genotypes (1 and 2) and several variants. Interestingly, multiple variants of the RepMP2/3 and RepMP4 elements exist at other sites within the bacterial genome. Because these variants are closely related in sequence, but not identical, it has been hypothesized that they have the capacity to recombine with their counterparts within MPN141, and thereby serve as a source of sequence variation of the P1 protein. In order to determine the variation within the RepMP2/3 and RepMP4 elements, both within the bacterial genome and among strains, we analyzed the DNA sequences of all RepMP2/3 and RepMP4 elements within the genomes of 23 *M. pneumoniae* strains. Our data demonstrate that:

(i) recombination is likely to have occurred between two RepMP2/3 elements in four of the strains,

(ii) all previously described P1 genotypes can be explained by inter-RepMP recombination events and

(iii) the difference between the two major P1 genotypes can be found in all RepMP elements, such that subtype 1 and 2 strains can be differentiated on the basis of sequence variation in each RepMP element.

Data in this study imply that subtype 1 and subtype 2 strains represent evolutionary diverged strain lineages. Finally, a classification scheme is proposed in which the P1 genotype of *M. pneumoniae* isolates can be described in a sequence-based, universal fashion.

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THE USE OF NEW MOLECULAR LABORATORY TECHNIQUES IN THE DIAGNOSIS OF BRONCHIOLITIS: WORTH THE EFFORT?

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Background and aims: While advanced laboratory diagnostics have enabled the identification of a variety of pathogens underlying the majority of bronchiolitis cases, how particular etiological agents affect the course of the disease remains uncertain.

Methods: 475 infants age< 2 years admitted with bronchiolitis during the 2005- 2006 winter were evaluated prospectively at three Israeli hospitals. Epidemiological and clinical data were collected. A nasopharyngeal specimen was tested for RSV and 8 other pathogens including adenovirus, rhinovirus, influenza and bocavirus, employing DFA, RT-PCR, PCR-DNA and ELISA. Subjects were categorized as follows: (1) Those in whom only RSV was identified, "ONLY RSV," (2) Those RSV-positive co-infected with at least one other pathogen "ALSO RSV," (3) Those RSV-negative with some alternative pathogen "NO RSV," and (4) Those in whom no pathogen was identified, "NO PATHOGEN."

Results: RSV, rhinovirus and adenovirus were identified in 72.8%, 27.2% and 6.9% of the children, respectively. 47.6%, 25.3%, 13.3% and 13.9% were categorized as "ONLY RSV," "ALSO RSV," "NO RSV," and "NO PATHOGEN," respectively. There were no epidemiological differences between groups. There were more reported eating difficulties among the "RSV ONLY" (55.8%) compared with "NO PATHOGEN," (32.5%) P=0.007. Clinical course during hospitalization did not vary significantly by group.

Conclusions: The results reaffirm that RSV is the most common cause of bronchiolitis. However, the clinical course of the disease was not found to vary as a function of a particular pathogen(s) leading us to question the added value of using new molecular diagnostics to identify the etiological agent(s) underlying bronchiolitis.

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PHARMACOKINETIC ASSESSMENT OF CLARITHROMYCIN IN SERUM, BRONCHOALVEOLAR LAVAGE (BAL) FLUID AND LUNG TISSUE: INFLUENCE OF DOSE ESCALATION ON MYCOPLASMA PNEUMONIAE

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Background and aims: *Mycoplasma pneumoniae* (Mp) infection is a common cause of acute respiratory disease in children and adults. Clarithromycin is often considered for treatment of Mp respiratory disease. However, the emergence of macrolide-resistant Mp strains and increases in Mp MIC have been recently reported. We developed a robust analytical method to determine clarithromycin content in biologic matrices as part of *in vitro* and *in vivo* studies to optimize clarithromycin therapy of Mp respiratory infections.

Methods: Clarithromycin was measured using LC/MS-MS system. Equal volumes (100 µL) of serum, BAL fluid, or lung tissue samples and internal standard (IS, roxithromycin) were extracted. The organic phase was evaporated and reconstituted with 200 µL acetonitrile for injection. Following injection (10 µL), chromatographic separation was performed using a C18 column, isocratic elution, 40ºC, and 5 minute run time. Clarithromycin and IS were analyzed using positive electrospray ionization combined with multiple reaction monitoring.

Results: The observed recovery of clarithromycin was excellent (98%). The standard curve was linear (r = 0.9995). The lower limit of quantitation (sensitivity) was 2 ng/mL and the upper limit of quantitation was 10 µg/mL. The method was demonstrated to be accurate, reproducible, and sensitive for quantitation of clarithromycin in serum, BAL fluid, and lung tissue using small sample volumes (100 µL).

Conclusions: The method has been successfully employed to study the effect of increasing dosages of clarithromycin for treatment of acute Mp respiratory infection using an experimental mouse model, supporting complex requirements of preclinical and clinical trials with small sample volumes.

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COMPARISON BETWEEN C REACTIVE PROTEIN AND PROCALCITONIN IN PATIENTS WITH RESPIRATORY TRACT INFECTION AND AUTOIMMUNE DISEASE

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Background and aims: C reactive protein (CRP) and procalcitonin (PCT) are markers of inflammation. The aim of this study was to compare CRP and PCT in patients with infectious disease and in those with autoinflammatory disorder.

Methods: Hospitalized children with respiratory tract infection (RTI) (n=61) and children with autoimmune disease (AD) (n=47) were prospectively enrolled. At admission, blood samples were taken to determine the level of CRP (automated enzyme-linked immunoassay, negative value < 0.5 mg/dL) and PCT (immunoluminometric assay, negative value < 0.25 ng/mL). Clinical data were collected during hospitalization.

Results: Among children with RTI, PCT < 0.5 ng/mL was identified in 30/36 (83.3%) children with confirmed viral etiology, whereas CRP < 1 mg/dL was observed only in 4/36 children (11.1%; p< 0.0001). Conversely, PCT $\geq$0.5 ng/mL was identified in 23/25 (92.0%) children with confirmed bacterial etiology, whereas CRP $\geq$1 mg/dL was detected in 24/25 children (96%). Among children with AD, in the active and in the stable phase of the disease PCT was always < 0.5 ng/mL, whereas PCR < 1 mg/dL was observed only in 11/32 children in active phase (34.4%; p< 0.0001) and in 2/15 of those stable (13.3%).

Conclusions: PCT seems a sensible and specific marker that permits to distinguish bacterial from viral etiology in patients with RTI. In contrast with CRP, the value of PCT does not seem to be affected by the inflammatory status. These findings suggest to use PCT for deciding when to start antimicrobial therapy in children with RTI or AD.

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PAIN AND GENERAL CONDITION OF CHILDREN HAVING UPPER RESPIRATORY INFECTION WITH OR WITHOUT ACUTE OTITIS MEDIA BEFORE AND AFTER DIAGNOSIS

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Background and aims: Symptoms related to acute otitis media (AOM) are unspecific and overlapping with the concomitant upper respiratory infection (URI). Earache is considered as an indicative of AOM but the evaluation of pain is difficult especially in young children. We compared pain and general condition between children with AOM and children with uncomplicated URI before and after diagnosis.

Methods: We asked a detailed history of preceding symptoms from 221 children (6 to 35 months) having URI and parental suspicion of AOM. Parents evaluated pain using faces scale (0, 2, 4, 6, 8 and 10) and their child's general condition using AOM faces scale (1-7) before ear examination and six hours after diagnosis. We strongly encouraged parents using analgesics in every case.

Results: The AOM group (117 children) and the URI group (104 children) were similar according to age (mean 1.3 years), gender, and the mean number of previous AOM (AOM group 1.6 vs. URI group 1.8). The intensity of pain was similar in both groups before (medians 6) and after diagnosis (medians 2). The general condition by AOM faces scale showed no significant difference between the groups before or after diagnosis, even though medians were slightly higher in AOM (6 before and 4 after) than in URI group (5 and 3).

Conclusions: Parental evaluation of pain and general condition does not differ in children with AOM from those with uncomplicated URI. The pain related to AOM seems to diminish rapidly after diagnosis when analgesic use is advised.

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MULTICENTER STUDY OF PERTUSSIS (P) ASSOCIATED HOSPITALIZATIONS IN COSTA RICAN (CR) CHILDREN (CH) DURING A SEVERE OUTBREAK

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Background: The burden of P is unknown for many Latin American countries. In CR, a severe P outbreak started at the end of 2005, being it the worst during the last 40 years. As a response to this public health problem and targeting the main source of infection for young infants, for the first time in the world nationwide maternal Tdap vaccination was started within 48-hrs post-partum on 4-30-2007. This study describes paediatric hospitalizations at 4 urban hospitals (H) prior to this intervention.

Methods: Multicenter retrospective survey of ch with laboratory-confirmed P (PCR, DIF, and/or culture) hospitalized in 1 paediatric tertiary referral H, and 3 general H with paediatric beds, from 1-1-2004 to 4-29-2007.

Results: 132 ch were identified. 43% were < 2 months of age and therefore had not been vaccinated; overall, 104 (78.8%) pts were < 6 months. 51.5% were boys. Symptoms included cough (94%), respiratory distress (73%), cyanosis (72%), vomiting (42%), and apnea (11%). 19 (14.4%) pts required PICU admission, among which all were mechanically ventilated. Nine (6.8%) pts died, of whom the mean age was 48.9 days ($\pm$ 27.4d). Annual deaths distribution was: 2004(0), 2005(1), 2006(4), and 2007 (4, first quatrimester); 6 deaths occurred from 12-24-06 to 02-23-07. Other complications included: severe pneumonia,15.2% pts; respiratory failure, 13.6% pts; and pulmonary hypertension, 7.6% pts.

Conclusions: P outbreaks can cause severe morbidity and mortality in CR infants. This study demonstrates the need for continuous epidemiologic surveillance of vaccine-preventable diseases, in order to adopt timely public health interventions.

SURGICAL INFECTIONS

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OUTCOME IN PEDIATRIC SMALL BOWEL TRANSPLANTATION

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Background: Infections represent a major cause of morbidity and mortality in patients with solid organ transplantation due to significant immunosuppression.

Methods: The charts of patients who underwent isolated or composite SBT between January 2003 and December 2007 were reviewed for demographic information, histology of the surveillance allograft biopsies, immunosuppressive regimen, episodes and treatment for rejection, and outcome. Univariate and bivariate analysis were performed to determine significant risk factors for mortality.

Results: We included 98 patients who underwent 110 transplants; 53.06% were male and 46.94% female. The median age at transplantation was 1.58 years (SD 3.9, range 0.33-18.5). Rejection was proven by biopsy in 45 (40.91%) of 110 transplants, but only 27 (24.54%) episodes required treatment. Median time to rejection was 1.87 months (SD 8.75). Median survival time after transplantation was 9.17 months (SD 11.59) with lower age being a risk factor for mortality (p=0.05). There was no significant statistical difference in mortality between the patients with or without rejection. Overall mortality in this series was 30.61% (30 patients). Mortality at one year was 18.18% (20 transplants). The cause of death was not available for 4 patients. Infections were primary and secondary contributory cause for death in 46.15% and 50% cases respectively. In 19 of 26 cases, sepsis was the primary, secondary or tertiary contributory factor for death.

Conclusions: Our data suggest that infections are important contributory factors to mortality in pediatric isolated and composite SBT. A suggested relationship between younger age at transplantation and increased risk of mortality was observed.

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POSSIBLE RISK FACTORS FOR A COMPLICATED SURGICAL SITE INFECTION AFTER CARDIAC SURGERY IN CHILDREN

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Background and aims: To determine the epidemiology, microbiology, clinical features and risk factors to develop deep infections after cardiac surgery in children.

Methods: We reviewed charts of children with surgical infection after cardiac surgery between 2000 and 2008. Children were classified as having superficial (SI) or deep infection (DI) according to development of bacteremia, surgical debridement or systemic symptoms. We examined risk factors for DI, including demographics, previous disease, time of surgery, delayed sternal closure, length of invasive devices, days and complications in PICU, need for re-surgery, and antibiotic therapy.

Results: Forty children were enrolled; 37% with DI. Median age was 16 months, 60% male. Most of heart diseases and surgical procedures were complex (hypoplastic left heart syndrome (37,8%); Glenn procedure (27%)). There were not differences between groups in any pre-surgical conditions including antibiotic prophylaxis. Median duration of surgery was 296 minutes (no differences between groups). The most common pathogens were S. aureus (30%) and coagulase negative Staphylococcus (28%). Relevant clinical findings were redness (100%), purulent drainage (84%) and fever (52%). Duration of antibiotic therapy was longer in DI (10 vs 35 days). Other significant differences included need for ECMO or hemofiltration, days on pressors, venous central lines or thoracic drains, and days in PICU.

Conclusions: The main etiology of infection after cardiac surgery was S. aureus. Several factors were significantly associated with DI, most of them related to invasives procedures. Pre-existing condition or characteristics of surgery were not associated with DI. Children with DI had a more complicated outcome.

URINARY TRACT INFECTIONS

P487

ATTEMPTS FOR DETECTION OF NANOPARTICLES-NANOBACTERIA AND DISTRIBUTION OF THEIR ANTIBODIES IN JORDANIAN PATIENTS WITH UROLITHIASIS

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Introduction: In 1998 calcifying nanoparticles (CNPs) or nanobacteria was proposed as an explanation of certain kinds of pathologic calcification and stone formation.

Background and aims: The study was conducted to assess the incidence of the anti-CNP Abs in Jordanian patients and to investigate the living nature of these CNPs.

Methods: Enzyme Linked Immunosorbent Assay (ELISA), bacterial culturing and staining techniques were used to investigate the incidence of calcifying nanoparticles IgG antibodies (anti-CNP Abs) in serum of Jordanian patients with urolithiasis and the living nature of these CNPs in the renal stones. Serum samples from 65 patients and related 20 healthy individuals were tested for anti-CNP Abs. Renal stones retrieved from the kidneys of 20 patients were processed and subjected to mammalian cell culture conditions then bacterial growth and staining were observed from these cultures.

Results: Results revealed the detection of anti-CNP Abs in 96% of patients and in 40% of healthy individuals. We couldn´t grow these CNPs by the techniques described, no bacterial growth was detected by usual staining.

Conclusions: Although, high anti-CNP Abs incidence were correlated strongly with the presence of CNPs and urolithiasis, no CNPs or bacterial growth was detected following the applied staining and turbidity methods, which may reflect the non living nature of such particles. The findings of this study can be used as a tool for early prediction of kidney stone formation.

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PROTECTIVE ROLE OF BREASTFEEDING AGAINST ACUTE PYELONEPHRITIS

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Aim: To evaluate the possible protective effect of breastfeeding against the development of lesions of acute pyelonephritis (APN) among infants with first time urinary tract infection (UTI).

Methods: We studied 137 (males:78,girls:59) infants aged 0.5-12 months (median 3.1) admitted to the hospital with their first time UTI and we evaluated the effect of breastfeeding on the results of the Technetium-99m-dimercaptosuccinic acid (DMSA) scintigraphy during the acute phase of infection as well as after 6 months or later.

Results: Sixty-nine patients (50%) were breastfed at the time of infection whereas 45 infants (33%) had interrupted breastfeeding before the episode of infection. On the other hand, 23 infants (17%) had not been breastfed at any time. Findings of APN on DMSA scan were documented in 31/69 (45%) of breastfed infants, in 25/45 (56%) of infants who were being breastfed in the past for different periods of time and in 16/23 (70%) of infants, who had never been breastfed (p=ns). Among boys, APN was detected in 52%,48% and 56% of infants with ongoing breastfeeding, different duration of breastfeeding and no breastfeeding respectively (p=ns) whereas among girls the corresponding values were 29%,62.5% and 79% (p=0.008). No correlation was found between the prevalence of permanent renal damage and the duration of breastfeeding.

Conclusions: A protective role of breastfeeding against the development of APN lesions on DMSA scan was noted only in girls with UTI. Nevertheless, no significant correlation between the development of permanent renal damage and the duration of breastfeeding was detected in both sexes.

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PREDICTIVE FACTORS ASSOCIATED WITH THE SIZE OF ACUTE PYELONEPHRITIS LESIONS IN INFANTS WITH URINARY TRACT INFECTION

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Aim: To evaluate whether clinical, laboratory or imaging findings, present during the acute phase of urinary tract incection (UTI) could predict the size of renal lesion in 99mTc dimercaptosuccinic acid (DMSA) scan.

Methods: A total of 333 infants (Males:186, Females:147) aged 0.5-12 months (median age 3 months) with first time UTI were evaluated. All infants underwent a DMSA scan within 28 days following admission as well as a voiding cystourethrogram and ultrasonography. Renal lesions on DMSA scan were classified as small, moderate and large. The clinical, laboratory and imaging findings of these infants were correlated to the size of renal lesions on DMSA scan.

Results: Lesions of acute pyelonephritis (APN) were noted in 170 infants (51.1%). In 86 infants DMSA scan revealed small lesions, in 16 moderate and in 68 large lesions. Body temperature (p=0.025), the percentage of neutrophils (p=0.008) and the grade of vesicoureteral reflux (P=0.002) on admission were the only factors related to the severity of the renal lesions. On the other hand, factors such as age, gender, C-reactive protein level, white blood cells number, ultrasound findings, the presence of VUR and the therapeutic delay time were not related to the size of the renal lesions.

Conclusions: Infants with high temperature, increased number of neutrophils and high grade of VUR during the acute phase of urinary infection are more likely to develop more severe lesions on DMSA scan.

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THE SIZE OF ACUTE RENAL LESIONS AS PREDICTIVE FACTOR OF SCARRING IN INFANTS WITH URINARY TRACT INFECTION

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Aim: To evaluate whether the size of acute renal lesions on 99mTc dimercaptosuccinic acid (DMSA) scan in infants with urinary tract infection (UTI) could predict scarring formation.

Methods: A total of 98 infants (Males:55, Females:43) aged 0.5-12 months (median age 3.5 months) with acute changes on 99mTc dimercaptosuccinic acid (DMSA) scan had a second DMSA scan within 6 to 12 months (median 6.5 months). Renal lesions on the acute phase DMSA scan were classified as small, moderate and large. A voiding cystourethrography was also performed in all infants. The size of renal lesions on DMSA scan during the acute phase of infection and the frequency of renal scarring were correlated for each renal unit separately. Data were analysed with chi-square test. A p-value ≤ 0.05 was considered significant.

Results: Among the 98 infants, acute renal lesions were detected in 111 renal units. Large lesions were seen in 51 renal units (46%), moderate lesions in 8 (7%) and small lesions in 52 (47%). Sixty-one percent (31/51) of the large acute lesions and 37% (22/60) of the small or moderate lesions evolved into scars (p=0.019). This difference was signifant only in infants with vesicoureteral reflux (VUR) (76% vs 40%, p=0.045) and not in infants without VUR (53% vs 35%, p=ns).

Conclusions: Evolution of acute pyelonephritis to renal scarring in infants with vesicoureteral reflux is more frequent as the size of acute renal lesions increases.

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ACUTE PYELONEPHRITIS IN CHILDREN IN HERAKLION, CRETE, GREECE

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Background and aim: Acute pyelonephritis (AP) may be a serious acute illness in childhood. A protocol for AP admissions in the Pediatric Department of Venizelion General Hospital, in Crete, Greece, has been established since 2000.

Methods: The demographical findings, laboratory results and radiological imaging findings of children with AP admissions, during 2007-2008 were analyzed retrospectively.

Results: Of 2241 admissions, AP was diagnosed in 69 children. The age ranged from 32 days to 10 years. 57 (83%) were infants (0-12months), 4 (6%) were 12-24 months old and 8 (11%) were older than 24 months. 33 (48%) were boys and 36 (52%) were girls. The main bacterial pathogen was E. coli (90%), followed by Proteus spp. (4%), Klebsiella spp. (3%) and Pseudomonas spp. (3%). Empirical treatment consisted of a second generation cephalosporin or amoxicillin- clavulanate or a third generation cephalosporin in severely ill infants. Renal ultrasonogram was performed in all children during the first days of admission and was abnormal in 16%. 87% of children had voiding cystourethrogram 15-20 days after admission and vesicoureteral reflux was found in 15%. DMSA was performed 6 months later in 27 (39%) and it was abnormal in 8 (29%).

Conclusions: There is a prevalence of acute pyelonephritis in infants. The most common uropathogen is E.coli. The DMSA was abnormal in a high proportion of cases. DMSA is a very helpful imaging study in diagnosing the renal scars after acute pyelonephritis.

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CLINICAL AND LABORATORY FACTORS ASSOCIATED WITH PYELONEPHRITIS IN CHILDREN < 24 MONTHS OF AGE

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Background and aims: To evaluate clinical and laboratory variables for differentiating between acute pyelonephritis (APN) and lower urinary tract infections (UTIs) in children < 24 months of age.

Methods: We retrospectively reviewed the medical records of 296 children with febrile UTI seen from 1996 to 2005. On the basis of DMSA performed 7-14 days after admission, they were classified into APN or non-APN groups. Gender, age, clinical findings, white blood cell count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), urinalysis, renal ultrasound and voiding cystourethrographic findings were evaluated.

Results: APN was documented in 118 children (39.9%). Children with APN had higher fever (38.9±1 vs 38.3±1^{o}C; p=0.19) as well as higher levels of ESR (52.1±20 vs 32.2±17mm/h; p< 0.001) and CRP (6.5±3.3 vs 3.5±2.5mg/dl; p=0.003). ROC analysis indicated that the above factors had a poor overall predictive performance: AUC_{fever}:0.659, AUC_{CRP}:0.669 AUC_{ESR}:0.620. However, logistic regression indicated that fever >38.8^{o}C and CRP >5mg/dl could be considered as reasonable predictors for pyelonephritis. Vesicoureteral reflux (VUR) was documented in 40 children from the APN and in 22 from the non-APN group (p< 0,001). VUR ^{3}grade III was also significantly associated with pyelonephritis (logistic regression).

Conclusions: In febrile children < 2 years of age with suspected or documented UTI, fever >38.8^{o}C and CRP >5mg/dl could be reasonably used to differentiate between upper and lower UTIs. The presence of VUR ^{3}grade III is also predisposing to pyelonephritis in these children.

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INCIDENCE AND RISK FACTORS OF EXTENDED-SPECTRUM B-LACTAMASE-PRODUCING BACTERIA IN COMMUNITY-ACCUIQRED PEDIATRIC URINARY TRACT INFECTION

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Objective: Urinary tract infection(UTI) is one of the most frequent in pediatric febrile diseases. Empirical antimicrobial treatment is indicated before bacteriological results are available for it to reduce renal problems. While treated completely, it could be recurred in underlying urogenital anomalies. This study was performed to identify prevalence and risk factors for community-acquired UTI by extended-spectrum β-lactamase(ESBL)-producing bacteria in children.

Methods: We conducted a case-control study using medical records from Bundang CHA General Hospital from January 2004 to June 2008. Eligible patients were identified from microbiology laboratory records. Controls are matched in a 2:1 ratio to case patients by age and sex.

Results: The most common pathogen was *Escherichia coli* (594 cases), followed by *Klebsiella spp.* (52 cases), *Enterococcus spp* (34 cases), and *Enterobacter spp* (30 cases). The each prevalence of ESBL producers in the *E.coli* and *Klebsiella spp.* was 21 (3.5%) and 7 isolates (13.5%). Prior use of antibiotics within a month (p=0.007; odds ratio[OR], 4.5, 95% confidence interval[CI], 1.5 to 13.7) and previous hospitalization history of UTI (p=0.035; OR, 3.4, 95% CI, 1.0 to 11.0) were associated with community-acquired infection by ESBL-producing bacteria. However, no significant difference was noted in underlying urogenital anomalies and recurrence of UTI.

Conclusion: ESBL-producing bacteria has been identified in pediatric community-acquired UTI. Previous use of antibiotics within a month and hospitalization history of UTI were associated with the risk of infection by ESBL-producing bacteria. Therefore, well-timed follow-up after treating UTI completely and use of antibiotics should be considered.

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DELAY IN TREATMENT INITIATION DOES NOT AFFECT THE DEVELOPMENT OF RENAL SCARS IN CHILDREN WITH FEBRILE URINARY TRACT INFECTIONS (UTIS)

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Background and aims: The objective of the present study was to evaluate the relationship of the duration of fever before treatment initiation (FBT) on the levels of C-reactive protein (CRP), white blood count (WBC) and on the technetium-99m-dimercaptosuccinic acid scan (DMSA) findings in children with febrile UTI.

Methods: 189 children aged 4 days to 6.5 years (0.5 ± 0.9 years) with febrile UTI were studied. WBC counts and CRP levels were measured on admission and on the third afebrile day. DMSA scintigraphy was performed within 7 days after treatment initiation and after 6 months.

Results: On admission mean CRP levels, WBC and ANC counts were increased and were reduced after three days of treatment (p=0.001). When dividing the study population into 4 groups, according FBT: a.< 12h, b.13-24h, c.25-48h, d.49-96h, CRP levels and WBC increased in parallel with the FBT (CRP:46.0 vs 63.8 vs 82.2 vs 84.2 mg/L, p=0.001). However the frequency or severity of acute DMSA or repeat DMSA were not associated with the pretreatment duration of fever (positive acute DMSA: 42.8% vs 45.8% vs 42.8% vs 57.1% for groups 1-4 respectively, positive repeat DMSA: 33.3% vs 33.3% vs 28.6% vs 35.7%). The above groups were not significantly different in terms of the frequency of VUR. The above findings were similar in children < 1 year of age vs >1 year.

Conclusions: The delay in treatment initiation up to four days does not affect the development of permanent renal lesions, despite the increase of inflammatory indices.

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SEVERITY OF RENAL LESIONS IN CHILDREN WITH FEBRILE URINARY TRACT INFECTIONS (UTIS) ASSOCIATED WITH DURATION OF FEVER AFTER TREATMENT INITIATION

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Background and aims: The objective of this study was to evaluate the relationship of the duration of fever after treatment initiation (FAT) with technetium-99m-dimercaptosuccinic acid scan (DMSA) findings in children with febrile UTI.

Methods: In 189 children aged 4 days to 6.5 years (0.52 ± 0.93 years), admitted with the suspicion of febrile UTI, CRP levels were measured on admission and during treatment with antibiotics. Renal involvement was assessed by DMSA scintigraphy within 7 days after treatment initiation and after 6 months.

Results: The study population was divided into 4 groups, according FAT: a:< 12h, b:13-24h, c:25-48h, d:49-96h. CRP levels increased in parallel with FAT (CRP:45 vs 84 vs 66 vs 84 mg/L, p=0.001). The overall frequency of acute DMSA(+) was not significantly different among 4 groups (37.5%, 47.2%, 50%, 63.6%, for groups 1-4 respectively). However severe lesions (grade 3-4) in acute DMSA were more frequent in children with FAT>48h (4.1%, 8.4%, 0%, 27.3%, x^2=15.4%, p=0.017). In the repeat DMSA all grade 1-2 lesions disappeared, while frequency of grade 3-4 lesions were not different among 4 groups (35.3%, 30.5%, 21.7%, 55.5%). The frequency of VUR was not different among 4 groups. The above findings were similar in children aged< 1 year vs >1 year.

Conclusions: The increased duration of fever after treatment initiation in children with febrile UTI is associated with the severity of renal lesions in acute, but not in the repeat DMSA. The above findings underline the importance of the early response to antibiotic treatment in children with febrile UTI.

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DIAGNOSTIC VALUE OF SERUM PROCALCITONIN IN FEBRILE INFANTS UNDER 6 MONTHS OF AGE FOR THE DETECTION OF BACTERIAL INFECTIONS

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Background and aims: The aim of this study was to determine the diagnostic value of serum procalcitonin (PCT), compared with that of C-reactive protein (CRP) and total white-blood cell count (WBC), in predicting bacterial infections in febrile infants under 6 months of age.

Methods: A prospective study was performed with infants under 6 months of age, admitted to the paediatric emergency department with fever of uncertain source. Serum PCT levels were measured by using an enzyme-linked fluorescent assay.

Results: A total of 71 infants (median age: 2 months) were studied. 23 infants (32.4%) had urinary tract infections (UTI), and 20 infants (28.2%) had viral meningitis. Others had upper respiratory tract infections (n = 15), lower respiratory tract infections (n = 7), gastroenteritis (n = 4), and bacteremia (n = 2). Median WBC and CRP levels were significantly higher in infants with UTI than in infants with viral meningitis. However, there was no difference in median PCT levels between both groups (0.13 ng/mL vs. 0.11 ng/mL, P = 0.323). The area under the receiver operating characteristic curve was 0.90 (95% CI: 0.79-1.00) for WBC, 0.85 (95% CI: 0.72-0.99) for CRP, and 0.59 (95% CI: 0.41-0.76) for PCT. High WBC (>12,000/mm^3) and CRP (>13 mg/L) were retained as significant predictors of UTI in a multiple regression model.

Conclusions: Serum PCT concentrations should be interpreted with caution in infants younger than 6 months with fever of uncertain source.

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CHILDHOOD URINARY TRACT INFECTIONS AS A CAUSE OF SEVERE RENAL FAILURE IN ADULTHOOD

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Background and aims: The importance of childhood UTIs as a cause of end-stage renal disease (ESRD) is not known. Our aim was to find out, what is the significance of childhood UTIs to the development of ESRD in adulthood.

Methods: The hospital records of all the patients treated or followed because of ESRD in the Hospital District of Northern Ostrobothnia (382 000 inhabitants) during 2005-2006 were reviewed. The patients with possible infectious reason for ESRD were interviewed and background data of their illnesses were collected with a structured questionnaire. Their patient records were obtained from the community health centers where they were treated in childhood.

Results: Of the 349 patients with ESRD, 291 had an apparent spesific cause for renal insufficiency not associated with UTIs. Of the remaining 58 patients, 53 were interviewed and the information on five patients´ UTI history was based on the hospital records. Altogether, 13/58 patients had a history of UTI in childhood. Seven of these thirteen patients had a renal abnormality, which alone had most likely lead to the kidney failure. Four of the remaining six patients had had 1-2 UTIs in childhood. Thus, the prevalence of recurrent UTIs in childhood as a possible cause of ESRD in adulthood was 2/382 000.

Conclusions: In the absence of serious congenital anomalies, the significance of childhood UTIs as a cause of ESRD in adulthood appears to be very rare. After the first UTI in children, examinations to find severe abnormalities of the urinary tract are sufficient.

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ACUTE PHASE RENAL SCANNING FOR URINARY TRACT INFECTIONS. A COMPARISON STUDY OF CHILDREN WITH AND WITHOUT ACUTE PHASE RENAL DEFECTS

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Background and aims: Urinary tract infections (UTIs) are a common cause of morbidity in childhood. Renal ^{99}Tc DMSA scanning is useful in detecting parenchymal defects in the course of UTIs. We compared the characteristics of hospitalized children suffering from UTI, with (DMSA+) or without (DMSA-) defects on acute phase renal scanning.

Patients and methods: Medical records of 88 children aged 1 month to 11 years with a first episode of febrile UTI and acute phase renal scanning who were hospitalized from January 2001 to December 2008 were reviewed. Characteristics of 32 DMSA+ and 56 DMSA- children were compared using univariate and multivariate logistic analysis.

Results: DMSA+ episodes of UTI occurred in children that were older (mean±SE: 20.9±4.5 vs 8.4±2.6 months, $p< 0.01$), were followed by a longer history of any kind of symptoms (5.8±2.7 vs 3.9±1.6 days, $p< 0.01$) or fever alone (2.8±0.4 vs 1.5±0.2 days, $p< 0.01$) prior to admission than DMSA- UTI episodes. DMSA+ episodes had significantly higher CRP (85.8±11.8 vs 46.4±6.8 mg/l, $p< 0.01$) but not ESR (73.1±5.9 vs 59.5±4.3 mm/h, p=NS) than DMSA- episodes. On multivariate analysis only older age was independently associated with acute phase DMSA defects ($p< 0.05$).

Conclusions: Older children with UTI seem to have a higher risk of parenchymal defects in acute phase DMSA than younger ones, in agreement with other studies. Prompt diagnosis and treatment of UTIs is warranted at all age groups.

P499

CORRELATION OF LABORATORY VALUES WITH THE CLINICAL DATA IN PATIENTS WITH URINARY TRACT INFECTION

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Hospitalized children frequently are diagnosed with urinary tract infection. In the present study we evaluate the relationship of clinical and the laboratory data in patients with urinary tract infection (UTI).

Patients/method: 143 patients with positive urine culture were included in the study. The complete blood count values, number of leucocytes in urinalysis (LeUA), sedimentation rate (SR), C-reactive protein (C-RP) and the clinical data were documented.

Results: The mean patients' age was 24.1 (Sd 34 months), the length of hospitalization was 7.6 (Sd 3) days and the duration of fever was 3 (Sd 1.6) days. The patient's mean white blood count was 15.963 (Sd 7.436) $X10^3/mm^3$, the mean platelet count was 403.000 (Sd 138.000) $X10^3/ mm^3$) and the mean sedimentation rate (SR) was 37.6 (Sd 31.1) mmHg/h. Statistically significant differences were reported comparing the duration of fever with the SR ($p< 0.0001$) and the white blood cell count (WBC) ($p=0.01$). Additionally, the patients' age was significantly associated with the duration of fever ($p=0.002$), the platelet count (Plt) ($p< 0.001$) and the C-RP ($p=0.02$). Finally, significant relationship was documented between the LeUA ($p=0.001$) and the WBC ($p=0.001$) but not with the duration of fever and the length of hospitalization.

Conclusions: In children with UTI the inflammatory response (platelet count, C-reactive protein, duration of fever) is significantly associated with the patients' age. Additionally, the duration of fever is significantly related with the SR and the WBC. Finally, the number of leucocytes in urinalysis has no association with any other factors except the WBC.

P500

CORRELATION OF RENAL ULTRASOUND WITH THE CLINICAL AND LABORATORY VALUES IN PATIENTS WITH URINARY TRACT INFECTION

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The urinary tract infection (UTI) is a common illness in hospitalized children.

We compare the radiologic picture of renal ultrasound (U/S) with the other clinical and laboratory values in patients with UTI.

Patients/method: 143 hospitalized children with UTI, diagnosed by positive urine culture, were included in the study. A renal U/S was performed during the hospitalization.

Results: The mean patient's age was 24.1 (Sd 34) months, the length of hospitalization was 7.6 (Sd 3) days and the duration of fever was 3 (Sd 1.6) days. The patient's mean white blood count was 15.963 (Sd 7.436) $X10^3/mm^3$, the mean % of neutrophils was 55.2% (sd 20.3%), the mean platelet count was 403.000 (Sd 138.000) $X10^3/ mm^3$ and the mean sedimentation rate (SR) was 37.6 (Sd 31.1) mmHg. Normal U/S had 69% of the patients. Bilateral abnormalities were reported in 12%. Statistically significant relationship was documented between the presence of abnormalities in U/S and C-reactive protein (C-RP) (p=0.002). No relationship was documented with the other laboratory values. Additionally, significant association was reported between the renal U/S and the length of hospitalization (p=0.03). The presence of fever and the duration of fever showed no relationship with the picture in renal U/S.

Conclusions: In hospitalized patients with urinary tract infection, an abnormal picture in renal ultrasound accompanies higher C-RP values and longer hospitalization. The other laboratory values related to the degree of inflammation were not significantly altered by the presence of abnormalities in renal ultrasound.

P501

RESISTANCE PATTERNS OF COMMONLY USED ANTIBIOTICS AMONG PATHOGENS OF COMMUNITY-ACQUIRED URINARY TRACT INFECTIONS IN TAIWAN PEDIATRIC EMERGENCY DEPARTMENT

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Background: The aim of this study was to determine the distribution and antibiotic susceptibility patterns of bacterial strains isolated from patients with community acquired urinary tract infections (UTIs) at a teaching hospital in North Taiwan.

Methods: Urinary isolates from suspected UTI cases age from 1d/o to 36 m/o attending to the pediatric emergency department of Chang Gung memorial hospital at Taoyuan were identified by conventional methods. Antimicrobial susceptibility testing was performed by Kirby Bauer´s disc diffusion method. Isolates resistant to third generation cephalosporin were tested for ESBL production by double disk synergy test method.

Results: Of the 19812 patients age between 1 d/o to 36 m/o, 619 samples showed growth of pathogens among which the most prevalent were *E. coli* (69.9%) followed by *Klebsiella* spp (8.3%). The majority (53.5%) of the isolates were from male while the remaining were from female. Among the gram-negative enteric bacilli high prevalence of resistance was observed against ampicillin , piperacillin and co-trimoxazole. Most of the isolates were resistant to 4 or more number of antibiotics. 14 percent of isolates were detected to produce ESBL among which 93.33% were *E. coli* isolates.

Conclusion: This study revealed that *E. coli* was the predominant bacterial pathogen of community acquired UTIs. It also demonstrated an increasing resistance to ampicillin, piperacillin and Co-trimoxazole and production of extended spectrum β-lactamase among UTI pathogens in the community. This study is useful for clinician in order to improve the empiric treatment.

P502

FEVER WITHOUT SOURCE AND URINARY TRACT INFECTION IN CHILDREN 3-36 MONTH AGE

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Introduction: Fever is common presenting symptom in pediatric< 3 years. Approximately 20% of these children do not have identifiable source pf fever.

Aim & material: Aim of this study was to evaluate the prevalence of urinary tract infection in 3-36 month age with fever without source. This prospective study was conducted on 300 children age 3 to 36 months who were admitted to ali-ebne abitaleb hospital with temperature>39. After careful history and physical examination, those children who had clinically undetectable source for the history and physical examination, those children who had clinically undetectable source for the fever were enrolled in the study. All received a screening urinalysis and urine culture.

Result: This study included 300 children (175 male and 125 female). Ninety two patients (30.6%) that among them 8.6% (15 cases) were male and 16.6% (77cases) were female. This difference was statistically significant (p value < 0.0001) the mean age and breast feeding rate in children with and without UTI were similar. UTI was more frequent in children without circumcisions and in children with history of previous UTI.

Conclusions: Young children presenting with fever may have nonspecific symptoms of UTI, and a high index of suspicion is appropriate in this setting.

VACCINE AND PREVENTION

P503

DISSEMINATED BACILLE CALMETTE-GUERIN INFECTION AFTER VACCINATION IN IRANIAN CHILDREN

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Background: Bacille Calmette-Guerin (BCG) vaccine is routinely given to neonates in setting where tuberculosis is endemic. Published reports appear to underestimate the true rate of disseminated BCG infection.

Methods: We performed a retrospective study on 34 children hospitalized for disseminated BCG infection in Nemazee Hospital, affiliated to Shiraz University of Medical Sciences between 1990 and 2007. Clinical data were collected through medical file review. The main method used to confirm the identity of the isolate as BCG was a PCR specific for spacer regions 33 and 34 of the direct repeat region of the *Mycobacterium tuberculosis* complex.

Results: We identified 9 definite and 25 probable cases reported from 1990 through 2007. All of the patients were vaccinated at birth. One half of our patients had been associated with an abnormality in immunologic work-ups suggestive of immune deficiency. Thirty-one patients (91%) aged younger than 2 years old. About 41 percent of the patients were male. Response to therapy was poor, with an overall mortality rate of 50%. In 9 patients, disseminated BCG infection was confirmed by PCR which directly applied to 14 available clinical specimens.

Conclusion: Disseminated BCG disease is an uncommon but devastating complication of vaccination that should be considered in the appropriate clinical setting. The incidence of disseminated disease is probably greater than that previously reported. Confirmed or suspected cases of disseminated BCG disease should be reported to the appropriate authorities to reassess risk and benefit balance of BCG vaccination.

P504

EVALUATION OF SOCIAL AND HEALTH INTERVENTIONS FOR IMMIGRANT VACCINATION IN MADRID (SPAIN)

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A 14% of children aged 0-14 years and an 18% of women of childbearing age of the Community of Madrid are migrants. In 2005, a rubella outbreak happened, with an 80% of cases reported in immigrant women. The study objective was to evaluate the social and health interventions carried out to achieve adequate migrant population. immunization coverage.

Methods were applied, designing a proactive, participatory, internal and intermediate evaluation based con criteria of accessibility, effectiveness, quality and coverage, going through the following steps:

- delimitation of scope
- literature review
- key stakeholders involvement
- information needs assessment
- evaluation matrix development
- implementation (8 focus groups, 39 interviews)
- data analysis
- conclusions and recommendations formulation.

Main results and conclusions refer to access to regional health system (high availability, but obstacles in accessibility and acceptability of services) and to more specific issues (positive attitude towards immunization, opportunistic children immunization, difficulties for attracting women for rubella immunization, lack of coordination with social agents, usefulness of accelerated schedule, need for more technical information).

The numerous recommendations can be ordered in:

- information to give to migrant population (25%)
- development of coordination between health and social actors (21%)
- professional training and information, procedures design (20%)
- establishment of general strategies for migrant health attention (20%)
- decrease of access barriers (language, communication, surgery hours…) (10%)
- increased feedback from immunisation records (4%).

P505

EPIDEMIOLOGY OF THE SEROGROUP B *NEISSERIA MENINGITIDIS* (MNB) FACTOR H BINDING PROTEIN AND IMPLICATIONS FOR VACCINE DEVELOPMENT

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Background: A recombinant factor H binding protein (fHBP) vaccine (LP2086) is in development with the potential to provide broad protection against invasive MnB disease (IMDB) globally. MnB fHBP sequences are divided into two subfamilies (A and B); every isolate has the gene for one of these subfamilies. Preclinical studies demonstrated that a vaccine containing one variant from each subfamily elicits broadly protective anti-MnB serum bactericidal antibody (SBA). As with other meningococcal vaccines, clinical efficacy will be established using the SBA assay as a surrogate for protection. An unbiased scientifically based approach is needed for selecting MnB strains for phase 3 SBA assessment. As an initial step, a pool of systematically collected IMDB isolates (n=1,263) was characterized with regard to fHBP variation and expression. Isolates representative of this collection were selected to support phase 3. Isolates from additional national collections are being studied to monitor potential regional and temporal fHBP epidemiological shifts.

Methods: fHBP sequence and expression levels were determined from a collection of 539 systematically obtained IMDB isolates from Spain and Germany.

Results and conclusions: All IMDB isolates contained *fhbp* and >98% had antibody-accessible fHBP on their cell surface. Though the proportion of strains in subfamily A or B was variable depending upon the country surveyed, the fHBP sequences observed fell within the previously described subfamilies, and the surface expression profiles were similar both regionally and over time to those of the reference collection. These epidemiological observations support continued development of a bivalent rLP2086 vaccine as a universal MnB vaccine.

P506

IMPACT OF INFANT PNEUMOCOCCAL VACCINATION ON PNEUMONIA AND ACUTE OTITIS MEDIA HOSPITALISATIONS IN LIGURIA, ITALY

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Background: Liguria was the first administrative Region in Italy, since 2003, to introduce the heptavalent pneumococcal vaccine (7-PCV) according to a universal childhood immunisation strategy: a study aimed to evaluate the clinical impact of the program was carried out within a pilot-project, on a regional basis, on behalf of the Ministry of Health.

Methods: In-patient discharge information on pneumococcal-associated or potentially-associated hospitalisations was collected in children 0-2-years old, in accordance with the International Classification of Diseases, 9th revision, Clinical Modification: hospitalisation rates for all-cause pneumonia (480-487.0), pneumococcal pneumonia (481), and acute otitis media (382-382.0-382.9), used as main outcomes, were calculated and compared in children belonging to birth cohorts before, 2000-2002, (n=33946) and after, 2003-2005, (n=35452) the introduction of vaccination. Rates for urinary tract infections (599.0) were used as control.

Results: A statistically significant decline for all-cause and pneumococcal pneumonia ($p < 0.05$) and for acute otitis media ($p < 0.01$) was observed in children born after 2003, with preventive fractions of 15.2 (95% CI=2.8, 26.1), 70.5 (95% CI=9.7, 90.4) and 36.4% (95% CI=24.1, 46.7), respectively. As far as concerns admissions according to age class, all-cause and pneumococcal pneumonia and acute otitis media rates declined in the 0-6, 7-12 and 13-24 month age groups, with significant differences reached in the 7-12 month age group for otitis media admission ($p < 0.001$) and in children aged 13-24 months for otitis ($p < 0.001$) and all-cause pneumonia ($p=0.006$).

Conclusions: Our data support the introduction of the 7-PCV into the national immunisation program.

P507

ROUTINE IMMUNIZATION COVERAGE IN UNDERSERVED CHILDREN OF ALIGARH (INDIA)- AN EFFORT WITH UNICEF

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Background and aims: Under five children not only constitute a large group but they are vulnerable or high risk group. They may suffer from certain communicable diseases which are preventable by active immunization. routine immunization coverage remail low due to some misbliefs. During 2001-2002, 17.9 million infants were not immunized in India. The present study was carried out to find out the routine immunization coverage and to impart correct health education to the community.

Methods: This hospital and outreach session based cross sectional study was carried out by interview method. 2531 under five children and their mothers or family members were included in the population sample.

Results: In Shahjamal area, maximum number of children (86.5%) were immunized with DPT, OPV (86.5%) first doses followed by BCG (84.9%). DPT and OPV second and third doses were given in 64.5% and 54.8% respectively. Measles and DPT booster coverage was low as 39.0% and 11.4% respectively. Similarly, in Bhojpura, 99% children received DPT and OPV first doses followed by BCG (94.1%). DPT and OPV second and third doses were given in 67.7% and 47.4% children respectively. Measles and DPT booster coverage was low as 31.9% and 6.7% respectively.

Conclusions: The results reveal high coverage of DPT_1, OPV_1, BCG, DPT_2 and OPV_2 and comparatively lower coverage with DPT_3, OPV_3, measles and DPT booster in both areas. There is a need to give the correct message to the community that Universal Immunization Programme vaccines are free of side effects and safe.

P508

INFLUENZA ILLNESS BY AGE IN VACCINATED EUROPEAN AND ISRAELI CHILDREN AGED 6 MONTHS TO 17 YEARS

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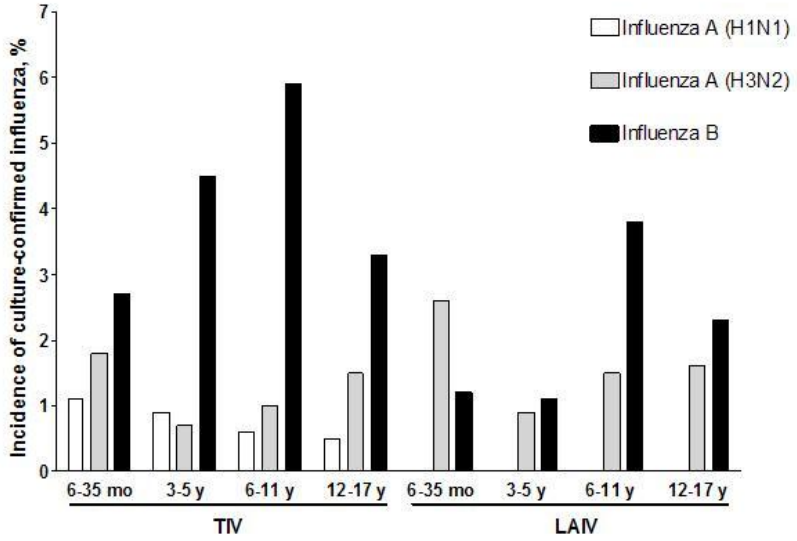
Background and aims: Limited culture-confirmed data exist regarding the burden of influenza in European children. In 2002-2003, two prospective, randomized, open-label studies evaluated the efficacy and safety of live, attenuated influenza vaccine (LAIV) versus trivalent inactivated vaccine (TIV) in children aged 6 months to 17 years in Europe and Israel. Data from these studies were analyzed to describe rates of influenza illness by age group and vaccine type.

Methods: Study 1 was conducted in children aged 6-71 months with recurrent respiratory tract infections who received 2 doses of influenza vaccine. Study 2 was conducted in children aged 6-17 years with stable, medically-treated asthma who received 1 dose of vaccine. Post-hoc analyses evaluated the rate of culture-confirmed influenza illness overall and by strain for 4 age groups (0.5-2, 3-5, 6-11, 12-17 years).

Results: The highest incidence of influenza occurred in subjects 6-11 years (51-75 per 1000). The differences were driven by influenza B, the most prevalent strain detected. The incidences of A/H1N1 and A/H3N2 were similar in all age groups.



[Incidence of culture-confirmed influenza]

Conclusions: Despite being from vaccinated children, these data support previous findings that the incidence of influenza B is highest in younger school-aged children. In all age groups analyzed, LAIV recipients had fewer cases of influenza illness than TIV recipients.

(Sponsored by MedImmune. LAIV is not approved outside of the United States.)

P509

SAFETY AND IMMUNOGENICITY OF NOVARTIS VACCINES' INVESTIGATIONAL QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE, MENACWY-CRM VERSUS MENOMUNE® IN CHILDREN AGED 2-10 YEARS

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Background: The incidence of meningococcal disease is highest in infants and adolescents, but a significant burden of disease occurs in children (2-10 years of age). The aim of this study was to evaluate the safety and immunogenicity of an investigational quadrivalent (A, C, W-135, Y) meningococcal CRM_{197}-conjugated vaccine (MenACWY-CRM) compared with a quadrivalent meningococcal polysaccharide vaccine (Menomune®) in children 2-10 years of age, at 1-month and 6-months post-vaccination.

Methods: In this study conducted in Argentina, 1500 healthy children (aged 2-10 years) were randomized 2:1 to receive either MenACWY-CRM or Menomune®. Safety was assessed by recording local and systemic reactions for 7-days and serious adverse events for 6-months post-vaccination. Immunogenicity was assessed by serum bactericidal assay using an exogenous human complement source (hSBA) 1 and 6-months post-vaccination in a subset of subjects.

Results: Both vaccines were well-tolerated. At 1-month post-vaccination, percentage of subjects with hSBA seroresponse in the MenACWY-CRM group were significantly higher versus the Menomune® group (lower limit of the two-sided 95% CI for the difference in seroresponse rate >0%), for serogroups A (93% vs 53%), C (82% vs 52%) W (74% vs 46%) and Y (82% vs 63%). At 6-months post-vaccination, antibody persistence was evident for all MenACWY-CRM serogroups and significantly more subjects in the MenACWY-CRM vs Menomune group maintained an hSBA titer ≥1:8 against serogroups C, W and Y.

Conclusions: MenACWY-CRM was well-tolerated and immunogenic in children aged 2-10 years, with evidence of persistence of bactericidal antibodies for at least 6-months post-vaccination.

P510

REVIEW OF IMMUNIZATION PROCESS FOR YEAR 2007 ON THE TERRITORY OF SKOPJE AND LOCAL DISTRICT AREAS

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Prevention, disease prevention is the key of preventive public health. It is always better to prevent a disease than to treat it. The most effective way to reduce disease and death from infections disease is to vaccinate susceptible populations.

Aim: Review of realised vaccination for year 2007 in the Public Institution Health centre-Skopje. The aim of preventive teams was to achieve high level, more than 90%, of the vaccinated plan, with results for high collective immunity. That will guarantee good epidemiological status on territory of Skopje and around.

Material and methods: In year 2007, vaccination was realised in 44 vacc. puncts.. Children, 0-6 years old, from city of Skopje and local district areas were included in vaccination program

Results: Plan/Realised.

BCG P.1495/R.1436 (96,1%), **DTPI** P.7423/R.7553(101,8), **DTPII** P.7590/R.7273(95,8%), **DTPIII** P.7796/R.7189(92,2%), **PolyoI** P.7432/R.7151(96,2%), **Polyo II** P.7558/R.7292(96,5%), **Polyo III** P.7789/R.7216(92,6%), **HepBI** P.443/R.426(96,2%), **HepBII** P.7244/R.6788(93,7%), **HepBIII** P.7343/R.6842(93,2%), **MPR** P.7534/R.6969(92,5%), **DTPIRev.** P.7384/R.6987(94,6%), **DTP IIRev.** P. 7345/R.6390(87,0%), **PolyoIRev.** P. 7459/R.6863(92,0%).

Conclusion: In year 2007, in the group of 0-6 years old children, realization of primo vaccination was higher than 90%; recruitment in the city area was better than in the district village areas. Perspective ideas for more quality realization of the children vaccination is supplement with personnel deficit, planning of more home visiting nurses in the village areas for better social mobilization.

P511

ECONOMIC EVALUATION OF A PENTAVALENT UNIVERSAL ROTAVIRUS VACCINATION PROGRAMME IN FRANCE

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Background: Rotavirus gastroenteritis (RVGE) is a major cause of hospitalisation in industrialised countries. In France, RVGE is estimated to result in 300,000 cases each year in children < 5, including 18,000 hospital admissions. The aim of the study was to assess the economic burden of RVGE as well as the full benefit of implementing a pentavalent rotavirus vaccination programme in France.

Methods: A decision-analytic model was developed to compare the impact of vaccinating a birth cohort of 790,000 children (85% coverage) with a no-vaccination strategy. The cohort was followed from birth to the age of 5. Economic impact of RVGE on healthcare resource use and budget impact of the vaccination programme were assessed from the third party payer (TPP) and societal perspectives. The potential impact of herd-immunity on these results was also evaluated.

Results: The economic burden of RVGE was estimated to be 33M€ for the TPP, 70% of which were mainly due to hospitalisation, and could cost up to 89M€ to the society. From year 1 and 2 following the introduction of RV vaccine, disease management cost would be reduced by about 40% and 60%, respectively. Thanks to this substantial cost reduction, 25% and 40% of vaccination costs would be payed-back (TPP perspective) the first and second year respectively following the introduction of the RV vaccine. Return on investment would be much faster in case of potential herd-immunity.

Conclusion: Implementing pentavalent rotavirus vaccination in France would reduce substantially the economic burden of RVGE allowing a rapid return on investment.

P512

A COST EFFECTIVENESS ANALYSIS OF ROUTINE VACCINATION WITH THE 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN-D CONJUGATE VACCINE (PHID-CV) IN SWEDEN

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Objective: To estimate the expected health benefits, costs and incremental cost-effectiveness ratio of routine vaccination with the new 10-valent pneumococcal non-typeable Haemophilus influenzae protein-D conjugate vaccine (PHiD-CV) compared with no vaccination and the 7-valent pneumococcal conjugate vaccine (PCV-7) in Sweden.

Methods: A cross-sectional population model was used to estimate the impact of vaccination over 1-year at vaccine steady-state and to perform an incremental cost-effectiveness analysis, comparing 3 different vaccination strategies. A 2+1 dose vaccination schedule was assumed. The effects of herd-protection, serotype replacement and serotype cross-protection were calculated separately. The main outcomes were measured by reduction in the disease burden, costs, QALYs and incremental cost-effectiveness ratio per QALY gained.

Results: Preliminary results indicate that PHiD-CV could prevent a considerable number of pneumococcal infections- particularly AOM. Annual healthcare costs (vaccine costs excluded) and indirect costs with PHiD-CV are estimated at 10% and 12% lower than with the no vaccination strategy, and 6% and 7 % lower than with PCV-7. Expected QALY gain from vaccination is twofold compared with PCV-7. At price-parity, health benefits can be achieved with a “low cost” per QALY (< €10, 000) compared with no vaccination and the estimated mean differences in cost and QALYs indicate that PHiD-CV dominates PCV-7. PHiD-CV was predicted to prevent 18,000 more antibiotic prescriptions than PCV-7.

Conclusion: Preliminary results indicate that the health benefits of PHiD-CV compared with no vaccination and PCV-7 can be achieved within a “low cost” per QALY gained, according to the Swedish National Board of Health and Welfare´s ranking.

P513

THE B-CELL RESPONSE TO A PRIMARY COURSE OF INVESTIGATIONAL MENACWY-CRM$_{197}$ VACCINE GIVEN AT 2 AND 4 MONTHS OF AGE

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Background and aims: A new investigational quadrivalent meningococcal vaccine conjugated to CRM$_{197}$ (MenACWY-CRM$_{197}$) has been shown to be immunogenic in young infants, in a 2- or 3- dose primary schedule. However, as with the serogroup C meningococcal conjugate vaccine, a decline in protective antibody was observed by 12 months of age, despite the induction of immunological memory (Snape *et al*. 2008). In this study we assessed the memory B-cell response at 5 months of age after priming with MenACWY-CRM$_{197}$ in infancy and the influence of maternal antibody present in infants at 2 months of age on the memory B-cell response.

Methods: 216 healthy children were primed with MenACWY-CRM$_{197}$ at 2 and 4 months of age. Blood samples were obtained from all children at 5 months of age and from a subset of children at 2 months of age before immunisation, and from all the mothers of the study children. The memory B-cell response was measured by ELISPOT and maternal antibody level by ELISA.

Results: Serogroup-specific memory B-cells were detectable in less than one fifth of children following priming immunisation with the two doses of MenACWY-CRM$_{197}$ vaccine. No influence of the maternal antibody was observed on the memory B-cell response at 5 months of age.

Conclusions: These data indicate that the decline in antibody after polysaccharide conjugate vaccination in early infancy might relate to the low frequency of memory B-cells induced in some infants during priming and support the importance of a booster dose of vaccine at 12 months of age.

P514

VACCINATION COVERAGE IN ADOLESCENTS (14 YEARS OF AGE) AND DETERMINANTS OF SUB-VACCINATION

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Background and aims: To measure the vaccination coverage in 14-year-old Flemish adolescents for Hepatitis B (HBV), Measles-Mumps-Rubella (MMR), Meningococcus serogroup C (MenC) and diphtheria-tetanus-polio (DiTe-Polio) booster vaccines.

Methods: A two-stage random cluster sample of 1319 adolescents born in 1994 and living in Flanders (Belgium) was selected. Their parents were interviewed in 2008 (EPI-cluster sampling survey method). Vaccination documents were verified and a questionnaire on socio-demographic indicators and vaccine-related factors was completed at home by trained interviewers. Only documented vaccination dates were accepted. Missing data were, when possible, retrieved from Vaccinnet (Flemish web-based vaccine registration system), school files or other vaccinators.

Results: Coverage estimates are shown in table 1. Only 83.5% of the adolescents had proof of both MMR-vaccines. Influencing factors were divorced parents or single parent, ethnicity of parents, education and work situation of parents, family income and failing one year in school or receiving special education.

	Dose 1	Dose 2	Dose 3
HBV	92.5 (90.9 - 94.1)	91.0 (89.4 - 92.7)	89.2 (87.4 - 90.9)
MMR	88.1 (86.1 - 90.0)	90.6 (89.0 - 92.2)	
MenC	86.4 (84.3- 88.6)		
DiTe	91.1 (89.6 - 92.7)		
Polio	90.8 (89.2 - 92.4)		

Conclusions: Even though the coverage improved considerably since 2005, coverage rates in adolescents are still below elimination thresholds in adolescents in Flanders. Special attention should be given to children of non-Belgian and underprivileged parents as well as adolescents who already failed in school.

P515

MEASLES ANTIBODIES AND RESPONSE TO VACCINATION IN CHILDREN AGED LESS THAN 14 MONTHS. IMPLICATIONS FOR AGE OF VACCINATION

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Background and aims: Passive acquired immunity against measles in children due to trans-placental transfer of maternal IgG antibodies decreases during the first months of life. In Catalonia two doses of Measles Mumps Rubella vaccine were scheduled at 15 months and 4 years of age. The objective of this study was to determine titres of measles antibodies in children aged 9-14 months before and after vaccination and in their mothers.

Methods: An experimental before-after study was conducted. Blood samples were collected by capillary puncture before and 28 days after vaccination. Mothers' samples were also collected by capillary puncture. Titres of specific measles IgG antibodies were determined by enzyme linked immunoassay. Seroconversion was defined as the presence of antibodies after vaccination in subjects without antibodies before. Maternal antibody interference was considered if children were seropositive before and seronegative after vaccination.

Results: Maternal antibodies were present in 37.7% of the 69 children included in the study. 45.2% were positive in the 9 months age group. Two samples were available from 51 children. From a total of 31 seronegative children, 61.3% seroconverted. The overall seropositivity was 64.7%. The interference of maternal antibodies was estimated at 30.0%. Of the 58 mothers enrolled, 67.2% had antibodies. Antibody titres were higher in infected mothers than in vaccinated mothers [240.4 vs 584 mUI/ml respectively (p=0.009)].

Conclusions: Advancing the first dose of measles vaccination from 15 to 12 months of age is an appropriate strategy given the increase in the period of infants' susceptibility to measles before vaccine administration.

P516

FACTORS UNDERLYING PARENTAL DECISIONS ABOUT CHILDHOOD VACCINATION: A SYSTEMATIC REVIEW

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Background and aims: A substantial literature explores parental vaccination decision-making, however the quality and findings of this literature were last assessed and synthesised systematically before the UK MMR controversy. This review focuses on combination vaccines and provides guidance for clinicians and policymakers on issues salient to parents, and to researchers on improving immunisation decision-making studies.

Methods: A comprehensive search strategy around the facets parent, decision, child and immunisation, along with handsearching, identified 440 articles. 409 articles were excluded following assessment against inclusion criteria (kappa for inter-rater reliability 0.71, $p < .001$). 12 qualitative and 19 quantitative studies were reviewed. Methodological quality was assessed using revised versions of validated scales. Content analysis was used to identify themes in the data, and code data to those themes.

Results: Study quality was frequently poor, with unrepresentative samples, self-report outcome measures and qualitative analyses open to bias, and a lack of prospective studies. There was substantial variation in factors reported and reporting/analysis methods, precluding systematic assessment of their predictive strength; however general safety concerns about vaccines were the most commonly assessed factor and these were consistently linked to lower uptake. Other factors linked to lower uptake were the perception that the vaccine is effective; that the disease is serious and the child is susceptible to it; and trust in healthcare system/Government policies around vaccination.

Conclusions: Parents acted in line with their attitudes and beliefs about vaccination. Interventions should focus on improving perceptions of vaccine safety and disease consequences. Research quality needs substantial improvement.

P517

EXPERIMENTALLY MODELLING IMMUNISATION DECISIONS: THE EFFECTS OF DISEASE, VACCINE REACTION AND HEALTH PROFESSIONAL FACTORS

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Background and aims: Most studies describing factors influencing immunisation decisions do so in specific vaccine or disease contexts, where unmeasured context-specific covariates may influence findings. We investigated the mechanisms underlying these decisions in a “sterile” experimental situation - a vital step before working with them in real-life.

Method: Participants imagined they were deciding whether to immunise their one-year-old child. In Study 1, disease and vaccine reaction likelihoods were presented; in Study 2, disease and vaccine reaction severity; and in Study 3, health professional opinion, consulting style and trustworthiness; all using vignettes. Each of these factors had multiple levels, e.g. low/medium/high, and all possible combinations of levels within each study were presented (full-factorial design). For each vignette participants marked how likely they were to accept the vaccine based upon the information given, on a Likert scale (range 0-100%, 10% intervals).

Results: Over 150 London Psychology undergraduates completed questionnaires. Disease and vaccine reaction likelihood and severity significantly predicted intention to immunise, and there were significant interactions between these factors (higher intention when disease common and serious and vaccine reaction uncommon and mild), suggesting that participants were mentally engaging in cost-benefit analyses. Health professional input significantly predicted intention to immunise and interacted significantly with other factors.

Conclusions: These data suggest that immunisation decision-makers use multi-factor information logically and effectively. This study demonstrates the utility of a context-free experimental approach to unpack sensitive immunisation decisions, and provides rationale for exploring these mechanisms with parents in hypothetical situations and validating the model in real situations.

P518

UK PARENTS' DECISIONS ABOUT THE MEASLES, MUMPS AND RUBELLA (MMR) VACCINE: A QUALITATIVE GROUNDED THEORY STUDY

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Background and aims: MMR uptake in the UK remains suboptimal, with measles outbreaks now commonplace. 75% of MMR non-immunisations are attributable to parental choice. Research into these choices is methodologically flawed and was conducted when disease prevalence was lower than today, thereby limiting its validity as a basis for modern interventions. We present a methodologically robust investigation of current MMR decision-making.

Method: 21 semi-structured interviews elicited beliefs and cognitions about MMR among London mothers deciding to accept, postpone or decline MMR for their children. Mothers were recruited purposively through General Practices and childcare organisations. Objective MMR uptake data were obtained from General Practices. Interview recordings were transcribed verbatim, and coding was double-checked.

Results: MMR-accepting mothers worried about outbreaks and disparaged MMR rejection based on autism fears, however all spontaneously mentioned the MMR controversy and few expressed total confidence in the vaccine. MMR postponement was more often attributed to unplanned delays than conscious choice. Some MMR-declining mothers believed that evidence on the number of autism cases causally linked to MMR exists but is impossible to find. Acceptors of expensive single vaccines were happy to pay for peace of mind.

Conclusions: MMR still worries UK mothers, though their dialogues and our difficulty recruiting MMR-declining parents suggest it is becoming less acceptable to refuse MMR, particularly if citing autism concerns. Whilst this normative change could improve uptake, interventions may be targeted inappropriately if MMR-declining parents feel unable to voice their true concerns.

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P519

STATE-SPECIFIC RESULTS OF VACCINATION ATTITUTE OF PAEDIATRICIANS - THE GERMANY VACCINATION STUDY

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Background: Vaccination rates for preventable diseases are in general unsatisfying in Germany, but show variations among the different states.

Until now, no representative study has analysed pediatricians' attitudes and behaviour of befind reasons of the low vaccination rate covering throughout Germany on a regional level.

Methods: A representative cross sectional survey of about 3020 paediatricians from all 16 German states received a standardised questionnaire. About eight weeks later, we sent a reminding letter and in a third turn a second questionnaire to increase the response rate.

Result: 2023 (67%) of all contacted paediatricians replied to the questionnaire. The recruiting efficiency (REP=fully received questionnaires divided by the number of all successfully contacted physicians) was at 62%.

61% of the questioned paediatricians declared to follow the recommendations of the STIKO (German committee for vaccination of the RKI). Concerning the states in detail, results varied from 83% in Saxony-Anhalt to 49% in Bavaria ($p< 0.0001$). In consideration of the state, where paediatricians received their degrees, independent from their place of practice, 57% (n=74) of those who studied outside Germany follow the STIKO-recommendations compared to 61% ($p=0.46$) of those who studied in Germany. In addition to this, 80% of the former students of Saxony-Anhalt follow these recommendations today, compared to 48% of the former students of Bavaria ($p< 0.0001$).

Conclusions: The study will contribute to better understand problems of the different situations in the German states in order to achieve a high vaccination rate nationwide.

P520

IMPACT OF INFLUENZA AND EFFECTIVENESS OF INFLUENZA VACCINATION IN CHILDREN WITH LEUKEMIA WHO HAVE COMPLETED CHEMOTHERAPY

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Background and aims: Influenza vaccination is recommended in patients with chronic disorders including those with leukemia because disease and chemotherapy impair immune function, thus making them more vulnerable to influenza viruses. Aim of this study was to evaluate whether children with leukemia who have completed chemotherapy could be really considered a high-risk category.

Methods: A total of 182 children with leukemia who have completed chemotherapy were randomized 1:1 to receive influenza vaccination (Inflexal V, Berna Crucell) or no vaccination. As control group, 91 age- and sex-matched otherwise healthy children unvaccinated against influenza were studied. Between 1 October 2006 and 30 April 2007, the surveillance of influenza-related morbidity among the study children and their households was performed.

Results: A significant reduction in influenza-related morbidity was observed among children with leukemia vaccinated against influenza off-therapy since less than one year than among those with leukemia unvaccinated against influenza off-therapy since less than one year ($p < 0.05$). Among this last group, influenza-related morbidity appeared significantly higher than among otherwise healthy children ($p < 0.05$). No significant difference in clinical and socioeconomic impact of influenza was observed between children with leukemia off-therapy since at least one year and the healthy ones, with reduced benefits even in the effectiveness of influenza vaccination.

Conclusions: Children with leukemia who have completed chemotherapy since less than one year appear at higher risk of influenza-related complications than those off-therapy since at least one year, who show an impact in influenza-related morbidity similar to that observed in otherwise healthy children.

P521

ENHANCED SURVEILLANCE FOR PNEUMOCOCCAL EMPYEMA THORACIS IN UK CHILDREN: THE FIRST 2 YEARS

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Introduction: The incidence of empyema has increased dramatically over the last decade with most cases *S. pneumoniae*, serotype 1. The heptavalent pneumococcal conjugate vaccine introduced into the UK immunisation schedule does not contain antigen for this serotype. Enhanced national paediatric pneumococcal empyema surveillance was introduced September 2006 in collaboration between the Health Protection Agency and the British Paediatric Respiratory Society.

Methods: An initial screening pneumolysin PCR is performed on culture negative empyema fluid. Positive specimens undergo serotyping using Bio-Plex serotype assay for serotypes. 1, 3, 4, 5, 6A, 6B, 7F/A, 8, 9V, 14, group 18, 19A, 19F and 23F.

Results: There was a 34% reduction in the number of samples received between years 1 and 2 (n=78 vs n=51, p=0.018). Mean patient age was 6.1yrs (range 0.2-16.7yrs). Serotype 1 was the most frequently detected serotype over the surveillance period (year 1 vs year 2; 62% vs 49%, p=0.012). Serotype 3 was the second most common serotype (year 1 vs year 2; 12% vs 27%, p=0.052). A significant reduction in disease due to vaccine serotypes 4, 6B, 14 and 23F was observed (year 1 vs year 2; n=13 vs n=2, p=0.014). Vaccine serotypes 18C and 19F were not detected. There is currently no evidence of “replacement disease” with non-vaccine serotypes.

Conclusions: Ongoing surveillance of changes in incidence and serotype distribution of empyema is important to monitor changes in the epidemiology of this condition, and to detect any influences of the new conjugate vaccine. This will inform future vaccine policy.

P522

ADVERSE LOCAL AND REGIONAL REACTIONS AFTER BCG SSI VACCINE: A 12 MONTH COHORT FOLLOW UP

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Background and aims: BCG Statens Serum Institute (BCG SSI®) is used in several countries for routine vaccination or for high risk children. Since 2006, BCG SSI® has been the only one available in France. A prospective study was set up to evaluate its safety.

Methods: Between February and June 2007, 227 physicians vaccinated 2599 children under 6 years of age. They recorded their training to intradermal vaccination, site of injection, dose and injection technique. Local and regional adverse events (AE) >1cm were prospectively recorded during a 12 months follow up.

Results: Among the 2435 children with a follow up, 433 (17.8%) had an AE: 12.4% for erythema, 12.2% for induration, 2.5% for abscess, 0.9% for ulceration, 0.1% for lymphadenitis. Two abscesses had led to surgery, and one to puncture. One practitioner presented a tenosynovitis following accidental prick. In multivariate analysis, age, sex, site of injection, dose, visible papule during the procedure, training were variables analyzed; factors associated with a reduction of AE were : age of vaccination < 1 year (comparing to age > 1year, OR = 0.35 [0.2-0.6] for age < 28 days, 0.29 [0.2-0.42] for age 29 days to 2 months, 0.53 [0.37-0.74] for age 3 to 11 months), visible papule (OR = 0.48 [0.36-0.63]), low dose (OR = 0.42 [0.31-0.58]).

Conclusions: In this active surveillance, AE following BCG SSI vaccination are frequent (17.8%) but rarely severe. However, rate of abscesses is higher (2.5%) than expected. Early vaccination and adequate procedures could reduce the risk of AE.

P523

COMMUNITY-WIDE BENEFITS OF PEDIATRIC INFLUENZA VACCINATION: INSIGHTS FROM THE MODELING OF INFLUENZA TRANSMISSION

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Background: The role of children as a reservoir and vector of influenza transmission is widely recognized. However, clear evaluation of the community benefits of recommending and funding influenza vaccination targeting children has not been performed in many countries.

Aim: Our objective was to develop a generic pediatric transmission model that can be adapted to any country to assess the public health and economic benefits of implementing pediatric vaccination programs.

Methods: We adapted a structured population model simulating influenza transmission within a community of 10,000 individuals during a typical epidemic season. Applying available data from UK and US, we then quantified the total number of influenza cases, hospitalizations, and deaths prevented by pediatric vaccination, with associated health related quality of life impacts and cost savings from public and societal perspectives.

Results: In the UK context, pediatric vaccination strategies were found to prevent between 10% and 23% of influenza cases with a whole-population based incremental cost effectiveness ratio from £420 to £3010 per quality adjusted life year gained. Depending on the vaccinated age group, from 79% to 84% of avoided influenza cases were prevented outside the targeted population. Results were similar in the US context.

Conclusion: Using UK and US data, this model suggests that implementing a pediatric influenza vaccination program is largely beneficial. Health and economic benefits were higher in the rest of the community than in the vaccinated pediatric population. This model is a useful tool to provide insights into the community benefits of pediatric influenza vaccination.

P524

EFFICACY OF HUMAN ROTAVIRUS VACCINE RIX4414 IN AFRICA DURING THE FIRST YEAR OF LIFE

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Background: Rotavirus vaccination is a potential strategy for diarrhea prevention among children in Africa, where disease burden is high and access to primary care is limited. This double-blind, placebo-controlled, multi-center trial (102248/NCT00241644) was conducted in Malawi and South Africa to evaluate the clinical efficacy of the oral, live-attenuated human rotavirus vaccine RIX4414.

Methods: 4939 healthy infants were randomised(1:1:1) and received 2-doses of RIX4414 (at 10 and 14 weeks; placebo at 6 weeks), 3-doses of RIX4414 (at 6, 10 and 14 weeks) or 3-doses of placebo. Routine EPI vaccines including OPV were co-administered. HIV-infected infants were not excluded. Vaccine efficacy (VE) against severe rotavirus gastroenteritis (RVGE), defined as >=11 on the 20-point Vesikari scale, was calculated from 2 weeks post last dose to age 1 year.

Results: During the efficacy follow-up, mean duration 7.6 months, severe RVGE developed in 1.9% of RIX4414 (n=2974, pooled groups) and 4.9% of placebo recipients (n=1443); overall VE 61.2% (95%CI:44.0%-73.2%). Despite lower VE in Malawian (49.4%[95%CI:19.2-68.3]) compared to South African children (76.9%[95%CI:56.9-88.4]), the burden of severe RVGE prevented among Malawian children was greater; 3.9 versus 2.5 episodes per 100 infants vaccinated, respectively. There was no difference in VE between children receiving 2 (58.7%;[95%CI:35.7%-74.0%]) and 3 doses (63.7%;[95%CI:42.4%-77.8%]) of rotavirus vaccine.

Conclusions: In challenging settings in Africa, RIX4414 significantly reduced severe RVGE during the first year of life. Efficacy of 2 and 3 doses was similar. Overall public health impact in Africa is anticipated to be substantially higher than developed settings due to the high disease burden.

P525

USE OF PARACETAMOL AFTER ADMINISTRATION OF INFANT VACCINATION IN THE NETHERLANDS, BEFORE AND AFTER THE TRANSITION TO ACELLULAR PERTUSSIS VACCINE

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Background: The Dutch enhanced passive surveillance system of the national vaccination programme includes relevant information of type and level of medical intervention. A questionnaire study addressing more severe adverse events after infant pertussis vaccination, inquired for vaccination related medication also. During the study transition from whole cell (wP) to acellular pertussis (aP) combination vaccine occurred.

Aims: To gain insight in the frequency of paracetamol use in routine infant vaccination and most important reported indications for medication.

Results: Response rate of the questionnaire survey was 54% (28.000), 15.000 for wP and 13.000 for aP. Paracetamol administration was significantly higher in wP group (7457, 49.5%; 95% CI 48.7-50.3%) compared to aP group (2513, 18.9%, 95% CI 18.3-19.6%). Distribution of prophylactic use, prophylactic and/or therapeutic or only therapeutic use of paracetamol was 25 -30%, 50 - 55% and ~20% for both vaccine groups. Use of paracetamol was constant in the first three doses for wP and aP vaccine groups (mean: 45.8% and 16.7%) however, significantly higher after the fourth dose (61.5% and 19.3%, for wP and aP, respectively).

Fever was the most important reason for paracetamol use after the fourth dose in both vaccine groups (range 43.6% - 49.9%), significantly more often after wP vaccination. Parents indicated crying and pain mostly after the 1st dose (range 33,5% - 41,8% and 18.8% - 22.9%).

Conclusion: Paracetamol use was significantly increased after wP vaccination, possibly due to previous experience with the vaccine and/ or an expected significantly decreased reactogenicity profile of the aP vaccine.

P526

PERTUSSIS DISEASE BURDEN WITHIN THE HOUSEHOLD: CAN WE PROTECT YOUNG INFANTS?

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Background and aims: Despite a successful infant vaccination program, infants are still at risk for severe pertussis during their first half year of life. We conducted a nationwide, prospective study to identify which family members introduced pertussis in infant households and estimated age-specific disease burden and vaccine-effectiveness within the household-setting.

Methods: In 2006-2008, all household members of infants ≤6 months of age hospitalised for pertussis were tested by PCR, culture and serology to establish *B. pertussis* or *B. parapertussis* infection. Also information on clinical symptoms and vaccination history was collected.

Results: Of the 204 included infants 148(73%) were unvaccinated, 37(18%) vaccinated once, 17(8%) twice and two infants (1%) three times. Among children eligible for one vaccination, median duration of hospital stay was 4 days in vaccinated and 11 days in unvaccinated infants (p=0.03). 397/749 (53%) household-members had laboratory confirmed pertussis, another 45 (5%) met the clinical case definition. Three siblings and one adult were hospitalised for one day. For 159/204 (78%) families a primary case could be identified: in one-child households mothers were most often (41%) the primary case, in two-child households siblings (38%) and in >2 child-households siblings and mothers equally. Vaccination did not protect against infection in children aged 1-3 years, however vaccine-effectiveness against clinical pertussis was 69% (37-85%) for the acellular vaccine and 58% (21-78%) for the whole-cell vaccine.

Conclusions: Vaccinating family contacts may reduce pertussis disease burden in infants. However, on the long term improved pertussis vaccines are required to tackle the pertussis problem.

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ANAMNESTIC IMMUNE RESPONSE 4 TO 8 YEARS AFTER PRIMARY HEPATITIS B VACCINATION SERIES

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Background: Hepatitis B vaccines are frequently administered during infancy. The duration of immunologic memory to hepatitis B after vaccination remains undetermined. This study evaluated the hepatitis B anamnestic response of children 4 to 8 years of age.

Methods: This open-label, randomized, multicenter, controlled study in Spain enrolled 1458 children previously immunised with recombinant hepatitis B vaccine (either RECOMBIVAX HB™ [rHBV-1] or ENGERIX B™ [rHBV-2]) during infancy.

Using a two-by-two design, participants were challenged with a single intramuscular (deltoid) dose of either modified process hepatitis B vaccine (mpHBV, 5 mcg) or rHBV-2 (10 mcg). Blood samples were collected immediately before and one month postimmunisation.

Results: Prior to receiving the challenge dose, 15.9 to 51.2% were seroprotected (% subjects with anti-hepatitis B surface antibody ≥ 10 mIU/mL). Approximately 91.6 to 97.3% of subjects achieved seroprotection post-challenge. There were no serious, vacine-related, adverse experiences, no discontinuations due to adverse experiences, and no deaths during this study.

		rHBV-1 Primary Series		rHBV-2 Primary Series	
		mpHBV Challenge Group (N=376)	rHBV-2 Challenge Group (N=375)	mpHBV Challenge Group (N=353)	rHBV-2 Challenge Group (N=354)
Parameter	Timepoint	Response (95% CI)	Response (95% CI)	Response (95% CI)	Response (95% CI)
SPR	Pre-Challenge	15.9% (12.2-20.2)	18.5% (14.5-23.1)	51.2% (45.7-56.6)	45.1% (39.6-50.7)
SPR	Post-Challenge	95.0% (92.1-97.1)	91.6% (88.1-94.3)	97.3% (95.0-98.8)	95.4% (92.6-97.4)
GMT	Pre-Challenge	4.3 (3.8-4.7)	4.2 (3.8-4.7)	13.1 (11.0-15.6)	11.4 (9.4-13.7)
GMT	Post-Challenge	476.9 (380.7-597.3)	561.2 (435.6-723.1)	1424.0 (1131.1-1792.8)	1216.1 (923.6-1601.2)

N: Number of subjects randomized in each treatment group; CI: Confidence Interval; SPR: Seroprotection rate (Anti-HBs Titer ≥ 10 mIU/mL); GMT: Geometric mean titer.

[Summary of Anti-HBs Responses]

Conclusions: The majority of children primed with rHBV-1 and rHBV-2 mounted an anamnestic response when boosted at 4 to 8 years of life. A single mpHBV dose is an adequate booster for children primed with rHBV-1 or rHBV-2.

P528

IMMUNE RESPONSE AND ANTIBODY PERSISTENCE AFTER A CONJUGATE MENC BOOSTER VACCINATION

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Aims: To assess the antibody persistence 12 months after receiving two different MenC vaccines given as a booster dose in the second year of life.

Methods: Open, randomized, multicentre clinical trial. Children 14 to 18 months of age previously primed with either 2 doses of NeisVac-C™ or three doses of Meningitec™, were boosted with any of the two vaccines together with Infanrix-IPV-Hib™.

Results: One month after the booster dose, children primed with two doses of NeisVac-C™ achieved higher SBA [6810 (95%CI: 5615 - 8259)] than those primed with three doses of Meningitec™ [1889 (95%CI: 1595 - 2236)], no matter which vaccine was used as a booster.

Twelve months after the booster, SBA was still significantly higher in subjects primed with NeisVac-C. Higher SBA titers were found in children boostered with NeisVac-C, compared to Meningitec (Table).

VACCINE	PRIMING			
BOOSTER	Meningitec ™		NeisVac-C ™	
	SBA GMT	% SBA≥1:128	SBA GMT	% SBA≥1:128
NeisVac-C ™	69.0 (43.2-110.1)	58.8	394.3 (255.4-608.7)	91.3
Meningitec ™	36,1 (21,7-60,3)	49.5	177,6 (101,5-310,7)	76.4
TOTAL	50,9 (36,0-71,8)	54.4	262,4 (183,4-375,3)	83.3

Conclusion: A booster with MenC and Infanrix-IPV-Hib™ vaccines induced high SBA and anti PRP antibodies no matter which MenC vaccine brand vaccine was used, however children primed and boosted with NeisVac-C maintained higher SBA GMT levels at 12 months after boosting.

P529

SAFETY AND IMMUNOGENICITY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN HEALTHY INFANTS AND TODDLERS RECEIVING ROUTINE VACCINATIONS IN SPAIN

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Aims: To compare the immune response of selected antigens included in routine childhood vaccines when administered concomitantly with PCV13 or 7-valent pneumocccal conjugate vaccines (PCV7), and to assess the safety and immunogenicity of PCV13 in infants and toddlers.

Methods: Healthy infants were randomized to receive PCV13 (n=315) or PCV7 (n=304) with DTaP-Hepatitis B-IPV-Hib at ages 2, 4, and 6 months and a meningococcal C vaccine (MnCC) at ages 2 and 4 months. Antibody response to selected antigens in both groups was assessed 1 month after doses 2 and 3 and 1 month after the toddler dose. Local and systemic events were reported for 4 days following vaccination.

Results: For all concomitant antigens, noninferiority was established at >-10% (lower limit of 95% CI for the difference in proportions between PCV13 and PCV7). Infant immune responses induced by DTaP, polio and MnCC antigens administered with PCV13 were noninferior to those observed with administration of PCV7. After infant dose 3 of PCV13, ≥97% of infants achieved pneumococcal anticapsular IgG concentrations ≥0.35 µg/mL (WHO antibody threshold for comparative assessment of pneumococcal vaccines) for all serotypes except serotypes 3 (90.3%) and 23F (94.6%). Following the toddler dose of PCV13, >98.7% achieved pneumococcal IgG antibody concentrations ≥0.35 µg/mL for all serotypes except serotype 3 (92.2%). Local and systemic reactions were similar between groups.

Conclusions: Immune responses for selected concomitantly administered vaccine antigens were comparable in both groups. PCV13 has an acceptable safety profile and elicits a likely effective antipneumococcal immune response in infants and toddlers.

P530

IMMUNE MEMORY AGAINST HEPATITIS B PERSISTS IN 7-8 YEAR-OLDS PRIMED WITH 3 DOSES OF HBV VACCINE IN ROUTINE CLINICAL PRACTICE

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Background and aims: Protection against hepatitis B disease after immunisation is considered to rely on both the persistence of protective serum antibodies and the ability of the immune system to mount an anamnestic response to a challenge with hepatitis B virus (HBV). This study was conducted to evaluate the persistence of the immune memory against HB surface antigen in 7-8 years old children that were vaccinated in infancy and live in a low endemic environment for HBV (Germany).

Methods: Open-label study [110474 / NCT00519649] conducted in 24 centres in Germany. 7-8 years old children, primed with 3-doses of HBV vaccine during infancy in routine clinical practice, were enrolled in the study. All subjects received a single challenge-dose of monovalent paediatric HBV vaccine. Blood samples were collected before and one month after vaccination. Anti-HBs antibodies were measured using ELISA.

Results: In total, 300 children were vaccinated; 280 were included in the per-protocol cohort for immunogenicity. Prior to challenge-dose, 83.5% of children had anti-HBs antibody concentrations ≥10mIU/ml and 37.4% had concentrations ≥100mIU/ml. One month post-challenge dose, the percentage of subjects increased to 100% and 98.2%, respectively. Anti-HBs Geometric Mean Concentrations increased 200-fold from 56.2 to 13099.3mIU/ml and 99.6% of subjects demonstrated an anamnestic response to the challenge dose of monovalent paediatric HBV vaccine. The HBV challenge vaccine was well tolerated.

Conclusions: Primary infant vaccination with monovalent HBV vaccine in routine clinical practice induces lasting seroprotection and strong immune memory for at least 7-8 years.

P531

PERTUSSIS OUTBREAK IN PAEDIATRIC CARDIAC SURGERY

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Introduction: Although pertussis immunisation is recommended for paediatric health care workers (HCW), vaccine uptake remains low and outbreaks may still occur. In 2008, a 6 month-old cardiac patient originating from Algeria, developed severe pertussis and was admitted to PICU.

Objective: To describe infection control intervention during a pertussis oubreak in our 16 beds paediatric cardiac surgery and 14 beds PICU unit.

Methods: Confirmed pertussis case: Positive PCR on nasopharyngeal aspirate (NPA). HCW, patients and parents were interviewed to search for cough and pertussis vaccine status. *B.pertussis* PCR detection was performed in all unvaccinated direct contacts of index case. Serology was performed in unvaccinated contact HCW and parents. Immunisation was proposed to all unvaccinated HCW. Contact patients and parents were given antibiotic prophylaxis and cardiac surgery unit was quarantined for 5 days. Active surveillance was performed for 10 weeks.

Results: 4/61 and 19/54 HCW had received a pertussis vaccine in surgery and ICU respectively. 151 NPA were performed and 7 confirmed cases have been identified (2 children, 2 nurses and 3 mothers), 2 of which were symptomatic. No cases were acquired in ICU. No children were identified with pertussis symptoms and 7 HCW had symptoms of cough, one was paroxysmal and one prolonged. No serology was positive (55 performed). Antibiotics treatments or prophylaxis were administered to 38 subjects. 110 HCW were vaccinated, 29 from surgery and 18 from ICU respectively.

Conclusions: Pertussis outbreak control required drastic containment measures. Pertussis immunisation of HCW should be actively recommended to avoid outbreaks.

P532

PRINCIPLES AND MAIN TASKS OF QUALITY ASSURANCE OF VACCINE TRIALS IN CHILDHOOD

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Background and aims: Vaccines are given to healthy children. In times of evidence based medicine they must be proven in randomized controlled trials (RCTs) with high qualitative and ethical standards. Quality assurance is necessary to guarantee that evidence on safety and efficacy of vaccines is based on high data quality. Consecutive inspections of the U.S. Food and Drug Administration found significant shortcomings in inquiries performed in RCTs in European countries. With this question in mind we performed a review about quality assurance in paediatric vaccine trials and propose a new model to improve data quality.

Methods: A literature research in Pubmed for quality assurance and vaccine trials was performed. The model was built on existing standard structures of quality assurance by implementing quantitative aspects.

Results: There was little evidence in the literature about data quality in vaccine trials. The model was built on queries posted from the data management to the investigator sites. By analysis of incorrect items in primarily collected data frequent problems can be identified. Resolutions on different stages from the case record form design to investigator initiating, data sampling and plausibility control can be developed.

Conclusions: Only meaningful results justify high efforts and possible risks for children within vaccine trials. But results depend on data quality, which must be assured. Mistakes are possible on all stages of inquiries. By quantifying incorrect items typical failure types can be identified and resolutions developed. The proposed strategy to minimize failures within vaccine trials has to be validated in further trials.

P533

IMMUNOGENICITY OF HEPTAVALENT PNEUMOCOCCAL VACCINE AND HEXAVALENT VACCINE, CO-ADMINISTERED TO ITALIAN INFANTS AT 3, 5 AND 11-12 MONTHS OF AGE

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Background: To evaluate the immunogenicity of heptavalent pneumococcal vaccine (PCV-7) and hexavalent Diphtheria-Tetanus-Trivalent Acellular Pertussis-Hepatitis B-Inactivated Polio Virus-Haemophilus influenzae Type B vaccine, when co-administered to infants according to a 3-dose course (2+1), an on-field clinical study was carried out in Genoa, Liguria, the first administrative Region in Italy, since 2003, to introduce the PCV-7 in the routine immunisation schedule.

Methods: Between 2006 and 2007 years, 151 and 43 healthy infants, immunised in co-administration with the vaccines under study and with the hexavalent vaccine given alone, respectively, were progressively enrolled in the local Public Health Units, at the third routine vaccination-visit. A blood sample from children, regularly immunised at 3, 5 and 11-12 months of age, was obtained one month after the third dose. Sera were tested by enzyme-linked immunosorbant and microneutralisation assays for measuring specific antibody response to the vaccine antigens, using standardised and validated methods.

Results: An excellent antibody response for PCV-7 was reached for all serotypes, with seroprotection levels [≥ 0.35µg/ml) ranging from 97.3% to 100% and Geometric Mean Concentrations (GMC) between 2.50 µg/ml (95% CI=2.16-2.90) for serotype 18C and 12.29 (95% CI=10.49-14.39) for serotype 14. Concerning the hexavalent vaccine, no significant differences emerged in the inter-group comparison, with seroptotection rates, between 97.7% and 100%, and Geometric Mean Titres, all well above accepted protective cut-offs.

Conclusions: Both vaccines resulted highly immunogenic, our results supporting the current strategy adopted in Italy for the routine immunization of newborns.

P534

ACCEPTANCE OF HPV VACCINATION AMONG PARENTS AND ADOLESCENTS IN ITALY

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Background and aims: Parental and adolescents' acceptance of HPV vaccine is critical for the success of the vaccination campaign. This study evaluated knowledge, attitudes, and behavioral intention towards HPV infection and vaccination in a random sample of Italian parents and adolescents.

Methods: A self-administered anonymous questionnaire covering demographics, knowledge about HPV infection and vaccine, perceived risk for HPV infections, perceived benefits of vaccinations including HPV vaccines, and willingness to receive an HPV vaccine was administered to families of adolescents aged 11-18 years in 8 schools.

Results: A total of 2,331 out of 3,062 (76.1%) parents and 863 out of 1,230 (70.1%) adolescents answered the questionnaire. An adequate knowledge on HPV infection and on the benefits of HPV vaccine was significantly higher among mothers than fathers ($p< 0.001$) and among female adolescents than among male adolescents ($p< 0.001$). Factors significantly related with willingness to use HPV vaccine were among the parents age >45 yrs, high education level, having a daughter instead of a son, being catholic, being in favour of vaccinations, having an adequate knowledge on HPV vaccination and among the adolescents age >16 yrs, being a female, having an adequate knowledge on HPV vaccination. The majority of parents (90.4%) and adolescents (82.6%) was interested in receiving more information on HPV and its prevention, identifying the school as the best setting where to improve their knowledge.

Conclusions: Parental and adolescents knowledge about HPV infection and vaccination should be urgently improved in order to ensure an adequate compliance to HPV vaccination's recommendations.

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SAFETY AND IMMUNOLOGIC NON-INFERIORITY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE GIVEN AS A 3-DOSE SERIES WITH ROUTINE VACCINES IN HEALTHY CHILDREN

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Background and aims: A 13-valent conjugate pneumococcal vaccine (PCV13) has been developed to improve protection against pneumococcal disease beyond that possible with the licensed 7-valent vaccine (PCV7). This study compared safety and immunogenicity of PCV13 with that of PCV7, when given as part of the vaccination schedule recommended in Italy.

Methods: 606 subjects were randomly assigned to receive either PCV13 or PCV7 at 3, 5 and 11 months of age; all subjects received Infanrix Hexa. Vaccine reactions were monitored. Antibody responses to Infanrix Hexa antigens, serotype-specific anticapsular polysaccharide IgG responses, and anti-pneumococcal opsonophagocytic activity (OPA) were measured 1 month after the 2-dose primary series and 1 month after the booster dose.

Results: Overall, the safety profile of PCV13 was similar to that of PCV7. There were no differences in immune responses to the Infanrix Hexa antigens. PCV13 elicited anti-pneumococcal capsular IgG antibodies to all 13 vaccine serotypes, with notable increases in concentrations seen after the booster dose (geometric mean concentrations ranged from 1.22 µg/mL for serotype 3 to 10.30 µg/mL for serotype 14). Responses against the 7 common serotypes were comparable between the PCV13 and PCV 7 groups when measured after the booster dose. PCV 13 also elicited substantial levels of OPA activity against all 13 serotypes following both the infant series and the booster.

Conclusions: PCV13 was comparable to PCV7 in safety profile and immunogenicity for common serotypes, demonstrated functional OPA responses for all 13 serotypes, and did not interfere with immune responses to concomitantly administered Infanrix Hexa.

P536

THE LONG-TERM HIGHEST PERTUSSIS INCIDENCE IN AGE COHORT 10-14 YEARS: IMPLICATIONS FOR INTRODUCTION BOOSTER VACCINATION

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Childhood vaccination against pertussis is obligatory in the Czech Republic. The vaccination started in 1958 and led to progressive and rapid reduction in pertussis incidence. Compulsory routine vaccination represents five doses in the Czech Republic. Despite of the fact the disease still circulates in the Czech population especially among school children. Since 1993 the pertussis incidence has been increased especially in age cohort 10-14 years. To understand epidemiological characteristics of this situation a descriptive analysis was undertaken.

All cases of pertussis were notified in nationwide communicable diseases mandatory reporting system (EPIDAT) to the National Institute of Public Health through regional public health offices. All cases of pertussis were laboratory confirmed by serology or culture.

From 1974 to 1993 the pertussis incidence did not exceed 1/100000 population. The lowest pertussis incidence rate was recorded in 1989 - 0.05/100 000. Since 1993 an increasing pertussis incidence and change in the age trend of reported cases have been recorded. The majority of pertussis cases (40-50%) have been reported among children in 10-15 years of age.

Data from 2008 indicate the highest increase in the reported cases from the 1980' in the Czech Republic - 767 cases (7.4/100000). The peak incidence was recorded in the age cohort 10-14 years - 380 cases (49.5%).

A descriptive analysis of situation of pertussis incidence led to changes in immunization policy in the Czech Republic. Changes in pertussis incidence were noticed by the national authorities and introduction of booster dose for children of 10-11 years was proposed.

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PHASE I STUDY OF A MVA-BASED MEASLES VACCINE - A SUPPLEMENTAL TOOL FOR MEASLES ERADICATION IN THE PAEDIATRIC POPULATION

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Background and aim: The current life-attenuated measles vaccine use from 9 to 15 months of age onwards, leaves a considerable gap of unprotected infants. The eradication campaign will open opportunities for alternative vaccines. Modified vaccinia Ankara-Bavarian Nordic (MVA-BN®) is a life, but non-replicating, vaccine vector with an extensive safety record. It showed a promising safety and immunogenicity profile in newborn and juvenile animals.

Method: In a single group, open label Phase I study 30 healthy adults, 18-32 years old, vaccinia-naïve and measles-experienced, received two subcutaneous immunizations of MVA-mBN85B, a recombinant MVA-BN® vectored measles vaccine, four weeks apart and were followed up for 6 months. The safety and immunogenicity were assessed.

Results: MVA-mBN85B induced a strong booster response with a geometric mean titer (GMT) of 8,420 mIU/ml in a measles-specific enzyme-linked immunoassay (ELISA) and a GMT of 789 in a measles plaque reduction neutralization test (PRNT) 14 days after the first immunization. This booster response was not compromised by pre-existing measles immunity. Measles ELISA and PRNT titers were strongly correlated (r=0.86). The peak of anti-vaccinia antibodies was reached 14 days after dose 2, all subjects seroconverted. No SAEs were recorded and the study vaccine was well tolerated.

Conclusion: This vaccine deserves further evaluation in children and infants and could make a substantial contribution in protecting infants earlier than the currently used live-attenuated measles vaccine. It also primes against smallpox.

Acknowledgement: Plasmids containing measles antigen sequences were received from Prof. A. Osterhaus, Head of Department of Virology, Erasmus University, Rotterdam.

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PROTECTIVE EFFICACY WITH CUBAN RECOMBINANT HEPATITIS B VACCINE IN HIGH RISK GROUPS CHILDREN. A 14-YEAR FOLLOW-UP STUDY

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Background: Long-term follow-up studies of populations that received recombinant hepatitis B (HB) vaccination beginning at birth are limited and the duration of protection after hepatitis B vaccination of infants is unknown.

Objectives: To determine the protective efficacy with Cuban recombinant hepatitis B vaccine in high risk groups children 14 year after primary vaccination.

Methods: The recombinant Heberbiovac-HB vaccine against hepatitis B was applied to 2 groups of children at 2 homes for the physically and mental disabled at doses of 10 mg (group A) and 5 mg (group B) with the scheme 0, 1 and 6 months and tested negative for HB surface antigen (HBsAg), and antibody to HBsAg (anti-HBs). Were followed up 14 years after primary vaccination.

Results: A year after primary vaccination, seroprotection was 100% (A=31/31 y B= 26/26) for the 2 groups of children and the GMT was 139,7 IU/L and 57,3 UI/L in the groups A and B respectively. At 14 years, none were HBsAg positive and none had clinic hepatitis B.

Conclusions: Fourteen years after primary vaccination starting at birth, the protective efficacy was 100% (none of participants had evidence of past HB virus infection, and none had clinic hepatitis B).

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VARICELLA VACCINATION AMONG ADOLESCENTS IN LAZIO REGION, ITALY

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Varicella is the most common infectious disease in Italy. In Lazio Region the trend is stable with an yearly incidence rate of 85/100,000. In 2001-2006, 21,978 out of 27,283 cases (80.6%) occurred in children 0-14 years old, and 5,305 in persons aged 15-99.

In Italy, the National Vaccination Plan recommends varicella vaccine be offered free of charge to groups at risk and susceptible adolescents. The Lazio Regional Program adopted this strategy, with the aim of controlling the disease while avoiding its shift towards older age groups where complications are more severe.

In June 2008, the 12 Regional Local Health Units (ASL) were asked about their strategy for immunizing adolescents. Only one ASL performed an active program, another stopped it due to low compliance. In the other ASL's, vaccine was given upon request of the family and alternative initiatives were undertaken in order to inform the population.

A meeting with the ASL's was organized in November 2008 where it was decided to adopt a proactive strategy to reach all adolescents. This included collecting data on prevalence of anamnestic negative adolescents and vaccine offer. In Italy, Human Papilloma Virus vaccine is offered to all 11 year old girls and it was agreed to promote synergies between the two vaccination programs.

Primary results from 3 ASL's confirmed the expected prevalence of approximately 20% susceptible adolescents, among them vaccine compliance was 50%. Complete data, expected shortly, will offer a picture of the regional situation and an epidemiological basis for future strategies.

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COST-EFFECTIVENESS ANALYSIS OF VACCINATION WITH 10-VALENT NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* (NTHI) PROTEIN-D CONJUGATE VACCINE(PHID-CV) VS. 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE(PCV-7) IN NORWAY

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Background and aims: To estimate the health benefits, costs and incremental cost-effectiveness ratio of vaccination switching from the current *PCV-7* to the new *PHiD-CV* vaccine in the Norwegian childhood immunisation programme.

Methods: A cross-sectional population model was used to estimate the impact of vaccination over 1-year at vaccine steady-state and perform an incremental cost-effectiveness analysis comparing 2 vaccines. Local epidemiological and unit cost data were used. Base-case analysis was performed using a 2+1 dose vaccination schedule. Vaccine cost is assumed to be equivalent. The effects of herd-protection for invasive disease, serotype replacement and serotype cross-protection (serotype 6A) were included. The main clinical outcomes were invasive pneumococcal disease (IPD), acute otitis media (AOM), tympanostomies, hospitalised pneumonia plus costs and the incremental cost-effectiveness ratio: cost per Quality Adjusted Life-year (QALY) gained and Life-years saved (LYS).

Results: Compared with *PCV-7*, *PHiD-CV* is predicted to prevent additionally 147 IPD cases, 16 hospitalised pneumonias, 1,441 tympanostomies and 7,150 AOM GP visits per year. *PHiD-CV* is expected to result in cost savings compared with *PCV-7* (51M Nkr (5.6M€) in direct costs and 76M Nkr (8.5M€) in indirect costs). Sensitivity analysis shows that the incidence of hospitalised IPD and the protection against AOM have the greatest impact on the results. Using probabilistic sensitivity analysis the results indicate that vaccination with *PHiD-CV* is cost-saving compared with PCV-7 in 99.6% of iterations.

Conclusions: The analysis predicts a significant health improvement and substantial cost savings to the Norwegian healthcare services and society by switching from the current vaccine to *PHiD-CV* in the Norwegian childhood immunisation programme.

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COMPLIANCE WITH A ORAL VACCINE AGAINST CHOLERA AND ENTEROTOXIGENIC *E. COLI* (ETEC)

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Background and aims: Among travel-related health problems, fecal oral infections are particularly relevant and are strictly related to the low level of hygiene, sanitation and water quality in several destinations. Primary prevention represents a fundamental tool in order to decrease the impact of important infections such as diarrhoeal diseases. The aim of this study was to evaluate the compliance with a oral vaccine against cholera and enterotoxigenic *E. coli* (ETEC).

Methods: An oral, inactivated diarrhoea and cholera vaccine, indicated for adults and children 2yrs of age or older, was offered to travellers to areas at risk in the period Jun.-Dec. 2008. A telephone-administered questionnaire was filled in at the end of the travel collecting information on destination, health problems, vaccination and any adverse effect following immunization. Oral inactivated vaccine contained killed whole *V. cholerae* O1 bacteria and the recombinant non-toxic B-subunit of the cholera toxin (CTB).

Results: Questionnaires were completed in 8 Travel Health Centers. The mean duration of the travel was 20.2 days; the most frequent destinations were Africa (52.2%) and Asia (33.8%). 40 subjects did not accept vaccination. The oral vaccine was used by 112 enrolled subjects; no severe adverse reactions have been registered. During the travel, 22/112 immunised subjects had diarrhoea.

Conclusions: The incidence of diarrhoea in vaccinated subjects was 19.8%, accordingly to other published studies (17.4-23%) that have demonstrated a vaccine efficacy against travellers' diarrhoea of 43-56% and greater than 80% against cholera.

P542

SAFETY AND IMMUNOGENICITY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE WITH/WITHOUT POLYSORBATE 80 IN HEALTHY INFANTS IN POLAND

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Background and aims: A 13-valent pneumococcal conjugate vaccine (PCV13) is under investigation to extend serotype coverage against invasive pneumococcal disease. Inclusion of polysorbate 80 (P80) results in a more robust manufacturing process. We investigated the safety and immunogenicity of PCV13 formulated with (PCV13+P80) and without P80 (PCV13-P80), given with routine pediatric vaccines, to evaluate whether P80 could be included in the formulation.

Methods: Healthy infants were randomly assigned (1:1) to receive 13vPnC+P80 or 13vPnC-P80 at 2, 3, 4 and 12 months of age, along with routine pediatric vaccines. Concentrations of capsular-binding IgG against the PCV13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) were evaluated 1 month after the infant series and 1 month after the toddler dose. Safety data were collected.

Results: The primary non-inferiority criterion (responders at WHO threshold concentration ≥0.35 µg/mL) was achieved for 11 of the 13 serotypes after the infant series (exceptions were serotypes 6B and 23F) and for 13 of 13 serotypes after the toddler dose. When comparing IgG geometric mean concentration ratios, the non-inferiority criterion was achieved for all serotypes after the infant series and toddler dose. After both the infant series and toddler dose, the reverse cumulative distribution curves of the responses to each serotype showed comparable IgG immune responses between vaccine groups. Local reactions and systemic adverse event profiles were similar between groups.

Conclusions: PCV13+P80 demonstrated immune responses non-inferior to those of PCV13-P80, with a comparable safety profile.

P543

MEAN AGES OF MEASLES, MUMPS AND RUBELLA VACCINATION IN FRANCE - COMPLIANCE WITH JULY 2005 RECOMMENDATIONS

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Background and aims: To estimate the mean age of children vaccinated in Fance with a measles, mumps and rubella (MMR) vaccine according to applicable recommandations published in 2005.

Methods: An observational study was conducted between October and December 2007 in 13 french pediatric emergency units. MMR vaccination history of children born from October 1st 2004 was collected. Children were analysed in 2 groups: the “classic population” (group 1), for which first vaccination was to be administered at 12 months (community entrance after 12 months or no prior day care centre attendance), and the “anticipated population” (group 2) for whom first vaccination was advised from 9 months of age if the child was attending day care.

Results: 663 children were evaluable and had received one dose (second dose: n=218). For the group 1 (n=459), the median ages at 1st and 2nd MMR dose were 13 months (mean: 13.4±2.9) [IQ:12-14] and 24 months (mean: 23.2±4.9) [IQ:20-26] respectively. For the group 2 (n=204), the median ages were 12 months (mean: 12.9±3.0) [Q:12-14] and 25 months (mean: 23.2±4.0) [Q:21-26] respectively. The age of MMR vaccination was consistent with recommendations for 1st and 2nd dose in 32.2% and 51.2% of group 1 respectively and 19.6% and 4.0% for group 2. Mean age of vaccinations got closer to the actual recommended age over time for both groups statistically ($p< 0.01$).

Conclusion: Even not so good adequacy to recommendations, we observed an improvement of mean age of MMR vaccinations with time.

For Investigator´s Group, Pediatric Emergency Units, Clamart, Lille ,Colombes, Lyon, Nantes, Toulouse, Créteil, Paris, Limoges, Versailles, Nice, Bondy, France

P544

HPV VACCINATION - HAVE WE BEEN TOO HASTY?

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The UK introduced HPV vaccination to a defined group of girls last year. It was determined that a further catch-up programme was also justified.

It was claimed that this could save 800 lives per year, but the economic models made a number of assumptions.The US introduced the vaccination prior to the UK, prior even to the full research study results being available. Not only did they introduce it, they made it a requirement for attending senior school. These programmes are based on Phase 3 trials which only reported in mid-2007.

The trials only followed up participants for 5 years and detected a reduced rate of development of stages 2 and 3 of cervical intraepithelial neoplasia (CIN). It is not known if CIN development is merely delayed or eradicated.

Although there is much merit in the supposition that preventing infection with the 16 and 18 will virtually stop development of CIN, this is probably not so straightfoward. New oncogenic strains could become more prominent, much fewer women may attend for screening believing that they are immune to HPV infection and hence cervical carcinoma.

Parents may be ambivalent about having their child vaccinated (supported by a pilot study in Manchester), but all worry that the vaccine is not safe. Certainly it has a relatively high level of reports of side-effects (26 per 100 000) compared with Meningococcal vaccination (0.1 per 100 000).

It will take many years before we can answer this - let´s hope that 800 lives per year are saved.

P545

CANADIAN PARENTS' AND NURSES' OPINIONS REGARDING BACTERIAL ACUTE OTITIS MEDIA PREVENTION THROUGH VACCINATION

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Background and aims: Acute otitis media (AOM) is a common childhood infection. A new 10-valent vaccine (Synflorix™) with a larger spectrum of protection was approved in Canada in 2008. We assessed parents' and nurses' opinions regarding AOM and its prevention/treatment.

Methods: A random sample of 502 parents responded to a telephone survey and 301 nurses completed an anonymous mail-based survey. In parental survey we assessed opinions regarding routinely recommended vaccines and Synflorix™. For nurses we used standardized questions regarding 7 candidate childhood vaccines' perceived safety, efficacy, acceptability, usefulness, and intention to recommend them. Basic Priority Rating (BPR) was calculated and logistic regression models were estimated.

Results: Surveys were conducted in April-June 2008. 32.1% of 6 months to 6 year-old children had at least one AOM within last 12 months; ¾ of parents believe antibiotics are always useful in AOM treatment; 78% of parents manifested willingness to vaccinate their child with a vaccine with a larger spectrum of protection against AOM. Synflorix was perceived as acceptable and useful by 95-97% of nurses. 94% of nurses manifested willingness to recommend the vaccine if it were publicly funded; 26% if parents had to pay for it. Synflorix had the 4th BPR after Twinrix, DTaP-IPV-Hib-HBV and MMRV, mostly due to 15-20% of “Do not know” responses.

Conclusions: AOM is perceived as an important health problem and the majority of parents and nurses would like to prevent them through vaccination. Additional educational efforts are needed.

P546

CHANGING IMMUNIZATION PROGRAMS: EVIDENCE BASED APPROACH FOR HEPATITIS A VACCINATION IMPLEMENTATION IN A LOW ENDEMIC AREA

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Background and aims: In low endemic areas like Quebec both hepatitis A (HA) and B (HB) are rare in young children and the risk increases with age. To evaluate different immunization programs against HA and HB we conducted a series of studies. Collected data served for decision making regarding two-dose Twinrix-Junior school-based immunization program implementation in Quebec in 2008.

Methods: The effectiveness of existing immunization programs, the prevalence of antibodies in different age groups, trends of hospitalisation, interventions triggered by HA cases, long-term clinical trials data, cost-effectiveness, dynamic models, as well as health professionals perceived usefulness and acceptability of an eventual immunization against hepatitis A were assessed.

Results: During the last decade the incidence of HA and HB varied from 1.0 to 2.7 and from 0.5 to 2.4 cases/100000, respectively. 97-99% of teenagers were anti-HAV negative. 81% of HA related hospitalisations were in adults. The effectiveness of the targeted HA vaccination was estimated at 11%. Six out of 16 food handlers related incidents required post-exposure interventions for ~30000 individuals. Clinical trials show an excellent long-term immune memory after two doses of Twinrix-Junior. 50% of cost-effectiveness studies had a ratio of < 20000$ per QALY. The dynamic model predicts that universal vaccination at age 1-9 years would reduce reported incidence by 36-60% and mortality attributable to HA by 26-56%, relative to continued targeted vaccination. 94-97% of health professionals estimated routine HA/HB vaccination as useful and acceptable.

Conclusions: Systematic evidence-based data help decision-making about potential new publicly funded immunization programs.

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IMMUNOGENICITY OF TWO PAEDIATRIC DOSES OF TWINRIX AND RECOMBIVAX-HB AND THE EFFECT OF A BOOSTER DOSE GIVEN SEVEN YEARS LATER

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Background and aims: Several studies have shown low completion rates of the three-dose vaccination schedule. We assessed the persistence of anti-HBs and anti-HAV after two paediatric doses of Twinrix and Recombivax and the effect of a booster dose.

Methods: In 2000-2001, 704 8-10 year-old children were vaccinated with two paediatric doses of monovalent or bivalent vaccine following a 0, 6 month schedule. A paediatric booster dose was administered in 2008. Serological tests were done one month post-second dose, pre-booster and one month post-booster dose.

Results: Post-second dose 96.5% of Twinrix and 94.4% of Recombivax vaccinees had an anti-HBs titer ≥10mIU/ml (p=0.17). GMTs were respectively 3 248 and 742mIU/ml (p< 0.0001). Before booster dose 92% and 75% (p=0.0001) had detectable levels of antibody and 75% and 56% had ≥10mIU/ml (p=0.0001) in Twinrix and Recombivax group, respectively. GMTs were 60mIU/ml for Twinrix and 12mIU/ml for Recombivax vaccinees (p< 0.0001). Post-booster 100% of Twinrix and 98% of Recombivax vaccinees had anti-HBs titers ≥10mIU/ml (p=0.006). GMTs were respectively 39573 and 5114mIU/ml (p< 0.0001). In Twinrix group 100% post-second dose, 96% pre- and 100% post-booster dose had ≥33mIU/ml of anti-HAV; the anti-HAV GMTs were 5717mIU/ml, 275mIU/ml and 8203 mIU/ml respectively. Booster dose was well tolerated.

Conclusions: Two paediatric doses of Twinrix and Recombivax ensure the persistence of immune memory for at least 7 years in virtually all vaccinees.

P548

DECLINE IN ROTAVIRUS HOSPITALIZED CASES IN SPAIN AFTER THE INTRODUCTION OF ORAL ROTAVIRUS VACCINES

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Introduction: Rotavirus is the most frequent cause of severe acute gastroenteritis (AGE) in children up to 5 years of age worldwide. In Spain, two oral vaccines were licensed in 2006 and 2007 respectively. In 2008, the Spanish Association of Pediatrics recommended the inclusion of those vaccines in the vaccination schedule. The purpose of this study was to evaluate the impact of the rotavirus vaccines in the area of Almeria (Spain).

Methods: Two periods were analyzed using the database of hospitalizations. Children with AGE up to 2 years of age were included. The vaccination coverage was calculated using the data of vaccines sales and the number of newborns in the study area.

Results: In the season 2006-2007, of 88 hospitalized AGE cases, 42 were positive for rotavirus (47.7%), which meant an incidence rate of 6.14 cases/1000 inhabitants under 2 years of age per year. In the following season, 60 AGE cases were hospitalized with 19 positive cases for rotavirus (31.6%) (Incidence rate: 2.62 cases/1000/year), showing a 53.4% reduction in the incidence rate. In the current season, a 75.6% of reduction has been observed. The vaccine coverage ranged from 25% at the beginning of 2007-2008 season to 43% in 2007-2008 (full schedule).

Conclusions: Our results show that rotavirus hospitalized cases in children under two years of age declined markedly in both last and current season in agreement with the increasing coverage for rotavirus vaccines in our area. These data demonstrate the positive impact of the rotavirus vaccines on hospitalizations for this cause.

P549

ANTIBODY RESPONSE TO TETANUS-TOXOID VACCINE IN CHILDREN WITH RECURRENT INFECTIONS

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Background and aims: The recurrence of infections may be the first sign of an immunological defect. The immune response to vaccine represents a good correlate to immunity, thus vaccine-antibody response is part of the immunological evaluation. Our study focuses on the prevalence and pattern of antibody response to tetanus toxoid (TT) vaccine in children with recurrent infections.

Methods: Antibodies to tetanus (TT-Ab) were assessed using a double-antigen ELISA in 59 children with recurrent infections (RI) (age range: 6 months-14 years) and in 52 healthy age-matched controls (HC). All children were stratified by age as follows: 6-18 mo., 18-36 mo., 3-6 ys, 6-9 ys and 9-14 ys. Antibody values higher than 0.1 IU/ml were considered as protective.

Results: Tetanus protection was observed in 87% (51/59) of RI and in 88% (46/52) of HC. Non-responders were variously age-distributed in both categories of patients. TT-Abs reached the highest values at 6-18 months and 9-14 years in RI as well as HC. However, TT-Abs were significantly higher in the 6-18 months RI (mean 3.56 IU/mL) compared to the age-matched HC group (mean 1.60 IU/mL) ($p < 0.05$). No differences were observed in the other age groups.

Conclusions: Our data show the protective value of vaccination in RI children, however the effect of recurrent infections or co-infections might affect the different intensity of antibody response. Further studies are needed to predict what dose to give and how many doses to optimize vaccination programs in this category of children.

P550

SAFETY AND IMMUNOGENICITY OF A 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE GIVEN WITH ROUTINE PEDIATRIC VACCINATION TO HEALTHY CHILDREN IN FRANCE

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Background: A 13-valent pneumococcal conjugate vaccine (PCV13;CRM_{197} conjugated to pneumococcal serotypes 1,3,4,5,6A,6B,7F,9V,14,18C,19A,19F,23F,Wyeth) has been developed to broaden coverage for prevention of invasive pneumococcal diseases compared with licensed 7-valent pneumococcal vaccine (PCV 7; Prevenar® Wyeth).

Objectives: Safety and immunogenicity of PCV13 booster given as part of a 3+1 (2,3,4,12 months) vaccination schedule.

Methods: Subjects were randomly assigned (2:1:1 ratio) to receive either 4 doses of PCV13, 4 of PCV7, or 3 of PCV7 followed by 1 dose of PCV13 concomitantly with DTaP-IPV/Hib at 2, 3, 4 and 12 months of age. Antibody responses to PCV13 were measured at 13 months. Reactogenicity and adverse events were assessed.

Results: Of 613 randomized subjects, 495 (PCV13/PCV13; n=241; PCV7/PCV7, n=133; PCV7/PCV13, n=121) were evaluable for immunogenicity after 12-month dose. For the 7 common serotypes, IgG GMCs were similar in all groups. IgG GMCs among additional serotypes ranged from 0.99 µg/mL (3) to 9.50 (19A) in PCV13/PCV13 recipients, and from 1.14 µg/mL (5) to 5.33 (19A) in PCV7/PCV13 recipients. GMCs were higher for 5 serotypes (not serotype 3) in PCV13/PCV13 recipients, vs. PCV7/PCV13. GMCs for the 6 additional serotypes were higher in PCV13 recipients vs. PCV7/PCV7.

Conclusions: One dose of PCV13 booster, given at 12 months of age in children primed with PCV7, induced a robust antibody response to all 13 pneumococcal vaccine serotypes, as did a 4-dose series of PCV13. Higher GMCs to the 6 additional serotypes in the 13vPnC/13vPnC group is consistent with establishing memory from infant series vaccination.

For P.C.V. Multicenter Study Groups, Paris, France

P551

ROTAVIRUS ACUTE DIARRHEA AFTER INTRODUCTION OF A G1P8 VACCINE: A COHORT STUDY

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Background: Rotavirus acute diarrhea is an important cause of morbimortality all over the world. Brazil was one of the pioneers countries in the implantation of the rotavirus vaccine at the National Expanded Program for Immunization in march 2006.

Methods: Two vaccinated and not vaccinated children cohorts were studied at the Santa Maria district in Aracaju, a brazilian northeastern city, from November 2006 to November 2008. 250 children were allocated in each group, with age varying from 2 to 25 months. They were visited at home two times per month to verify the occurrence of acute diarrhea and, in case of diarrhea, stool samples were collected to be analized by ELISA, RT-PCR and eletropherotyping.

Results: There were 583 episodes of acute diarrhea, 47,2% (275) in not vaccinated and 52,8% (308) in vaccinated children. 512 samples were collected and 250 were already analized. Twelve were positive at ELISA, 8 from the vaccinated group and 4 from the not vaccinated group. Nine samples were genotyped: among vaccinated 3 were GNTPNT and 2 G2P4; among not vaccinated, 2 classified as GNTPNT, 1 G2PNT e 1 G2P4.

Conclusions: After the implantation of the rotavirus vaccine, we verified a change in the profile of acute diarrhea and of the circulating rotavirus strains.

P552

CLINICAL COURSE STUDY POST B.C.G VACCINATION

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Background and aims: The most common complication of post B.C.G vaccination is lymphadenopathy or lymphadenitis, usually in neck or axilla. The aim of this study were evaluation various manifestations of post vaccination adenopathy and effectiveness of different treatment modalities on them.

Methods: We studied 82 infants (range of age 2-26 months) within 2 years (May2003-2005). These patients who were affected by post B.C.G vaccination lymphadenitis referred to pediatric infectious clinic .The patients were follow up by physical examination monthly for 6-18 months and some time intervention treatment till adenopathy disappear or fistulized. We observed the duration of healing in affected lymph node.

Results: No specific treatment was performed on 50 patients who had only cervical and axillar lymph node. The lymph nodes were resolved spontaneously within 3- 9 months. In 30 patients out of 50 mentioned above resolution occurred without fistulization. In the others resolution of lymph node occult with fistulization.6 patients with disseminated adenitis required needle aspiration. The lymph nodes in these patients were resolved in 2 months. Oral Erythromycin was administered in 3 patients. These treatments not have any significant affect on duration.

Conclusion: Generally in adenitis post B.C.G vaccination surgery or needle aspiration rarely needs. Cleaning area of lymph node and careful following up patients are highly recommended.

P553

IMPLEMENTATION OF VACCINATIONS IN CHECHEN REFUGEES' CHILDREN IN POLAND [*]

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Aim of study: To assess the implementation of vaccinations in Chechen refugees' children.

Materials: The subjects were children from the Centre for Foreigners in Warsaw-Bielany. Their examinations were performed three times during the study: first-220 children in June; second-303 children in August; third-310 children in October 2008 (the varying numbers due to changes in the Centre's population).

Methods: Initially medical documentation including vaccination cards was assessed. During the consecutive two examinations realization of recommendations was analyzed and history was obtained on the causes of not having the child vaccinated.

Results: We found that in Chechnya, unlike in Poland, there are no obligatory vaccinations against mumps, rubella and *Haemophilus influenzae type B.* While during the first examination 19% of Chechen children had vaccination certificates, the numbers rose to 30 and 45% during the consecutive two examination. Most vaccination certificates were obtained in the first year of life (85%). The reasons for non-completion of vaccinations were:

a/ low parents' awareness

b/ lack of self-discipline (every other child did not come for established visits);

c/ relocation of refugees between different Centers;

d/ postponement of vaccination (in every fourth child). Refugees' children born in Poland were in much better health than Chechen children born abroad.

Conclusions: Because of differences between Polish and Chechen vaccination programs and low Chechen parents' awareness about the need for vaccinations in children, there is a great need for implementation of health care programs and monitoring of sanitary-epidemiologic conditions in Centre for Foreigners to avoid outbreaks of epidemics.

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P554

OVERVIEW OF THE POST-MARKETING SAFETY AND EFFECTIVENESS SURVEILLANCE PROGRAMMES FOR GARDASIL®

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Background and aims: Vaccines are introduced via population-based vaccination programmes as soon as their efficacy is shown to be higher than any potential risk. When introduced, their long-term effectiveness and full safety profile are usually unknown; they need to be assessed through post-marketing surveillance programmes. Gardasil has been shown to reduce the incidence of cervical cancer, precancerous cervical, vulvar and vaginal lesions and external genital warts causally related to HPV6/11/16/18. This vaccine was rapidly implemented in routine programmes of many countries because of expected important public health benefit on reduction of cervical cancer and other HPV-related diseases.

Methods: General vaccine-reporting structures, such as VAERS (Vaccine Adverse Event Reporting System) in the US, provide data on rare adverse events. HPV-specific surveillance programmes, using cross-sectional and longitudinal designs from cohorts and databases across three continents where Gardasil is used are monitoring long-term safety and effectiveness, including the follow-up of cohorts vaccinated in clinical trials.

Results: By September 2008 >36 million doses of Gardasil have been distributed worldwide. Passive surveillance systems, such as VAERS have not identified any safety issues. The extensive, multi-focal surveillance programmes will provide increasingly long-term safety data. Other programmes will provide effectiveness and duration of protection data, and impact on HPV type-replacement, sexual behaviour and cervical screening.

Conclusions: This is the most comprehensive vaccine surveillance programme to date reflecting the public health authorities and manufacturers intentions to enable early access to an intervention that will prevent cervical cancer, while taking all precautions to ensure its long-term safety and effectiveness.

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IMPACT OF LIVE ATTENUATED INFLUENZA VACCINE ON THE DEVELOPMENT OF ACUTE OTITIS MEDIA IN INFLUENZA-INFECTED CHILDREN 6-71 MONTHS OF AGE

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Background and aims: Acute otitis media (AOM) is a frequent complication of influenza in young children. Influenza vaccination is known to protect against influenza-associated AOM. We sought to determine whether live attenuated influenza vaccine (LAIV) provides additional protection from AOM beyond the vaccine's protection against influenza illness.

Methods: We pooled data on AOM from 6 randomized, double-blind, placebo-controlled trials in children 6-71 months of age (LAIV, n=7657; placebo, n=5437). Efficacy was measured against vaccine-similar strains in 9 influenza seasons. Influenza was detected by viral culture, and AOM was diagnosed clinically. Rates of AOM as an unsolicited adverse event through 10 to 15 days postvaccination were also evaluated.

Results: The pooled efficacy of LAIV against culture-confirmed influenza caused by matched strains was 81.0% (2.8% vs 14.6%, $p< 0.001$). Among influenza-infected children, AOM was diagnosed in 24 of 212 (11.3%) LAIV recipients and 134 of 794 (16.9%) placebo recipients, which represented a 32.9% relative reduction of AOM in the culture-positive LAIV recipients ($p=0.048$). Consequently, the overall efficacy of LAIV in reducing influenza-associated AOM was 87.2% (0.3% vs 2.5%, $p< 0.001$). Rates of AOM as an adverse event were higher in LAIV recipients versus placebo in 3 seasons and lower in 6 seasons.

Conclusions: In the studies analyzed, LAIV substantially reduced the development of influenza-associated AOM caused by matched strains in children by both preventing influenza and reducing complications in children who developed influenza illness despite vaccination.

(Sponsored by MedImmune. LAIV is not approved outside of the United States).

P556

TYPE-SPECIFIC EFFICACY OF INACTIVATED INFLUENZA VACCINE IN CHILDREN 9 MONTHS TO 3 YEARS OF AGE

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Background and aims: The burden of influenza in young children has been well established, and some countries have already started recommending vaccination of healthy children against influenza. There are, however, scarce data available on the efficacy of influenza vaccine in young children. We determined the efficacy of inactivated influenza vaccine against laboratory-confirmed influenza A and B infections in children 9 months to 3 years of age.

Methods: We followed a cohort of 631 pre-enrolled children throughout the influenza season of 2007-2008. Information about influenza vaccination of the children was received from the parents. The parents were asked to bring their children to the study clinic whenever they had fever or signs of a respiratory infection. Detection of influenza in nasal swabs from the children was based on viral culture, antigen detection, and PCR methods.

Results: Influenza was diagnosed in 7 of 154 (4.5%) fully vaccinated children and in 58 of 456 (12.7%) unvaccinated children, which constituted a vaccine efficacy of 64% (95% CI 23-83%, p=0.004) against any influenza. The efficacy of the vaccine against circulating influenza A viruses that were well matched with the vaccine strains was 83% (95% CI 30-96%, p=0.004). In contrast, no significant efficacy was observed against influenza B viruses that were mismatched with the vaccine strains (vaccine efficacy 38%, 95% CI -59-76%, p=0.3).

Conclusions: Trivalent inactivated influenza vaccine is effective in preventing symptomatic influenza in children 9 months to 3 years of age when the vaccine strains are well matched with the circulating strains.

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QUANTITATIVE AND QUALITATIVE IGG RESPONSES AFTER PRIMING AND BOOSTER VACCINATION WITH DIFFERENT PERTUSSIS VACCINES IN DUTCH CHILDREN

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Background and aims: Since whooping cough is reemerging, many changes in the pertussis vaccination program have been made in the Netherlands. We investigated the induction of IgG responses by different booster vaccines in children primed with either whole cell (DTwP) or acellular (DTaP) vaccination.

Methods: In this cross-sectional study DTwP and DTaP primed children 4 years of age were recruited in three groups (n=60); before, +10 and +28 days after booster vaccination with either Triaxis or Infanrix vaccine, as part of a larger study (ISRCTN65428640) that investigates the long term immunity to *Bordetella pertussis* after vaccination in children 3-9 years of age.

IgG levels to pertussis toxin (Pt), filamentous heamagglutin (FHA), pertactin (Prn) and fimbriae type 2 and 3 (Fim2/3) and avidities of Pt and Prn antibodies were measured using a multiplex immuno assay.

Results: Overall, post booster IgG levels to Pt, FHA and Prn were significantly higher in DTaP than in DTwP primed children. In DTwP primed children, IgG levels were higher after Infanrix booster vaccination than after Triaxis, due to the higher pertussis antigen concentrations in the Infanrix vaccine. Pre and post booster vaccination Pt- and Prn- avidities were significantly higher in DTaP than in DTwP primed children.

Conclusions: This study shows the importance of priming for the quantity and quality of the IgG responses elicited pre and post booster vaccination. After DTwP priming, a booster vaccine with high pertussis antigen concentrations must be used to elicit quantitative and qualitative higher IgG responses to pertussis antigens.

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BCG-INDUCED IMMUNE RESPONSES IN HIV-EXPOSED AND UNEXPOSED SOUTH AFRICAN INFANTS: A PHASE 2 RANDOMIZED CLINICAL TRIAL

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Background and aims: HIV-exposed infants are routinely BCG-vaccinated at birth in developing countries. There are limited data on the effects of delayed BCG vaccination and maternal HIV infection in infants. We investigated the effect of delayed BCG vaccination on cellular immune responses in HIV-exposed and unexposed infants.

Methods: A randomized controlled trial comparing intradermal BCG (Danish strain, 1331) at birth vs. delayed vaccination at 14 weeks of age was conducted (2006-2008) in the Khayelitsha district, Western Cape Province, South Africa (maternal HIV prevalence 29.4%; tuberculosis notification > 1500/100 000). IFN-γ production (pg/ml) was measured longitudinally by ELISA using a standard 7-day whole blood assay. Antigens included *M.tuberculosis* PPD, BCG, ESAT-6/CFP-10, TB 10.4 and *Staphylococcus* enterotoxin B (positive control).

Results: 180 infants, 120 HIV-exposed, 60 HIV-unexposed, were enrolled. The proportion of infants with positive IFN-γ response to *M.tuberculosis* PPD was 70.2% at week 14, 68.7% at week 24 and 25% at week 52 (birth group). In the delayed group 9.4% were positive at week 14, 58.0% at week 24 and 30.8% at week 52. The magnitude of IFN-γ response was lower in HIV-exposed infants at 14 weeks (276.49 pg/ml vs. 790.17 pg/ml; p=0.048), but was similar at 24 and 52 weeks of age.

Conclusions: Delayed BCG vaccination had limited effect on IFN-γ responses, which waned considerably during the fist year of life. Delayed BCG vaccination was feasible in a setting with high HIV and tuberculosis burden. HIV-exposed infants may be more susceptible to tuberculosis even in the absence of HIV infection.

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PERTUSSIS KNOWLEDGE, ATTITUDE AND PRACTICES AMONG EUROPEAN HEALTH CARE PROFESSIONALS IN CHARGE OF ADULT VACCINATION

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Background: Despite high infant vaccination coverage, pertussis is increasing in many developed countries, predominantly due to waning immunity in adolescents and adults, who involuntarily transmit *Bordetella pertussis* to susceptible infants.

Methods: 517 internet interviews were conducted amongst Healthcare Professionals (HCPs) to assess their current level of knowledge, attitude and practices with respect to adult pertussis vaccination. The study was performed in Finland (n=105), Germany (n=156), Poland (n=101) and Spain (n=155).

Results: Most HCPs consider providing adult vaccination against tetanus, but only 17% mentioned pertussis vaccination. Pertussis was generally considered to be less serious than other adult respiratory tract infections, with a low perceived need for adult vaccination. Only half of the HCPs reported seeing adult pertussis, but where encountered, approximately 8 cases were seen annually.

Generally, few HCPs either discuss adult pertussis vaccination [7/10 reported discussing pertussis vaccination with < 5% adult patients] or recommend or prescribe a pertussis-containing vaccine to adults. A key reason for not prescribing adult pertussis vaccination is the lack of official guidelines.

Conclusions: Pertussis transmission from adolescents and adults to vulnerable infants is a growing problem; representing the major cause of death due to bacterial infections for newborns < 2 months of age.[1] European HCPs have variable experiences of adult pertussis, generally driven by a low level of disease awareness and few recommend adult pertussis vaccination. Clear guidelines on vaccination are needed to help HCPs manage the consequences of waning pertussis immunity, and transmission to vulnerable infants.

[1]Floret D. Arch Ped 2001;8(Suppl):705s-11s.

P560

IMMUNOGENECITY AND SAFETY OF INACTIVATED JAPANESE ENCEPHALITIS VACCINE IN KOREAN CHILDREN

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Background and aims: The mouse-brain inactivated Nakayama strain Japanese encephalitis vaccine (inactivated JEV) which was introduced in 1971, has not been supported by objective data on its immunogenecity and safety in children < 3 years of age in Korea. Therefore, we need a reliable data by the prospective study on the immunogenecity and the safety of inactivated JEV.

Methods: We measured the neutralizing antibody(NTAb) titers from samples in normal 1-3 year old healthy 80 children during the pre-vaccination period and 4-6 weeks after the 2nd dose for inactivated JEV. The 2nd dose of the inactivated JEV vaccinated 1-2 weeks after 1st dose. Active monitoring was done through phone calls 1-2 weeks after the 1st and 2nd doses of the inactivated JEV. The adverse reactions were recorded on the diary cards by parents, for 4 weeks from the second dose of the inactivated JEV.

Results: The children who received the 2 doses of the inactivated JEV were tested positive for NTAb as 93.8% which was defined as a serum titer greater than 1: 10. The geometric mean of the NTAb was 30.5. The adverse reactions were noted in 52.2%. After the 1st dose, localized reactions were 13.0% and systemic reactions were 13.0%. After the 2nd dose, the localized for 16.3%, and the systemic for 7.6%.

Conclusion: From the current schedule of inactivated JEV, appropriated level of neutralizing Ab was achieved, The adverse reactions were reported higher than previous Korean studies, but most of them were mild.

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IMMUNOGENICITY OF BOOSTER DOSES OF13-VALENT PNEUMOCOCCAL CONJUGATE AND HIB/MENC VACCINES GIVEN AT 12 MONTHS OF AGE IN THE UK

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Background: We report the toddler stage results of a randomised, double-blind study of a CRM_{197} conjugated 13-valent pneumococcal conjugate vaccine (PCV13) directed against serotypes 1, 3, 5, 6A, 7F, 19A, in addition to serotypes 4, 6B, 9V, 14, 18C, 19F, 23F contained in the currently licensed 7-valent vaccine (PCV7).

Methods: Children previously randomised 1:1 to receive PCV7 or PCV13 at age 2 and 4 months received a further dose of their designated vaccine at age 12 months. A *Haemophilus influenzae* type b/serogroup C meningococcus conjugate vaccine (Hib-MenC-TT) was given concomitantly. Pneumococcal serotype specific and anti-PRP (Hib) IgG concentrations were measured 1 month after the toddler dose, as were MenC rabbit complement serum bactericidal antibody (SBA) titres.

Results: Of 278 infant participants, 120 (PCV7) and 130 (PCV13) completed the toddler stage. Prior to the booster vaccine, serum pneumococcal IgG antibody concentrations ≥0.35µg/ml (WHO threshold concentration) were observed in 12.6% (serotype 3) to 92.0% (serotype 14) of PCV13 recipients. After the booster dose this percentage was 88.2% for serotype 3, and ranged from 97.1% to 100% for the remaining serotypes. Following Hib-MenC-TT, MenC SBA titres ≥1:8 were seen in 91.8% (PCV7 group) and 91.7% (PCV13 group) of participants, while anti-PRP IgG concentrations ≥1.0µg/ml were seen in 100% and 99% respectively. Day 1-4 fever rates were 7.7% (PCV13) versus 19.4% (PCV7); otherwise reactogenicity and safety profiles were similar.

Conclusions: A 12 month dose of PCV13 effectively boosts antibodies against all vaccine serotypes, without interfering with the response rates to concomitantly administered Hib-MenC-TT.

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EVALUATION OF NATIONAL VACCINATION PROGRAM IMPLEMENTATION AMONG CHILDREN IN WARSAW(*)

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Aim of study: We aimed to evaluate the implementation of obligatory and recommended vaccination program among children aged 12-36months.

Materials and methods: The analysis involved 107patients. We evaluated the implementation of vaccinations by checking the entries in each Child's Health Books. We used questionnaires filled by parents for evaluation of the parents' awareness and attitudes to the vaccination program.

Results: 98% of children (105/107) were vaccinated (without payment) in compliance with the current National Vaccination Program. 35 children (33%) were administered (paid) recommended vaccinations. 25% of children (27/107) were vaccinated against *Streptococcus pneumoniae*, while others in the recommended vaccinations group received vaccines against chickenpox, *Neisseria meningitidis* type C, influenza, rotaviral diarrhea, viral hepatitis type A and tick-borne encephalitis. 20% of patients (21/105) received vaccinations against Producer's Guidelines. In 67% of cases (72/107) recommended vaccinations were not administered because of their high cost. In 24% (26/107) of cases a negative parents' attitude to vaccination was found. Family doctors vaccinated only 73% of the children who received vaccines under the Program.

Conclusions: In Poland, obligatory vaccinations are administered to almost all children, mainly in GP practices. The recommended vaccinations are implemented only in a small group of children, due mainly to high cost. The most often recommended vaccination was against *Streptococcus pneumoniae.* Importantly, in fully 24% of cases a negative attitude to vaccination Program was found. Hence it is extremely important to raise parents' awareness on the need for vaccination and to introduce gradual reimbursement for the recommended vaccines.

[1]CMKPgrant 501-2-1-19-56/08

P563

THE IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINE ON MYRINGOTOMY WITH VENTILATION TUBE INSERTION IN AUSTRALIA, 1998-2007

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Background: The heptavalent pneumococcal conjugate vaccine (7vPCV) has been shown to reduce myringotomy with ventilation tube insertion (MVTI) procedures in a 4 dose schedule, both in randomized controlled trials and post-marketing studies. In Australia, a 3 dose schedule is used routinely for non-Indigenous children, beginning in January 2005. Our aim was to determine if a reduction in MVTI has occurred despite absence of the booster dose.

Methods: All episodes of MVTI July 1998 to June 2007 among children aged ≤9 years were identified in the National Hospital Morbidity Database. Monthly age-stratified rates of were determined, with Poisson regression modelling used to evaluate the vaccine impact after adjusting for background and seasonal trends.

Results: 238,634 hospital separations were identified. In the 2.5 year period after routine 7vPCV, there was a significant adjusted reduction in MVTI in children aged < 1, 1 and 2 years of 23%, 16% and 6% respectively. A non-significant reduction was observed in those aged 3 and 4 years, while a significant increase of 5% was observed for the 5-9 years age group.

Conclusion: The differential effects observed by time period and age group are suggestive of a vaccine effect. Although impact may have been greater with a booster dose, this finding has important implications for the cost-effectiveness of 7vPCV, particularly in developing countries where WHO recommends a similar 3+0 schedule.

P564

PERSISTENCE OF IMMUNITY 5 YEARS AFTER IMMUNISATION WITH TD_5AP-IPV, TD_5AP + OPV OR DT_2AP-IPV AS PRESCHOOL BOOSTER VACCINE

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Background and aims: The Td_5ap-IPV vaccine (Repevax®) was licensed for use in pre-school children in 2002 following a study evaluating the immunogenicity and reactogenicity of 3 vaccines; Td_5ap-IPV, Td_5ap (Covaxis®) +OPV and DT_2aP-IPV (Tetravac®). We evaluated the persistence of antibodies to the vaccine antigens 5 years post vaccination.

Methods: 299 children completed the initial study and were eligible to participate in the persistence phase of the study. An antibody titre of ≥0.1 IU/ml was used as correlate of protection against diphtheria (seroneutralisation assay) and tetanus (ELISA). For poliomyelitis types 1, 2 and 3 a titre of ≥1:8 (seroneutralisation assay) was considered as a correlate of protection. In the absence of an agreed correlate of protection, no thresholds of response for pertussis antigens were defined. Geometric mean titres/concentrations were calculated for all antigens, including pertussis.

Results: Five years after immunisation seroprotection rates for the 3 vaccines, Td_5ap-IPV, Td_5ap+OPV and DT_2aP-IPV, were 75%, 67% and 79% for diphtheria and 100%, 96% and 89% for tetanus, respectively. All children had antitoxin titres ≥0.01 IU/ml for both diphtheria and tetanus. All 3 vaccines induced persisting antibody responses against pertussis. The seroprotection rate for poliomyelitis for the 3 groups was achieved in >95% of children except for poliomyelitis type 3 in those who received OPV (83%).

Conclusion: Td_5ap-IPV provided good persistent immunity for all antigens up to five years after receipt of the booster. Similar results were generally seen in the Td_5ap + OPV and DT_2aP-IPV groups.

P565

AVIDITY OF MEASLES, MUMPS AND RUBELLA ANTIBODIES INDUCED BY MMR VACCINATIONS

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Background: The two-dose nation-wide MMR vaccinations have been used in Finland since 1982.

By the mid-1990s, indigenous measles, mumps and rubella were eliminated from Finland, and after that only a few cases of measles, mumps and rubella have been imported. Antibody follow-up in a vaccinated cohort has shown that MMR vaccine-induced antibodies wane over time. This study's aim was to investigate the avidity of measles, mumps and rubella antibodies after MMR vaccinations, and the avidity's possible role in protection.

Methods: Antibody avidity was determined from the samples of 69 vaccinees collected about half a year and 20 years after the second MMR dose. The avidity of measles, mumps and rubella antibodies was measured by commercial EIA tests and was expressed as avidity index (low < 30%, intermediate 30-50%, high >50%).

Results: Half a year after the second MMR dose, antibodies of low-avidity were measured in 62/69 samples for mumps, but in none for measles and rubella. The avidity of rubella antibodies was high in all samples throughout the follow-up. The mean avidity index was lowest for mumps and highest for rubella both half a year and 20 years after the second MMR dose.

Conclusions: In recent mumps epidemics twice-vaccinated individuals have also fallen ill, whereas measles is relatively rare in vaccinated individuals, and only a few rubella cases appeared in vaccinees. This may be partly explained by differencies in antibody avidity induced by MMR vaccinations, which possibly means different levels of protection against measles, mumps and rubella.

P566

GENERATION OF HUMAN SERUM COMPLEMENT LOTS THAT PERFORM CONSISTENTLY FOR USE IN *NEISSERIA MENINGITIDIS* SEROGROUP B (MNB) VACCINE CLINICAL TRIALS

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Background: MnB is the etiological agent for 40-70% of invasive meningococcal disease (IMD) cases in the US and Europe. Wyeth is developing a MnB vaccine (rLP2086) composed of two variants of the MnB factor H binding protein (fHBP). Since IMD cases are rare, MnB vaccine efficacy will be assessed using a surrogate of protection, the serum bactericidal antibody (SBA) assay. The assay measures complement-mediated bacterial killing in the presence of immune serum. There are no standardized MnB SBAs; assays must be carefully controlled and validated. The source of human complement is a critical component for this assay. SBA titers obtained using human complement from different individuals can vary considerably. This will affect the assignment of responder status in meningococcal vaccine trials. We developed a method to generate complement lots for use in MnB fHBP vaccine trials that perform reproducibly in SBAs.

Methods: Thirty individual human serum complement sources were screened in an SBA assay using human positive “test” sera from rLP2086 vaccinees. A statistical algorithm was used to identify complement sources that yielded “average” titers. These average individual complement sources were pooled and tested for performance using a proficiency panel of sera from human vaccinees.

Results: Two pooled complement lots were generated and their performance in the SBA compared. The mean bias ratio was 1.01 (90% CI: 0.93-1.10) indicating statistical equivalence.

Conclusion: Pooling of statistically-identified individual human serum complement sources yields lots that perform consistently and reproducibly, thereby facilitating reliable within- and between-clinical study SBA titer comparisons.

P567

REACTOGENICITY OF A COMBINED DT-IPV AND A MMR VACCINE IN HEALTHY 9-YEAR OLD CHILDREN

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Background: In the Netherlands, children receive simultaneously a booster DT-IPV and their second MMR vaccinations at nine year of age. Little is known about the rates of adverse events to the DT-IPV and MMR injection at this age.

Aim: Gain insight in the occurrence of adverse events after vaccination at nine years of age.

Method: Two questionnaires about local and systemic reactions were distributed one and three weeks after vaccination in the same group of 1250 healthy children (response: 57.0% and 46.5%, respectively).

Results: 86.5% of the children had local reactions (LR's) within one week after vaccination, which were more reported at the DT-IPV (83.4%) than at the MMR site (32.7%). Pain was mostly reported (80.8% at the DT-IPV site; 29.1% at the MMR site). 33.4% had systemic events (SE's) in the first week after vaccination, from which headache was mostly reported (20.8%). 20.9% of the children reported SE's 2-3 weeks after vaccination. From children with LR's only at the DT-IPV site, 31.7% reported SE's in the first week after vaccination, and 20.6% reported SE's 2-3 weeks after vaccination. For children with LR's only at the MMR site this was 22.9% and 21.4%, respectively. From children with no LR's, 16.3% and 11.9% reported SE's within one week and 2-3 weeks after vaccination, respectively. No serious adverse events were reported.

Conclusion: Although the frequency of LR's is high, simultaneously administration of DT-IPV and MMR vaccine at nine year of age is safe. These results maintain the confidence in the vaccination programme.

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PERSISTENCE OF ANTIBODY RESPONSE FOLLOWING A BOOSTER DOSE OF HIB-MENC-TT GLYCOCONJUGATE VACCINE: A PHASE IV OPEN RANDOMISED CONTROLLED TRIAL

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Aims: Antibodies against *Haemophilus influenzae* type b (Hib) and serogroup C *Neisseria meningitidis* (MenC) wane after infant immunisation, but can be boosted by toddler immunisation with a dose of a combined Hib and MenC glycoconjugate vaccine (Hib-MenC-TT). This study assessed the persistence of seroprotection one year following this booster dose.

Methods: This open-label randomised controlled trial was conducted across the UK and Poland (109664/NCT00454987). Children previously immunised at 2, 3 and 4 months of age with either the routine UK immunisations of the time (DTPa-IPV-Hib and MenC-CRM_{197} (control group)) or DTPa-IPV and Hib-MenC-TT (Hib-MenC group) received Hib-MenC-TT co-administered with MMR vaccine at 12-15 months of age. Anti-PRP Ig (Hib) and MenC bactericidal antibodies (rSBA) were measured on sera collected approximately one year after the Hib-MenC-TT booster dose.

Results: Blood was drawn from 271 participants (mean age 27.8 months) at a mean of 14.6 months (range 12-18 months) following Hib-MenC-TT boosting. MenC seroprotection (rSBA ≥1:8) was demonstrated in 178/200 of the Hib-MenC group (89%, 95% C.I. 83.8%-93.0%) and 41/59 of control group participants (69.5%, C.I. 56.1%-80.8%). Hib seroprotection (anti-PRP Ig ≥1.0µg/ml) was seen in 188/198 (94.9%, C.I. 90.9%-97.6%) of the Hib-MenC group and 52/63 (82.5%, C.I. 70.9%-90.9%) of control group participants.

Conclusion: This is the first study reporting persistence of anti-PRP Ig and MenC SBA one year following a Hib-MenC-TT booster dose. The maintenance of seroprotection at 2 years of age in the majority of participants supports the 2006 introduction of Hib-MenC-TT at 12 months into the UK immunisation schedule.

P569

A SURVEY FOR THE PRESENT STATE AND VALIDITY OF TESTS TO HEPATITIS B IN KOREA

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Background and aims: A survey for the present state and validity of rapid tests for anti-HBs as a health screening in kindergartens and work places in Korea were needed. This survey was planned to be used as basic data in Korean National Immunization Policy as well as to suggest a guideline about tests to hepatitis B.

Methods: Information on the types of tests to anti-HBs as a health screening in kindergartens or work places was collected from various institutions by telephone. Also, we validated 10 different commercial kits (1 chemiluminescence microparticle immunoassay, 1 chemiluminescent immunoassay, 1 electro- chemiluminescence Immunoassay, 5 immunochromatographic assays, and 2 passive hemagglutination assays) for anti-HBs using with self-preparing pooled serum (range of anti-HBs: 1 to 100 mIU/mL).

Results: The usage rates of immunochromatographic assay or passive hemagglutination assay for anti-HBs as screening methods in kindergartens or work places in Korea were 83.3% and 64.4%, respectively. There were no qualitative test kits to get positive results to a sample with 10,9 mIU/mL titers of anti-HBs. Additionally, only one out of 7 to samples with 21.5 and 4 out of 7 to samples with 34 mIU/mL were positive results in the same qualitative test kits.

Conclusions: Inaccurate test for anti-HBs were performed with high percentage as a screening test in kindergartens or work places in Korea. This situation evokes medical confusions as well has remarkably increased unnecessary burden to the national finance. The guideline for test to hepatitis B in Korea should be decided.

P570

VALIDATION OF A NEW ENZYME IMMUNOASSAY FOR THE QUANTITATIVE MEASUREMENT OF HUMAN IGG ANTIBODIES SPECIFIC FOR HIB CAPSULAR POLYSACCHARIDE

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Background and aims: The purpose of this study was to validate a new ELISA method for the evaluation of the immunogenicity of *Haemophilus influenzae* type b (Hib) vaccine using the capsular polysaccharide polyribosylribitol phosphate (PRP) as an antigen.

Methods: For the validation of the new ELISA method, the specificity, precision (intermediate precision, repeatability), accuracy, lower limit of quantification (LLOQ) and stability was evaluated.

Results: The results indicated that this ELISA showed specificity to HbO-HA antigen and repeatability and intermediate precision were within acceptance criteria (repeatability: CV ≤15%, intermediate precision: CV ≤20%). Anti-PRP IgG titers correlated well (R=0.93) with the radio antigen binding assay (RABA) (R=0.93), and also the standardized ELISA using HbO-HA (R=0.96). The precision and accuracy of samples in LLOQ were from -6.2 to -25.4% in nominal values, which were within acceptance criteria (precision: CV ≤25%, accuracy: ±25%). Freeze-thaw stability and short term temperature stability were within ±20% of acceptance criteria.

Conclusions: We conclude that the ELISA with PRP Ag is specific, sensitive, accurate and a precise assay. The ELISA is an appropriate serologic assay which can be used for quantitation of anti-PRP IgG antibodies in human sera.

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PUBLIC HEALTH AND ECONOMIC IMPACT OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN THE NETHERLANDS

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Background: Incidence of pneumococcal disease in children < 2 years of age has dropped dramatically since 7-valent pneumococcal conjugate vaccine (PCV7) introduction. Thirteen-valent pneumococcal conjugate vaccine (PCV13) covers 6 additional important serotypes, including 19A. We examine the public health and economic value of pediatric vaccination with PCV13 in the Netherlands.

Methods: A decision-analytic model was developed to estimate the impact of vaccination with PCV13 relative to not vaccinating in invasive pneumococcal disease (IPD), pneumonia, and otitis media (OM). The model takes an epidemiological approach from a societal perspective in tracking incidence, serotype coverage, disease sequelae, death, and costs. Incidence, serotype coverage, disease sequelae, and mortality were obtained from Dutch surveillance and registry data. Direct effects for all 13 serotypes were assumed similar to direct effects observed for PCV7 among its covered serotypes. Indirect effects and utilities were obtained from the published literature. Costs include direct medical and non-medical costs and were obtained from Dutch registries. Costs and outcomes were discounted at 4.0% and 1.5% respectively.

Results: Assuming 95% of Dutch children vaccinated, considering only direct vaccine effects, the reduction in IPD cases is 89% in children and the incremental cost per quality-adjusted life year (ICER) of vaccinating is €32,200. When considering indirect effects in the full population, the number of IPD cases reduced by 50% overall and the ICER reduces to €4,600.

Conclusion: A national immunization program with PCV13 for children in the Netherlands is expected to have dramatic public health impact and be a highly cost-effective use of resources.

P572

ANTIBODY PERSISTENCE AND IMMUNE MEMORY 15 MONTHS AFTER MENINGOCOCCAL TETRAVALENT TETANUS-TOXOID CONJUGATE (ACWY-TT) VACCINE IN TODDLERS AND 3-5 YEAR-OLDS

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Background: The highest incidence of meningococcal disease is in young children. Existing polysaccharide vaccines against serogroups A, C, W, Y offer short-lived protection and do not induce immune memory. An investigational ACWY-TT conjugate vaccine was immunogenic and well tolerated in a first study in toddlers and children.

Methods: Blood samples in this follow-up, phase II, open randomized study (104704/NCT00126984) were collected 15 months after a single dose of ACWY-TT or control vaccine (monovalent MenC-CRM at 12-14 months, and ACWY-polysaccharide [MenACWY-PS] at 3-5 years of age). Subjects vaccinated toddlers received 1/5th dose of MenACWY-PS vaccine and were assessed one month after for boostability of the primary response. Serum bactericidal antibodies were assessed using rabbit complement source (rSBA, cut-off ≥1:8).

Results: The percentage of subjects with persisting rSBA titres ≥1:8 was significantly higher after ACWY-TT than control for all serogroups, except W-135 in the 3-5 year-olds (Table). One month after MenACWY-PS challenge in toddlers, GMTs (adjusted values) were significantly higher (for A: 3246.0vs.529.9, W-135: 9675.6vs.1439.2 and Y: 5840.6vs. 521.8) or not significantly different (for C: 6094.2vs. 5264.0) in ACWY-TT versus MenC-CRM primed subjects, indicating boostability by ACWY-TT priming.

		Persistence: % with rSBA titre ≥1:8			Difference (ACWY-TT – Control)	
Toddlers	**N**	**ACWY-TT**	**N**	**MenC-CRM**	**%**	**[95% CI]**
A	40	97.5	36	30.6	66.94	[49.16; 80.21]
C	39	92.3	40	60.0	32.31	[14.30; 49.29]
W-135	40	97.5	41	41.5	56.04	[39.16; 70.39]
Y	40	97.5	40	75.0	22.50	[8.60; 38.24]
Children		**ACWY-TT**		**MenACWY**	**%**	**[95% CI]**
A	45	100	29	89.7	10.34	[1.88; 26.52]
C	46	100	32	59.4	40.63	[25.44; 57.84]
W-135	46	100	32	93.8	6.25	[-1.84; 20.27]
Y	46	100	33	78.8	21.21	[10.63; 37.87]

[Table]

Conclusion: The ACWY-TT vaccine induced persisting immune responses to all four serogroups in ≥ 92.3% of toddlers and 100% of 3-5 year-olds. Boostability after priming was successfully demonstrated.

P573

MUMPS EPIDEMIC IN BULGARIA, 2006-2008

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An increased mumps incidence has been reported in Bulgaria since 2006, with a total of 11792 cases reported during 2006-2008. This is the first mumps epidemic since the adoption in 2001 of a two dose MMR immunization schedule (at 13 months of age and 12 years of age). The aim of the study is to analyze the epidemic features and reasons provoking it in the conditions of high national immunization coverage, preceded however by interruption of the mumps immunization during 1982-1986.

The analysis is based on the data from the National communicable disease surveillance system requiring compulsory notification and information about case laboratory confirmation. The data on the national immunization coverage and the immunization status of the patients are obtained from the Immunization information system and the Regional inspectorates for public health protection and control.

Out of total of 5299 cases in 2007, 68.5% were in patients older than 15 years of age and out of total of 5 582 cases in 2008, 63.1% were in the same age groups. In 2007, 44.4% of cases had received 1 dose mumps vaccine, 8.5% - 2 doses and 5.6% have not been vaccinated or there is no data available (41.5%).

The shift of the age-specific incidence to the older age groups is clearly demonstrated. Mumps epidemic affected mostly adolescents and young adults, who were exposed to a higher risk because of the inadequate vaccination (suspended mumps immunization in 1982-1986 and a history of a single dose of vaccine, or no vaccine).

P574

VACCINE-RELATED ADVERSE EVENTS [VAE] OBSERVED IN 2006-2008 IN THE DEPARTMENT OF PAEDIATRIC NEUROINFECTIONS, JOHN PAUL II HOSPITAL IN CRACOW, POLAND

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Background: Despite a spectacular reduction of infectious diseases due to widespread vaccinations, media report on their harmfulness. We hospitalise the majority of VAE in the province of Małopolska therefore we can evaluate the safety of vaccines used in Poland.

Objective: Assessment of vaccination complications among children from Małopolska requiring hospitalisation between 2006 and 2008.

Method: Retrospective analysis of diseases supposedly associated with vaccination among patients hospitalised in 2006-2008 versus the whole vaccinated population.

Results: 64000 children up to 2 years of age are vaccinated annually in Małopolska. The vaccination coverage in 2006-2008 was 98%. 250000 doses of the DTP vaccine were given every year (750000 doses in 3 years). A mean of 70 VAE were reported annually, including 21 hospital admissions. In 2006 - 2008 62 children with suspected VAE were admitted excluding causal relationship with vaccination in 12 cases. In 39/50 cases, VAE was secondary to vaccination against tetanus, diphtheria and pertussis [DTwP and DTaP] in combination with other vaccinations. HHE occurred in 6 cases, including 2 after DTaP, persisted crying [1 after DTaP] in 6, and seizures [1 after DTaP] in 5. In the remaining cases the reason for hospitalisation was parental anxiety rather than a real necessity. Single children were hospitalised after meningococcal C vaccine, hepatitis B vaccine, tetanus and diphtheria anatoxins, polysaccharide pneumococcal vaccine and MMR. All hospitalisation were short-term, without permanent consequences.

Conclusions: A low percentage of VAE indicates that the vaccines used at present in the National Immunisation Programme in Poland are safe.

P575

HSP70-P24 FUSION DNA VACCINES AS NEW CANDIDATES FOR HIV VACCINES

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Background and aims: Heat shock proteins (Hsp´s) are known to have an important role in presentation of peptide antigens on MHC molecules. It is supposed, that Hsp´s can serve as an adjuvant in the development of new types of vaccines. Aim of our study was to determine adjuvanticity of murine Hsp70 as a fusion partner for HIV-1 p24.

Methods: To eliminate possible side effects of contaminants present in recombinant protein produced in E. coli, we used DNA vaccination approach. Plasmids expressing p24 in fusion with Hsp70 either on C' or N' terminus under control of CMV promoter were used for vaccination of experimental mice. Effect of immunization was evaluated by ELISA analysis of serum p24-specific antibodies and by FACS analysis of antigen specific T cells.

Results: DNA vaccines encoding fusion antigens induced higher levels of specific antibodies that DNA vaccines encoding p24 alone. Furthermore, fusion DNA vaccines induced higher antigen specific T cell production of IFN-γ. IL-4 and IL-10 levels remain unchanged. Most effective was the DNA vaccine encoding p24 N' terminally fused with Hsp70.

Conclusions: HIV p24 antigen fused N' terminally with murine Hsp70 showed during DNA vaccination higher immunostimulatory effect than vice versa construct or DNA encoding p24 antigen alone.

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P576

PRODUCT-SPECIFIC VARICELLA VACCINE EFFECTIVENESS DURING SIX OUTBREAKS OF VARICELLA IN CHILD DAY CARE CENTRES IN BERLIN AND POTSDAM, GERMANY

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Universal varicella vaccination for children ≥11 months old was introduced in Germany in 2004. In 2008, the Robert Koch Institute investigated six outbreaks in Day Care Centres (DCCs) in order to evaluate post-licensure varicella vaccine effectiveness (VE).

We performed a cohort-study among a total of 971 children. Self-administered questionnaires on varicella disease and vaccination histories as well as vaccination records were reviewed. A case was defined as a child attending investigated DCCs at the time of an outbreak with acute onset of varicella clinical signs. VE was calculated comparing attack rates among vaccinated (at least one dose) and unvaccinated children. Children with a previous history of varicella, younger than 11 months, vaccinated at age < 11 months or < 42 days before disease onset were excluded from VE analysis.

Information on vaccination and disease status was available for 500 (51%) children (median age: 3.8 years, 51% males). After exclusions, 321 (33%) children were eligible for VE calculation. Attack rate in vaccinated individuals was 13% compared to 46% in non-vaccinated. Overall VE was 72% (95%CI 59-82) but differed by vaccine products ($p < 0.05$). One-dose effectiveness of Varivax® was 81% (95%CI 51-93), of Varilrix® 47% (95%CI 16-67), and of Priorix-Tetra® 63% (95%CI 25-82). Two-dose effectiveness of Priorix-Tetra® was 100% ($p < 0.001$). Relative risk of breakthrough varicella in 1-dose vaccinated children with Varivax® was 0.36 (95%CI 0.129-0.996, $p < 0.05$) compared to Varilrix®.

VE among children attending DCCs in varicella outbreaks differs significantly by vaccine product. We strongly recommend two-dose varicella vaccination schedule.

P577

OPPONENTS OF VACCINATIONS IN THE INTERNET - EVALUATION OF THE 21 MOST POPULAR ENGLISH AND GERMAN WEB SITES

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Background and aims: The Internet has emerged in modern society as a primary source of information including information about vaccinations. However, where only vaccinations are being considered, there is a common matter of dispute and there are a great many fanatical opponents. Our aim was a systematic evaluation of English and German language anti-vaccination sites which pay attention to content and form of presentation.

Methods: Using a popular Google search engine and key words: vaccination (and) adverse effect (Impfen, Impfschaeden) we reviewed and analyzed the first 15 English and 6 German language displayed Web sites that promulgated anti vaccination information. Using a standardized form, 2 authors systematically evaluated these sites based on specific content and attributed forms.

Results: The typically found content claims were that vaccines cause idiopathic illness (21/21 sites), vaccines compromise immunity (21/21), adverse vaccine reactions are under reported and vaccinations are motivated by profit (19/21). The most common design attributes were the presence of links to other anti vaccination sites (21/21 sites) and the use of emotionally charged stories of children who had allegedly been harmed by vaccines (19/21). The form of presentation was similar to scientific publications (citations, using scientific titles: M.D. Ph.D. Prof.) and seemed to be reliable.

Conclusions: It is very likely that parents seeking information on the web will find Anti vaccination Web sites that may be considered convincing and reliable by internauts without proper background. Therefore, information regarding vaccinations must be made more widely available on the Internet.

P578

THE EFFECTİVİNESS OF ONE DOSE OF VARICELLA VACCINE

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Aim: Varicella vaccine is immunogenic, but effectiveness of one dose of varicella vaccine is varied. In last years, outbreaks of varicella in vaccinated children are reported from a lot of countries, including Turkey. In this study, we investigated that the effectiveness of varicella vaccine in vaccinated children who had received a single dose.

Methods: This study was conducted in 4 elementary schools and 9 nursery schools in Izmir, Turkey from October 1 to December 31, 2008. We distributed a questionnaire to parents to collect demographic information, history of varicella and vaccination. Varicella disease was defined as varicella like rash that developed >6 weeks after vaccination in vaccinated children. Informations about the numbers and forms of lesions, pruritis and fever were registered by a questionnaire.

Results: In the study, 3630 questionnaire were distributed and 2523 of them were resumed. One thousand three hundred and eighty-four children who had received 1 dose of vaccine were included in the study. The median age at vaccination was 13 months. Of 1384 vaccinated children, 424 (30.7%) had a history of varicella. In 90%, the disease has been diagnosed by a doctor. Children vaccinated 5 or more years were at greater risk for varicella disease that was more than twice as high as that among children vaccinated more recently.

Conclusions: A single dose of varicella vaccination provided suboptimal protection against varicella, although it provided sufficient protection against moderate and severe disease. A longer duration since vaccination was associated with an increased risk of varicella infection.

P579

SERUM ANTIBODY RESPONSE TO TETANUS TOXOID IN CHILDREN WITH DOWN SYNDROME

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Children with Down Syndrome (DS) have an increased frequency of infections, hematological malignancies, and auto-immune diseases, suggesting immunological changes. We investigated the antibody response to tetanus toxoid (TT), which is part of the Dutch immunization program. TT is a highly immunogenic T-cell-dependent antigen and therefore useful to test for more severely disturbed specific antibody response. Quantitative (titer) and qualitative (avidity) TT responses were investigated after booster vaccination at 4 and 9 years of age in 15 and 7 DS children, respectively. Samples were taken before and 3-4 weeks after vaccination. TT-specific IgG and IgG-subclass antibodies were measured by quantitative enzyme linked immunosorbent assay (ELISA), avidity of IgG_1-anti-TT by an avidity ELISA. The results were compared with reference values from the laboratory.

At 4 years, post-vaccination geometric mean total IgG, IgG_1, IgG_2 and IgG_4 anti-TT-titers were decreased. At 9 years, DS children had lower post-vaccination geometric mean IgG_4 anti-TT-titers only. Post-vaccination avidity levels of IgG_1-anti-TT were decreased in 8/15 DS children at four years and 4/7 DS children at nine years of age. The quantitative and qualitative anti-TT-responses of the DS group as a whole are shifted downwards compared to the reference values. Although the anti-TT-response increases towards normal titers with increasing age in DS children, the quality of the antibodies, as measured by their avidity, is still abnormal at that age, showing that DS children have profound and lasting difficulties with specific anti-TT antibody formation.

P580

LONG-TERM IMMUNOLOGICAL FOLLOW-UP OF CHILDREN WITH *HAEMOPHILUS INFLUENZAE* SEROTYPE B (HIB) VACCINE FAILURE IN THE UNITED KINGDOM

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Background: It is not known how long children with Hib vaccine failure retain protective Hib antibody levels after infection. This study aimed to determine anti-polyribosylribitol phosphate (PRP) antibody concentrations in children several years after Hib infection and to identify risk factors for low antibody levels.

Methods: The families of UK children with Hib vaccine failure diagnosed between 1992 and 2005 were asked to complete a questionnaire and a blood sample was obtained from the child.

Results: Of 323 families approached, 260 (80.5%) returned a completed questionnaire and 175 (54.2%) children provided a blood sample. The median age at follow-up was 8.4 years (IQR 6.2-15.4 years) and median follow-up time was 4.1 years (IQR, 3.5-9.7 years). Twenty seven children (16.1%) had been born prematurely and/or had underlying disease and eighteen (10.8%) had immunoglobulin deficiency. The median anti-PRP antibody concentration was 0.70 µg/ml (IQR 0.22-5.8 µg/ml). Overall, 95 children (56.9%) had anti-PRP levels < 1.0 µg/ml, while 27 (16.2%) had anti-PRP levels < 0.15 ug/ml. All three children with Down's syndrome and 42% (10/24) of children aged < 5 years at follow-up had Hib antibody levels < 0.15 µg/ml. An antibody level < 0.15 µ/ml was independently associated with underlying conditions, young age at Hib disease and shorter time interval between Hib disease and follow-up.

Conclusions: Over half the children with Hib vaccine failure had antibody concentrations below those considered to confer long-term protection, suggesting that they might be at further risk and so benefit from another dose of Hib conjugate vaccine.

P581

EARLY EVIDENCE FOR DIRECT AND INDIRECT EFFECTS OF THE INFANT ROTAVIRUS VACCINE PROGRAM IN QUEENSLAND, AUSTRALIA

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Background and aims: To identify an impact on routinely collected health-related data following the first 18-months of the publicly-funded infant rotavirus vaccination program (RotaTeq) introduced in July 2007.

Methods: We analysed age group specific data from 2007 and 2008: Health Department rotavirus notifications compared to 2006 data, and laboratory testing behaviour and results compared to mean 2000 to 2006 values.

Results: Each of the three outcome measures fell in the targeted age-group, children less than two years of age, in 2007 and 2008, when compared with data available from the pre-vaccine era: rotavirus notifications fell by 53% (2007) and 65% (2008), laboratory tests performed fell 3% and 15%, and the proportion positive fell 45% and 43%, respectively. Indirect effects of infant vaccination were seen: notifications and the proportion of tests positive for rotavirus fell in all other age-groups. The number of rotavirus tests performed increased in adult age-groups, possibly related to routine screening of specimens from aged-care and health facility gastrointestinal outbreaks.

Conclusions: The first 18-months of publicly-funded rotavirus vaccination program in Queensland has had an early, direct and indirect impact on rotavirus disease as assessed using routinely collected data. These outcomes have been achieved with completed three-dose vaccine coverage of approximately 75 and 80% for the first two quarterly birth cohorts assessed. Improved benefits are anticipated as more birth cohorts are immunised and with better course completion. Further observational studies are required to assess vaccine effectiveness, changing rotavirus ecology, and to identify barriers to additional gains.

P582

IMPACT OF POSTPARTUM INFORMATION ABOUT PERTUSSIS BOOSTER TO PARENTS IN A UNIVERSITY MATERNITY HOSPITAL

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Background and aims: Parent to infant transmission of pertussis remains an issue in France. In 2004 the French Technical Committee of Immunization recommended pertussis booster in a cocooning vaccination strategy including parents to prevent severe pertussis. These recommendations are still insufficiently implemented. The objective of this study was to determine the impact of postpartum information about pertussis booster to parents in a university maternity hospital and its effect on vaccination rates.

Methods: During a three months period, all parents of recent delivered babies were informed orally and by an information letter about pertussis infection and the benefits and risks of pertussis booster. Immunization was recommended as soon as possible after discharge. Two months after birth, parents were called by phone about pertinence of the information previously given and the effectiveness of this policy.

Results: From January to March 2008, 983 deliveries and 659 recall acceptations were registered. 65% (426/659) of women answered to the questionnaire. Information about pertussis was delivered especially by paediatricians and midwives during the mother's hospitalisation and was considered clear and pertinent in 97% of cases. 68% (267/393) of mothers and 63% (245/388) of fathers who received a pertussis vaccine prescription before discharge were vaccinated. Vaccination was done by a generalist practitioner (94%) and mostly in the first month after birth (69%).

Conclusion: Postpartum information about pertussis was successfully implemented and well understood by parents in maternity and should contribute to increase pertussis vaccination coverage in parents of young children.

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P583

MEASLES ANTIBODIES IN NEWBORNS IN RELATION TO MATERNAL IMMUNIZATION STATUS

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Background and aims: The protection provided by transplacentally transmitted maternal antibodies against measles is changing since most women are vaccinated, age of primigravida is increasing and boosting effect of circulating natural infections is decreasing. This study aims to measure passive transmission of measles maternal antibodies to newborns, in relation to mother's medical history of natural infection or vaccination status against measles.

Methods: Maternal and neonatal serum samples were collected 2-3 days after delivery. Measles natural infection history or vaccination status was noted. IgG antibody levels against measles were detected by Measles IgG Capture Enzyme Immunoassay (Microimmune Ltd, UK).

Results: One hundred and eight mothers (16 to 38 years old) and their neonates were included in this study. Most women (99/108, 91.7%) had been immunized against measles, only 5 mothers had history of past natural infection and 4 mothers had no knowledge of their immunization status. Most mother-newborn pairs had concordant results (98 positive and 7 negative) whereas 3 neonates of mothers with detectable IgG antibodies were found seronegative. Ten newborns born to immunized women (10.1%) had undetectable measles IgG antibodies.

Conclusions: In this cohort of children, 1 in 10 neonates born to immunized mothers had undetectable measles antibodies at birth. Prospective follow up of this cohort at 3 and 6 months of age, will further support recently accumulating data suggesting that infants' window of susceptibility is increasing and earlier immunization against measles may be necessary.

P584

PUBLIC HEALTH OFFICERS OPINIONS ON NEW VACCINATION PROGRAMS IN ITALY

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Background and aims: Public health officers and gynaecologists attending to a Congress were requested to express their opinion on whether HPV immunization of women older than 12 years, varicella immunization with combined MMRV vaccine and rotavirus immunization should be included in the National Immunization Plan in Italy.

Methods: For each of the 3 immunization program, a specific 12-14 questions list was prepared following the 8 steps of the WHO Vaccine Introduction Guidelines (VIG) algorithm (WHO/IVB/05.18). For each immunization strategy, a logistic regression model was used to identify the set of topics which, jointly considered, showed the strongest influence on the final responder's statement.

Results: Eighty-seven responders (82% of which were Public health officers) out of 127 participants provided 247 evaluable questionnaires. The final statement “to introduce the vaccine” was voted by 89%, 84,4% and 59,1%, for HPV, MMRVand rotavirus, respectively. The public health priority, the burden of disease, the economic and financial issues and the vaccine presentation were the most important topics. However, the pattern of relevant topics was different among the 3 immunization strategies.

Conclusions: To our knowledge, this is the first report of a survey on immunization programs carried out by using the WHO VIG. The results of this assessment suggest that, apart from the public health priority, the key topics on which a positive decision is reached differ from one immunization strategy to another even in the same Country.

P585

THE U.S. EXPERIENCE WITH THE VARICELLA VACCINATION PROGRAM

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Background and aims: In 1995, the United States implemented a universal one-dose childhood varicella vaccination program with goals of achieving >90% vaccine coverage among young children and reducing varicella disease by >90%. In 2006, a routine two-dose program was adopted. We present the US experience with the one-dose program, scientific considerations for the policy change, and program priorities.

Methods: PubMed search: varicella, varicella vaccine, herpes zoster (HZ). Analysis of available data to update published results.

Results: By 2007, 1-dose varicella vaccine coverage among young children reached 90%. One-dose provided ~85% protection against any varicella disease and 100% against severe disease. National and active sentinel surveillance indicated reduced varicella incidence (92%), and related hospitalizations (75%-88%), deaths (87%), and health expenditures (74%); however, outbreaks among highly vaccinated school populations and other considerations prompted adoption of a 2-dose policy. The vaccine had an excellent safety profile but some recipients developed vaccine-strain HZ. Preliminary post-marketing surveillance data suggested a higher risk for febrile seizures in the first-to-second week after dose one of combination measles-mumps-rubella-varicella vaccine compared with MMR and varicella vaccines administered simultaneously. Data suggest a lower risk for HZ among vaccinated children but are inconclusive regarding an impact of the varicella vaccination program on HZ epidemiology.

Conclusions: The one-dose vaccination program significantly reduced varicella morbidity and mortality, but optimal protection and sustained achievement of program goals require greater effectiveness. Program priorities include evaluating impact of the 2-dose vaccine program, monitoring vaccine-induced immunity and the possible impact on HZ epidemiology.

P586

EVALUATION OF THE VACCINE TO PREVENT HERPES ZOSTER AND POSTHERPETIC NEURALGIA

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Background and aims: Varicella-zoster virus causes mainly varicella, frequently in children, and could reactivate in adults, in this case it causes Herpes Zoster disease(HZ). One of the most common complications of HZ is postherpetic neuralgia (PHN). This review assesses the safety, efficacy and efficiency of the new vaccine (Zostavax^{R}) for the prevention of HZ and PHN in adults.

Methods: Systematic Review, data source: MedLine, Embase, Center for Reviews and Dissemination, Cochrane Library, EMEA, FDA, ClinicalTrials.gov register, CEA Registry, and Euronheed. The inclusion criteria were clinical trials, and economic studies about the vaccine. Quality was evaluated using CASP checklist and Jadad scale.

Results: Three clinical trials, one report of a Health Technology Assessment Agency and seven economic analysis were included. A clinical trial about efficacy showed a decrease of pain in the vaccination group of 61.1% ($p< 0.001$). Duration of pain was lower in vaccination group (21 vs. 24 days, $p=0.03$). The reduction of incidence of HZ in the vaccination group was 51.3% and a reduction of incidence of PHN of 66.5%. A higher percentage of adverse effects in the injection zone was shown in the vaccination group. Economic analysis reports outcomes in range 6,670-200,734$/QALY.

Conclusions: The vaccine is safe, severe adverse effects have only appeared occasionally. The vaccine has demonstrated efficacy in the incidence of HZ and PHN, it has shown a decrease of duration and severity of pain related to them. Economic analysis reflects that vaccination, except in optimistic scenarios about efficacy, presents values higher than considered threshold (50,000$/QALY).

P587

UPDATE ON GARDASIL® (QUADRIVALENT HUMAN PAPILLOMAVIRUS [HPV] 6/11/161/18 VACCINE) CLINICAL TRIAL EFFICACY RESULTS

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Background and aims: At licensure (2006), GARDASIL was shown to prevent HPV16/18-related high-grade lesions (CIN2/3 and AIS) with up to two-year follow-up (protocols 013/015, women aged 16-26). Here we present end-of-study vaccine efficacy (VE) for up to four years; VE for women aged 24-45 (protocol 019), men aged 16-26 (protocol 020), and long-term VE for the HPV16 monovalent prototype-vaccine (protocol 026).

Methods: Review of protocols 013/015, 019, 020, and 026.

Results: In the per-protocol-population of women aged 16-26, end-of-study VE for HPV16/18-related CIN2/3 or AIS was 98% (95%CI:94-100); VE for HPV6/11/16/18-related condyloma, VIN1-3, and VaIN1-3 was 99%, 100% and 100%, respectively. In PCR-negative subjects for HPV6/11/16/18/31/33/35/39/45/51/52/56/58/59 pre-vaccination, Gardasil significantly reduced CIN2-3/AIS associated with the 10 non-vaccine HPV types which cause ~20% of cervical cancers. In women aged 16-26 who had cleared a previous infection with one of the vaccine-HPV types at the time of vaccination, Gardasil recipients were protected against recurrence of disease from that type, unlike placebo recipients. Among women aged 24-45, per-protocol VE for any HPV6/11/16/18-related disease was 92% (95%CI:50-100). In men aged 16-26, VE against any HPV6/11/16/18-related external genital lesion in the per-protocol-population was 90% (95%CI:69-98). In the extended follow-up of 16-23 year old women up to 9 years after vaccination with the HPV16 monovalent prototype-vaccine, per-protocol VE against HPV16 CIN was 100%.

Conclusions: Disease prevention remains the most important measure of long-term VE. Vaccination with GARDASIL is expected to reduce significantly the burden of cervical and other cancers, dysplasia, and genital warts in women and men.

P588

SAFETY AND IMMUNOGENICITY OF 13 VALENT PNEUMOCOCCAL CONJUGATE VACCINE GIVEN WITH MENINGOCOCCAL C CONJUGATE AND OTHER PEDIATRIC VACCINATIONS IN SPAIN

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Aims: The safety and immunogenicity of 13-valent pneumococcal conjugate vaccine (PCV13, serotypes 1, 3, 5, 6A, 7F, 19A, added to PCV7, serotypes 4, 6B, 9V, 14, 18C, 19F, 23F) were assessed. The immune responses of selected antigens in concomitant routine infant vaccines were compared when coadministered with PCV13 or PCV7.

Methods: Healthy infants aged 42-98 days were randomized to receive PCV13 (n=223) or PCV7 (n=226) with DTaP-Hepatitis B-IPV-Hib at ages 2, 4, and 6 months and MnCC at ages 2 and 4 months. Response to diphtheria, tetanus, and MnCC antigens was assessed 1 month after the infant series. Response to PCV13 serotypes was assessed 1 month after doses 2 and 3. Local and systemic reactions were reported for 4 days following vaccination.

Results: For selected antigens, noninferiority was established at >-10% (lower limit of 95% CI for the difference in proportions between PCV13 and PCV7). Approximately 99% of both groups achieved MnCC SBA antibody titers ≥1:8. In both groups, >96% achieved an IgG antibody concentration ≥0.10 IU/mL for diphtheria and tetanus. Postdose 3, ≥93% of PCV13 subjects achieved pneumococcal anticapsular IgG concentrations ≥0.35 µg/mL (WHO antibody threshold for comparative assessment of pneumococcal vaccines) for all serotypes except serotype 3 (86.2%). IgG GMCs for 13 serotypes were 0.85-4.51 µg/mL. Local and systemic reactions were similar between groups.

Conclusions: PCV13 can be given safely with concomitant routine infant vaccines without immunological interference. Compared with PCV7, PCV13 has an acceptable safety profile and elicits a likely effective antipneumococcal immune response.

P589

IMPACT OF THE REMOVAL OF THE 18 MONTH DTPA DOSE ON PERTUSSIS INCIDENCE IN AUSTRALIA

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Background: Acellular pertussis containing vaccines (DTPa) were introduced into the routine childhood immunisation schedule in 1999 with a primary course at 2, 4 and 6 months and booster doses at 18 months and 4 years. The 18-month dose was removed in 2003. This study evaluated the impact of this change on notified pertussis to 2006.

Methods: Pertussis notifications for children < 5 years were obtained from the National Notifiable Diseases Surveillance System. Vaccine Effectiveness (VE) was estimated using the screening method.

Results: Following removal of the 18 month dose point estimate for VE was higher with a 4 dose schedule (87.6% vs 80.3%), but with the numbers of cases available, not statistically significant. Incidence rates per 100,000 for children 1-4 years decreased overall from 2003-2006 (22.6 vs 14.8), but this period did not include an epidemic.

Conclusion: Any increase in notified pertussis must be considered in the context of the documented reduction in local reactions among children receiving three vs four doses of DTPa prior to 4 years of age. The available data support the current schedule, but should be monitored over a longer time including at least one pertussis epidemic period.

P590

BURDEN OF ENDEMIC AND EPIDEMIC MENINGOCOCCAL DISEASE IN THE MIDDLE EAST AND NORTH AFRICA (MENA)

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Background: Acute bacterial meningitis (ABM) remains an important public health problem worldwide. *Neisseria meningitidis* is one of the three most important organisms causing ABM. Globally an estimated 500,000 cases and 50,000 deaths are attributed to meningococcal disease every year. Existing epidemiological data in the Middle East and North African (MENA) region appears to be fragmented and non-standardised.

Methods: Published and unpublished data from 1990 onwards was systematically reviewed to describe the epidemiology and meningococcal burden of disease in MENA. Unpublished data was obtained from authors and key experts in the region.

Results: Results from over 170 publications showed that meningococcal disease causes endemic disease in most MENA countries, and is associated with epidemics in Sudan and Saudi Arabia. Disease incidence was 0-5 cases per 100,000 population in most countries, with incidences up to 13.3 per 100,000 in Sudan. Infants, young children and male adults are mostly affected. Serogroup A, followed by B and W-135 are most prevalent.

Clinically, meningococcal disease presents as meningitis (29-80%) and meningococcaemia (4-61%). Case fatality ratio ranges between 4-15%. Higher mortality is associated with serogroup W-135. Between 2-11% survivors develop sequelae. Carriage rates range between 0-8% being highest in infants and adolescents.

Conclusions: Data in MENA highlight a substantial burden especially in infants, young children and adults. Clinically, meningococcal disease causes severe disease with high morbidity and mortality. Burden monitoring provides key information to assist policy makers to prevent epidemics and potential global spread. Meningococcal conjugate vaccines offer a unique opportunity for effective disease control.

P591

THE IMMUNOGENICITY AND SAFETY OF REPEATED ADMINISTRATION OF DTPA BOOSTER IN ADOLESCENTS AND YOUNG ADULTS

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Background: The incidence of pertussis is rising amongst adults and adolescents in industrialised countries. By replacing the commonly recommended 10-yearly tetanus and diphtheria (Td) booster with reduced-antigen-content dTpa vaccines, additional protection against pertussis could be conferred. This abstract describes the repeated administration of dTpa in adolescents and young adults.

Methods: Adolescents who had previously been vaccinated with DTPa (4 doses) plus reduced-antigen-content dTpa (1 dose) at 4-6 years of age, received an additional dose of dTpa vaccine 6 years later (Trial: 100406). In another trial, young adults (20-24 years) received a second dose of dTpa 10 years after a previous one in an open, phase IV trial (NCT00610168).

In both trials, antibodies against the dTpa antigens were measured before and one month post-vaccination. Solicited local and general symptoms, unsolicited symptoms and SAEs were recorded.

Results: One-month post-booster, all subjects in both studies were seroprotected/seropositive against all vaccine antigens. In the 83 adolescents (10-12 years), the GMCs for the three pertussis antigens increased by 8-10 fold compared to pre-vaccination. In the 82 young adults (mean age 21.1 years), a 10-15 fold increase in pertussis GMCs was documented.

During the 4-day follow-up, the adolescents recorded the following Grade 3 solicited symptoms: pain (2.4%), redness (13.3%), swelling (13.3%), headache (1.2%), gastrointestinal symptoms (1.2%) and fatigue (1.2%). The young adults recorded Grade 3 pain (9.9%), redness or swelling ≥50mm (16.0%), fatigue (2.5%) and gastrointestinal symptoms (1.2%).

Conclusions: Repeated dTpa boosters are well tolerated in adolescents and young adults and induce a vigorous immune response.

P592

DECENNIAL ADMINISTRATION OF REDUCED-ANTIGEN DTPA VACCINE IN YOUNG ADULTS - INCIDENCE OF SOLICITED LOCAL SYMPTOMS CLASSIFIED BY PRE-VACCINATION ANTIBODY CONCENTRATIONS

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Background: Decennial vaccination of adolescents and adults with reduced-antigen-content-diphtheria-tetanus-acellular pertussis (dTpa) vaccines is currently being evaluated. Previous studies have demonstrated that successive doses of acellular pertussis vaccine are associated with increased rates of local reactions.[1] This post-hoc analysis was undertaken to study patterns in local reactogenicity and the influence of antibody concentrations (NCT00610168).

Methods: Young adults, who had received a dTpa booster 10 years previously, were vaccinated with a second dose of dTpa (GSK). Pre- and post-vaccination antibody concentrations against D, T, pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN) were determined. Solicited local symptoms were recorded for 4 days after vaccination and their incidence in relation to pre- and post-vaccination antibody concentrations were investigated.

Results: 82 subjects received the dTpa booster. Grade 3 pain, redness and swelling post-booster occurred in fewer subjects with the lowest anti-diphtheria concentrations (< 0.1IU/ml) 6.7%, 0%, 13.3%, compared with the highest (>1.0IU/ml) 17.6%, 23.5%, 23.5%, respectively. Similar observations were seen according to pre-vaccination tetanus concentrations: < 0.1IU/ ml: no subjects; >1.0IU/ml: 8.5%, 14.9%, 21.3%, respectively. No such correlations were observed in relation to pre-vaccination PT and FHA antibody concentrations.

Conclusions: The incidence of Grade 3 local symptoms seemed to be higher with high pre-vaccination diphtheria and tetanus antibody levels but not with PT and FHA. Repeated dTpa boosters in adults may be expected to have similar reactogenicity as repeated dT boosters.

[1]Rennels M, et al. *Pediatrics* 2000;105:e12.

P593

IMPORTANCE OF SPONTANEOUS REPORTING OF ADVERSE EVENTS (AE): EXPERIENCE IN MENINGOCOCCAL C VACCINATION IN BRAZIL FROM 2003 TO 2008

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Background and aims: The meningococcus group C is nowadays the most important agent involved in meningitis cases in infants and children and is the most relevant agent in these infections in Brazil. This disease can lead to a variety of complications and even to death, which demands prevention that can be done through vaccination of susceptible children. However, it is also very important to monitor the safety and tolerability of the vaccine available for use, in way that the AE can be prevented or adequately handled, and the interactions with concomitant vaccines and treatments can be predicted.

Methods: Retrospective study. Data obtained from manufacturer records based on patients spontaneous notifications of AE from September 2003 to November 2008. These patients were also contacted by phone for the follow-up and outcome of the event.

Results: The postmarketing data showed that of the 1,040,634 doses of meningococcal vaccine applied only 27 patients (0,0026%) presented any AE post-vaccination. From these patients, we managed to find 4 types of notified AE, which included gastrointestinal, neurological, immunological and reactions in the application site. All cases had satisfactory clinical resolution in the follow-up. Vaccine failure was not reported.

Conclusions: Although vaccine reaction causality cannot be established in all cases, this monitoring is of great importance once it allows providing a means for detecting new or previously unreported vaccine-related AE, determining the number of AE reported nationwide, allows collection and analysis of vaccine-specific AE event information and assists in the assessment of potential risk factors for AE.

P594

VACCINE COVERAGE IN PRIVATE SCHOOLS' CHILDREN AGED 4-9 IN CURITIBA (BRAZIL), 2008

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Background and aims: Review vaccine coverage (basic and boost regimen) of both National Immunization Program (NIP) included and non-included vaccines in children attending elementary private schools in Curitiba in 2008.

Methods: In Curitiba, there are 122 private schools where 5,773 children are attended.A representative sample of 23 schools was selected, and 415 children attended in 23 of that schools were selected. Their parents were interviewed for filling a form containing questions about the children and their families. The registers of immunization were verified and parents were inquired about the reasons for not immunize children with vaccines included and not-included in the routine calendar.

Results: The median age of the children was 6 years (range, 4 to 9 y). The average family income was US$1,900 and the median was US$1,700. The coverage for the routine schedule vaccines included in NIP schedule was 96%; however, only 59% received the fifth dose of the pertussis vaccine. The coverage for vaccines not included in NIP (CI95%) was: Varicella: 39% (29.-48); MenC-conjugated: 37% (29-45); Hepatitis A: 35% (26-43), Pn7-conjugated: 20% (13-27); Influenza: 14% (9-18) and Pneumo-23: 10% (7-13). The main reason for children not receiving the vaccines not included in the NIP schedule was the unawareness of their relevant benefits.

Conclusions: Despite of the fact of 100% of the children had access to medical services in Curitiba, their families were not offered guidelines about the use of vaccines not included in the routine immunization calendar.

P595

HEPATITIS A VACCINATION´S RATES IN SCHOOLCHILDREN: NECESSITY FOR MORE MEDICAL AND PUBLIC EDUCATION ABOUT RISKS AND BENEFITS

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Background and aims: It has been estimated that hepatitis A is responsible for up to 39% of the liver transplants in children between 2 months and 15 years of age in the southern region of Brazil. Hepatitis A vaccine (HAV) has been recommended by the Brazilian Society of Pediatrics for healthy children aged 1 year and older since 1997; however, it has not been included in the routine calendar and there is few data about the vaccine coverage in Brazil. The aim of this study was to evaluate the HAV coverage in children from families with good socioeconomic conditions and attending private schools in Curitiba.

Methods: 415 schoolchildren (median, 6 years) were selected from 23 private schools of Curitiba city, and their relevant parents/guardians were interviewed to obtain information about the child, checking the vaccination registers and identifying the reasons for not using HAV.

Results: The HAV coverage was 34.5% (25.5-43.4) and the main reasons for the child not receive the vaccine were: unawareness of the vaccine = 23.1% (IC95%:17.0-29.2%), vaccine cost = 41.8% (IC95%: 35.5-48.1%), medical contraindication 20.9% (IC95%:14.5-27.3%). None of the children had a real contraindication for HAV use.

Conclusions: Pediatricians not perceive hepatitis A as severe enough to recommend the immunization. It is necessary to educate pediatricians and parents about the risks of hepatitis A and the benefits of vaccination.

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RIX4414 IS PROTECTIVE AGAINST SEVERE RVGE CAUSED BY DIVERSE ROTAVIRUS SEROTYPES DURING THE FIRST YEAR OF LIFE IN AFRICAN INFANTS

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Background: The efficacy of the oral, live attenuated human rotavirus(RV) vaccine RIX4414 against severe RV gastroenteritis(RVGE) was examined in a double-blind, placebo-controlled, multi-center phase III trial (102248/NCT00241644) conducted in Malawi and South Africa. Infants were followed up to one year of age to evaluate vaccine efficacy(VE) of RIX4414 against severe RVGE caused by specific RV types.

Methods: Healthy infants (N=4939) were randomised(1:1:1) and received 2 doses of RIX4414 (at 10 and 14 weeks; placebo at 6 weeks) or 3-doses of RIX4414 or 3-doses of placebo (at 6-10-14 weeks of age). Routine EPI vaccines including OPV were given concomitantly. HIV-infected infants were included in the analysis. VE was calculated from 2-weeks post-last dose of RIX4414/placebo until one year of age. Severe RVGE was defined using the 20-point Vesikari scale(score>=11). Diarrhoeal stool samples were analysed for RV by ELISA and genotyped by RT-PCR followed by a reverse hybridization assay.

Results: G1, G2, G3, G8, G9, G12, P[4], P[6] and P[8] were the circulating RV types detected during the surveillance period (mean duration 7.6 months). G1 was most prevalent in South Africa and G12 in Malawi. VE against severe RVGE caused by all RV types observed(pooled RIX4414 group): G1: 64.1%(95%CI:29.9-82.0), G2: 79.2%(95%CI:8.9-96.5), G3: 83.8%(95%CI:9.6-98.4), G8: 64.4%(95%CI:17.1-85.2), G12: 51.5%(95%CI:< 0-77.9) and P[4]: 70.9%(95%CI:37.5-87.0), P[6]: 55.2%(95%CI:< 0-81.3), P[8]: 59.1%(95%CI:32.8-75.3). Results between 2-dose and 3-dose groups were similar.

Conclusions: Two or three doses of RIX4414 provide protection against diverse circulating RV types and significantly reduce severe RVGE in African infants during the first year of life.

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HPV VACCINATION PROGRAM HEALTH DISTRICT BAHIA DE CADIZ - LA JANDA (CÁDIZ, ANDALUSIA, SPAIN): PLANNING, TARGET POPULATION, COVERAGE, SIDE EFFECTS

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Background and aims: HPV vaccine is used to protect against 'high-grade' cervical intraepithelial neoplasia and cervical cancer that are caused by some HPV types that progress to cancer if untreated. VPH vaccine is effective and immunogenic in girls and women aged 10 to 25 years. **Cervarix**(GSK) is the vaccine used in the Andalusian Health Service vaccination Program. It contains purified L1 proteins for types 16 and 18 of the human papillomavirus. All girls born in 1994(14 years) will be the group to be immunised. The aims are to present the first result of the vaccination program after three months from the starting date.

Methods: Selection of target population was made based on the start sex activity survey in our community. Preparation of briefs for parents and professionals, centralised phone number for appointments and a reminder of subsequent doses and additional information (“Salud Responde”). Writings to every professional and personal dose distribution by health centers with recordings in health digital history (“Diraya”).

Results: After three months, “Road Map” (planning) is met optimally in all its sections. 1,918 girls (75%) have been vaccinated. The vaccine has a good safety profile, the most common adverse reaction is mild to moderate short-lasting pain at the injection site. Only one case (0.05%) of allergic reaction was reported to the Andalusian Center of Pharmacovigilance.

Conclusions: The vaccination was well accepted by the population. The safety of the vaccine is important; it has a good safety profile. It complements the vaccined with safe sex information, control cytology.

P598

AN OUTBREAK OF MEASLES IN CAMPO DE GIBRALTAR AREA, ALGECIRAS, SPAIN, FEBRUARY - JULY 2008: POBLATIONAL CONTROL MEASURES

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Background and aims: Several European countries have notified measles outbreaks in specific population groups. The Andalusia Vaccination Calendar includes two doses of measles, mumps and rubella (MMR) at the ages of 15 months and three years. On the 4th of February 2008, two cases of measles from "Campo de Gibraltar", a sanitary area in the south of Spain were notified to the Andalusian Epidemiological Surveillance Network ("SVEA"). The aims are to characterise the outbreak and the population control measures.

Methods: The following steps have been taken to control the outbreak: respiratory isolation of the cases; vaccination (**Priorix**GSK) or immunoglobulin to susceptible contacts, with close surveillance at work, schools, nurseries, and health centres; vaccination of infants aged between 6 and 15 months and catch-up to 3 years old and health workers.

Results: Highest incidence in the group younger than 2 years and in the group of 20 - 29 years. 148 cases were confirmed (All the viruses isolated were of the Enfield genotype D4 strain). Vaccination: 90% age 6-11 months, 100% age 11-15 months, Cath-up 50%, and 273 health workers.

Conclusions: The disease mainly affected the adult population with low immunization coverage, as well as children under 15 months and still unvaccinated. Since it was not a strain previously isolated in indigenous cases, it would be presupposed as imported although it has not been possible to locate the index case. Pockets of family members not vaccinated at social risk were detected that indicates the need for a more comprehensive immunization coverage.

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INFLUENZA VACCINE COVERAGE AMONG PRESCHOOL CHILDREN AGED 0-6 YEARS IN WARSAW, POLAND

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Background: Influenza vaccinations are highly recommended for healthy children aged 6 months - 5 years.

The aim of our study was to find influenza vaccination coverage among preschool children in Warsaw.

Material and methods: We analyzed medical documentation of 1466 children aged 0-6 years from three out-patient clinics in Warsaw.

Results: We found 44 children who had a written prove of vaccination against influenza, so the influenza vaccine coverage was estimated as 3%. The average age of a vaccination against influenza was 4,4 years. Most of vaccinated children (54,5%) were vaccinated at the age 1-2 years, 34% at the age 3-6 years, 11% were vaccinated before 1st year of life. 50% of children vaccinated for the first time in their life were given only one dose of vaccination (the course of vaccination was incomplete). 20% of this children continued vaccinations against influenza during next years after the first vaccination. For 95% of children vaccination against influenza was the only one given during a visit in the medical office. Medical history of vaccinated against influenza children revealed that 89% of them were also previously vaccinated with combined vaccines (hexavalent or pentavalent), 75% of them were given monovalent vaccines which made their vaccination schedule wider.

Conclusions: Influenza vaccination coverage among preschool children in Warsaw was low (3%). Most of children were vaccinated at the age between 1st and 2nd year of life and half of individuals vaccinated for the first time in their life did not completed vaccination scheme.

P600

REALIZATION OF VACCINATION SCHEDULE AMONG CHILDREN WITH CONGENITAL HEART DEFECTS

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Introduction: Congenital heart defects (CHD) occur in 1% of newborns. Heart defect is not a contraindication for vaccination but children with CHD have often difficulties with a realization of vaccination schedule.

The aim of our study was to estimate realization of vaccination schedule among children hospitalized with CHD.

Materials and methods: We analyzed medical documentation of 60 children age 0-8 years (mean age 4, 2 years). Diagnosis of CHD was: PDA (32%), VSD (26%), ASD II (24%), CAVC (18%). 52% of children were after cardio surgery procedures. We also asked patents to fulfill the survey with questions concerning their knowledge about vaccinations.

Results: We found that the vaccination schedule was properly realized in 87% of children, but in 40% there were observed delays. The reasons of delays were: cardio surgery procedures and prolonged hospitalizations (37%) and acute infections (30%). Only 10% of children with CHD had monovalent recommended vaccinations against Streptococcus pneumoniae, 7% against hepatitis A, 4% against Neisseria meningitidis, 4% against varicella.Most of parents knew that congenital heart defects are not contraindications for vaccinations (80%). The main source of knowledge about vaccinations for parents was a pediatrician (50%) only for 12% of them - a general practitioner.

Conclusions: Realization of a vaccination schedule among children with diagnosis of CHD is on a high level. Parents' knowledge about vaccinations is enough but they require more information concerning recommended monovalent vaccines. General practitioners should be more active in education of parents of children with CHD concerning vaccination schedule.

P601

IMPACT OF HERD IMMUNITY ON *STREPTOCOCCUS PNEUMONIAE* CARRIAGE DURING COURSE OF TRIAL OF 11-VALENT PNEUMOCOCCAL CONJUGATE IN FILIPINO CHILDREN

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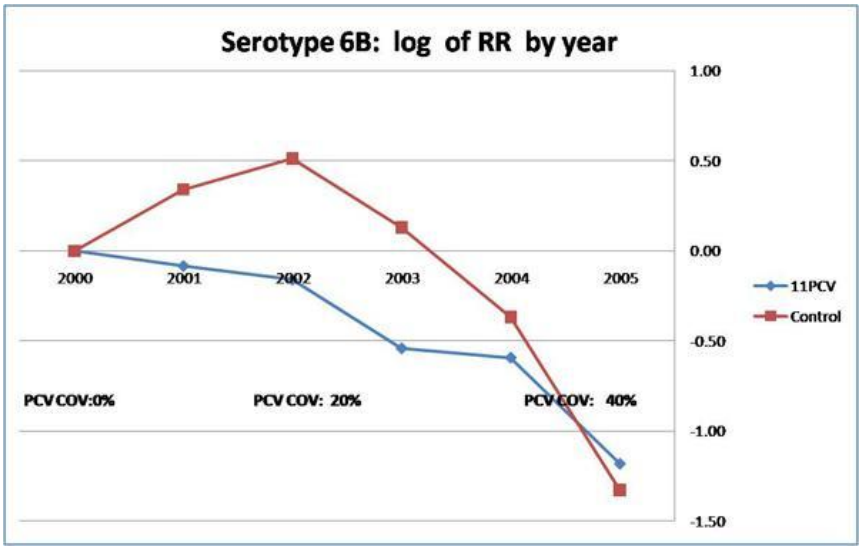
Background and aims: Rapidly evolving herd immunity, optimal from programmatic perspective, may bias vaccine efficacy (VE) estimates towards zero in case pathogen under study becomes rare during course of trial.

Methods: 1,108 infants (9% of total 12 190 enrolled) were recruited into an immunogenicity and carriage study nested in an individual randomized phase III trial (ARIVAC) which lasted 4.5 years (7/2000-12/2004). They received 11PCV (N=554) or saline placebo (N=554) at scheduled 6, 10, and 14 weeks of age. WHO standard methodology was used to study nasopharyngeal (NP) Pnc serotypes at 2, 5, 9 and 24 months. Adjusting for age, number of siblings and seasonality, we analysed Pnc carriage using GEE binary regression with log link.

Results: Total 4236 NP-swabs were taken. Among placebo recipients, Pnc was isolated in 27% at 2, 48% at 5, 53% at 9 and 42% at 24 months. After 2 years of trial and 11PCV coverage of approximately 20% in target child population; vaccine type (VT) NP Pnc incidence started diminishing also among placebo recipients. Decrease was most pronounced in Pnc 6B (Figure).



[Figure 1]

Conclusion: As herd impact of 11PCV against VT Pnc carriage appears rapidly, even individually randomised trials may detect a combined direct and indirect VE. This is good news for implementation of PCV, but problematic for trials aiming to demonstrate maximal direct VE.

P602

IMMUNOGENICITY OF A ROTAVIRUS VACCINE (RIX4414) IN EUROPEAN PRE-TERM INFANTS WITH DIFFERENT GESTATIONAL AGE

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Background: The live-attenuated human rotavirus(RV) vaccine RIX4414 was immunogenic in full-term infants in trials across Asia, Latin and North America and Europe. This phase IIIb, randomised(2:1), double-blind placebo-controlled trial was conducted in Europe to assess the immunogenicity of RIX4414(*Rotarix*™) based on gestational age of pre-term infants. This vaccine has been proven to be safe in pre-term infants.

Methods: Enrolled infants(N = 1008) randomised into two groups received two doses of RIX4414/placebo as per 0, 1-2 month schedule and stratified by gestational age [20% early pre-term infants = 27-30 weeks(N=206) and 80% late pre-term infants = 31-36 weeks(N=802) in each group]; Dose1 was given at 6-14 weeks after birth. Anti-RV IgA seroconversion(SC) rate(ELISA cut-off = 20 U/mL) and geometric mean concentration(GMC) were calculated one-month-post-Dose2.

Results: Mean gestational age of infants were 29 and 34 weeks in early and late pre-term groups, respectively; mean chronological age at Dose1 was 10 weeks in early pre-term and 8 weeks in the late pre-term groups. The anti-RV IgA SC rates were 75.9% (95%CI:56.5-89.7) in early pre-term and 88.1% (95%CI:80.9-93.4) in the late pre-term infants who received RIX4414 vaccine (N=147), while anti-RV IgA SC rates in infants who received placebo(N=81) were 23.1% (95%CI:5.0-53.8) and 14.7% (95%CI:7.3-25.4) in the respective groups. GMC calculated on seropositive infants receiving RIX4414 were 236.5 (95%CI:133.4-419.3) in early-preterm and 359.1 (95%CI:280.6-459.5) in late-preterm.

Conclusion: Two doses of RIX4414 were immunogenic in both early and late pre-term European infants supporting the implementation of RV vaccination not only in the full-term infants but also in this population.

And Rota-054 study group.

P603

VACCINATION OF PRETERM INFANTS WITH THE 10-VALENT PNEUMOCOCCAL NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* PROTEIN D-CONJUGATE VACCINE (PHID-CV)

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Background and aims: PHiD-CV (GlaxoSmithKline Biologicals), designed to protect infants against pneumococcal and non-typeable *H. influenzae* diseases, is immunogenic in full term infants. This study examined the immunogenicity and safety of PHiD-CV in preterm infants.

Methods: In this open study (107737/NCT00390910) conducted in Spain and Greece, infants born after gestation periods of 27-30 weeks (Preterm I, N=50), 31-36 weeks (Preterm II, N=87) or >36 weeks (Full term, N=149) were enrolled to be vaccinated at 2-4-6 months of age with PHiD-CV coadministered with DTPa-HBV-IPV/Hib. Antibodies were measured 1 month post-dose 3 with ELISA (22F-inhibition) and opsonophagocitic assay (OPA). Local and general solicited/unsolicited symptoms and SAEs were recorded.

Results: The mean (±SD) body weight at dose 1 was: 3.1±0.55kg (Preterm I), 4.2±0.75kg (Preterm II), 5.2±0.7kg (Full term). A high percentage (≥92.7%) of subjects had antibody concentrations ≥0.2 µg/mL for all serotypes in all groups. At least 93.2% of subjects had OPA titers ≥8 for most serotypes except for serotypes 1 (≥58.8%) and 6B (≥81.7%) across groups, 5 (85.3%) and 19F (88.6%) in preterm I group only. Fever >39°C (rectal temperature) was observed after 1.0% and 2.1% of doses in preterm and full term groups, respectively. Only one SAE out of 31 was causally related to vaccination (pyrexia, full term group).

Conclusions: PHiD-CV was immunogenic for all 10 vaccine serotypes and presented a good safety profile both in preterm and full term infants.

This study was funded by GlaxoSmithKline Biologicals, Belgium.

P604

MASS VACCINATION IMPACT ON VARICELLA CASES IN FRANCE: MODEL-BASED COMPARISON USING A TRADITIONAL VERSUS AN EMPIRICAL CONTACT MATRIX

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Background and aims: Varicella mass vaccination is not recommended in France. In 2007, 778,000 varicella cases occurred (median age of infection 3 years). Mean age of infection could increase following vaccination, leading to more severe complications. Since vaccination affects both vaccinated and unvaccinated individuals, dynamic mathematical models are needed to predict population-level consequences. Structure and frequency of contacts between individuals, at the heart of such approaches, have been based on unverified assumptions. A key recent advance is the development of social contact pattern matrices using empirical (survey) data. The objective was to re-assess the impact of vaccination with respect to this crucial component.

Methods: Two age-structured mathematical models were developed. one using an empirical (EMP) contact matrix from Mossong, and the other using the hypothesized (HYP) contact matrix from Brisson. Both models were calibrated to reproduce varicella incidence in France (with highest incidence among 1-4 year olds). The consequences of vaccination (with 80% coverage) were compared.

Results: Both models predicted that vaccination significantly reduces incidence among 1-4 year olds, but increases incidence in an older age group (“age shift”). The age shift was predicted among 15-24 year olds with the HYP matrix versus 10-14 year olds with the EMP matrix.

Conclusions: Despite an age shift, overall varicella incidence declined significantly after vaccination. Mean increases in age of infection depended on structural assumptions, with the empirical matrix predicting a shift to a younger age than previously thought. Accordingly, there should be fewer complications, which should be considered when evaluating vaccination benefits.

P605

FINIP: A CLUSTER-RANDOMIZED TRIAL OF THE NEW PNEUMOCOCCAL *HAEMOPHILUS INFLUENZAE PROTEIN* D CONJUGATE VACCINE (PHID-CV) IN FINLAND - OBJECTIVES AND DESIGN

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Background and aims: We aim to demonstrate the overall effectiveness of the PHiD-CV vaccine (GlaxoSmithKline Biologicals) against diseases caused by *S.pneumoniae* or *H.influenzae* both in vaccinated and unvaccinated population. Thus far we have evaluated the feasibility of a nationwide study.

Methods: A phase III/IV cluster-randomized, double-blind trial has been designed. Two thirds of clusters will receive PHiD-CV; one third hepatitis A or hepatitis B vaccine as control. The study is conducted in Finnish municipal health care centers (HCC). Children < 18 months of age are enrolled to receive 2-4 doses according to age. Half of infants aged < 7 months receive 4 doses and the other half 3 doses to assess effectiveness of different schedules. Outcome data will be obtained through national health registers. We aim to enrol 91000 children (1.5 birth cohorts), during 14 months starting in spring 2009. In addition, 7000 children will be enrolled in a nasopharyngeal carriage, immunogenicity and acute otitis media surveillance study.

Results: Around 80% of the HCCs accepted to participate in the study. There are >700 cases of invasive pneumococcal disease (IPD), >20000 cases of hospital-diagnosed pneumonia, >12000 cases of tympanostomy tube placements and millions of antimicrobial prescriptions notified annually in the health registers, which will be searched. The 10-valent PHiD-CV is assumed to cover 75% of IPD in Finnish infants.

Conclusions: Field trial design, municipal well-baby clinic network, availability of register data, and research-oriented health care personnel enable to carry out this huge clinical trial to obtain valid results on population level.

P606

THE COST-EFFECTIVENESS OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) COMPARED TO 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7) FOR CHILDHOOD VACCINATION IN GERMANY

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Background and aim: To evaluate the potential cost-effectiveness of a new Pneumococcal Conjugate Vaccine PCV13 (additional serotype coverage 1, 5, 7F, 3, 6A and 19A) compared to the currently recommended PCV7 for childhood vaccination in Germany.

Methods: A steady state, static cohort model was constructed to estimate the incidence of meningitis, bacteraemia, pneumonia and Acute Otitis Media (AOM) in children and invasive pneumococcal disease (IPD) and pneumonia in adults. Change in IPD occurrence was taken from US surveillance following PCV7 introduction and adjusted to German serotype distribution. Mortality, morbidity and cost resulting from pneumococcal disease were estimated using recent published literature. A 4-dose paediatric schedule was assumed, with vaccine price per dose assumed to equal PCV7.

Results: In addition to PCV7, the model estimated that introducing PCV13 would prevent 158 cases of bacteraemia and 37 cases of meningitis annually in children; 2365 cases of IPD would be prevented in older children and adults due to herd immunity effects. A total of 620 more deaths per year would be prevented and 10,060 life years gained. Medical costs would fall by an additional 21.2 million Euros per year, 3.5 million Euros in children and 17.7 million Euros in adults.

Conclusions: The model found that paediatric PCV13 vaccination in Germany would further reduce the burden of pneumococcal disease with substantial health and economic benefits. Final cost-effectiveness will depend on the emergence of herd immunity benefits in Germany, impact on AOM and pneumonia, vaccination schedule and price.

P607

THE EFFECT OF A NATIONAL VACCINATION PROGRAM ON THE INCIDENCE OF ROTAVIRUS-GASTROENTERITIS-ASSOCIATED HOSPITALISATIONS IN AUSTRIA

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Background and aims: In Austria vaccinations against Rotavirus gastroenteritis (RV-GE) have been adopted to the National Immunization Program since July 2007 for all children starting at six weeks up to six months of age. Since then vaccination coverage rates have increased to 85%.

Methods: Surveillance data was collected between January 2001 and December 2008 from a sentinel network covering one third of all Austrian paediatric beds. Cases were eligible for analysis from all children up to the age of 15 years who were admitted to an Austrian children's hospital and suffered from RV-GE.

Results: Between January 2001 and December 2007 on average 4500 children per year were admitted to hospital because of RV-GE. In 2008 we registered 2900 cases of hospitalised children with RV-GE. The incidence rates in children below one year of age decreased from 2100 per 100,000 (2001-2006) to 1450 per 100,000 in 2007 and 600 per 100,000 in 2008. In children one year of age incidence rates declined from 1850 (2001-2007) to 1350 per 100,000 in 2008, respectively. In children two years of age and older incidence rates remained unchanged.

Conclusion: This data clearly shows that even shortly after the introduction of a general immunization program against RV-GE the number of hospitalized children below 2 years of age has decreased drastically.

P608

HUMAN ROTAVIRUS VACCINE RIX4414 IS HIGHLY EFFICACIOUS IN ASIAN INFANTS DURING THE THIRD YEAR OF LIFE

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Background: Two doses of the oral live-attenuated human rotavirus(RV) vaccine RIX4414(*Rotarix*™) has been shown to be highly efficacious in preventing severe RV gastroenteritis(GE) during the first two years of life in Asia(96.1%). Infants participating in a double-blind, randomised, placebo-controlled and multi-centre trial conducted in Singapore, Hong Kong and Taiwan(e-track107070, 107072, 107076/NCT444563/028/029/030) were followed up to three years of age to assess the protection offered by RIX4414 against severe RVGE.

Methods: 8687 healthy infants, 5-17 weeks of age at Dose 1 were enrolled and randomised into two groups(1:1) to receive 2 doses of RIX4414-vaccine/placebo following a 0,1-2 month schedule. Routine vaccinations were given concomitantly. Vaccine efficacy(VE) was calculated from approximately 2 years of life of infants until 3 years. Severity of RVGE was assessed using the 20-point Vesikari scale(severe RVGE ≥11). Diarrhoeal stool samples were analyzed for RV by ELISA and typed by RT-PCR.

Results: During the third-year efficacy follow-up period (mean duration: approximately 1 year), 0 and 13 severe RVGE episodes were reported in RIX4414(n=4222) and placebo group(n=4185), respectively corresponding with a VE against severe RVGE of 100.0%(95%CI:67.5-100.0,p< 0.001). VE against wild-type G1 was 100.0%(95%CI:< 0-100.0;p< 0.031) (5 reported severe RVGE episodes in placebo and 0 in RIX4414 group) and 100.0%(95%CI:41.9-100.0,p< 0.004) against pooled non-G1 RV types(G2,G3,G9) (8 reported severe RVGE episodes in placebo and 0 in RIX4414 group). Efficacy against hospitalized RVGE was 100.0%(95%CI:60.5-100.0;p< 0.001).

Conclusions: The third-year efficacy results demonstrate that the RIX4414-vaccine offers sustained protection against severe RVGE during the third year of life without any reduction in efficacy.

P609

SEROPERSISTENCE OF TICK-BORNE ENCEPHALITIS (TBE) ANTIBODIES IN CHILDREN AND ADOLESCENTS

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This study investigated the seropersistence of TBE antibodies and the response to a booster vaccination with FSME-IMMUN in subjects aged 3 - 18 years. Seropersistence was assessed at 24 and 34 months after the third vaccination with FSME IMMUN 0.25 ml administered in the context of the primary immunization. The first booster was planned at 3 years after the third vaccination, however, the booster vaccination was postponed for subjects who still showed high TBE antibody levels (ELISA > 1000 VIE U/ml and positive NT result). Further follow-up was done at 46 and 58 months, and a booster vaccination was offered at either 4 or 5 years after the third vaccination, depending on the antibody level. The booster response was assessed 21 - 35 days after vaccination. A total of 358 subjects were enrolled in the study, and 174 received the booster 3 years after the third vaccination. Of these, 163 were still seropositive, however, showing ELISA levels below 1000 VIE U/ml. At 46 and 58 months 172 children were further followed for antibody persistence. At 4 years after the third vaccination a booster vaccination was administered to 29 subjects - all of whom were still seropositive - and at 5 years after the third vaccination only one subject was vaccinated. A total of 130 children did not receive the first booster vaccination during the entire study as they still had high TBE antibody levels. Overall a very good booster response was observed in all age groups.

P610

MARKERS OF HBV INFECTION IN 10-12-YEAR OLD CHILDREN VACCINATED AGAINST HEPATITIS B IN INFANCY

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Background: Vaccination is the best method of protection against hepatitis B (HB). The efficacy of immunization is high, estimated at about 95% in healthy population. However, the duration of protection remains unknown.

Aim: The aim of the study was to determine the direct efficacy of HB vaccine in 10-12-year old children immunized in infancy.

Material and methods: In 121 children aged 10-12 ys. immunized against HB with recombinant vaccine in infancy (with 4-dose schedule, first dose given at birth, 10 µg) markers of HBV infection: HB surface antigen (HBsAg - marker of chronic hepatitis) and antibodies to HB core antigen (anti-HBc total - marker of past HBV infection) as well as anti-HBs antibodies (as a marker of seroprotection against HB) were determined. Titers of anti-HBs ≥ 10 IU/l were defined as protective.

Results: Of the 121 participants, 97 (80%) had protective levels of anti-HBs. None were HBsAg positive nor had history of hepatitis. In 4 children (3,3%), despite protective titers of anti-HBs (54 to ≥ 1000 IU/l), anti-HBc were positive. Amongst anti-HBc positive children everyone had risk factors of HBV infection in anamnesis (hospitalization, surgery, HBV-infected parents). In one child, in which HBV DNA using PCR method was additionally determined, it was negative. In other three HBV DNA is to be examined.

Conclusions: Vaccination is highly effective in preventing chronic HB for 10 to 12 years after infant vaccination. However, a number of children becomes HBV infected, which needs to be considered due to the risk of occult hepatitis.

P611

EVIDENCE OF *BORDETELLA PERTUSSIS* INFECTION IN VACCINATED ONE-YEAR-OLD DANISH CHILDREN

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Background and aims: In Denmark, pertussis immunization is carried out with a PT toxoid vaccine. Because there is ample evidence that single component (PT toxoid) vaccines have less efficacy than multicomponent pertussis vaccines, we studied IgG and IgA antibody titers to PT and FHA in one-year-old Danish children to estimate the circulation of *Bordetella pertussis* in the population.

Methods: We followed 228 healthy children from 2004-06. The children were scheduled to receive routine immunizations with D-T-aP-IPV-Hib at 3, 5 and 12 months of age. Blood samples were obtained from 204 of the children by age 12 months. IgG and IgA antibodies against PT and FHA were measured by ELISA.

Results: At the time of blood sampling 100% had received one dose, 98% had received two doses and 23% had received three doses of PT toxoid vaccine. Ten children had IgA antibody to PT and 18 had IgG antibody to FHA. Seven of the 10 PT IgA responders had received three doses of vaccine.

Conclusions: Infection stimulates both an IgA and IgG antibody response to PT. The IgA response after a first infection is often minimal. However, subsequent vaccination will bring out this response. Our data indicate that 5% of our cohort had a *B. pertussis* infection. This indicates that *B. pertussis* was circulating in the community even though few clinical cases were recognized. The finding of FHA antibody in 9% also might suggest a high *B. pertussis* rate. However, the FHA antibody could be due to cross-reacting antibodies.

P612

INFORMATION, KNOWLEDGE, BELIEFS AND ATTITUDES OF TEENAGERS IN VALENCIAN REGIONAL COMMUNITY ABOUT HUMAN PAPILLOMAVIRUS' VACCINATION

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Background and aims: At the time of implant strategies in public health will have to identify knowledge and attitudes of the target population. The aim of the study has been to know the information and risk perception by teenagers on the Human Papillomavirus (HPV) and identify their sources information.

Methods: Analytical transverse study using a survey by a total of 212 students aged 13 and 14 years old from public and private schools in Valencian Regional Community.

Results: 78 males and 134 women with an average age of 13,62. The 79,85% of women knew that the vaccine is used to prevent cervical cancer, but only 5,97% of them knew that it serves to prevent transmission of HPV infection. The 11,19% of women and 16,67% men were unaware of the mechanism of transmission of HPV. A percentage of teenagers surveyed more than 6% thought that one of the mechanisms of HPV transmission is through blood transfusion. The 52,56% of males and 58,96% of women answered correctly that HPV infection is more risk in women.

Conclusions: Teenagers aged 13 and 14 years old have an inadequate knowledge about HPV, they confuse it with HIV. It's necessary to make interventions aimed at health Promotion among teenagers and general population by health institutions and health professionals.

P613

IMMUNOGENIC AND SAFE VARICELLA VACCINATION IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS AFTER EVALUATION OF THEIR HUMORAL AND CELLULAR IMMUNITY TO VARICELLA

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Objectives: Humoral and cellular immunity are needed to protect against Varicella zoster virus (VZV). Our objectives were to develop more sensitive and specific assays to measure both immunities in pediatric orthotopic liver transplant (OLT) recipients, and to assess their response to varicella vaccination, currently not recommended after transplantation.

Methods: A new ELISA-based assay was developed using lectin affinity purified glycoprotein from human dermal fibroblasts. VZV-specific CD4+ memory T cells were quantified through a whole blood assay. Cells were stimulated with anti-CD28 and CD49d costimulatory antibodies with or without VZV-gp. A dual antibody was added to capture IFN-g produced by CD45+ cells, and CD4+ and CD8+ T cells were analyzed by FACS.

Pediatric OLT recipients, at least one year after transplantation and seronegative for VZV, were vaccinated with a live-attenuated varicella vaccine. Their antibody titers were measured after VZV vaccination.

Results: VZV immunity was assessed into 46 OLT recipients (mean age 10.1 years, at transplantation 3.1 years). IgG antibodies to VZV were detected in 58/106 samples with our assay. The number of IFN-g producing T cells was similar in children with past infection or immunization.

23 seronegative OLT recipients were vaccinated with 2 or 3 doses of varicella vaccine. No adverse events were associated with vaccination. All children had protective antibody titers after vaccination.

Conclusion: Sensitive assays identify a significant proportion of pediatric OLT recipients without detectable VZV antibodies. Cellular assays contribute to better estimate past exposure and immunity. Varicella vaccine vaccination is safe and immunogenic in pediatric OLT recipients.

P614

REDUCED IGG ANTIBODY AVIDITY IN SOLID ORGAN TRANSPLANT RECIPIENTS AFTER VARICELLA-ZOSTER-VIRUS VACCINATION

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Background and aims: Varicella-zoster virus (VZV) infection may cause significant morbidity and mortality in the immunocompromised patient. The study was designed in order to answer the question as to whether or not solid organ transplant recipients have a lower VZV IgG antibody avidity, despite having protective IgG antibody levels after vaccination.

Methods: The levels of serum IgG antibodies against VZV were evaluated by ELISA. The avidity of serum IgG antibodies against VZV was determined by using a commercial test kit, which involved the removal of low-avidity antibodies via urea treatment and measurement of the remaining bound IgG by ELISA.

Results: Median IgG antibody levels were 800 U/ml for 36 wild-virus infected controls, 810 U/ml for 14 vaccinated controls and 630 U/ml for 28 transplant recipients. Median relative avidity index (RAI) was 89% for wild-virus infected controls, 94% for vaccinated controls and 82% for transplant recipients ($p=0.01$ compared to wild-virus infected controls, $p=0.002$ compared to vaccinated controls).

Conclusion: In conclusion, IgG antibody avidity in solid organ transplant recipients may serve as an additional marker to evaluate humoral immunity against VZV. This may be of particular importance in the clinical setting of exposure to VZV in immunosuppressed patients regarding clinical relevant reinfection and varicella-caused complications.

P615

IMMUNOGENICITY AND SAFETY OF VARICELLA VACCINE GIVEN AS A TWO-DOSE COURSE IN THE SECOND YEAR OF LIFE

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Aim/background: One dose of varicella vaccine is highly effective in preventing typical chickenpox disease, however two doses provide better control of the breakthrough cases. This study assessed the immunogenicity and reactogenicity of a two-dose course of live attenuated (OKA strain) varicella vaccine (*Varilrix*™, GlaxoSmithKline Biologicals) in the second year of life.

Methods: 121 healthy children, aged 11-21 months at first dose, received two doses of varicella vaccine (42-56 days interval between doses). Pre- and post-vaccination blood samples were collected. Anti-varicella titres were measured by immunofluorescence. Solicited local (day 0-3 after each dose)/general, unsolicited (day 0-42) symptoms and serious adverse events (SAEs, throughout the study period) were recorded.

Results: Post-dose 1, seropositivity was 99.1% and rose to 100% post-dose 2. A 9-fold increase in geometric mean titers (GMT) of varicella antibody was observed following the second dose *versus* the first dose (GMT=154.3 post-dose 1; GMT=1395.4 post-dose 2). The most commonly reported solicited local reaction after both doses was redness (27.9% post-dose 1 and 38.0% post-dose 2). The observed incidence of any fever (axillary temperature³37.5°C) was 42.6% post-dose 1 and 43.8% post-dose 2. Rash (localized or generalized) was reported rarely (3.3% post-dose 1; 2.5% post-dose 2). No varicella-like rash was reported after either dose. Eight SAEs were reported for five subjects. None of them were considered to be vaccine-related and all events resolved.

Conclusion: Two doses of varicella vaccine are well-tolerated and highly immunogenic in the second year of life. The second dose induces a strong increase in antibody titres (109705/NCT00568334).

P616

REDUCTION IN HOSPITALIZATIONS AND AMBULATORY VISITS EIGHT YEARS AFTER INTRODUCTION OF UNIVERSAL MASS VACCINATION AGAINST VARICELLA IN URUGUAYAN CHILDREN

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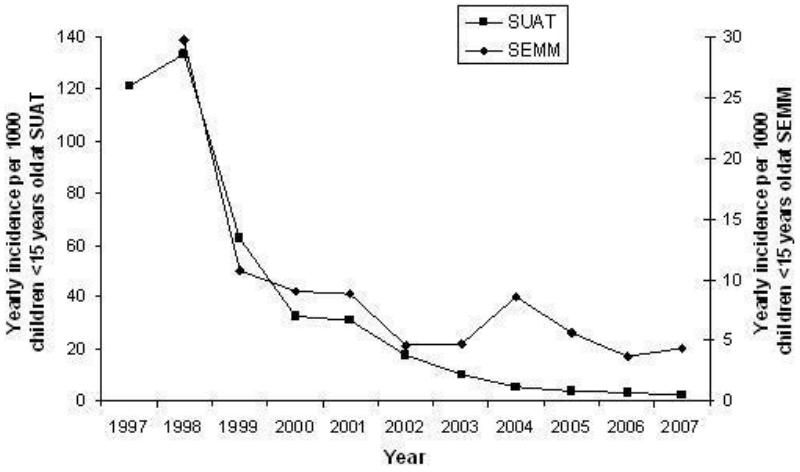
Background/aims: Although chickenpox is sometimes considered a benign childhood disease, it represents a significant public health concern, and can have a wide spectrum of complications. Varicella vaccination was introduced free of charge at the end of 1999 into the Uruguayan immunization schedule as one dose of *Varilrix*™ (GlaxoSmithKline Biologicals, Rixensart, Belgium) at 12 months of age. In this study, the impact of the Uruguayan varicella universal mass vaccination (UMV) eight years after its introduction was assessed.

Methods: Information on hospitalizations was collected from the main paediatric referral hospital in Montevideo. The proportion of admissions for varicella was compared to the overall number of admissions. Age-specific incidence of ambulatory visits for varicella cases in children aged < 15 years was also calculated. The vaccine coverage exceeded 90%.

Results: Hospitalizations decreased by 97% and 98% in 2006 and 2007, respectively, compared to years 1997-1999. In 2006, 22 out of 15105 hospitalizations, were varicella-related; the respective numbers for 2007 were 14 out of 15365. The overall incidence of varicella ambulatory visits among children < 15 years was 3.5/1000 in 2006; and 3,4/1000 in 2007, which corresponds to a 91% reduction since the introduction of the varicella UMV program (compared to 1997-1999).

Conclusion: Varicella incidence among Uruguayan children decreased dramatically after vaccine introduction in the target population.

(106278-106282)



Incidence of varicella in children aged <15 years, Uruguay 1997–2007. SEMM, Servicio de Emergencia Medico Movil; SUAT, Servicio de Urgencia Asistencia y Traslado.

[Figure 1]

P617

THE EFFECT OF VACCINEPROFILAXON MORBIDITY AND EPIDEMIOLOGY OF THE PERTUSIS

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Instruction: Contagious diseases have been following mankind since ancient times knowing no boundaries and have been spread very quickly from one part of the world to the other.

Aim of the work: To present the state of this contagious disease and the percentage of coverage on children with primovaccine and revaccine against pertusis in the period between 1994-2008 in the Medical Centre in Negotino.

Materials and methods used: For the production of this work, materials from the annual reports in the department of immunization and epidemiological service in the town has been used. The work represents retrospective study where descriptive and analytical methods have been used, data is statistically processed and represented numerically, tabularly and graphically.

Results: Vaccineprofilax has been carried out with the classical three typal diteper vaccine, starting on the third month within the period of thirty days, and revaccination in the second and the forth year.

planned done %

- primovaccine 1488 1479 99.3
- I revaccine 1602 1600 99.8
- II revaccine 1554 1550 99.7

Conclusion: In the country of Negotino in this period there is only one example of pertusis. It is about one year old unvaccinated child. The percentage of vaccination is quite high and ranges between 98.8-100%. Vaccineprofilax is the only method of extermination of pertussis.

P618

IMMUNOGENCITY AND SAFETY OF PEDIACEL® COMPARED WITH INFANRIX®-IPV+HIB AT 2, 3 AND 4 MONTHS OF AGE, BOTH CO-ADMINISTERED WITH PREVENAR®

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Objective: PEDIACEL ($DTaP_5$-IPV-Hib) or Infanrix-IPV+Hib ($DTaP_3$-IPV reconstituting Hib) was co-administered with Prevenar (7-valent conjugate pneumococcal vaccine) in infants 2, 3, and 4 months of age, and these treatment groups were compared with respect to immunogenicity and safety.

Design: Single blind, randomised, 2-arm, multicentre study in France and Poland.

Results: In the per-protocol population, seroprotection rates after primary series vaccination with PEDIACEL or Infanrix-IPV+Hib were 91.0% versus 80.8% for PRP (≥0.15 mg/mL) and 99.2% versus 100% for diphtheria (≥0.01 IU/mL); both regimens achieved 100% for tetanus (≥0.01 IU/mL) and poliovirus 1-3 (≥8 1/dilution). With these seroprotection rates, PEDIACEL was non-inferior to Infanrix-IPV+Hib for PRP (delta of -10%) and for diphtheria, tetanus and polio 1-3 (delta of -5%). Seroprotection rates and GMTs for PRP were higher for PEDIACEL. Seroresponse rates against the pertussis antigens PT, FHA and PRN were similar in both groups. A response to FIM was observed in the PEDIACEL group; however FIM is absent from Infanrix-IPV+Hib vaccine. Seroprotection rates for 7 pneumococcal antigens (≥0.35 mg/mL) in the PEDIACEL group were non-inferior to the Infanrix-IPV+Hib group (delta of -10%), and GMTs were similar. The safety profiles of both treatment groups were also similar.

Conclusions: When coadministered with Prevenar using a 2,3,4 month schedule, vaccination with PEDIACEL elicited robust immune responses non-inferior to those of Infanrix-IPV+Hib, and similar safety profiles were observed. Although not a predefined hypothesis, PEDIACEL PRP response was higher than that of Infanrix-IPV+Hib.

P619

EFFECTIVENESS OF ACELLULAR PERTUSSIS VACCINES: DURATION OF PROTECTION

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Background: The effectiveness of acellular pertussis vaccines needs continuous monitoring. One possibility of studying possible changes in effectiveness is to estimate the duration of protection after the last vaccine dose.

Methods: A total of 100 consecutive cases among children and adolescents whose nasopharyngeal swabs were positive for Bordetella pertussis-DNA by real-time PCR (IS 481) were analyzed. After consenting to the study, the medical records of all individual cases were screened for symptoms, vaccination history and contacts. Families were contacted and case contacts as well as the vaccination history of the family were recorded. Estimates for the duration of protection were derived from the time interval between the time of infection and the last vaccine dose.

Results: The 100 cases had a mean age of 8.2 years (median age 8.45, range: 0.8 - 12.3 years), and 57 were female. In contrast to a mean vaccination coverage of more than 95% found in a cohort study in Germany [1], 52 % of children in this cohort were unvaccinated. Of these, 5% were too young to be vaccinated, but 47 % should have received a primary course of three doses. In cases vaccinated according to the vaccination calendar, the mean duration between the last vaccine dose and the infection was 6.07 years (95% CI: 0.80 - 9.92 years), and the median duration was 6.44 years.

Conclusions: The estimated duration of protection in this effectiveness estimate derived from routine data did not differ from results of previous efficacy studies into the duration of protection.

P620

CHANGES IN CARRIAGE OF *STREPTOCOCCUS PNEUMONIAE* IN CHILDREN ATTENDING DAY CARE CENTRES (DCC) IN COIMBRA, PORTUGAL

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Background and aims: Carriage of pneumococcus changes in response to vaccination in children attending DCC, with reductions in vaccine serotypes reported. This study aims to monitor the carriage rates in this population to assess the changes that may be attributable to PCV7.

Methods: A cross-sectional study of children (aged 6 to 77 months) from DCC, in an urban setting in Coimbra, Portugal, was preformed in January 2008. A nasopharyngeal swab was taken and serotyping and sensitivities obtained for pneumococcus positive samples.

Results: The number of samples taken was 561, with isolation of *S. pneumoniae* from 311; a carriage rate of 55.4%. 82.5% had received PCV7 with 73.6% being age-appropriately vaccinated. 23 (7.4%) vaccine types were detected (14 - 0.6%, 6B - 0.3% and 19F - 6.4%). In 13 of these cases (19F =12 and 14=1) the subject had been age-appropriately vaccinated. 76 (24.4%) of isolates were resistant to penicillin (10 were serotype 19F). The carriage of vaccine related types was high (serotypes 19A, 23B and 6A accounting for 32.1%) with 12.2% showing resistance to penicillin, mainly 19A.

Conclusions: There was an increase in the vaccination rate in this community with a corresponding decrease in carriage rate of vaccine types compared to previous years. 19F continues to be carried in spite of vaccination. Penicillin resistance has increased in conjunction with an increase in the carriage of resistant 19A.

P621

ATTITUDES OF PARENTS TOWARDS CHILDHOOD IMMUNIZATIONS IN POLAND

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Background and aims: A very high coverage for virtually all vaccines included in the childhood immunization schedule indicates their good acceptance in Poland. The parents' attitudes toward immunization were however never investigated. The objective of the study was to assess parents' attitudes towards vaccine safety and vaccinations.

Methods: Computer-assisted telephone interviews were collected from parents of children < 2 years. Two-stage sampling was used: first, a list of 3,000 households with children < 2 years was quota-selected from a consumer database collecting contact information from 95% mothers during deliveries; random digit dialling was used to attempt the interview with parents. The 30-item questionnaire covered spontaneous awareness of parents, sources of information, and parents' attitude towards vaccinations.

Results: A total of 1045 interviews were collected, 960 from mothers, and 85 from fathers. Mean age of parents was 28.9 (±5.4). Overall, 98% of parents have never refused or delayed any immunization their children has been offered, and almost 92% have no reservations regarding mandatory vaccination. As much as 398 parents (38.0%) have paid for a vaccine recommended for their child. Up to 15% of parents find some immunizations carrying a greater risk than the disease they protect against. Pneumococcal vaccine was the vaccine over which the greatest percentage of parents' expressed concern (27 persons, 2.6%).

Conclusions: The present study revealed good acceptance of childhood immunizations among Polish parents. However, increased activity of anti-vaccination movements is observed which necessitates improved communication on vaccine safety with the society, and continued monitoring of parents attitudes.

P622

ROTAVIRUS VACCINES IN CHILDREN, EVALUATION OF SAFETY, EFFICACY AND EFFICIENCY

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Background and aims: Rotavirus is the main agent which causes gastrointestinal disease in infants. It could provokes severe diarrhoea, often requires hospitalization and sometimes causes death, majority in developing countries. Prevention of the infection could be considered an important objective in Public Health, and vaccination could contribute to this proposal. This study assess safety, efficacy and efficiency of rotavirus vaccines.

Methods: Systematic review of rotavirus vaccines (Rotashield®, Rotarix®, RotaTeq®). Data Source: MedLine, Embase, Center for Reviews and Dissemination Database, Cochrane Library, EMEA, FDA, ClinicalTrials.gov register, CEA Registry and Euronheed. We included studies with healthy children. Interventions was vaccination versus no vaccination. The quality was evaluated by means of the criteria of the CASP checklist and Jadad scale.

Results: Ten clinical trials, a systematic review, and 14 economic studies were included. Majority of the studies showed no significant differences between groups about adverse effects or cases of intususception. Vaccine efficacy was superior to 50%. The value range for QALY gained was 21,900-155,077€ and for DALY gained was 34.25-164,386 €.

Conclusions: Rotavirus vaccines are safe, with typical adverse reactions. The efficacy is high, they could prevent acute gastroenteritis and reduce the number of hospitalizations and medical visits. The variability in the economics results, together with the vaccine cost, meant the cost-effectiveness was substantially influenced by the assumptions of the models and that vaccination could be expensive for the health system.

P623

IMMUNOGENICITY AND IMPACT ON CARRIAGE OF PNEUMOCOCCAL SCHEDULES INVOLVING FEWER DOSES OF CONJUGATE VACCINE WITH OR WITHOUT A POLYSACCHARIDE BOOSTER

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Background: Current pneumococcal vaccination schedules may not be optimal for use in developing countries.

Methods: 552 Fijian infants were randomized to receive 0, 1, 2 or 3 doses of 7-valent pneumococcal conjugate vaccine (PCV) between 6 and 14 weeks of age, and further randomized to receive or not 23-valent polysaccharide (PPS) vaccine at 12 months. All children received a 20% dose of PPS at 17 months. ELISA antibody levels and avidity were measured to 23 serotypes, and opsonophagocytic assays to 11 serotypes. Impact on carriage was assessed.

Results: Following three doses of PCV, geometric mean concentrations (GMC) of antibody to all 7 serotypes were >1.0 ug/ml. Following two doses GMCs were significantly lower for 3 serotypes (6B, 14, 23F) but higher for one (19F). A single dose provoked significant responses for all serotypes. The 12 months dose of PPS vaccine provoked strong booster responses to the PCV serotypes and good primary responses to 15 of the remaining 16 serotypes, and levels remained elevated until 17 months. Following the 17 months micro-dose of PPS, children who did not receive the PPS at 12 months had good responses, while those who did receive the PPS at 12 months had poorer responses for all serotypes.

Conclusions: Two doses of PCV produced similar primary responses to 3 doses, while a single dose produced a reasonable antibody response. PPS at 12 months provoked strong responses to most serotypes, but lead to reduced capacity to respond to a micro-dose of PPS at 17 months.

P624

CONSTRUCTION OF *OPA*-DEFICIENT MUTANT STRAINS OF *NEISSERIA MENINGITIDIS* TO EVALUATE A POTENTIAL SEROGROUP B MENINGOCOCCAL VACCINE

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Background and aims: Opacity-associated adhesin (Opa) proteins are major meningococcal outer membrane proteins. A limited number of Opa variants have been associated with hyperinvasive serogroup B meningococci globally over the last 60 years, suggesting their use as a potential novel vaccine. Recently, immunisation of mice with Opa elicited high levels of meningococcal-specific bactericidal antibody, demonstrating proof in principle. Opa proteins are critical in meningococcal pathogenesis, mediating bacterial adherence to host cells, and modulating human cellular immunity via interactions with T cells and neutrophils, although there are conflicting data regarding their effects. We have constructed *opa*-deficient meningococci to enable these interactions to be more fully understood before Opa can be exploited as a vaccine component.

Methods: All 4 *opa* genes from *Neisseria meningitidis* strain H44/76 were amplified by PCR, cloned into the plasmid vector pBluescript, and disrupted using the antibiotic resistance genes *aph* or *ermC* (conferring resistance to kanamycin or erythromycin, respectively) or using *lacZ* (allowing blue/white selection of colonies). The resultant plasmids were used to transform H44/76. Mutant bacteria were identified by growth on kanamycin or erythromycin-containing media, or by their blue colour, and confirmed by PCR.

Results: *N. meningitidis* strains deficient in one or more *opa* genes were constructed by sequential transformation and homologous recombination of different disrupted *opa* genes.

Conclusions: These mutant strains will allow precise evaluation of bactericidal antibody responses to Opa and will be used to assess the effects of Opa on T cells and neutrophils, assisting vaccine formulation and increasing understanding of meningococcal pathogenesis.

P625

OBSERVATIONAL SAFETY STUDY OF FEBRILE CONVULSION FOLLOWING MMRV VACCINATION IN A U.S. MANAGED CARE SETTING

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A combined measles, mumps, rubella, varicella live vaccine (MMRV, Merck and Co., Inc., US) was licensed in the US in 2005. Pre-licensure clinical trial data showed a significant increase in fever following vaccination as compared to the vaccines given separately (MMR+V). This post-licensure retrospective cohort study was undertaken to assess the incidence of febrile convulsion following MMRV.

31,298 children 12-60 months of age who received MMRV in February 2006-June 2007 in a managed care organization were included in the study. Subjects were matched on age, sex, and calendar date of vaccination to children who received MMR+V concomitantly in January 2004-January 2006, before MMRV availability. Potential cases of febrile convulsion were identified through administrative data and adjudicated by expert panel, according to pre-specified criteria.

During the 30 days post-vaccination, there were 128 and 94 cases with a convulsion code in the MMRV and MMR+V groups, respectively. After review of available medical charts and adjudication, there were 84 cases of confirmed febrile convulsion, 44 (1.41/1000) and 40 (1.28/1000) in the MMRV and MMR+V cohorts, respectively (RR= 1.10, 95% CI= 0.72, 1.69). In days 5-12 following vaccination, a pre-specified period of interest, the respective numbers were 22 (0.70/1000) and 10 (0.32/1000) (RR=2.2, 95% CI=1.04, 4.65).

These data suggest that the risk of febrile convulsion is not different in children vaccinated with MMRV vs. MMR+V in the month following vaccination but increased in days 5-12 when post-vaccination fever is most likely to occur. It may be important to monitor fever during this time period.

P626

HOSPITAL-BASED SURVEILLANCE TO EVALUATE THE IMPACT OF ROTAVIRUS VACCINATION IN BRAZIL

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Background and aims: Brazil implemented routine immunization with a monovalent, human rotavirus vaccine in 2006 and vaccination coverage reached 89% in 2008 in Sao Paulo, making it imperative to assess the impact of immunization on the incidence of severe rotavirus gastroenteritis (RVGE).

Methods: According to WHO guidelines, we performed a five-year (2004-2008) prospective surveillance in a sentinel hospital from Sao Paulo, with routine testing for rotavirus in all children under 5 years of age hospitalized with acute gastroenteritis (AGE). Genotypes were determined by reverse-transcription polymerase chain reaction (RT-PCR) analysis of positive stool samples.

Results: During the study 655 children were hospitalized with AGE; of which 169 (25,8%) were positive for rotavirus.

We observed a 59% reduction (p=0,001) in RVGE hospitalizations in the post-vaccine period (mean of 18/year for 2007-2008 vs. 44/year for 2004-2006), with reductions for all age groups.

Before vaccine introduction, an average of 535 tests were done annually, of which 164 were positive (30,6%). In 2008, 457 tests were done, of which 61 were positive (13,3%), representing a 56% reduction in the positivity rate (p< 0,001).

The peak incidences of RVGE occurred two months later in 2007 and 2008 compared to previous years.

RT-PCR showed that G2 accounted for 15%, 70% and 100% of all cases identified, respectively, in 2006, 2007 and 2008.

Conclusions: A marked decline in RVGE hospitalizations was demonstrated with evidence of herd immunity, likely attributable to the introduction of rotavirus vaccine. The predominance of genotype G2P[4] highlights the need of continuing post-licensure surveillance studies.

P627

CAN THE BOOSTER INTERVAL OF THE ADULT/PEDIATRIC *FSME-IMMUN*® TBE VACCINE FORMULATIONS BE EXTENDED FROM 3 TO 5 YEARS?

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Background: The question if the booster interval of *FSME-Immun® Adults* and *FSME-Immun® 0.25 ml Junior* can be extended from 3 to 5 years has not yet been satisfactory answered due to absence of reliable data.

Methods: A post-authorization open-label multi-center observational study was performed in 2.915 subjects aged ≥6 years. Subjects could participate if they had received at least one TBE vaccination, and exceeded the recommended interval until the next vaccination by ≥20%. Subjects received a single dose of *FSME-Immun® Adults* or *FSME-Immun® 0.25 ml Junior* (according to age). Blood was collected immediately before and 21-84 days after vaccination for TBE IgG antibody measurement (Enzygnost® test). Seropositivity was assumed at ≥10 and seroprotection at ≥25 U/ml. Cohort reported here: n=1,204; regular primary immunization with (B+) or without (B-) booster; time since last vaccination ≥4.5 to < 5.5 (T1), ≥5.5 to < 8 (T2), and ≥8 yrs (T3). Age stratification: Children < 16, young adults ≥16 to < 50, and elderly ≥50 years.

Results: Seropositivity before study vaccination (T1/T2/T3): Children (B-) 100.0/93.5/96.0%, (B+) 100.0/100.0/100.0%; young adults (B-) 100.0/87.9/84.8%, (B+) 97.7/99.0/97.8%; elderly (B-) 83.3/60.0/54.4%, (B+) 88.9/83.7/79.6%. Seroprotection after study vaccination was ≥96.5% irrespective of age and booster status.

Conclusions: Subjects aged < 50 years had a sufficient seropositivity rate up to 5.5 years after primary immunization, supporting booster interval extension to 5 years if backed by other study data. Subjects aged ≥50 years had a seropositivity rate of < 90% under all circumstances and should maintain a booster interval of 3 years.

P628

LONG-TERM SAFETY AND IMMUNOGENICITY OF A HUMAN PAPILLOMAVIRUS (HPV)-16/18 AS04-ADJUVANTED CERVICAL CANCER VACCINE IN GIRLS AGED 10-14 YEARS: 36-MONTH FOLLOW-UP

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Background and aims: A strong and long-lasting immune response against high-risk HPV types is critical when prophylactic vaccination against cervical cancer takes place prior to sexual debut. The HPV-16/18 AS04-adjuvanted vaccine has previously been shown to be highly immunogenic and generally well-tolerated when administered to pre-teen and adolescent girls. This open extension (104904/NCT00316706) of a phase III, randomized, controlled, multi-country study was designed to evaluate the long-term immunogenicity and safety of the vaccine. We report interim results up to Month 36.

Methods: Immunogenicity (ELISA) and safety were assessed in girls aged 10-14 years who had received 3 doses of the HPV-16/18 AS04-adjuvanted vaccine (n=601) at 0, 1 and 6 months.

Results: 36 months after the first vaccine dose, 100% of girls (n=575, ATP cohort) were seropositive for anti-HPV-16 and -18 antibodies. Anti-HPV-16 GMTs were 2688.6 EL.U/mL (95% CI: 2503.6, 2887.3) and anti-HPV-18 GMTs were 995.0 EL.U/mL (95% CI: 918.1, 1078.4). Anti-HPV-16 and HPV-18 antibody levels peaked at Month 7 then gradually declined. At Month 36, antibody titers were notably higher than the plateau level observed in a phase IIB efficacy study (580299/007; NCT00518336), which was associated with sustained protection against HPV-16 and HPV-18 infections. No vaccine-related SAEs, or withdrawals due to adverse events, were reported over the 36-month follow-up.

Conclusions: The HPV-16/18 AS04-adjuvanted vaccine was immunogenic and generally well-tolerated in girls aged 10-14 years through 36 months, with antibody levels likely to result in sustainable long-term protection.

On behalf of the HPV Adolescent Study Investigators Network.

P629

CO-ADMINISTRATION OF AS04-ADJUVANTED HPV-16/18 CERVICAL CANCER VACCINE WITH DTPA-IPV IN 10-18-YEAR-OLD GIRLS: MONTH 7 RESULTS FROM A RANDOMIZED TRIAL

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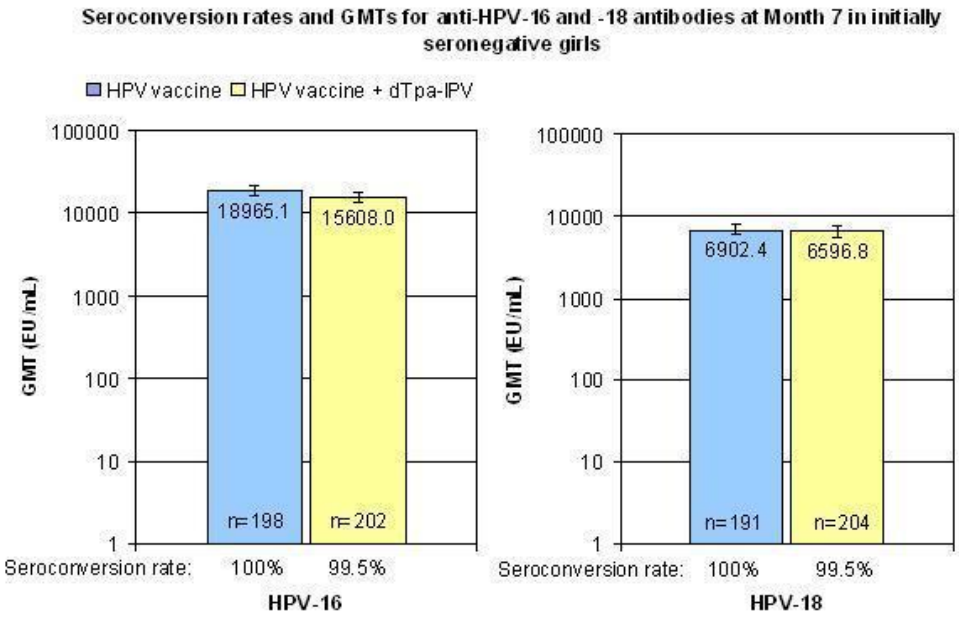
Background: Human papillomavirus (HPV) vaccination in adolescent girls occurs at an age when other vaccines are routinely administered.This randomized, open, multicenter study (108464/NCT00426361) evaluated co-administration of HPV-16/18 AS04-adjuvanted vaccine with diphtheria-tetanus-acellular pertussis-inactivated poliovirus vaccine (dTpa-IPV).

Methods: Healthy girls aged 10-18 years were randomized to receive HPV vaccine at Months 0, 1 and 6 (n=248), HPV vaccine co-administered with dTpa-IPV at Month 0 and HPV vaccine at Months 1 and 6 (n=255),or dTpa-IPV at Month 0 followed by HPV vaccine at Months 1, 2 and 7 (n=248). Immunogenicity was evaluated at Months 0, 1, and 7/8.

Results: The dTpa-IPV immune response at Month 1 (primary objective) was non-inferior when dTpa-IPV vaccine was co-administered with HPV vaccine, versus dTpa-IPV alone, for seroprotection rates for anti-diphtheria, anti-tetanus and anti-poliovirus (≥99.2%), and GMTs (EU/mL) for anti-pertussis toxoid (84.2 and 75.4), anti-filamentous haemagglutinin (611.7 and 615.2) and anti-pertactin (426.2 and 360.0), respectively. The HPV-16/18 immune response at Month 7 (secondary objective) was non-inferior when HPV vaccine was co-administered with dTpa-IPV, versus HPV vaccine alone (see figure).Co-administration was generally well-tolerated. Reactogenicity of dTpa-IPV and HPV vaccines post-dose-1 was generally similar. No subjects withdrew due to adverse events and no vaccine-related SAEs were reported.



[Graph 1]

Conclusions: Immunogenicity and tolerability results support co-administration of HPV-16/18 AS04-adjuvanted cervical cancer vaccine with dTpa-IPV in girls aged 10-18 years.

For HPV Vaccine Adolescent Study Investigators Network.

P630

POTENTIAL OF SYNTHETIC P4 PEPTIDE AS A VACCINE AGAINST *H.INFLUENZAE* INFECTIONS

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Background & aims: H.influenzae infections are one of the leading causes of childhood mortality & morbidity globally. Due to the increased recognition of NTHi as a pathogen the need to have a uniform vaccine has become essential. The potential of P4 as a protective agent has been under scrutiny but conclusions were elusive. Hence efforts were put to map the immunodominant regions of P4 protein, design synthetic peptide as well as evaluate its protective efficacy.

Methods: Prospective population study of children < 2 years was conducted to capture H.influenzae isolates from the community. Conserved protein was identified by comparative proteomics and epitope mapping done based on artificial neuronal network algorithms. Synthetic peptide generated corresponding to the region of potential antigenecity. Immunogenecity assayed *in vitro* while protective efficacy was evaluated *in vivo.*

Results: H.influenzae type b & NTHi isolates obtained from the prospective population study yielded a conserved protein of molecular mass around 29 kDa. N-terminal sequencing of the protein showed a 100% homology with P4 OMP. P4 protein epitope mapping done immunoinformatically localized region of immunodominance. Synthetic peptide on immunization in rabbits showed significant immunogenecity & also showed significant reduction of viable bacteria in lung from rats.

Conclusion: The study effectively used immunoinformatics to explore the immunogenic potential of P4 protein. The conserved nature, protective efficacy of P4 Protein reinstates its significance as a candidate vaccine. These observations answer the queries with regard to protective ability of P4 and emphasize its inclusion in multicomponent vaccine.

P631

BREAKTHROUGH DISEASE AFTER VARICELLA VACCINATION IN GERMANY - IS THERE A PROBLEM?

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Background: Since introduction of routine varicella vaccination of children >11 months of age in Germany in 2004, sentinel surveillance showed decreasing numbers of varicella cases in children. Varicella vaccine uptake for first and second doses according to licensed vaccines was increasing, but breakthrough disease appeared. We investigated its extent and influencing factors.

Methods: Approximately 1000 primary care physicians complete monthly questionnaires with aggregated numbers of varicella cases by age group, numbers of varicella vaccine administered as first and second doses as well as case based questionnaires on vaccinated persons with varicella. A case with breakthrough disease (BTC) was defined as a person with clinical signs of varicella ≥42days after last dose of varicella vaccination. Severe BTC showed >50 skin lesions.

Results: From August 2006 to October 2008, a total of 35,232 varicella cases and n=268 (21) BTC after one (two) doses of any varicella vaccine administered at that time were reported. Numbers of BTC and their proportion on all varicella cases increased over time. The reported 156,445 first and 51,238 second varicella vaccine doses until August 2008 accounted for 1.8 (0.4) BTC per 1000 first (second) doses within 2 years after vaccination. The number of BTC after one dose and their severity differed by vaccine brand.

Conclusion: The number of BTC after one dose of varicella vaccine is still rising. Two doses of varicella vaccine can reduce BTC. Revaccination of one dose recipients should be considered. The optimal interval between doses and the differences by vaccine brands need further investigation.

P632

EUROPEAN PAEDIATRIC INFLUENZA ANALYSIS (EPIA): ESTABLISHING MULTIPLE REGRESSION MODELING NEEDED TO ESTIMATE THE PAEDIATRIC DISEASE BURDEN OF INFLUENZA

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Background: EPIA is an international collaborative research project aimed at estimating the paediatric burden of influenza in European countries. Its goal is to provide data to individual countries for decision making regarding paediatric influenza vaccination.

Methods: Weekly virological data (sentinel+non-sentinel) for influenza and RSV, along with age-specific influenza-like illness (ILI; acute onset of fever >38°C and one of the following symptoms: cough, coryza, sore throat, headache or myalgia) data were analyzed from 2002-2008. Participating countries included Denmark, England, Finland, Italy, the Netherlands, Scotland, Spain, and Wales. An initial study of Dutch children aged 0-19 was undertaken. Multiple regression modeling was used to attribute proportions of ILI to RSV and influenza virus sub-types. Sensitivity analyses included an investigation of the consequence of overlapping RSV and influenza epidemics.

Results: Model form: ILI rate = b_0+b_1*RSV+b_2*InfA(H3)+b_3*InfA(H1)+b_4*InfB. The model fit the data well (adjusted R^2, range: 71-89%). For the 6 seasons, 63% of ILI was attributed to influenza [30% influenza B; 33% A(H3)], 22% to RSV, while 22% was unexplained. When restricting the time frame to 2002-2005 (a period featuring two well-spaced RSV-influenza epidemics), the influenza attribution rose to 77%, while RSV dropped to 12%.

Conclusions: Across 6 seasons, 63-77% of ILI was attributed to influenza A+B, while RSV unexpectedly contributed only 12-22%. The model tended to underestimate the influenza burden and overestimate the RSV burden for periods with overlapping RSV and influenza epidemics. Future EPIA analyses of more countries, age groups and outcomes data will explore the robustness of these findings.

P633

OPSONOPHAGOCYTIC ACTIVITY OF ANTIBODIES AFTER VACCINATION WITH AN INVESTIGATIONAL 11-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN AN EFFECTIVENESS TRIAL IN THE PHILIPPINES

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Background and aims: *In vitro* opsonophagocytic activity (OPA) of antibodies to pneumococcal capsular polysaccharides is recommended to be measured for serological evaluation of pneumococcal vaccines. We present here OPA results for an investigational elevenvalent pneumococcal conjugate vaccine (11PCV) that was evaluated in a nested study of a phase III trial with pneumonia as the primary endpoint in 12,194 infants in The Philippines (controlled-trials.com registry no. ISRCTN62323832).

Methods: 1,111 infants recruited into a nested immunogenicity study received three doses of 11PCV or saline placebo at 6, 10, and 14 weeks of age. OPA for six vaccine serotypes (VT; 4, 5, 6B, 14, 18C, and 19F) and two vaccine-related serotypes (VRT; 6A and 19A) was determined in a subset of 201 serum samples taken at 18 weeks of age. A fourfold multiplexed opsonization assay (MOPA4) was used.

Results: Geometric mean (GM) OPA titers were significantly higher for 11PCV (N=87-89) than for placebo group (N=107-109) against all 8 serotypes. Serotype 4 induced the highest GM OPA titer of 1685, followed by serotypes 5 (1202) and 19F (843). Proportions of infants with detectable OPA (titer of ≥4) for 6 VTs varied from 74% (6B) to 100% (4 and 5). GM OPAs for serotypes 6A and 19A remained low (≤5) and proportions of infants with detectable OPA were 18% and 24%, respectively. In general, antibody concentration and OPA correlated well or modestly.

Conclusion: Three doses of 11PCV in early infancy induced antibodies with good OPA for the six VT. OPA for the VRT remained low.

P634

PERTUSSIS-VACCINATION IN ADULTS WITH COMBINATION VACCINES AT A UNIVERSITY HOSPITAL

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Background and aims: In adults pertussis symptoms are not as severe as in children, for which reason an infection is often not diagnosed. Protective immunity lasts less than 10 years. Since 2004 only combination vaccines such as TdaP or TdaP-IPV have been available. The reactogenity of TdaP doses was evaluated in medical staff who had previously been vaccinated with Td.

Methods: Medical staff who had not been vaccinated against pertussis within the last ten years and who had not been known to have had whooping cough previously, were vaccinated with one dose of TdaP-IPV. In contrast to the previous research, we also vaccinated clients even less than 1 year after the previous Td injection. Local and systemic adverse events were documented for 14 days after injection. A classification was done, depending on when the last dose of Td was administered: less than 5 years ago (group1), 5-9 years ago (group2), more than 10 years ago (group3).

Results: So far, 154 adults have been vaccinated according to the above schedule. No severe adverse events or systemic reactions have been observed. The most local events were documented in group 1, fewer in group 2, and even fewer in group3.

Conclusions: The results indicate that the period of time of 5 years for administering Tdp-combination vaccines after vaccination with Td vaccines, recommended by the STIKO and the manufacturers of the vaccines, can be reduced.

P635

SELECTED NON-ENTERIC VACCINES CAN INFLUENCE GROWTH OF THE FETUS AND INFANT: RANDOMIZED CONTROLLED STUDY DATA FROM BANGLADESH

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Background: Infections are known to reduce growth in the fetus and young infant, but there are few data that vaccine prevention of respiratory infections can ameliorate these effects. We analyzed the separate effects of two vaccines on growth, in a secondary analysis of a recent RCT.

Design/methods: Pregnant women were randomized in the third trimester to receive either influenza or pneumococcal 23V vaccine (control). We analyzed the effect of maternal influenza vaccine on birth weights, during the period of antigenic match between flu vaccine and local circulating flu viruses. Infants were separately randomized to pneumococcal PCV7 vaccine or Hib vaccine at 6, 10, and 14 weeks. We compared length and weight in the 2 infant groups at 6 months.

Preliminary results: For infants *in utero* during the circulation of vaccine-related influenza viruses, birth weights were ≈200 gm higher, compared to infants of control mothers. ($p = 0.02$) The effect on birth weights was not seen during circulation of non-vaccine-related flu strains. At 6 months, male infants who received PCV7 vaccine had small increases in length and weight compared to controls (+0.3 kg, +4%, $p = 0.08$). In female infants the difference between the PCV7 recipients and controls in length and weight (+0.6 kg, +9%, $p < 0.0001$) were substantial.

Conclusion: These unique RCT observations in this Asian setting suggest that some resipiratory vaccines can improve growth of infants:

1) prevention of influenza infections in the mother increases fetal growth, and

2) infant pneumococcal conjugate vaccine increases 0-6mo infant growth.

P636

PRELIMINARY COST-UTILITY ANALYSIS OF NATIONAL INFANT VACCINATION AGAINST MENINGOCOCCAL SEROGROUP B DISEASE IN ISRAEL

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Background and aims: *Neisseria meningitidis* is a major cause of childhood meningitis and septicaemia. The leading pathogen in Israel is Serogroup B. The expected availability of a vaccine that may potentially protect against most meningococcal serogroup B (MEN B) strains prompts an a-priori evaluation of a nationwide vaccination programme.

Methods: A spreadsheet model was used to estimate intervention costs and the expected decrease in the burden of MEN B disease in terms of QALYs and treatment costs.

Results: During 1999-2008, an average of 74.9±12.2 invasive meningococcal disease (IMD) cases was reported annually in Israel. Most cases (75%) occurred in children aged 0-14 years. Serogroup B comprised two-thirds of bacterial isolates.

Assuming a range of vaccine costs between $1-$10 four dose MEN B immunization schedule (at ages 2,4,6 and 12 months) will cost between $1.1-$6.3 million. Based on an assumed vaccine efficacy of 95% and vaccine coverage of 93%, around $0.67 million will be saved in discounted averted treatment costs, including special education and institutionalization costs for long-term sequelae (deafness, neurological disorders). Around 181 discounted QALYs will be added, 88% from averted mortality, 10.5% from averted permanent sequelae and 1.5% from averted morbidity. Cost per QALY ranges from a very-cost effective $2,635 to a cost-effective $32,773 per QALY. At vaccine costs below $0.21 per dose, the intervention becomes cost-saving.

Conclusions: Depending on the vaccine price and what other interventions are competing for funds, the adoption of a national MEN B vaccination program is probably medically and economically justifiable.

P637

WHO ARE THE CHILDREN AT RISK FOR MEASLES? LESSONS FROM THE 2007-2008 JERUSALEM OUTBREAK

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Background and aims: During 2007-2008, an extensive measles outbreak emerged in ultra-orthodox communities in Jerusalem.

Methods: We studied cases under-five years and conducted a case-control study (age and address-matched).

Results: During August 2007-June 2008, 1527 cases were reported nationally, of which 992 (65%) were in Jerusalem district. the genotype involved was D4. Of the 992 cases in the district: 711 (71.7%) were under-15 years old; 419 (42.2%) under-five years. The peak incidence rate was in children aged 6-12 months (1387/100,000). The outbreak started in a town where 142 cases occurred, 74 (52.1%) under-five years. These 74 cases were compared to 148 controls. Cases were significantly less likely to be registered in a well-baby clinic (63.5% vs. 98.6%); if registered - it was at a later age and lower compliance with routine well-child care. A higher child's ranking in the family associated with lower compliance. The cases had lower immunization coverage (HBV3, DTaP-IPV-Hib3 - 37.8%, 33.8% vs. 81.1%, 82.4% in controls). Only 10.8% of cases received DTaP-IPV-Hib4 and only two (3.1%) received MMR1, vs. 59.2% and 83.8% respectively in controls. Cases´ siblings were significantly less likely to be immunized with MMR than controls´ siblings (47.9% vs. 94.4%). Siblings´ rank in the family was inversely related to MMR immunization coverage.

Conclusions: Children who contracted measles were either under the recommended age for MMR1 or showed inadequate compliance with routine well-baby services, immunization overall and MMR specifically. Decreased MMR coverage was evident among cases´ siblings and associated with increasing rank in the family.

P638

COST-EFFECTIVENESS OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION RELATIVE TO 7- VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN THE UNITED KINGDOM (UK)

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Background: While 7-valent pneumococcal conjugate vaccine (PCV7) has demonstrated a dramatic public health impact and is considered highly cost-effective or cost saving, 13-valent pneumococcal conjugate vaccine (PCV13) covers 6 important additional serotypes. We examine the incremental public health impact and cost-effectiveness of PCV13 vs. PCV7 in the UK.

Methods: A decision-analytic model (payer perspective) was developed to estimate impact of PCV13 vs. PCV7 on invasive pneumococcal disease (IPD), pneumonia, and otitis media (OM). We used an epidemiological approach to track incidence, serotype coverage, disease sequelae, death, and costs. Incidence, serotype coverage, disease sequelae, indirect effects, utilities, and mortality data were obtained from national surveillance systems, national vital statistics, and published literature. Direct effects for PCV13 serotypes were assumed similar to direct effects for PCV7 serotypes. Costs and outcomes were discounted at 3.5%. A 3-dose schedule and parity pricing were assumed.

Results: Direct effect of PCV7 and PCV13 pediatric vaccination would eliminate 66% and 83% of IPD in vaccinated children in the UK, respectively. Assuming 80% coverage of the 3 dose schedule, and considering indirect effects (herd impact), IPD would be reduced by 24% (PCV7) and 45% (PCV13) for the entire population. With and without inclusion of indirect effects, PCV13 would be cost saving relative to PCV7 (5-17 million additional pounds saved), with a more dramatic reduction of the burden of all forms of pneumococcal disease.

Conclusion: A PCV13 national pediatric immunization program in the UK would provide additional protection against pneumococcal disease and be a highly cost effective intervention.

P639

TO INVESTIGATE THE EFFECT OF PAEDIATRIC VACCINATION ON ROTAVIRUS DISEASE BURDEN IN BELGIUM

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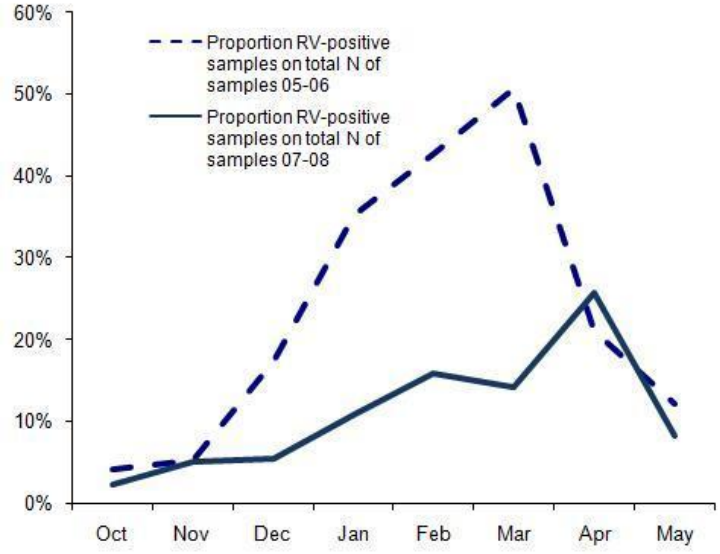
Background and aims: To investigate the impact of paediatric rotavirus vaccination on rotavirus disease burden in Belgium.

Methods: Paediatric vaccination against rotavirus was reimbursed in Belgium from November 2006. We retrospectively analysed results from stool samples collected from children aged ≤ 5 years during outpatient visits or hospitalization at 11 paediatric hospitals distributed across Belgium. Data from the period October 2005-May 2006 (pre-vaccine) were compared with October 2007-May 2008 (post-vaccine).

Results: After the introduction of rotavirus vaccination, the peak percentage of test results positive for rotavirus was approximately half the percentage in the pre-vaccine period, and the peak was delayed (Figure 1).



[Figure 1: % RV-positive test results/month]

Conclusions: The 2007-8 rotavirus season appears delayed in onset and diminished in magnitude compared with the 2005-6 season. These changes coincide with the introduction of rotavirus vaccination. The comparison pre-vaccine and post-vaccine (estimated coverage >80% birth cohort) would be consistent with vaccination impact on RV-disease burden. These findings were consistent with previously published results from the US, where rotavirus vaccination was recommended in February 2006. Data from the US National Respiratory and Enteric Viruses Surveillance System (NREVSS) showed that rotavirus activity was delayed in onset and diminished in magnitude by >50% in the period July 2007-May 2008 (post-vaccine) compared with June 1991-July 2006 (pre-vaccine). (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5725a6.htm)

P640

IMPACT OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION ON COSTS AND OUTCOMES IN GERMANY AND THE UNITED STATES

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Background: 7-valent pneumococcal conjugate vaccine (PCV7) has had a profound public health impact and is considered highly cost-effective or cost saving. Thirteen-valent pneumococcal conjugate vaccine (PCV13) covers 6 important additional serotypes, including 19A. We examined public health and economic impact of PCV13 pediatric national vaccination programs (NIP) in Germany and the US, two of the world's three largest economies.

Methods: A decision-analytic model was developed to estimate impact of PCV13 on invasive pneumococcal disease (IPD), pneumonia, and otitis media (OM) relative to no vaccination. We used an epidemiological approach from a payer (Germany) and societal (US) perspective to track incidence, serotype coverage, disease sequelae, death, and costs. Incidence, serotype coverage, disease sequelae, indirect effects, utilities, and mortality data were obtained from country-specific surveillance systems, national vital statistics, and published literature. Direct effects for PCV13 serotypes were assumed similar to PCV7 direct effects. Costs, discounted at country-specific rates, were obtained from standard country-specific costing sources and published literature.

Results: In an NIP, PCV13 direct effects would eliminate 85.9% and 86.5% of IPD in German and US vaccinated children, with an incremental cost per quality-adjusted life year (ICER) of €66,600 and $47,800, respectively. Assuming 80% vaccination coverage and considering indirect effects, 50.5% and 54.7% of IPD cases would be eliminated from the entire population and PCV13 would be cost saving in both countries.

Conclusion: Pediatric national immunization programs with PCV13 in Germany and the US are expected to have dramatic public health impact and be highly cost-effective or cost-saving.

P641

BACTERICIDAL ACTIVITY AGAINST AN EXTENDED PANEL OF MENINGOCOCCAL STRAINS FOLLOWING IMMUNISATION WITH NOVEL SEROGROUP B MENINGOCOCAL VACCINES IN INFANCY

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Background: We previously reported that ≥93% of infants completing an early infant (2, 4, 6 and 12 month) or a late infant (6, 8 and 12 month) course of a serogroup B meningococcal (MenB) vaccine (rMenB+OMV) had human complement serum bactericidal antibody (hSBA) titres ≥1:4 against 3 meningococcal strains (44/76-SL, NZ98/254 and 5/99) expressing the vaccine antigens.

Methods: Sera obtained after completion of early or late infant courses of rMenB (containing factor H binding protein (fHBP) sub-variant 1.1, NadA and GNA2132) or rMenB+OMV (rMenB plus outer membrane vesicles from strain NZ98/254, expressing PorA P1.7-2,4) were tested for hSBA using 4 additional MenB strains: M00-242922 (ST:41, fHBP1.4, NadA-ve, PorA:P1.7-2,4); M01-240101 (ST:1049, fHBP1.11, NadA-ve, PorA:1.19-1,15-11); M01-240355 (ST:213, fHBP3.4, NadA low expression, PorA:P1.22,14) and M01-240364 (ST:11, fHBP 3.4, NadA+ve, PorA:P1.5,2).

Results: After an early infant course of rMenB+OMV, 80% of participants had hSBA titres ≥1:4 against M00-242922 (PorA homologous), 57% against M01-240101 (contains related fHBP), 11% against M01-240355 (fHBP, PorA and NadA heterologous) and 78% against M01-240364 (NadA homologous). After a late infant rMenB+OMV course, 100% of participants had hSBA titres ≥1:4 against M00-242922, 70% against M01-240101, 17% against M01-240355 and 90% against M01-240364.

For these four strains, rMenB alone was only immunogenic for M01-240364 (hSBA ≥1:4 in 70% (early infant) and 88 % (late infant) participants).

Conclusion: These data confirm that a course of rMenB+OMV in early or late infancy induces bactericidal antibody against strains expressing the vaccine antigens, further demonstrating the potential for improved vaccine prevention of MenB disease.

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A SMALL CONSERVED HEMAGGLUTININ PEPTIDE INDUCED INFLUENZA A (H3N2)-SPECIFIC ANTIBODIES AND IFN-Γ PRODUCTION

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Background and aims: The Influenza hemagglutinin (HA) and neuraminidase (NA) are antigenic surface glycoproteins responsible for viral attachment and release, respectively. Immunological responses to HA and NA play an important role in immunity to influenza infection. Mutations in these molecules also lead to seasonal outbreaks and pandemics.

Methods: A small highly conserved peptide region on the HA molecule has been identified that is present on H1, H3, and H5 influenza A virus strains from birds and humans. This small HA peptide sequence is conserved across several vaccine and field strains obtained since 1995. A unique construct of this peptide was conjugated to a protein carrier and mice were immunized with 5 µg and 20 µg doses of this prototype vaccine at 0 and 4 weeks.

Results: The conjugated viral peptide induced antibody responses by enzyme-linked immunosorbant assay (ELISA) at both 5 µg and 20 µg doses. In addition, 75% of the mice developed antibodies by day 42 that bound to live influenza virus H3N2 (Wuhan strain). Further studies showed that the peptide or H3N2 virus induced IFN-γ production in spleen cells on subsequent exposure.

Conclusions: These studies suggest that a unique construct of a highly conserved region of the HA molecule of influenza A can induce humoral and cellular immune responses to live influenza virus.

P643

SAFETY AND IMMUNOGENICITY OF A TODDLER DOSE OF A LIQUID HEXAVALENT DTAP-IPV-HIB-HEPB VACCINE FOLLOWING PRIMARY SERIES

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Background: We previously reported the safety and immunogenicity of 3 infant doses of a liquid hexavalent diphtheria-tetanus-acellular pertussis-inactivated poliovirus-*Haemophilus influenzae* b-outer membrane protein complex conjugate-hepatitis B vaccine (DTaP-IPV-Hib-HepB) manufactured with a modified hepatitis B process. The safety and immunogenicity of the toddler dose administered at 15 months (4th dose) is now reported.

Methods: Healthy toddlers, who completed 3 infant doses of DTaP-IPV-Hib-HepB, received a fourth dose at 15 months, given either concomitantly with, or 1 month before pneumococcal conjugate vaccine (PCV7). A control group received DTaP-IPV/Hib (at 2,4,6,15 months) + HepB (2,4,6 months) concomitantly with PCV7. Solicited local and systemic reactions were recorded for 7 days. Antibody concentrations were measured 1 month post-vaccination.

Results: Of the DTaP-IPV-Hib-HepB +PCV7 recipients: 38.5% reported fever, 48.0% tenderness, 41.2% erythema and 28.4% swelling. No related serious adverse events were reported for DTaP-IPV-Hib-HepB. One febrile seizure was reported in the control group. Of DTap-IPV-Hib-HepB +PCV7 recipients, 97% had anti-HBs ≥10 mIU/mL, and 99% had anti-PRP levels ≥ 0.15µg/mL.

Conclusions: A booster dose of DTaP-IPV-Hib-HepB, given alone or concomitantly with PCV7, was well tolerated and elicited robust immune responses in toddlers. NCT00362427.

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INCIDENCE OF FIRST EPISODE FEBRILE SEIZURES IN CHILDREN HOSPITALIZED WITH VARICELLA

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Introduction: Universal vaccination with MMRV vaccines is expected to rapidly improve the uptake of varicella vaccination. Since last year ACIP does not express a preference for use of MMRV vaccine over separate injections of equivalent component vaccines in response to new surveillance data showing an increased risk of febrile seizures following vaccination with the first dose of MMRV vaccine. To estimate the incidence of first episode febrile seizures associated with varicella disease, a retrospective study of children hospitalized in our center between 1985 - 2002 was conducted.

Methods: An existing database of all children hospitalized with varicella during the study period was reviewed and children with the admitting diagnosis of “febrile seizures” were identified.

Results: During the study period, 1791 children (median age of 4.5 years) were hospitalized secondary to varicella. One hundred and three children (5.8%) were admitted due to their first episode of febrile seizures (median age of 2.5 years). Children with diagnosis of viral or postinfectious encephalitis and children with preexisting neurological disease were excluded.

Conclusions: The incidence of febrile seizures in children hospitalized with varicella is lower than that reported in children hospitalized with febrile upper respiratory tract infections (16-20%). However, when consulting parents about the pros and cons of using combined MMRV vaccination it is important to inform them about the incidence of febrile seizures in children with varicella. The results of this retrospective study provide further data supporting the use of combined MMRV vaccine especially in population where compliance is an issue.

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SUPPORTING AND IMPEDING FACTORS IN A METROPOLITAN MMR CATCH-UP PROGRAMME: SURVEY OF IMMUNISATION PROVIDERS

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Background: A MMR catch-up programme was conducted among school age children across London in 2004-05. Primary care trusts (PCTs)delivering the programme reported anecdotally a range of difficulties delivering the programme. A systematic enquiry was conducted to assess organisational factors affecting programme delivery.

Methods: Immunisation coordinators of all PCTs were surveyed covering their views on aspects of programme planning, implementation and evaluation. Surveys included both closed and open questions.

Results: Twenty of 28 PCTs (74%) responded. Key issues in the planning phase were adequate lead in planning time, the importance of existing relationships with schools, and staff training. Implementation issues included the use of schools to distribute campaign information, issue around confirming consent, the importance of printed support materials, and logistic issues with vaccine delivery, distribution and storage. Evaluation in most PCTs was limited.

Conclusions: Catch-up of MMR un- and under-vaccinated children at school age has emerged as an important issue for reducing the risk of measles epidemics in developed world settings. Evidence for how to achieve this is lacking. This study, together with the quantitative programme evaluation, gives subjective programme provider evidence for supporting and impeding factors in implementing such programmes in the school setting.

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PAEDIATRIC VACCINATION PROGRAMMES AGAINST HPV: AN INDIVIDUAL-BASED SIMULATION MODEL

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Background and aims: Models are needed to estimate the long-term effect of immunisation programmes on the age-specific prevalence of HPV-types (16, 18, 31, 45 and 6/11) targeted by new vaccines. To represent the sexual transmission of HPV infection, we developed an individual-based discrete event simulation model that incorporated details of individuals' sexual behaviour. As an intermediate step towards estimating the response to vaccination and compliance with the national cervical cancer screening programme, we sought to calibrate the model to pre-vaccination data.

Methods: A hypothetical population of 20,000 individuals with demographic characteristics sampled from UK population data was used to obtain the age-specific prevalence of HPV before the introduction of vaccination. Input parameters to describe the sexual behaviour of individuals in the model, as well as validation of other output measures, were obtained from the Natsal 2000 UK national survey of sexual behaviour. Input parameters describing the progression and remission of each HPV type were taken from published compartmental transmission models, and other sources.

Results: A sufficiently accurate mechanism to account for observed sexual behaviour is obtained by specifying partnership formation rates, and fitting the simulation output to the mean observed annual number of sexual partners by sex and age. The resulting age-specific prevalence for each HPV type accurately reproduces those reported in the literature.

Conclusions: Having obtained a realistic model of sexual behaviour and HPV transmission, future work will address issues concerned with changes in behaviour following vaccination on screening uptake, and in modelling the impact on cervical cancer cases.

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VACCINNET, A VACCINE ORDERING SYSTEM LINKED TO A VACCINATION DATABASE IN FLANDERS, BELGIUM

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Background and aims: The increased number of vaccines in Flanders' vaccination program made it necessary to develop a uniform vaccine ordering system, Vaccinnet. Its vaccination database opens new perspectives for evaluating the vaccination program and immunization coverage.

Methods: Vaccinnet, an online vaccine ordering system linked to a vaccination database, was established in 2004 and made available in 2005-2006. Follow-up of each vaccinator's vaccine stockpile facilitates vaccine ordering, when a critical threshold is reached. As an intrinsic condition all users of Vaccinnet have to register recent vaccinations in a population-linked database. This vaccination database is made available to them.

Results: Vaccinnet currently covers all vaccinations administered by preventive well-baby clinics and school medicine. According to a recent EPI-survey in Flanders, this accounts for about 84% of infant vaccinations and 82% of school-age vaccinations. Additionally, about 40% of active vaccinating GPs and paediatricians are using Vaccinnet so far.

We estimate that about 90% of recent vaccinations in infants and 89% of recent vaccinations of school children are registered in the database. Automatic upload from electronic medical files may increase the use of Vaccinnet and complete the database. This can help to identify under-vaccinated groups by surveys, starting from children without or with incomplete data in Vaccinnet.

Conclusions: A central database containing all known vaccination data of the population, in particular of children and adolescents, can be helpful to improve the quality of the vaccination program in Flanders and to detect under-vaccinated groups in society if used in well designed vaccination surveys.

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PRIMARY VACCINATION OF ADULTS WITH REDUCED ANTIGEN CONTENT DIPHTHERIA-TETANUS-ACELLULAR PERTUSSIS (DTPA) VACCINES

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Background: Despite effective infant immunisation schedules, pertussis is still circulating in industrialised countries. Universal adolescent and adult booster vaccination against pertussis have been advocated and increasingly implemented in industrialized countries to prevent transmission to vulnerable infants.[1,2] This double-blind controlled trial evaluated if dTpa vaccine can also be used for primary vaccination of adults.

Methods: Adults (≥40 years; N= 460) without Td vaccination for 20 years or with unknown vaccination history, were randomized to receive 3 vaccine doses according to a 0-1-6-month schedule [Group1 (G1): dTpa (3 doses); G2: dTpa-IPV (1 dose) + Td (2 doses); G3: Td (3 doses)]. Blood samples were collected pre-dose 1 and one month after each subsequent dose. Local and general symptoms were solicited for 15 days after each dose.

Results: Of 460 enrolled adults, >48% had no protective antibody concentrations against diphtheria and tetanus prior to vaccination. At one month post-dose 3, >99% had seroprotective anti-diphtheria and anti-tetanus antibody concentrations (G1 and G2). One month post-dose 1, ≥96.4% subjects vaccinated with either dTpa or dTpa-IPV had antibody concentrations above the assay cut-off for each pertussis vaccine antigen (PT, FHA, PRN) and ≥92.2% demonstrated a vaccine response (seroconversion or 2-fold titre increase) to all 3 pertussis antigens (G1 and G2). The data from this study did not raise clinically significant safety concerns.

Conclusions: Primary vaccination of adults with dTpa and dTpa-IPV is immunogenic and well tolerated and provides useful protection against pertussis.

[1]Campins-Marti M, et al. Vaccine 2002;20:641-6

[2]Forsyth KD, et al. CID 2004;39:1802-9

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NATIONAL IMMUNIZATION PROGRAM FOR PREVENAR (PCV7) RESULTS IN REDUCTION OF INCIDENCE OF IPD IN GERMAN CHILDREN

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Background and aims: In July 2006 a general recommendation for the vaccination with a 7-valent pneumococcal conjugate vaccine (PCV7) was issued for all German children up to the age of 24 months. We present the impact of the national immunization program with PCV7 (3+1 doses) on the incidence of IPD in Germany.

Methods: Cases of IPD in children were reported by two independent sources: microbiological laboratories and pediatric hospitals. Serotyping was performed at the German National Reference Center for Streptococci. The population under surveillance was 12,124,937 children under the age of 16 years. Incidence rates with regard to age groups and pneumococcal serotypes are based on capture recapture estimates combining the two reporting sources.

Results: As from January 2007, not more than 80% of all newborns had received full vaccination with PCV7. The rate of IPD in children under 16 years of age was reduced from 4.0/100,000 pre vaccination to 3.1 post-vaccination. The reduction in incidence was attributed to significant reductions in children younger than two years (20.0/100,000 to 10.7). In this agegroup the incidence of all vaccine serotypes was strongly reduced (4: 0.9to0.2; 6B: 1.7to0.9; 9V: 0.7to0.2; 14: 5.7to1.2; 18C: 1.0to0.3; 19F: 1.6to0.8; 23F 1.7to0.2). The incidence of non-vaccine serotypes remained stable. There were no significant changes in IPD incidence among children of 2 years and older.

Conclusions: One year after a general vaccination recommendation the incidence of vaccine-serotype IPD in German children under 2 years of age was significantly reduced, further contributing to the impact of PCV7 worldwide.

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COLLAPSE (HYPOTONIC HYPORESPONSIVE EPISODE; HHE) FOLLOWING THE FIRST INFANT VACCINATION: A CASE CONTROL STUDY ON RISK FACTORS AND SEQUELAE

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Background: Collapse is a known adverse event following immunization, defined as sudden onset of pallor, limpness and hypo-responsiveness. For years collapse was a contraindication for pertussis containing vaccines. In the Netherlands this has been abandoned with good results. However, risk factors and sequelae are unknown.

Aim: Identify risk factors on the occurrence of collapse and assess its influence on growth and development, measured at 2-3 years of age.

Methods: Infants with collapse following first DTP-IPV-Hib vaccination were compared with controls, matched for month of birth, sex and region. Data on demographic and predisposing factors, vaccinations, health, growth and development were extracted from medical file. We computed a prediction model on risk factors of collapse, using logistic regression analysis. Goodness of fit was expressed by Bayesian Information Criterion (BIC).

Adjusted odds ratios (ORs) were calculated to assess influence of collapse on growth and development. We corrected overestimation of ORs with Zhang-method.

Results: Duration of breastfeeding (OR 1.03; 95%CI 0.99-1.06) and smoking during pregnancy (OR 2.14; (95%CI 0.37-12.50) were identified as possible risk factors. -2LogLikelyhood was 45.215 and BIC was -34.83 (obviously better than full model).

OR of collapse on growth was 0.16 (95%CI 0.04-0.70), adjusted for sex, age, interaction of collapse*hearing-test and overestimation.

OR of collapse on development was 0.22 (95%CI 0.03-1.78), adjusted for sex, age, interaction of collapse*feeding at first vaccination and overestimation.

Conclusion: Smoking during pregnancy and duration of breastfeeding seems to be non significant risk factors for collapse. Collapse had no negative influence on growth and development.

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EFFECT OF REDUCED DOSE SCHEDULES WITH PCV-7 ON PNEUMOCOCCAL CARRIAGE IN CHILDREN AND ADULT CONTACTS: A RANDOMIZED CONTROLLED TRIAL

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Background and aims: The effects of reduced dose schedules of heptavalent pneumococcal conjugate vaccine (PCV-7) on pneumococcal carriage in children as well as adult contacts are largely unknown, though highly relevant in the context of subsequent herd effects.

Methods: In a randomised, controlled, trial, 1003 healthy infants were randomly assigned to receive either 2 doses of PCV-7 (Prevenar™) at 2 and 4 months of age, 2+1-doses at 2, 4 and 11 months or none (controls). Nasopharyngeal swabs were collected from children and a parent during two years of follow-up with a 6-months interval and cultured for presence of *S. pneumoniae*.

Results: At 12 months of age, vaccine-type (VT) pneumococcal carriage was significantly reduced after both PCV-7 schedules, with VT-carriage rates of 25%, 20% and 38% in the 2-dose, 2+1-dose and control-group respectively (both $p < 0.001$). Corresponding figures at 18 and 24 months of age were 24%, 16% and 38%, and 15%, 14% and 36% respectively (all p-values< 0.001). Despite an increase in carriage of non-vaccine serotypes (NVT) in both vaccine groups, at 24 months of age an absolute reduction in overall pneumococcal carriage of 10% was observed for both vaccine schedules ($p < 0.05$). In parents of vaccinees in both vaccine groups, we observed a trend towards reduced VT-carriage but also doubled NVT-carriage rates compared to parents of controls at the child's age of 24 months.

Conclusion: Reduced dose PCV-7 schedules are effective in reducing VT pneumococcal carriage in children and therefore direct effects and herd effects will be sustained.

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RISK FACTORS FOR NASOPHARYNGEAL BACTERIAL CARRIAGE IN CHILDREN AND THE EFFECT OF PCV-7

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Background and aims: Young children are an important reservoir and source of spread of bacterial pathogens in the community. Identifying risk factors can be useful for prevention strategies.

Methods: Data from a randomised controlled trial in 1003 healthy infants assigned to receive 2, 2+1 or no PCV-7 doses. Nasopharyngeal swabs cultured for *S. pneumoniae* (SP), *S. aureus* (SA), *M. catarrhalis* (MC) and *H. influenzae* (HI) were collected. Univariate and multivariate analyses were performed to identify factors associated with bacterial nasopharyngeal carriage at 12 months of age.

Results: In 987 collected swabs, carriage rates were: HI 50%; MC 66%; SP 62%; SA 8%. Eleven percent of the children carried none; 25%, 34%, 30% and 1% of the children carried 1, 2, 3, and 4 bacterial species respectively. Multivariate analysis showed that day-care attendance, siblings and current URTI were positively associated with SP, HI and MC-carriage but negatively with SA. Use of antibiotics < 2 months was associated with lower pneumococcal carriage. PCV-7 vaccination was associated with lower risk of pneumococcal carriage but increased risk of SA carriage.

Conclusions: Day-care exposure is the most important risk factor for bacterial nasopharyngeal colonization with SP, HI and MC but lowers the risk for SA. PCV-7 vaccination is associated with lower pneumococcal carriage but increases the risk for *S. aureus* at 12 months of age.

Table 1 Multivariate analysis of risk factors for bacterial nasopharyngeal carriage in children at the age of 12 months

	S. pneumoniae	*H. influenzae*	*M. catarrhalis*	*S. aureus*
	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Day-care attendance				
Low*	1.3 (0.8-2.0)	1.4 (0.9-2.3)	1.3 (0.8-2.0)	1.0 (0.5-1.9)
High**	3.8 (2.8-5.4)	3.6 (2.6-5.1)	3.8 (2.8-5.3)	0.3 (0.2-0.6)
Immunized with PCV-7	0.6 (0.5-0.9)	1.2 (0.9-1.7)	0.7 (0.5-1.0)	2.1 (1.2-3.8)
Siblings	2.7 (2.0-3.6)	3.0 (2.3-4.1)	2.2 (1.6-3.0)	0.6 (0.3-0.9)
Current URTI	1.6 (1.1-2.3)	2.4 (1.7-3.3)	2.4 (1.7-3.5)	0.4 (0.2-0.8)
History of wheezing	0.9 (0.6 -1.4)	1.1 (0.8-1.7)	1.5 (0.9-2.3)	0.5 (0.2-1.3)
Previous use of antibiotics				
< 1 month	0.1 (0.1-0.2)	0.8 (0.4-1.6)	0.6 (0.3-1.1)	1.3 (0.4-4.0)
> 1 month but < 2 months	0.3 (0.2-0.7)	0.7 (0.3-1.5)	0.5 (0.2-1.1)	2.2 (0.7-6.9)
> 2 months	0.8 (0.5-1.4)	0.7 (0.4-1.1)	0.9 (0.6-1.6)	0.6 (0.2-1.9)
Use of pacifier	1.0 (0.8-1.4)	0.9 (0.7-1.2)	1.2 (0.9-1.6)	1.3 (0.8-2.1)
Tobacco smoke exposure	1.2 (0.7-2.1)	0.8 (0.4-1.3)	0.7 (0.4-1.2)	0.7 (0.3-2.0)
Swab during RSV-season	0.9 (0.6-1.3)	0.9 (0.7-1.3)	1.7 (1.2-2.5)	0.8 (0.4-1.4)

Factors from univariate analysis not included in multivariate analysis: gender

PCV-7: 7-valent pneumococcal conjugate vaccine; URTI: upper respiratory tract infection.

* Low day-care: ≤ 2 days and/or group size ≤10 children ** High day-care: > 2 days and group size >10 children

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ASSESSING THE POTENTIAL EFFECTS OF HERPES ZOSTER VACCINATION AMONG ELDERLY IN THE NETHERLANDS

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Background and aims: A vaccine to prevent herpes zoster (HZ) is available. To facilitate a decision on including the vaccine in the National Immunization Programme (NIP), we assessed the potential effects of HZ-vaccination among elderly in the Netherlands. This assessment could also be useful when childhood varicella vaccination is considered, because of the possible raise in HZ-cases in the mid term.

Methods: The assessment was done according to the vaccination evaluation model of Kimman et al., a checklist that structures all relevant data for decision making on introduction of a new vaccine.

Results: The mean annual incidence of HZ based on GP-consultations (2002-2007) and hospital admissions (2000-2007) in the Netherlands amounted to 332 and 2.3 per 100,000 respectively. In the period 2000-2007 18 deaths with HZ as primary cause were registered.

Assuming vaccination coverage of 75% and a vaccine efficacy as published by Oxman et al., most HZ-cases are prevented by vaccination at the age of 60 years. However, the lowest number of persons needed to be vaccinated to gain one QALY is at the age of 70 years. Assuming a vaccine price of €77, the most optimal cost-effectiveness ratio is €21,716 (95%CI €11,569 - €31,870) for vaccination at the age of 70 years.

Conclusions: The cost-effectiveness ratio of HZ-vaccination at the age of 70 years lies just above the often socially accepted threshold of €20,000 per QALY. This assessment could be of use in considering the necessity and desirability of both HZ- and varicella vaccination in the Netherlands.

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CELLULAR AND HUMORAL IMMUNE RESPONSES OF PRE-TERM INFANTS TO THE PRIMING WITH PERTUSSIS VACCINES

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Background and aims: As protection against *Bordetella pertussis* is mediated by both specific antibody and T cell responses, and as it is recommended to vaccinate preterm infants against *B. pertussis* according to chronological age, we have determined whether highly pre-term infants (≤ 30 weeks) are able to mount these immune responses during vaccine priming.

Methods: 46 premature infants were vaccinated at 2, 3 and 4 months of chronological age with a Tetravalent diphtheria-tetanus-pertussis-polio vaccine mixed with an *Haemophilus influenzae* Type b vaccine. 22 received an acellular (Pa), and 24 received a whole cell (Pw) pertussis vaccine. Blood samples collected at 2, 3 and 6 months of age were analyzed for specific IgG titers and avidities, as well as for antigen-induced IFN-γ, IL-5 and IL-13 secretions.

Results: In Pa-vaccinated infants, anti-filamentous haemagglutinin and anti-pertusiss toxin IgG were detected in the sera from 6 months-old infants at similar titres and nearly same avidities as age-matched vaccinated full-term infants. Most of the Pa- or Pw-vaccinated infants developed at 3 or 6 months of age an IFN-γ response to the *B. pertussis* antigens, accompanied by an IL-5 and IL-13 secretion for the Pa-vaccinated infants.

Conclusions: Like full-term infants, most pre-term infants are able to mount at 6 months of age adequate specific humoral and cellular immune responses to the administration of prime pertussis vaccination at chronological age. However, since most severe cases of infection occur before 2 months of age, additional efforts should be made to protect infants already at birth against *B. pertussis*.

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CONCOMITANT VACCINATION OF QUADRIVALENT HPV 6/11/16/18 VACCINE (GARDASIL®) WITH EITHER REPEVAX® OR MENACTRA®/ADACEL® IN HEALTHY ADOLESCENTS 10-17 YEARS OF AGE

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Background: Co-administration of GARDASIL® (quadrivalent HPV [types 6/11/16/18] L1 VLP vaccine) with other vaccines was evaluated in two studies: 1. with REPEVAX® (diphtheria/tetanus/acellular pertussis/poliomyelitis vaccine); and 2. with MENACTRA® (meningococcal A/C/Y/W-135 conjugate vaccine) and ADACEL® (tetanus/diphtheria/acellular pertussis vaccine).

Methods: Two open-label, randomized studies were conducted in males and females aged 10-17 years. In one study (protocol 024) 843 subjects received GARDASIL at day 1, month 2, and month 6 and REPEVAX either on day 1 (opposite limb) or at month 1 (non-concomitant). In the other study (protocol 025) 1042 subjects received GARDASIL at day 1, month 2, and month 6 and MENACTRA and ADACEL on day 1 (opposite limb) or at month 1 (non-concomitant). Antibody levels for all vaccine components were measured. Adverse experiences (AE) were closely monitored.

Results: Seroconversion for HPV 6/11/16/18 was $\geq$99% in all vaccination groups. Immune response following concomitant administration of the vaccines was demonstrated non-inferior to non-concomitant administration: $p < 0.001$ for all GARDASIL, REPEVAX, MENACTRA and ADACEL antigens based on geometric mean titers and seroconversion rates. Concomitant administration of the 2 or 3 vaccines was generally well-tolerated. One serious vaccine-related AE (transient muscular weakness) was reported; no subjects withdrew due to AEs.

Conclusion: Concomitant administration of GARDASIL with either REPEVAX or with MENACTRA/ADACEL was generally well-tolerated and was not immunologically inferior to non-concomitant administration. By reducing the number of visits required for full adolescent immunization, concomitant administration of vaccines could increase compliance.

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IMMUNOGENICITY AND SAFETY IN INFANTS OF A HIB-HEPATITIS B VACCINE WITH A MODIFIED PROCESS HEPATITIS B COMPONENT

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Background and aims: A hepatitis B vaccine was manufactured with a modified process (mpHBV) that incorporated double the usual amount of phosphate. After having studied the mpHBV in young adults, it is now evaluated in infants in a combination hepatitis B and Haemophilus influenzae b vaccine (mpHBV-Hib).

Methods: The mpHBV-Hib was compared with the licensed bivalent HBV-Hib vaccine COMVAX™ (Merck&Co., Inc.) for immunogenicity and safety. Both vaccines contained 5 mg/0.5 ml of HBsAg and 7.5 mg/0.5 ml of PRP-OMPC. A total of 543 infants were randomized 1:1 to receive either vaccine at 2, 4, and 12 months of age. A pneumococcal conjugate vaccine (PCV) was given concomitantly. Immunogenicity was assessed at 1 month post-dose 3.

Results: Seroprotection rates (% subjects with anti-HBs ≥10mIU/ml) were 100% and 99% for mpHBV-Hib and the licensed control (COMVAX™), respectively. Geometric mean titers (GMTs) were 4204 (95% CI, 3411 to 5182) and 1683 (95% CI, 1350 to 2099) mIU/ml, respectively. Anti-PRP seroprotection rates (SPR) at ≥0.15 mg/ml and at ≥1.0 mg/ml were 97% and 94%, respectively, for mpHBV-Hib and 96% and 92%, respectively, for the control. Anti-PRP GMTs were 7.1 mg/ml for mpHBV-Hib and 8.0 mg/ml for the control. Reactogenicity of the two vaccines was similar.

Conclusions: The mpHBV was compatible in combination with Hib and with co-administered PCV. The safety profile of mpHBV-Hib was comparable to the licensed control. Both the control and mpHBV-Hib met acceptability criteria for seroprotection rates to hepatitis B, with higher anti-HBs GMTs noted for mpHBV-Hib.

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IMMUNOGENICITY OF ONE DOSE OF AN INVESTIGATIONAL MENINGOCOCCAL TETRAVALENT TETANUS-TOXOID CONJUGATE (ACWY-TT) VACCINE IN 2-10 YEAR OLDS

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Background: Currently no multivalent conjugate vaccine is available for use in the EU in children under 11 years of age. The immunogenicity and reactogenicity of a single dose of an investigational tetravalent ACWY-TT conjugate vaccine developed by GSK was evaluated in 2-10 year old children.

Methods: In this Phase II study (108658/NCT00427908), healthy children (N=309) were randomised 3:1 to receive one dose of ACWY-TT vaccine (5µg of each meningococcal polysaccharide conjugated to tetanus toxoid) or control (polysaccharide ACWY vaccine [ACWY-PS]). Serum bactericidal antibodies were assessed using baby rabbit complement source (rSBA, cut-off ≥1:8) before and 1 month post-vaccination. Reactogenicity was assessed for 4 days using diary cards.

Results: One month after vaccination 100% of subjects in both groups had rSBA titres ≥1:8 against all 4 serogroups. The vaccine response (4-fold rise, or, in initially seronegative; titre ≥1:32) in ACWY-TT recipients was statistically significantly higher versus control (98.4%vs. 91.9%, 94.3%vs. 81.2%, 100%vs 95.6%, 99.1%vs. 82.9% against serogroups A, C, W135, Y, respectively). GMTs were statistically significantly higher for all 4 serogroups in ACWY-TT compared to ACWY-PS vaccinated subjects. The vaccines were well tolerated.

Conclusion: The ACWY-TT conjugate vaccine induced statistically significantly higher vaccine responses against all four meningococcal serogroups compared to the polysaccharide vaccine in 2-10 year-old children.

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INCIDENCE OF INFLUENZA ILLNESS IN EUROPEAN CHILDREN: DATA FROM TWO PROSPECTIVE PLACEBO-CONTROLLED STUDIES CONDUCTED DURING THREE INFLUENZA SEASONS

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Background and aims: Limited data exist describing the burden of influenza in European children. From 2000-2003, during 3 influenza seasons, 2 prospective, randomized, double-blind studies evaluated culture-confirmed influenza illness in European children who had received placebo or live attenuated influenza vaccine (LAIV). Study data were analyzed to describe the incidence of influenza illness in European children.

Methods: Study 1 was conducted in 2000-2002 in children aged 6-35 months at enrollment attending daycare in Belgium, Finland, Spain, UK, and Israel. Study 2 was conducted in 2002-2003 in children aged 11-23 months in Europe (Belgium, Finland, Germany, Poland, Lithuania), Asia, and Mexico. Post-hoc analyses were conducted using data from placebo recipients in European countries to calculate the rate of culture-confirmed influenza illness by season, age, and country.

Results: During the 2000-2001, 2001-2002, and 2002-2003 seasons, 507, 320, and 82 European children were followed. The incidence of culture-confirmed influenza illness was 12.6%, 30.6%, and 11.8%, and the dominant strains were A/H1N1, A/H3N2, and A/H3N2 & B, respectively. Rates were similar among children 6-23 and 24-47 months of age. In study 1, the cumulative 2-year incidence was similar by country (16.2%-25.3%). Rates were highest in the 2001-2002 season when A/H3N2 strains were dominant after absence in the previous season.

Conclusions: Over 3 influenza seasons, the incidence of influenza illness in European children aged < 4 years ranged from 13 to 31%, confirming a high burden of influenza in young children in Europe.

(Sponsored by MedImmune. LAIV is not approved outside of the United States.)

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IMMUNOGENICITY OF ONE DOSE OF AN INVESTIGATIONAL MENINGOCOCCAL TETRAVALENT TETANUS-TOXOID CONJUGATE (ACWY-TT) VACCINE IN 1-2 YEAR OLDS

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Background: Meningococcal disease is common in toddlers, but no multivalent conjugate vaccine is yet available for this age group. An investigational ACWY-TT conjugate vaccine developed by GSK was evaluated for its immunogenicity and reactogenicity after one dose in toddlers.

Methods: In this Phase IIb, open study (108658/NCT00427908), healthy toddlers of 1-< 2 years (N=304) were randomised 3:1 to receive one dose of ACWY-TT vaccine (5µg of each meningococcal polysaccharide conjugated to tetanus toxoid) or control vaccine (monovalent MenC-CRM). Serum bactericidal antibodies were assessed using baby rabbit complement source (rSBA, cut-off ≥1:8) before and 1 month post-vaccination. Reactogenicity was assessed for 4 days using diary cards.

Results: Postvaccination, MenACWY-TT was non-inferior to MenC-CRM in terms of percentage of subjects with rSBA-MenC titres≥1:8 (100% vs 98.5%). All ACWY-TT vaccinees reached rSBA titres ≥1:8 against serogroups A, W135 & Y, significantly above the background responses in MenC-CRM controls (< 74.2%).The percentage of subjects with a rSBA titre 1:128 and the GMTs were both significantly higher for all four serogroups in ACWY-TT compared to MenC-CRM vaccinated subjects. Both vaccines were well tolerated. The reactogenicity and safety profile of ACWY-TT was similar to MenC-CRM.

Conclusion: The ACWY-TT vaccine induced immune responses against all four serogroups in 100% of toddlers. A, C, W-135 and Y conjugate vaccines could expand coverage against devastating meningococcal diseases in toddlers 1-2 years of age.

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EFFICACY OF ROTATEQ® AGAINST ROTAVIRUS GASTROENTERITIS-ASSOCIATED HEALTHCARE RESOURCE UTILIZATION FOR UP TO 3.1 YEARS POSTVACCINATION IN FINLAND

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Background and aims: The Rotavirus Efficacy and Safety Trial (REST) enrolled 23,429 infants in Finland. In the Finnish Extension Study (FES), 20,736 of the Finnish infants were followed beyond the 1-year period in REST to evaluate the impact of vaccination with RotaTeq against rotavirus gastroenteritis (RVGE)-associated healthcare resource utilization (HCRU), defined as a hospitalization or emergency department (ED) visits, for up to 3.1 years postvaccination.

Methods: FES infants were contacted every 12 weeks to determine whether they had any RVGE-related HCRU. RVGE was defined as in REST; follow-up started 14 days after dose 3.

Results: In Finland, the number of RVGE-associated HCRU cases observed in REST was 320 (17 vaccine, 303 placebo); the FES captured 156 additional cases (11 vaccine, 145 placebo). FES showed that RotaTeq reduced RVGE-associated HCRU, regardless of rotavirus serotype, by 94% (95% confidence interval [CI]: 91,96) up to 3.1 years after vaccination, while in the Finnish cohort of REST, it was 95% (95 CI: 91,97) for up to 2 years after vaccination. In the Finnish population (REST+FES), the efficacy of RotaTeq against HCRU for RVGE by rotavirus serotypes was: G1 (95% [95% CI: 92,97]), G2 (67% [95% CI: < 0,76]), G3 (92% [95% CI: 44,100]), G4 (67% [95% CI: < 0,94]), and G9 (92% [95% CI: 49,100]).

Conclusion: In Finland, vaccination with RotaTeq continues to provide protection against RVGE up to 3.1 years postvaccination and supports the decision by the Finnish government to recommend routine rotavirus vaccination and introduction of universal vaccination with RotaTeq in 2009.

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THE DIFFICULTIES OF MASS IMMUNIZATION CAMPAIGN AGAINST MEASLES AND RUBELLA IN UKRAINE

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Background: Mass immunization campaign against measles and rubella started in Ukraine on May 2008. For immunization was used vaccine ZA30-X manufactured by Serum Institute of India Ltd. The immunization was stopped in two weeks because of death of 17 years boy from septic shock after a broad antivaccination campaign. The questions about safety of vaccine were aroused and discussed in the mass media. The negative relation to all vaccination programs enhanced in parents and health workers through the country. The investigation of postvaccinal health status of adolescents was performed in Cherkassy region.

Methods: The school children of 16-17 years old were examined for post-vaccinal reactions after vaccination by vaccine ZA30-X during May-June 2008 and answered a specific questionnaire.

Results: 798 school children participated in the survey: 474 immunized against measles and rubella and 324 non-immunized children. For medical help asked 4 vaccinated children: two had signs of upper respiratory infections, one diagnosed the acute cystitis and the last one - psychogenic reaction after vaccination. Pain from shots was not common and observed in 19,2% vaccinated children. There was no evidence in difference of clinical signs in vaccinated and not vaccinated adolescents: malaise (36,9% versus 35,1%), fever (22,5% and 24,0%), cough (29,7% and 28,1%), rhinitis (39,7% and 42,7%), headache (53,0% and 54,7%), myalgia (13,2% and 19,5%), eye pain (14,0 and 12,5%), stomach ache (13,4% and 14,0%), dizziness (19,6% and 14,6%), irritability (28,1% and 37,6%), sleepiness (32,5% and 34,6%). The different complains were related mostly to respiratory infections.

Conclusions: The vaccine ZA30-X against measles and rubella is safe. It is not necessary to do active monitoring of adolescents after vaccination. The trough information about vaccination should be spread in population to enhance the trust to vaccination programs.

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TRAINING OF NURSE, MIDWIFE AND MEDICAL STUDENTS IN VACCINOLOGY: BENCHMARKING EXERCISE IN EUROPE

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Background: Most health consumers consider the healthcare worker as their major source of information on immunisation and vaccine safety. Within the Vaccine Safety, Attitudes, Training and Communication (VACSATC) EU-project a specific work package is focusing on the possible improvements of the pre-service training.

Methods: Surveys to benchmark the pre-service training about knowledge, skills and competences towards immunisation were distributed to students and curriculum managers of medical schools, universities and nursing training institutions in the participating EU countries.

Results: Valid responses of 178 medical and paramedical students and 82 curricula managers were collected from 5 countries (Belgium, Bulgaria, Italy, Slovenia and Sweden). Although the response rate was low in most countries, consistent trends were observed. In most institutions training on vaccines and immunisation is disseminated over a wide range of courses over several academic years. Topics as immunology and vaccine preventable diseases are well covered during the pre-service training. Major gaps in knowledge and competences were identified towards vaccine safety, communication with parents, addressing anti-vaccine arguments and practical skills. 97% of the students confirmed that vaccination is an important medical act and 85% indicated they needed more training on immunization.

Conclusions: Immunisation is one of the corner stones of public health. Doctors, nurses and midwives, regardless if they are involved in immunisation or not, are an important source of information for the public and should be appropriately and timely trained for that role. Opportunities for improvement of the pre-service training were identified.

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COMMUNITY BASED BCG VACCINATION IN AUCKLAND, NEW ZEALAND

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Background: Tuberculosis remains an important health issue in New Zealand (population 4 million) with an average annual notification rate of 10 cases per 10,000.[1] Neonatal Bacillus Calmette-Guérin (BCG) vaccination is selectively offered free of charge to high risk infants in New Zealand.

Waitemata District Health Board (WDHB) services the north and west regions of Auckland. BCG vaccination is available to eligible babies born in the WDHB area in Outpatient Clinics after discharge from hospital.

Aim: To investigate neonatal BCG eligibility of babies born in the WDHB area and BCG vaccine uptake by infants born at Waitakere Hospital (West Auckland).

Methods: A database search of WDHB hospital births from 1/1/2006 -31/3/2006 was conducted using ethnicity to determine BCG eligibility. Vaccination records from community BCG clinics were checked to ascertain uptake and timing of vaccination delivery by one year of age.

Results: A total of 23% of the babies delivered in WDHB were eligible for BCG vaccination. Of the babies born at Waitakere Hospital (n=593), 34% were eligible for the BCG vaccine. Vaccine uptake of eligible babies was 46% by one year of age and only 46% did so before 6 months of age.

Conclusion: A large population of babies in WDHB are at risk of tuberculosis infection. Timely delivery of vaccination could be improved by education and offering BCG vaccination to eligible newborns in hospital prior to discharge.

Reference: *[1]Ministry of Health. Guidelines for Tuberculosis Control in New Zealand 2003. Wellington: Ministry of Health; Dec 2002. URL:http://www.moh.govt.nz/moh*.

P664

SAFETY AND IMMUNOGENICITY OF A 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ADMINISTERED TO OLDER INFANTS AND CHILDREN NAÏVE TO PREVIOUS VACCINATION

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Background: 7-valent pneumococcal conjugate vaccine (PCV7, Prevenar®, serotypes 4, 6B, 9V, 14, 18C, 19F, 23F) is effective against vaccine-serotype invasive pneumococcal disease in children. The 13-valent conjugate vaccine (PCV13) contains additional serotypes 1, 3, 5, 6A, 7F, and 19A, broadening coverage worldwide.

Objectives: Safety and immunogenicity of PCV13 in healthy older infants and children naïve to previous pneumococcal vaccination.

Methods: Subjects were vaccinated according to 3 catch-up schedules currently recommended for PCV7. Group 1: 2 doses of PCV13 at 7 to < 12 mo with a booster dose at 12-16 mo. Group 2: 2 doses at 12 to < 24 mo. Group 3: a single dose at ages 24 to < 72 mo. Antibody responses to PCV13 were measured 1 month after final dose. Adverse events, local and systemic reactions were assessed.

Results: Of 355 subjects enrolled, 352 completed the study. The median ages for the 3 groups were 8.0 mo, 17.5 mo, and 41.0 mo, respectively. The pneumococcal anticapsular IgG geometric mean concentrations (GMC) were comparable within each of the 13 serotypes for the 3 groups. Overall, GMCs ranged from 1.94 to 8.04 µg/mL for Group 1, 1.86 to 6.45 µg/mL for Group 2, and 1.42 to 6.03 µg/mL for Group 3. Adverse events, systemic and local reactions were similar in the 3 groups.

Conclusions: Immune responses to PCV13 were comparable within each serotype across all 3 age groups. The 3 catch-up schedules are appropriately immunogenic for the respective age groups, with acceptable tolerability and safety profiles.

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CONSENSUS ON PERTUSSIS BOOSTER VACCINATION IN EUROPE (C.O.P.E)

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Background: When introduced, infant immunisation against pertussis dramatically reduced the number of reported cases in children. Recently, pertussis has been increasingly recognised, particularly amongst adolescents and adults (peak incidence: 10-19 and 35-64 years), who transmit the disease to vulnerable infants. Many healthcare providers underestimate the impact of pertussis and do not consider adult vaccination.[1]

Methods: A panel of European experts recently discussed the need for pertussis booster vaccinations in adolescents and adults.

Results: The panel recommended that:

Adolescents (10-18 years) should receive a single dose of combined reduced-antigen-content-tetanus-diphtheria-acellular pertussis (dTpa) vaccine instead of dT, irrespective of a complete primary vaccination schedule.

Adolescents with a history of pertussis should receive dTpa according to routine recommendations.

Adults (≥19 years) should receive a single dTpa dose instead of Td for active booster vaccination if their last dT dose was ≥10 years earlier, irrespective of disease history.

The cocoon strategy (vaccinating close-contacts of newborns with dTpa) should continue until immunisation coverage in adults is sufficient for herd protection.

The need for improved surveillance with standardised biological diagnoses, health economic analyses and education to raise disease awareness and capitalise on the opportunities to administer booster vaccinations was emphasised.

Conclusions: Control of *B. pertussis* circulation is crucial and will require regular boosters for the whole population. As an initial step, practical recommendations for booster vaccination of adolescents and adults in Europe have been proposed. Implementation of these recommendations is likely to increase protection of the population as a whole.

[1]Hoffait M et al, ESPID 2009

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DELAYED ANTIBODY RESPONSE TO TICK-BORNE ENCEPHALITIS VIRUS VACCINATION IN CHILDREN AFTER THYMECTOMY

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Background: Thymectomy in early childhood due to open heart surgery leads to premature aging of the immune system (immunosenescence), which is characterized by a decrease of naive T cells in later life. The study was aimed to investigate whether children after thymectomy may show a poor antibody response to new antigens like vaccines.

Methods: Thus, 44 thymectomized and 56 non-thymectomized age-matched children were vaccinated with tick-borne encephalitis virus (TBEV) vaccine (FSME Immun Junior, Baxter, Vienna) following a three-dose regimen. IgG antibody levels were evaluated 4 weeks after each vaccine administration.

Results: Thymectomized children showed 2.2-fold lower TBEV IgG antibody levels after the second vaccination when compared to controls (p=0.03), but a normal response after the third vaccination.

Conclusion: Our results showed a delayed increase of TBEV IgG antibody levels after vaccination in thymectomized children. This may indicate alterations of the primary T cell immune response to new antigens but a normal memory function. Thus, it is mandatory to monitor the antibody response to new antigens and vaccinations as well as infection rates in thymectomized children to avoid long-term complications.

VIRAL INFECTIONS

P667

PATTERN OF ROTAVIRUS G/P GENOTYPE DISTRIBUTION IN TUNISIA FROM 1995 TO 2007

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Background: An epidemiological survey investigating the rotavirus infections in children was undertaken in Tunisia between January 1995 and December 2007.

Methods: A total of 2428 faecal specimens were screened by ELISA for the presence of group A rotavirus antigen. Rotavirus-positive samples were used for G and P typing by multiplex semi-nested reverse transcription-PCR.

Results: Rotavirus detection rate was 21% (N = 509 positive stool). G genotypes found were G1 (32.9%), G2 (23.7%), G3 (26.3%), G4 (7.3%), G8 (0.4%), and G9 (2.1%). Thirty four specimens (7.3%) had mixed G profiles. P genotypes detected were P[8] (54.9%), P[6] (11.2%), and P[4] (24.1%). Mixed P profiles were also detected (9.8%). Although the distribution of the annually detected genotypes was always changing, G1P[8] rotavirus strains were always predominating until 2004, but in 2005 the G3P[8] has emerged as the most predominant strains, than between 2006 and 2007 the most common combination circulating in Tunisia became G2P[4]. In this study the rate of mixed rotavirus infections has increased from 9% in the first ten years to 16% during the four last years. This higher rate has coincided with changes in the distribution of VP7 genotypes in the country.

The study demonstrated a decrease of incidence of G1P[8] and emergence of G3P[8] and G2P[4] as the most common genotypes in Tunisia between 2004-2007 with an a considerable increase of mixed infections. These data imply that the distribution of group A rotavirus genotypes circulating in Tunisia, changes over time.

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NOROVIRUS - THE SECOND MOST FREQUENT AGENT OF VIRAL ACUTE GASTROENTERITIS IN A PAEDIATRIC PORTUGUESE POPULATION

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Background and aims: Noroviruses (NoVs) constitute a genetically diverse group of viruses in the *Caliciviridae* family, and are recognized as an important cause of acute non-bacterial gastroenteritis worldwide. The aim of this study was to evaluate the causal agents of viral gastroenteritis and to estimate the prevalence of NoV infection in the paediatric population of a tertiary hospital in Portugal.

Methods: Faecal samples were collected between January 2008 and September 2008, from children less or equal to 16 years, attending emergency room or hospitalized with symptoms of acute gastroenteritis (AGE). The stool samples were investigated for the presence of NoVs, rotaviruses, enteroviruses, and adenoviruses using reverse transcription polymerase chain reaction (RT-PCR).

Results: A total of 207 stool samples from children between 1 month and 16 years (median 17 months) with symptoms of AGE were collected. During the study period, rotavirus was the most prevalent viral agent (18.8%), followed by NoVs (11.6%). Adenovirus and enterovirus were identified in 7.2% and 3.4%, respectively. Rotavirus was the most prevalent in all months, except on July, August and September, when NoVs was more frequent than rotavirus.

Conclusions: NoVs was the second most frequent agent causing viral AGE and it was the most prevalent in the summer months. Due to the absence of a national surveillance system for viral AGE, the role of NoVs and other viral pathogens in diarrhoeal disease remains underestimated, and further studies are needed.

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RISK OF HEPATITIS C INFECTION IN CHILDREN IN CONTACT WITH INDEX CASES

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Introduction: Hepatitis C virus (HCV) infection characterized by persistent viremia is a major cause of liver disease. Household contact as a route of infection has been reported. There is a paucity of data on risk behaviors associated with HCV transmission through nonsexual household contact, especially in children.

Methods and materials: A descriptive study was conducted to evaluate 82 family members under 19 years old who had contact with 41 index cases with hepatitis C in Zahedan, South-Eastern Iran. Data including hepatitis C virus antibody , sex, history of addiction, staying in jail, transfusion, intra-venous drug users, tattooing, unsafe sex, surgery, needle stick and hematologic disorders were registered. For patients who were confirmed for HCV infection, serum aminotransferases and HBS Ag were requested.

Results: From 82 children who where in contact with 41 index cases, 51 (62.2%) were male. The mean age of the children was 12.3 ±5.4 years old. The most common risk factors were history of transfusion 11 (13.4%), thalassemia 7 (8.5%), hemophilia 3 (3.7%) and tattooing 4 (4.9%). Eight patients were seropositive. Five of them had abnormal aminotransferase but none of them were HBS positive. The most common risk factors in seropositive children were history of transfusion and hematologic disorders.

Discussion: Children under 19 years old in contact with seropositive patients are at risk of infection in the family. The rate of infectivity is approximately 10%. Preventive measures such as genetic consultation before marriage and prevention of tattooing could reduce the rate of hepatitis C in children.

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ACUTE DISSEMINATED ENCEPHALOMYELITIS: CASE REPORT DUE TO HUMAN HERPESVIRUS-6 INFECTION

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Acute disseminated encephalomyelitis (ADEM) is an immune mediated demyelinating disease of the Central Nervous System, arising after infections or immunizations. The initial clinical presentation is not specific, but includes systemic and neurological symptoms. Magnetic resonance neuroimaging is the exam of choice.

A previously healthy 16 months old girl is admitted for acute loss of walking, refusal to feed and irritability, two weeks after a febrile illness. On neurological examination she was alternating periods of irritability and drowsiness, lack of spontaneous movements of the lower limbs with hypotonia and arreflexia, ataxia and urinary retention.

The cerebral spinal fluid (CSF) analysis showed pleocytosis, normal proteins and a positive polymerase chain reaction for Human Herpesvirus-6 (HHV-6). A T2-weighted magnetic resonance neuroimaging revealed a spinal cord focal lesion in D2-D3 and through D6 until the *conus medullaris,* compatible with the ADEM diagnosis.

She was treated with intravenous corticotherapy and immunoglobulins, with gradual improvement.

This is a clinical report of ADEM with a major spinal cord involvement, which requires a differential diagnosis with other acute flaccid paralysis.

The identification of HHV-6 in the CSF, in the context of a preceding viral infection, allows considering a causal relation between this virus and the ADEM.

By reporting this case the authors wish to highlight the possibility of neurological manifestations after a HHV-6 infection, rarely described in the literature.

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TREATMENT OF HEPATITIS C IN CHILDREN´S HOSPITAL - DAMASCUS UNIVERSITY

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Background and aim of the study: Cases of hepatitis C were more in recent years in the children´s hospital. This study was to determine the treatment of these cases.

Methods: Seventy five cases of hepatitis C were diagnosed by PCR in years 2003 and 2004 at the Children´ Hospital. All these cases were treated and surveyed for one year. AST, Gamma GT, PT, WBC, and HCV-RNA were done before treatment and 3, 6, 12 months after the beginning then 3 month after the end of treatment. Thirty tow patients were treated by Interferon of them 25 patients were of type I and 7 were of type IV, 45 patients were treated by Interferon and Ribavirin (2 of them were treated by Interferon then changed to this treatment), 30 patients were of type I and 15 were of type IV.

Results: In treatment with Interferon alone AST was normalized in 53%, Gamma GT in 62.5% and PT in all patients. Early Virologic Response (ETR) was 48% in type I and 28.6% in type IV. Sustained Virologic Response (SVR) was 36% in type I and 28.6% in type IV. In treatment with Interferon and Ribavirin AST was normalized in 80%, Gamma GT in 82.7% and PT in 97.8% of Patients. ETR was 76.6% in type I and 73.3% in type IV, SVR was 60% in type I and 53.4% in type IV.

Conclusions: Treatment by Interferon and Ribavirin was better than Interferon alone. Prognosis of type I was better than type IV.

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PREVALENCE, SEASONALITY, AND GENOTYPING OF ROTAVIRUS GROUP A ISOLATED FROM HOSPITALIZED JORDANIAN CHILDREN

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Aim: This study was carried out in the capital of Jordan (Amman) to determine the prevalence, seasonality and the circulating VP4 and VP7 genotypes of rotavirus group A. Also to determine the efficacy of the recently introduced Rotavirus vaccine, according to genotypes isolated.

Methods: A total of 698 fecal specimens were collected from hospitalized children aged less than 5 years who were admitted to the Islamic Hospital between October 2006 and September 2007. An immunochromatographic kit (Operon, USA) was used. Electropherotypes were determined by electrophoresis in 0.9% agarose gel. Nested/Multiplex RT-PCR was carried out to determine the circulating VP4 and VP7 genotypes.

Results: Rotavirus was detected in 35.5% of patients.Infection peaked: in December 2006 and June 2007. The long electropherotype pattern was found to predominate (87.9%) over the short pattern (12.1%). The most common G/P combination was G1P[8] (57.26%). This combination comprised 58.7% (128/218) of the overall long electropherotypes, and 46.7% (14/30) of the overall short electropherotypes. Of all genotypes, G1P[4], G3P[8], G1P[11], G1P[6] and G1P[10] represented 2.82%, 0.81%, 0.81%, 0.4%, 0.4%, respectively.This is the first report for the G1P[11] genotype. Thirty percent of the isolates were partially typed, in which either G or P types were determined, and 7.26% of the isolates neither G nor P types could be determined.

Conclusion: The efficacy of monovalent vaccine containing G1P[8] genotype would be significantly high in Jordan. Continuous monitoring of genotypic changes among Jordanian isolates due to reassortment should be carried out for future assessment of the efficacy of this vaccine.

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MULTI-DRUG RESISTANT HERPES SIMPLEX VIRUS INFECTION IN UNDIAGNOSED IMMUNODEFICIENCY - A MANAGEMENT CHALLENGE

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Aims: To describe an unusual case of severe multi-drug resistant herpes simplex virus infection in a child with undiagnosed immunodeficiency.

Results: A 12 month old girl of middle-eastern origin born to consanguineous parents was admitted to paediatric intensive care unit (PICU). She had a history of recurrent chest infections and otitis media since 4 months of age. At 11 months of age, she developed severe herpes simplex virus type 1 infection. She required intensive care for secondary streptococcal pneumonia and septic shock. She was treated with aciclovir and antibiotics in the Middle -East and subsequently transferred to PICU in London. She had extensive herpetic lesions involving the face, cornea, neck, chest and possibly gut mucosa, with detectable viral DNA in blood as secondary Pseudomonas infection. The herpetic lesions resulted in nasal and laryngeal stenosis which compromised the airway and lungs. She underwent tracheostomy and required prolonged ventilation. Serial anti-viral susceptibility tests showed acquired resistance to aciclovir, and subsequently also to foscarnet. She was managed with prolonged anti-viral dual therapy using various combinations of intravenous aciclovir, foscarnet and cidofovir, and finally with oral brivudin and trifluridine eye drops. Despite extensive investigations, other than a low level of IgM, the underlying cause of immunodeficiency was not elucidated. She is awaiting bone marrow transplantation in an attempt to correct the immunodeficiency.

Conclusions: Prolonged antiviral therapy in immunodeficient patients could lead to emergence of multi-drug resistance. This is a major challenge in the context of undiagnosed immunodeficiency.

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SURVEILLANCE OF ACUTE FLACCID PARALYSIS(AFP) IN ORAN(ALGERIA) IN 2008

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The national program of eradication of poliomyelitis in Algeria was established in 1993 and redynamized in 1997.The evaluation has made a number of insuffisiences concerning surveillance.

Aim: To describe epidemiological characteristics of acute flaccid paralysis in Oran.

Methodology: Retrospective study of cases of AFP fellowed during 2008.

Clinical and virological data were studied.

Results: Two girls were fellowed for AFP.

They were immunized against poliomyelitis.

The notifications were done in the 7 days after onset of AFP.

Two stools were sent to the loratory in good conditions.

The virological results were received in 28 days after onset of AFP.

Virological data:no polioviruses were isolated.

Conclusion: Poliomyelitis has been eradicated in Algeria and no polioviruses have been identified.

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ENTEROVIRAL INFECTION OF A CARDIAC PROSTHETIC DEVICE

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Introduction: Patients with Congenital Heart Disease are at risk for developing infective endocarditis (IE), especially on foreign material. As 5 to 7% of the IE episodes remain culture negative, identification of the causative pathogen may represent a challenge.

Case report: A 4 month-old trisomic boy with operated congenital atrioventricular septal defect presented 3 episodes of dehiscence of his interventricular prosthetic patch, attributed to IE. Clinical presentation was remarkable with heart failure, but neither fever, nor inflammatory syndrome. Operative and histopathological findings confirmed the diagnosis of IE but all blood cultures remained sterile. Extensive microbiological, serological, molecular, and anatomopathological workup failed to evidence any clue of bacterial or fungal etiology. However, a Coxsackie B2 virus (identification confirmed by sequence determination) was cultured from the excised patch. The virus was also recovered from nasopharynx and stools, indicating a disseminated infection. As no specific treatment of Enterovirus is currently available, high doses of intravenous immunoglobulins were administered. After a prolonged critical period, the evolution has been satisfactory.

Conclusions: Although Enteroviruses are known agents of myocarditis in children, isolated viral IE was only described in animal models. So far, the part played by viruses in IE with persistently sterile blood cultures is unknown. This case is the first description of an IE with a demonstrated viral etiology. We suggest that viral etiology should be ruled out in cases of culture negative IE.

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VARICELLA: DISEASE´S IMPACT AND SOCIAL DISPARITIES IN VACCINATION COVERAGE IN SCHOOLCHILDREN FROM CURITIBA, BRAZIL, 2008

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Background and aims: In Brazil, the varicella vaccine is only available in the public system for risk groups. The aim of this study was to review the impact of the disease and the main reasons for not immunize children attended in private schools.

Methods: In 2008, parents of 415 children attending the first year of elementary schools from Curitiba city were interviewed to collect data about the children, family income, varicella disease and vaccine coverage and the reasons for not receiving the vaccine.

Results: 34% of the children had positive antecedents to varicella (median, 3 years); from these, 56% required medical assistance, 75% missed school (average, 9 days) and 9% developed complications (CI95%:4-14%). In 26% of the cases, the mother was absent from work (average, 6 days). Eleven children developed the disease after receiving the vaccine (84% effectiveness). The vaccine coverage was 39% (CI95%:29-48) and varied with income (median US$1,900) from 10% (CI95%: 3-17%) in low income families (< US $2,000) till 66% (CI95%: 56-75) for children with income family > US$ 8,000. The cost of the vaccine was the main reason for not immunize children of low income families, and lack of information about varicella vaccine benefits in the other group. Only 24% of the vaccinated children received the vaccine at 12 months.

Conclusions: Varicella causes significant morbidity and social impact. Public vaccination could reduce disparities in varicella coverage and inequities in healthy care.

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RAPID INFLUENZA TEST IN YOUNG FEBRILE INFANTS FOR THE IDENTIFICATION OF LOW RISK PATIENTS

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Background: Management of young infants with fever without known source (FWS) is often aggressive. Febrile infants with confirmed viral infection are at lower risk for serious bacterial infections (SBI).

Objective: To assess if the use of a rapid Influenza test (RIT) in infants less than 3 months with FWS can help to identify low risk patients.

Patients and methods: A prospective study was performed during 5 influenza seasons in the Emergency Department of two Spanish hospitals including infants less than 3 months with FWS. RIT and blood culture (BC) were always performed.

Results: 381 infants were included, RIT was positive in 113 (29.7%).

The prevalence of SBI was significantly lower in patients in the positive RIT group (3/113; 2.65%; CI 95%: 5.5-7.6 vs 47/268; 17.5%; CI 95%: 13.2-22.6. p< 0.001).

No patient in the positive RIT group had a positive BC vs 8 in the negative, 3.07%, CI 95% 2.09-4.05.

Of 299 UC obtained, 32 (10.7%) had urinary tract infection (UTI). The prevalence of UTI was lower in the positive RIT group (4.17%, CI 95%: 0.9-11.7, vs 12.78%, CI 95%:8.7-17.8).

CSF was cultured in 110 (28.9%), 97 in the negative group. CSF culture was positive in 5, all of them had a negative RIT.

Conclusion: The use of RIT in young infants with FWS during influenza seasons can help to identify those with a lower risk to have a SBI. Approachment to febrile infants with a positive RIT may be more conservative and routine BC may be no longer necessary.

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ISOLATED CYTOMEGALOVIRUS MENINGITIS IN AN HEALTHY 10 MONTHS-OLD BOY PRESENTING AS UNEXPLAINED FEVER

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Cytomegalovirus(CMV) causes serious diseases in immunocompromised patients and in neonates. Beyond the postnatal period in healthy children, CMV mostly gives a mononucleosis-like, self-limited infection and is rarely causing serious systemic manifestations.

Clinical case: A ten months old Romanian healthy child presented with a prolonged fever (> 39°C) for more than two months. Extensive infectious, immune or hemato-oncologic work-up was negative, with no response to antibiotics nor to a short steroid course. Biochemical investigations showed marked inflammatory syndrome and lymphocytic aseptic meningitis (cerebrospinal fluid: white blood cells 214/µl, lymphocytes 75%, neutrophils 16%, glucose 35mg/dl, protein 142mg/dl, lactic acid 3.3 mmol/L). Bacterial cultures, including tuberculosis were negative. CMV PCR was positive in blood and in the cerebral spinal fluid. PCR was negative for tuberculosis. Nuclear magnetic resonance of the brain showed marked thickening of the meningies. The child had no sign of congenital CMV infection and no immune deficiency. Under intravenous Gancyclovir (5 mg/kg every 12 hours) the child's condition progressively improved with disappearance of fever eighteen days after treatment onset and normalization of cerebrospinal fluid. After 28 days, ganciclovir was switched to oral valgancyclovir (20 mg/kg/day) for a planned period of two months. The child has fully recovered, with psychomotor catch-up.

We conclude that isolated CMV meningitis can occur in immunocompetent children, presenting as isolated fever and inflammation. Anti-viral treatment with gancyclovir was successful.

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EPIDEMIOLOGIC, VIROLOGIC AND CLINICAL INVESTIGATION OF COMPLICATED ENTEROVIRUS 71 INFECTIONS IN SOUTHERN VIETNAM

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Background and aims: Enterovirus 71 (EV71) may cause severe and fatal neurological complications in children. This study was to investigate the epidemiologic, virologic and clinical characteristics of complicated EV71 infection in southern Vietnam during 2007 to 2008.

Methods: Patients with hand, foot, mouth disease/ herpangina pulse either brainstem encephalitis, autonomic system dysregulation or pulmonary edema admitted to Children's Hospital No.1 in Ho Chi Minh City, Vietnam were enrolled. The demographic characteristics, hospital course and outcome were analyzed. Throat and stool swabs were collected for viral isolation. Nucleotide sequencing was performed of positive culture of EV71.

Results: Totally 73 children were enrolled to have severe EV71 infection. The peak age-specific incidence was in children 1-2 years. The mean fever duration before admission was 4 days. Fever (100%), skin rash (94.5%) and myoclonic jerk (86.3%) were noted frequently. The disease rapidly progressed into severe neurological complications within 12-24 hours. The mortality rate was 13.7% (10/73). Among severe patients, brainstem encephalitis was the major complication (97%). Acute flaccid paralysis was also observed in 12% of patients. EV71 was identified in 42 patients (57.5%). Phylogentic analysis of all the EV71 isolates belonged to subgenotype C5 which emerged and became the predominant strain since 2005.

Conclusions: EV71 infection has emerged as an important infectious disease in southern Vietnam. Our findings suggest that children under 3 years had high risk of complicated EV71 infection and may deteriorate rapidly. Brainstem encephalitis was the major neurological complication. Continuous surveillance and vaccine development are warranted to prevent severe complications.

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INFLUENZA RAPID TESTS (IRT) FOR CHILDREN IN PRIMARY CARE IMPROVES THE MANAGEMENT OF INFLUENZA

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Background: Previous studies showed that clinical diagnosis of influenza based on symptoms lacks of accuracy in children. The aim of this study is to evaluate the impact of IRT in the management of influenza like illnesses in children in primary care.

Methods: During the 2007-2008 influenza season, an observational prospective, multicenter study was carried out in France. Clearview influenza A&B tests® were used directly from nasal swabs.

Results: In a 22 weeks period, 565 pediatricians and general practitioners included 13660 children (mean age, 4.6 years) with clinical symptoms suggesting influenza. Among them 45.6% had positive IRT. For 71.6% of patients, onset of symptoms was < 48h. High risk children according to French recommendations for influenza vaccine represented 5.5% and among them 31.1% were vaccinated. Inaugural acute otitis media and/or pneumonia were diagnosed for 12.1% of children. In 25.8% of cases, an antiviral was prescribed for children with positive IRT and was associated with high risk patient (OR =1.5 CI:[1.1;1.9]), positive IRT (OR=40.7 CI:[31.1;53.3]) and duration of symptoms (OR>1). Antibiotic was prescribed in 22.8% of cases for children with negative IRT and associated with high risk patient (OR=1.7 CI:[1.3;2.3]), vaccinated patients (OR=1.9 CI:[1.2;2.8]), inaugural infection (OR =102.5 CI:[85.4;123.1]) and negatively associated with positive IRT (OR=0.3 CI:[0.2;0.3])

Conclusion: Even at the peak of influenza activity, positive IRT did not reach more than 50%, that underlines the uncertain clinical diagnosis. Moreover, even in vaccinated patients, IRT can be positive. More targeted influenza management with antivirals and antibiotics occurs when IRT results are available.

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HAND-FOOT-MOUTH DISEASE OUTBREAK IN ROMANIAN CHILDREN

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Background: Hand-foot-mouth disease (HFMD) produced by enteroviridae, generates mouth sores and blistering on hands and feet. Seasonal epidemics were documented.

Aim of study: To describe the impact on a tertiary hospital, during the 2008 HFMD-outbreak in Bucharest.

Methods: Retrospective case series analysis of ER-patients.

Including criteria - presence of complete triad of hand-foot-mouth syndrome.

Results: 67 children, 39 male patients are analyzed. Mean age 2.34 years (extremes 8mo - 5.5y). 42 admitted and 25 treated as outpatients in ER. Clinical picture of complete HFM was associated with fever in 65, severe dehydration in 32, meningismus in 7 and seizures in 5 children. Another 87, presenting only mouth sores and fever, were excluded.

Lab results: important electrolyte imbalance, metabolic acidosis, leucocytosis with differential evocative for viral infection were documented. 7 LP's documented normal CSF aspects. Abnormal EEG-pattern was present in 4 children. Mean hospital length-of-stay was 3.4days (10h -9days).

Discussion: 7HFMD were diagnosed between 1 Jun-31 Aug 2007 (of 6099 ER-patients). In 2008: 10-fold increase in the same period of time (67 of 7118 ER-patients). Probably some of the 87 herpangina patients were incomplete HFMD.

Case-presentation for residents increased awareness about HFMD and empiric antibiotic treatment was not initiated as often, in 2008 (14% vs 71% in 2007).

Conclusions:

1. In 2008 was documented an outbreak of HFMD in Bucharest, with a 10-fold increase in presented patients in ER.
2. Frequence 9.41/1000 ER patients.
3. Severe cases were 16.4%.
4. Recognition of HFMD can be increased by educational strategies.

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SEVERE HEPATITIS A IN FRENCH CHILDREN - 11 YEARS ANALYSIS AND POSSIBLE IMPLICATIONS OF VACCINATION

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Background and aim: Severe hepatitis A could have a major impact on French children and families' quality of life and generates important financial burden.

The aim of study: To evaluate clinical and evolutive aspects of severe disease and correlate these findings with possible benefits of hepatitis A vaccination.

Methods: Retrospective study of children presenting during eleven years in Kremlin-Bicêtre Hospital (January 1997 - December 2007).

Inclusion criteria - confirmation of severe hepatitis by anti-HAV IgM antibody titration.

Results: 71 children, 43 boys were included. Mean age 8.3 years - extremes 2.2-14 years. 58 were inpatients. Average hospital-length stay: 12.5 days (1 - 128 days).

Risk-factors analysis: 51 developed disease after traveling in endemic areas, 11 after having contact with another documented patient. Seasonal distribution: 56% were admitted during Sept-Nov period.

Clinical picture was dominated by jaundice (98%), abdominal pain (96%), vomiting (79%). Lab results documented severe disease (mean values: ALT 2992 UI, AST 2947 UI, bilirubin 171 µmol/L, PT 60.8%).

Course: 7 patients had fulminant hepatitis, 5 required hepatic transplantation (HT), one 2, another 3HT. One patient died.

Estimated direct-cost was 2.3 million euros. This represents immunization cost for 150,000 children.

Conclusions:

1. Hepatitis A can produce fulminant disease, with huge costs.
2. Most patients developed disease after traveling in endemic areas.
3. Only 10% of families were informed about hepatitis A immunization.
4. Immunization could be a cost-effective option and advocacy measures should focus on education and co-funding for a greater hepatitis A vaccination rate.

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HUMAN BOCAVIRUS INFECTION IN BELGIAN CHILDREN WITH ACUTE RESPIRATORY TRACT DISEASE

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Background: Acute respiratory tract infections are a leading cause of hospitalisation in young children. Human bocavirus (hBoV) is a newly described parvovirus, recently detected in the respiratory tract of children, but only few reports provide data proving the link between hBoV and respiratory tract disease.

Methods: In order to determine the importance of hBoV as a cause of respiratory tract infections among children admitted to the hospital, 284 children younger than 5 years and admitted to our hospital for respiratory tract infection were prospectively included from November 2006 till October 2007, after written permission of the parents. Records from the patients were analysed for demographic data and clinical symptoms. Nasal swaps were taken and processed by using Polymerase Chain Reaction (PCR) techniques for viral diagnosis.

Results: Respiratory viruses were detected in 143 children. Respiratory syncytial virus (RSV) was detected in 79 (27.8%) of the children, adenovirus in 41 (14.4%), parainfluenza type 1, 2 and 3 in respectively 6 (2.1%), 4 (1.4%) and 7 swaps (2.5%). hBoV was found in only 8 samples (2,8%) and human Metapneumovirus (hMPV) was detected in 17 specimen (5,9%). Co-infection with another virus was observed in 4 (50%) of the hBoV-positive children. Cough and fever were the most common symptoms in all patients.

Conclusions: Our data suggest that 50% of acute respiratory illnesses in young hospital-admitted children are of viral origin. Clinical symptoms of hBoV infection are similar to those of RSV infection, but the prevalence is much lower and co-infection with another virus is frequent.

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DETECTION OF ENTEROVIRUS IN THE CEREBROSPINAL FLUID OF CHILDREN WITH MENINGITIS

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Background and aims: Enteroviruses (EV) are an important cause of central nervous system (CNS) infection in childhood, ranging from meningitis to meningo-encephalitis. EV CNS infections can be diagnosed with culture or polymerase chain reaction (PCR) of cerebrospinal fluid (CSF). This study aimed to describe the rate of detection of viral pathogene in CSF of Dutch children with EV meningitis.

Methods: Clinical data of children aged 0-16 years with clinical EV meningitis and in whom CSF was available for analyses, in 2 major Dutch general hospitals together with a drainage area of > 500.000 individuals between 2003 and 2008 were analysed retrospectively.

Results: A total of 149 children had EV infection. In 49 (86%) of 57 children with documented meningitis an EV was isolated from the CSF. Children with EV meningitis (median age=36 days, range 0-11.6 years) were younger than the total group with EV infection (median age=128 days, range 0-14.8 years). Of the 49 children with isolated EV in CSF, 25 (51%) did not have any pleocytosis (elevated WBC in CSF). Children without pleocytosis were significantly younger than those with pleocytosis (median age 3.9 vs 25.1 months; $p < 0.05$), had significantly lower blood leukocyte counts and higher blood C-reactive protein (CRP) levels ($p < 0.05$). There was however no difference in duration of symptoms.

Conclusions: EV meningitis without pleocytosis is more often seen in younger children. The clinical relevance of this observation is not known. However, this finding may reflect a difference in immune maturity between the age groups.

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ENTEROVIRUS IS AN IMPORTANT CAUSE OF CENTRAL NERVOUS SYSTEM INFECTION IN DUTCH CHILDREN

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Background and aims: Enteroviruses (EV) are an important cause of childhood infection, with different clinical spectra, from gastroenteritis to meningo-encephalitis. EV is diagnosed with culture or polymerase chain reaction (PCR). EV infection is not registered nationwide in the Netherlands. This study describes the clinical features of EV infection in Dutch children.

Methods: Epidemiological study, involving children 0-16 years who visited two major general hospitals, between 2003 and 2008, and diagnosed with EV infection (positive PCR or culture).

Results: Hundred-and forty-nine children had an EV infection, median age of 4.3 months (range 0-14.8 years). Eighty-seven (58%) were male.

The most frequent presenting symptoms were fever in 113 (76%), diarrhea in 69 (46%) and irritability in 61 (41%).

Fifty-seven children (38%) had meningitis, 51 gastro-enteritis and 41 other organ involvement; respiratory infection (n=8), Bornholm (n=5), lymfadenitis mesenterica (n=2), acute disseminated encephalomyelitis (n=1), encephalitis (n=1), myeloradiculitis (n=1), cardiomyopathy (n=1), coxitis fugax (n=1). Seventeen had fever of unknown origin and in 4 no specific organ involvement.

Hospital admission was necessary in 121 children. The median duration of admission was 4 days (1-57 days). Viral culture (n=241) was more frequent performed than PCR (n=88). In 17 children with a positive PCR but a negative culture, the diagnosis would have been missed if PCR was not performed.

Conclusions: This study confirms that fever is the most frequent symptom of EV infection in childhood. It shows importance of EV as cause of meningitis in Dutch children and the need for a nationwide registration and follow-up.

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CLINICAL-LABORATORY FINDINGS AND PROGNOSIS OF GANCILOVIR-TREATED INFANTS WITH CYTOMEGALOVIRUS INFECTION: A SINGLE CENTER EXPERIENCE

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Introduction: Although, treatment of CMV infection is indicated in immunocompromised patients, there are no established guidelines or the effect of ganciclovir therapy in infancy.

Patients: 25 patients with CMV infection (infants with systemic clinical findings and positive anti CMV-IgM, low avidity and increased CMV viral load) and which have been treated with ganciclovir were evaluated.

Results: Median age was 4 months (10 day-12 months) and mean first complaint date was 2.1±0.4 months. Clinical findings were: 84% fever, 36% seizures, 68% of respiratory system findings, 84% malnutrition, 52% gastrointestinal system findings (4 infants with cholestasis), 28% splenomegaly, 12% ocular findings, 32% CNS findings. Two of these infants were admitted to our clinic with adrenal failure associated with CMV infection. Impaired liver function test were observed 92% of these patients and 84% of anemia, 16% thrombocytopenia. One infant have secondary hemophagocytosis associated with CMV infection. All patients were treated with intravenous ganciclovir 10 mg/kg/day for 9 to 21 days. No adverse events associated with ganciclovir therapy were reported. CMV antigenemia were negative after ganciclovir therapy in 18 infants and were considerably low in 3 children without clinical symptoms. During follow-up period among 21 survived infants, 6 infants have various degrees hearing impairment. We could not demonstrate risk factors or clinical findings associated with mortality or hearing loss in ganciclovir-treated infants with CMV infection.

Conclusion: Ganciclovir might be used a treatment choice of symptomatic infants with CMV infection. For the determination of risk factors associated with mortality and morbidity, further large studies needed.

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CHARACTERISTIC OF SPLEENOMEGALY IN MONONUCLEOSIS INEFCTIOUS

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Background and aim: Mononucleosis infectious (MI) is generalized lymphoproliferative disorder mostly coused by Epstein Barr virus (EBV).Fever, angina and lymphadenopathy together with splenomegaly are the most common symptoms.

The Aim of study was to analize frequency and characteristic of splenomegaly in patients with acute MI

Methods: In this prospective study we evaluated 50 children aged from 3-18 years hospitalized in Infectious Disease Clinic with acute IM infection from 2007 year.The diagnosis of acute MI was werrified with standard ELISA test (positive IgM antibody against EBV). We used standard clinical, laboratory and additional analyses. Abdominal ultrasond examination was done in 2, 3, 4, 6, 8 week of illness onset, and additional when necessery.

Results: All patients had fever, angina and lymphadenopathy. Spelnomegaly was founded in 40 patients (80%), and it resolved to normal range between 3-4 weeks. In one case, splenomegaly mainteined for 3 months. Ten patients among all had mild trombocytopenia as a result of spleen secvestration and it resolved to normal range.

Conclusion: Splenomegaly is frequent clinical finding in MI, and it usually rersolvs to normal range between 3-4 week Mild trombocytopenia can be foundded and is usually transitory.

Keywords: Spleomegaly, IM, EBV, ultrasond.

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DETECTION OF PARVOVIRUS B-19 INFECTION IN SAUDI CHILDREN WITH SICKLE CELL DISEASE

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Objective: To detect parvovirus B-19 DNA together with its antibodies in the sera of Saudi children with Sickle cell disease.

Study design: This is a prospective, observational study included fifty children with Sickle cell disease. Patients' sera were compared with those of thirty healthy children regarding presence of parvovirus B-19 IgG and IgM as well as detection of its DNA by PCR technique.

Results: There were statistically significant differences in the prevalence of Parvovirus B-19 IgM, IgG and PCR among patients when compared with controls ($P = 0.006$, 0.001 and < 0.001 respectively). Acute Parvovirus B-19 infection detected by positive IgM and PCR was found 44% of the patients while chronic Parvovirus B-19 infection detected by positive IgG and PCR was detected in 24% of the patients. Anemia was worse in children with acute than in chronic than in old Parvovirus B-19 infection.

Conclusions: Parvovirus B-19 infection is detected in high rates among Saudi children with Sickle cell disease and it may result in severe anemia. So, Parvovirus B-19 must be suspected and screened for in such group of patients. More studies for quantification of the virus will be more useful for diagnosis and staging of infection.

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PARENTAL-COLLECTED NASAL SWABS AS A VALID METHOD FOR INFLUENZA VIRUSES DETECTION IN CHILDREN

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Background and aims: Parental collection of nasal swabs could be an easy method to monitor epidemiology of respiratory infections and to evaluate viral transmission and vaccine efficacy. The objective of this study was to calculate sensitivity values for the detection of influenza viruses in children by using parental-collected nasal swabs.

Methods: Children who presented to the emergency room with symptoms of influenza-like illness were enrolled, and paired nasal specimens were collected. Parents were asked to collect the specimen from the right nostril using a middle turbinate flocked swab (Copan, Italy) and a trained pediatrician had to collect the specimen from the left nostril using a pernasal flocked swab (Copan, Italy). The two swabs were performed in opposite nostrils in randomized order. Real-time polymerase chain reaction for the detection of influenza A and B viruses was performed. Patient discomfort was evaluated by a visual discomfort scale (1-5).

Results: Paired nasal swab specimens were collected during 90 illnesses, with a least one virus detected in 18 (20.0%) patients (15 influenza B, 2 influenza A, one influenza A+B). Viral detection rate was 94.4% with parental collection and 83.3% with pediatrician's collection, with no significant difference in sensitivity between the two methods. The degree of discomfort was 1.99 for parental collection and 3.76 for pediatrician's collection ($p < 0.05$).

Conclusions: Parental-collected nasal swabs are a less invasive diagnostic respiratory specimen with adequate sensitivity and better tolerability in comparison with pediatrician-collected swabs. These results encourage the use of parental-collected nasal swabs in large-scale community studies.

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SPONTANEOUS CLEARANCE OF HEPATITIS C VIRUS IN VERTICAL INFECTED CHILDREN

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Chronic hepatitis C virus (HCV) infection is one of the leading causes for end-stage liver disease in industrialized countries. However, in contrast to the well-known clinical course of hepatitis C infection in adults, little information on the natural history of hepatitis C in infants and toddlers is available. In general, age is considered an important factor in longterm-development of HCV-infection, since a higher age is associated with more rapid and progressive disease.

In our patient cohort, we observed spontaneous clearance of HCV in two boys and one girl, at the age of 3 to 4 years. None of the infected patients showed clinical signs of liver disease. Two of the infected children showed high ALT and/or AST values during the first two years of age. Subsequently, liver function tests (LFTs) remained in the normal range.

Spontaneous clearance in vertically infected HCV-positive children has been documented in several studies. Our observation provides additional information on a potent inflammatory response preceding viral clearance. Given the disadvantageous side-effect profile of interferon, high LFTs in the absence of clinical signs in HCV-infected small children do not justify therapy, since hepatic inflammation might be associated with a high rate of viral clearance. Larger case-based studies are necessary to further clarify the clinical outcome of congenital HCV infection and facilitate the decision making process for or against combinational therapy.

P691

NEONATAL HERPES ENCEPHALITIS: LOW INCIDENCE BUT HIGH MORBIDITY

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Herpes simplex virus (HSV) is the leading cause of severe sporadic encephalitis at all age. In neonates, signs and symptoms of illness typically appear between first and second week of life. They are limited to poor feeding or lethargy. Fever and seizures are common.

HSV PCR is the diagnostic test of choice. It's sensitive and highly specific. False-negative results are reported especially in neonates and young infants. Repeat essay should be performed. EEG and MRI can highly contribute to diagnosis.

When clinical features, moreover EEG and MRI findings, strongly suggests diagnosis, acyclovir should be initiated empirically. Indeed, sequelae are frequent. Potential deficits can be intellectual, motor, psychiatric, epileptic, visual or auditory in nature.

A 15-day-old boy is admitted into hospital for lethargy and moderate fever. Clinical and biological findings on admission are reassuring. Antimicrobial prophylaxis is started.

Soon after, focal right-sided seizures appear. EEG shows left-sided discharges. Anticonvulsant therapy is started and acyclovir is given empirically.

HSV PCR on cerebrospinal fluid is reported negative. But, MRI findings are significant for focal areas in temporal cortex and both thalami. Acyclovir is continued, though, because some results are characteristic. A second lumbar punction is performed. HSV PCR and viral culture are reported positive. Acyclovir is maintained to complete a 21-day course.

Neonatal herpes encephalitis is rare but potentially severe. Diagnosis should be foreseen in infants with compatible clinical presentation. Empirical antiviral therapy should be initiated, as it is crucial to a good outcome. Repeat sample for HSV PCR should be considered.

P692

EVALUATION OF THE UTILITY OF AN INFLUENZA RAPID TEST IN CHILDREN WITH A RESPIRATORY INFECTION DURING AN INFLUENZA SEASON

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Introduction: Influenza infection is highly epidemic in winter having similar clinical symptoms to other respiratory infections. We used a rapid influenza test (RIT) to evaluate its usefulness in the management of children with suspected respiratory infection.

Methods: Children with positive RIT belonged to a cohort prospectively studied in an Emergency Department between December 2006 and March 2007 during an influenza season, were compared with children with an influenza infection diagnosed by nasopharyngeal culture in whom the viral results was initially unknown. The following parameters were analyzed: family contacts, clinical symptoms, laboratory analyses, rate of admission and use of antibiotics.

Results: Thirty children with positive RIT (PRIT) were compared with 21 children with delayed diagnosis obtained by viral culture with influenza infection. There were no differences in age, gender, past medical history and family contacts. In addition, we did not find differences in respiratory symptoms, maximum temperature and length of fever. When we analyzed the laboratory results we did not observed any differences in the number of leukocytes, percentage of neutrophils or CRP. PRIT group had a significant fewer rate of admissions (10% vs 52%), including those infants with fever without a source (0% vs 24%), and less antibiotic use (10% vs 38%) compared with the group with delayed diagnosis of influenza. There were no patients with invasive bacterial infection in either group.

Conclusions: RIT contributes to a better use of resources, decreasing hospital admissions and reducing the use of antibiotics in infants with respiratory infections during influenza season.

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EVALUATION OF AN INFLUENZA RAPID TEST FOR DECISION MAKING AND A BETTER USE OF HEALTH RESOURCES

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Background and aims: Influenza infection is highly epidemic in winter due to its high infectivity. There are rapid diagnostic methods that allow us to make clinical decisions and optimize resources.

Methods: Prospective study between December 2006 to March 2007, during an influenza season. We performed a rapid influenza test (RIT) in children with suspected influenza infection, including infants with fever without source. Children with negative RIT (NRIT) were included in a standard protocol of fever without source, whereas children with a positive RIT (PRIT) underwent blood and urine cultures, with 24 hours follow-up without antibiotic treatment.

Results: Seventy children received RIT, with 30 having a positive result and 40 negative result. There were no differences in age, gender, past medical history and family contact. No differences were found in frequency of respiratory symptoms and fever before ED evaluation. Patients with PRIT had less leucocytosis (and left shift deviation) than NRIT, without differences in CRP values. NRIT had fewer admission rates than PRIT (10% vs 50%), and less unnecessary admissions (7% vs 34%). There was also a trend towards less antibiotic use in PRIT compared to NRIT with a positive viral culture. All bacterial infections (n = 4) occurred in NRIT. The positive predictive value of this RIT during a flu season of 96,6%.

Conclusions: RIT offers a reliable diagnosis in patients with suspected influenza infection during the flu season, allowing an ambulatory follow-up of children with this infection, reducing antibiotic use and permitting a more optimized use of health resources.

P694

IMPACT OF RAPID INFLUENZA TEST (RIT) DURING INFLUENZA EPIDEMIC IN FEBRILE CHILDREN LESS THAN 6-YEARS OLD

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Aim: To determine the impact of the RIT on prescription of additional tests, antibiotics and oseltamivir, and the influence of oseltamivir on the fever, clinical evolution, and parents' day work stoppage.

Methods: Prospective study in the pediatric emergency department of Nice University Hospital from 01/21 to 2008/03/28 including children from 1 month to 6 years old with fever ≥ 38.5°C for less than 48 hours. Virologic research on naso-pharyngeal aspiration was: immunofluorescence, cell culture and RIT Clearview®. Oseltamivir was proposed to the children older than 1 year with positive RIT. Evolution at 7 days and one month was evaluated by phone contact.

Results: 138 children were included. The RIT was positive in 36.2% (n=50): 60% influenza A, 38% influenza B, 2% A and B. Sensibility, specificity, positive predictive value and negative predictive value of the RIT were 90.5%, 90.3%, 80.9% and 95.5% respectively. Clinical signs significantly correlated to influenza were: cough, rhinitis, nausea or vomiting. In the RIT positive group, there was no significantly less additional tests (38% vs 46.6%), significantly less antibiotic prescription at day 7 for patients treated by oseltamivir, but no difference for hospitalization. There was no more complication at day 7 or at 1 month with or without treatment by oseltamivir. There wasn't any difference in parents' day work stoppage neither patients with or without influenza nor in those treated or not with oseltamivir.

Conclusion: During influenza epidemic, RIT allow reduction of antibiotic prescription at day 7 for patients with positive RIT and treated by oseltamivir.

P695

HORIZONTAL TRANSMISSION OF HEPATITIS B THROUGH SALIVA?

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Background and aims: For children, the most common route of acquiring hepatitis B virus (HBV) infection is vertical from mother to child. Horizontal transmission plays another important role in childhood, but the mechanism of viral spread among children remains to be elucidated. Saliva containing HBV has previously been demonstrated to be infectious to chimpanzees. The aim of this study was to investigate the quantitative relationship between HBV in saliva and blood in children.

Methods: Between May 2006 and December 2008, paired plasma and saliva samples were collected from 46 children aged 0-16 years with chronic hepatitis B. HBV DNA in plasma and saliva was quantitatively measured by TaqMan PCR. Statistical analyses were performed using mixed models with random intercepts in R-2.8.1.

Results: There was a high correlation between HBV DNA in plasma and saliva. In the HBeAg positive children, mean log HBV DNA was 17.6 in plasma and 10.4 in saliva. In the HBeAg negative children, mean log HBV DNA was 6.8 in plasma. HBV DNA was undetectable in saliva of HBeAg negative children (lower detection limit 50 IU/ml). There was a 38 times higher level of HBV DNA in saliva of the HBeAg positive children than in plasma of the HBeAg negative children. (HBV $DNA_{HBeAgPositiveSaliva}$ =33,860 IU/ml; HBV $DNA_{HBeAgNegativePlasma}$=880 IU/ml).

Conclusion: We found a high level of HBV DNA in saliva of HBeAg positive children. Our results suggest that saliva could be an important vehicle for horizontal transmission of HBV among children.

P696

ESTIMATING IMPACT ON QUALITY OF LIFE DUE TO ROTAVIRUS AND NON-ROTAVIRUS GASTROENTERITIS IN DANISH FAMILIES

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Background and aims: In industrialized countries, gastroenteritis (GE) remains a significant economic burden and may have a major impact on the quality of life (QoL) of affected families. Rotavirus (RV) is the leading cause of GE in children under five years of age. The aim of this study was to estimate the impact on QoL of children with RVGE and non-RVGE and their respective parents.

Methods: Children under five years of age with acute GE were recruited during 2008 at Department of Paediatrics, Hvidovre Hospital and at General Practitioners (GP) clinics nationwide. The parent was, at time of enrolment, asked to rate the present health status with respect to themselves and their child according to the visual analogue scale (VAS) and the EuroQol questionnaire (EQ-5D).

Results: In total 147 children were included. Rotavirus was detected in 43% and 36% of hospital cases and GP cases, respectively**.** For children with RVGE and non-RVGE mean EQ-5D score was 0,41 and 0,50, respectively; the mean VAS score was 47 for both groups. For parents of children with RVGE and non-RVGE mean EQ-5D score were 0,76 for both groups; the mean VAS score was 77 and 74, respectively.

Conclusions: No satisfactory generic QoL instrument has been developed for use in children below the age of five years. However, for a contemporary adult population the mean EQ-5D and VAS score are 0,93 and 87, respectively. We conclude that both RVGE and non-RVGE severely impact the QoL of not only the child but also the parents.

P697

MUTATION FREQUENCY OF NS5A IN PATIENTS VERTICALLY TRANSFECTED WITH HCV GENOTYPE 1 PREDICTS SVR TO PEGINTERFERON-ALFA-2B AND RIBAVIRIN COMBINATION THERAPY

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Viral genome analyses performed in adult HCV-patients to elucidate the mechanisms of viral resistance to treatment yielded very inconsistent results and are not transferable to the paediatric patients who are, in contrast to adults, often infected vertically during a state of high immune tolerance.

We analysed the mutational frequency in the PKR-binding domain (PKR-BD) of NS5A as well as PePHD of E2 protein before and after treatment with peginterferon-alfa-2b and ribavirin in children chronically infected with HCV genotype 1 - either vertically (n=15) or horizontally (n=11). After cDNA-synthesis the amino acid sequence of NS5A (2209-2274) and E2 (618-681) was determined by sequencing of the PCR-amplified HCV genome.

Concerning the PKR-BD a significant higher number of mutations could be observed in vertically compared to horizontally infected patients (2.14 vs 1.24, p-value=0.03). This difference was exclusively based on the increased number of mutations in responders versus non-responders in vertically infected patients (2.95 vs 1.33; p-value=0.02). While all patients with at least 4 mutations (n=3) did respond to therapy, no other predictive parameters could be identified. In the PePHD no differences could be observed between either of these groups.

These findings support the idea that the mode and therewith the time of infection in terms of immune tolerance is an important factor that has to be taken into consideration in children. Also the number of mutations in the PKR-BD might be a useful parameter in vertically infected children to predict virological response. However, the relative small number of subjects limits final considerations.

P698

HERPES SIMPLEX ENCEPHALITIS IN CHILDREN - CASE REPORT

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Background and aims: Herpes simplex encephalitis remains a serious illness with significant risks of morbidity and death.

Methods: We present 2 cases hospitalized in our pediatric clinic with herpes simplex encephalitis. The diagnostic was established: clinical symptoms (fever, headache, seizures, vomiting) and laboratory findings (serologic evaluation of blood and CRF analysis). Also, the diagnostic was completed with imagining studies (MRI) and electroencephalography (EEG).The patients were treated with acyclovir (10 mg/kg iv q8h) and symptomatic medications.

Results: All patients require admission to intensive care unit. First case is a boy, one age old, hospitalized for fever, vomiting, seizures, and lethargy. Diagnostic serologic and CRF was positive. IRM imagining was suggestive for herpes simplex encephalitis. EEG show focal abnormalities, such as spike and slow sharp-wave patterns. The evolution was favorable with etiologic, pathogenic, depletive and symptomatic treatment. Complications and sequelae: hydrocephaly, seizures and neurological deficits. The second child is a girl, two ages old, was admission in our clinic for: fever, irritability, tremor and paraplegia. Serological diagnostic was positive. IRM cervical spinal marrow showed: diffuse lesions of spinal marrow (C4 - T5). The treatment was etiologic, symptomatic and pathogenic. The evolution was favorable with complete recuperation of deficits in 3 months.

Conclusions: Herpes simplex encephalitis in children is a severe disease complicated with neurological squeals and death without specific treatment. Even with complete treatment the risk of mortality is increase. The reason for which, we recommend the use of treatment with acyclovir in acute encephalitis when this etiology is even suspected.

P699

NOSOCOMIAL GASTROENTERITIS IN PEDIATRIC BURN UNIT

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Background and aim: Rotaviruses are recognized as an important cause of nosocomial infection in infants and children. The incubation period is short (1 to 2 days). So this diagnosis is relatively easy as a nosocomial infection. We performed active surveillance of hospital outbreaks of gastroenteritis to determine incidence, microbiologic cause and effectiveness of control measures.

Methods: We active monitored in pediatric burn unit for hospital-associated gastroenteritis from January through December 2007 for one year. Nosocomial cases were defined as those cases in which rotavirus was shed beyond the third day after admission. To trace nosocomial transmission, we mapped the ward at the time of detection of rotavirus. Stool samples were obtained from 43 acute diarrheal children in burn unit. The main technique used was virus culture method.

Results: The median age was 1.25 age. And the mean of revealed periods were 8 days after admission in burn unit. Viruses were detected in 20 of 43 patients(47%). Rotaviruses were 17 cases(40%), noroviruses were 2 cases(5%) and astrovirus was 1 case. The mean admission periods were 20 days for burn care. The peak incidence were March and April.

Conclusions: We have detected nosocomial rotavirus infection rates of 40%. Nosocomial infections demonstrated transfer of infection within single rooms or wards. The principle for control of rotavirus is the institution of single room or cohort isolation with enteric precautions. We recommend that rigorous disinfection and hand washing are the key features of current infection control. Vaccines have been development.

P700

THE DEMOGRAPHIC PROFILE, PATTERN OF CLINICAL PRESENTATION AND THE OUTCOME IN A COHORT OF CHILDREN HOSPITALIZED WITH DENGUE INFECTION

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Background: Although children are the main group affected by dengue, little published data are available on the clinical profile of dengue infections in children and even fewer reports on children living in the Latin America and the Caribbean.

Objectives: To describe the demographic profile, pattern of clinical presentation and the outcome in a cohort of children hospitalized with dengue infection.

Methods: This study was carried out at the Queen Elizabeth Hospital in Barbados. Children admitted with sign and symptoms suggestive of Dengue infection or where diagnosis is elusive are routinely screened for dengue infection using the ELISA test for the IgM antibody in the serum. All the children with confirmed dengue infection who were admitted to the pediatric ward of this hospital during 2007 were included in this study.

Results: A total of 115 children (male 53%, female 47%) were studied during one year period. Dengue infection accounted for 6% of all admissions in children. 52% had secondary dengue infection while 48% had primary dengue infection. Seventeen (15%) had dengue hemorrhagic fever (DHF), 35 (30%) had dengue fever (DF) with typically described clinical features where as 44 (38%) had dengue fever with atypical features (ADF). There were 2 deaths and both were neonates with DHF.

Conclusions: Severe illness in children necessitating hospitalization can result either from primary or secondary dengue infection. Atypical manifestation can occur in over one third of cases. Beyond the neonatal period dengue infection in children carry very low mortality.

P701

RAPID DETECTION OF ENTEROVIRAL RNA IN CEREBROSPINAL FLUIDS BY ONE STEP-SNRT-PCR IN PATIENTS WITH ASEPTIC MENINGITIS IN EGYPT

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Background: Human entreroviruses are the most common cause of aseptic meningitis particularly among children. In Egypt, the role of enteroviruses associated meningitis, demographics and clinical presentations wasn´t investigated before.

Subjects: 68 aseptic meningitis patients (14 patients < 1 year, 21 patients from 1-5 years, 22 patients 6-10 years and 11 patients > 10 years.

Methods: Chemical (glucose, proteins), microbiological and molecular detection of enterovirus RNA using snRT-PCR in CSF specimens were investigated.

Results: Enteroviruses were detected in 31 of 68 (45.6%) of aseptic meningitis patients by sn RT-PCR assay. Among the different age groups, Enteroviruses were detected in (50%) of patients < 1y, in (43%) of patients between 1-5 years, in (50%) of patients 6-10y, and in (36%) of patients > 10 years. There was no significant difference among males and females with enteroviral meningitis with male to female ratio 1.4:1. Peak of enteroviral meningitis was in July (25.8%). The significant clinical presentations among patients with enteroviral meningitis were lethargy, skin rash and diarrhea (p= 0.017, 0.004, and 0.000 respectively). Headache and photophobia were observed with increasing age (p= 0.001 and 0.04 respectively). Disturbed level of consciousness, skin rash, diarrhea and neurological sequelle were found to be more frequent among younger ages ≤5 years (p = 0.048, 0.033, 0.020 and 0.048 respectively). Children with positive enterovirus PCR had shorter hospital stay as compared to patients with negative PCR (p=0.000).

Conclusions: snRT-PCR allows rapid diagnosis and management of enteroviral meningitis by reducing hospital stay and antibiotic use.

P702

ALTERATIONS OF THE TUMOR SUPPRESSOR PROTEIN P16INK4A EXPRESSION IN BASAL AND SUPERIOR EPITHELIAL CELLS IN HPV-ASSOCIATED LARYNGEAL PAPILLOMAS

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Background: Human papillomavirus is able to affect oral epithelial cells resulting in respiratory papillomatosis. After integration of HPV genome into cellular chromosomes viral protein E7 interacting with retinoblastoma protein (pRb) may induce cell malignant transformation. p16INK4A is an element of the pRb pathway and can cause G1 cell cycle arrest.

The aim of the work was to investigate the expression of p16INK4A in the basal and superior epithelial cells of laryngeal papillomas associated with HPV types 6/11 infection.

Methods: 36 randomly selected biopsy specimens from laryngeal papillomas were immunostained with the commercially available antibodies against p16INK4A according to the standard protocol. The type of virus was detected by PCR.

Results: P16INK4A + cells were found in the basal layer of epithelium of the majority of patients. The quantity of clusters of p16INK4A+ cells correlated with the number of operations. The evaluation of staining intensity in the basal as well as in the upper layers of epithelium showed more apparent binding of anti-p16INK4A antibodies to the cells in the biopsy samples of patients who underwent 3 and more operations and suffered from the disease more than 3 years ($p \leq 0.01$). Eleven out of 15 biopsy samples with high intensity of p16INK4A staining of cell clusters were found positive for HPV 11, one - for both HPV types 6 and 11 and only 3 - for HPV type 6.

Thus, our study has shown that immunohistochemical staining for p16INK4A is a promising marker for prognosis of respiratory papillomatosis severity.

P703

CHICKENPOX ACUTE DISSEMINATED ENCEPHALOMYELITIS IN CHILDHOOD

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Background: Acute disseminated encephalomyelitis represents almost 1/3 of post infectious encephalitis often appears during viral diseases (chicken pox, measles, and mumps). Is generally accepted that acute disseminated encephalomyelitis is due to immune response induced by viral illness either by the stimulation of B lymphocytes by a viral agent inducing a polyclonal antibody secretion.

Material and methods: We present the case of 6 years old patient, being in the 14-th day of chicken pox eruption admitted in our clinic with a rapid and obvious deterioration of neurological status (seizures, coma).The diagnosis was based on clinical manifestation, EEG, cerebral MRI and CSF examination.

Results: delta and theta waves on EEG; Cerebral MRI shows many areas of increased signal on T2-weighted, sequences which could also suggest multiple sclerosis in other circumstances. He was treated with methylprednisolon pulse therapy (30 mg/kgc/day for 3 days), antiviral therapy (acyclovir) for 10 days and anticonvulsinants. With slow recovery.

Conclusions: This was the first case of ADEM associated with chickenpox hospitalized in our clinic, among the other cases of viral diseases with ADEM (mumps, measles, and influenza). The diagnosis of ADEM was concluding only after the long term evolution (clinical and imagistic). Cerebral and spinal MRI was normal after 6 months and after 1 year. The patient didn't present other neurological signs during follow-up.

P704

THE ANTIROTAVIRUS COW DRY ORAL LACTOIMMUNOGLOBULIN (ACDOL) APPLICATION FOR THE TREATMENT AND THE PREVENTION ROTAVIRUS GASTROENTERITIS (RGE)

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The aim of our research was to study efficiency of ACDOL application, developed by The Epidemiology and Microbiology State-Research-Institute for prevention and treatment of patients with the RVI.

Materials and methods: ACDOL consists from the basic lactoimmunoglobulin fraction (secretory Ig G (94 %)). The action main mechanism is creation of passive immunity in gut. The clinical research was performed at the Pediatric-Infectious diseases Hospital at 2007-8. The diagnosis RVI was confirmed by detection of a rotavirus-antigen in stools by EIA.

Results: We observed 84 children with RGE at the age of 6 - 60 months ($p>0.05$). All of them had basic therapy (rehydratation, diet). ACDOL was prescribed at 1 doze (500 mg) 3 times a day till 5 days. This treatment was started at 1-11 day from the beginning of disease Me 2.0 (1.0-3.0). The control group was 53 patients. They had basic therapy only. After the ACDOL treatment the improvement of the condition was observed (restoration of appetite ($p< 0.05$), normalization of diarrhea ($p< 0.05$), discontinuance of vomiting ($p< 0.05$); normalization of temperature ($p< 0.05$). The disappearance of RA from stools was observed in 35 from 84 cases (41.7%) of patients with ACDOL and 18 (33.9%) patients with RVI ($p< 0.5$) from controls. 14 patients from close contacts with other RVI patients had preventive treatment with ACDOL. At 13 of these children rotavirus-antigenes in stools were not found for all supervision time.

Conclusion: ACDOL may be useful in RVI prevention in close contacts and for treatment children with RGE.

P705

HUMAN METAPNEUMONOVIRUS IN NON-HOSPITALISED GREEK INFANTS WITH ACUTE RESPIRATORY TRACT INFECTION

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Background and aims: Human metapneumovirus (hMPV)**,** a recently discovered respiratory pathogen classified in the *Paramyxoviridae* family, has been associated with acute respiratory tract infections (ARTI) in infants and children. The aim of our study was to determine the frequency and clinical features of hMPV infection in non-hospitalised Greek infants with ARTI.

Methods: Routine nasal swabs were obtained from 63 infants, younger than 12 months of age, who attended with ARTI the Paediatric Emergency Department of 'Penteli' Children's Hospital in Athens during the winter season 2007-2008. All specimens were tested for the presence of hMPV antigens using a validated enzyme-linked immunoassay.

Results: The mean age of the infants of our sample was 4 months (range 20 days to 12 months). hMPV was detected in 6 (9.5%) children, 3 boys and 3 girls. In five children, hMPV was identified as a unique viral pathogen, while only one child was co-infected with hMPV and respiratory syncytial virus (RSV). Bronchiolitis was diagnosed in all hMPV-positive cases. The month with the highest number of hMPV detections was January. All hMPV-positive children were discharged home without requiring hospitalization or supplemental oxygen therapy.

Conclusions: Our results provide further evidence of the importance of hMPV as a pathogen associated with community-acquired ARTI in Greek infants, with a tendency to have mild clinical course.

P706

LOW PREVALENCE OF INVASIVE BATERIAL INFECTION IN FEBRILE INFANTS UNDER 3 MONTHS WITH ENTEROVIRUS INFECTION

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Objectives: To determine the prevalence of enterovirus (EV) infection in infants under 3 months with fever without source (FWS) and to describe their clinical and analytical characteristics and the prevalence of invasive bacterial infection (IBI).

Methods: A prospective study (August 2006 - August 2008) was performed including infants under 90 days admitted with FWS. EV PCR in blood and/or CSF samples was determined and also blood and urine culture were collected in all patients.

Results: Of 381 patients, EV infection was diagnosed in 64 (16.8%, 95% CI: 13.2-20.9%). Of those, 24 (37.5%) were diagnosed during summer months. EV infection was more common in infants under one month (65.4% vs. 34.4% ($p < 0.01$)). EV positive patients had lower white blood cell count (10,296 vs. 13,038 ($p < 0.001$)). Only 2 EV positive patients had a procalcitonin value greater than 2 ng / mL. In 46 cases (71.9%) IV antibiotic was administered. One case of invasive bacterial infection (IBI) was detected in an EV positive patient (S. agalactiae urinary tract infection) while 83 were detected in negative ones (prevalences difference: 24.6%, 95% IC: 18.9% - 30.3%, $p < 0.001$). No complications were seen in EV infected patients.

Conclusions: EV infected children have significantly lower incidence of IBI than negative ones. The EV PCR determination in blood and/or CSF in the management of infants under 90 days with FWS would allow a more conservative approach, especially in infants under 30 days in spring and summer months.

P707

SELECTIVE ROTAVIRUS VACCINE PRESSURE AGAINST P[8] STRAINS, AND POSSIBLE IMMUNE EVASION BY SPECIFIC G1 LINEAGES AFTER VACCINE INTRODUCTION IN BELGIUM

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Background: Recently, two rotavirus vaccines were introduced in Belgium. A dramatic decline in rotavirus incidence in our hospital based surveillance prompted us to collect 628 rotavirus positive stool samples isolated throughout Belgium in the 2007-2008 rotavirus season.

Methods: Samples were G- and P-genotyped by sequencing.

Results: Although a further decline of hospitalisations due to rotavirus infection was observed, the proportion of G1P[8] strains remained comparable to the previous season. The most frequently observed genotypes were G2P[4] (40,9%), G1P[8] (31,8%), G9P[8] (13,1%), G4P[8] (8,1%), G3P[8] (3,8%) and G12P[8] (1,3%), as well as one rare G6P[14] strain. Vaccination status was known for 283 patients of which 29,0% were vaccinated. Vaccinated infants were more likely to become infected with G2P[4] strains than unvaccinated infants (OR=2,05 (1,21-3,46)). Infections caused by P[8] strains were significantly less detected in vaccinated infants compared with unvaccinated infants (OR=0,49 (0,29-0,83)). However, infections with G1P[8] strains were not significantly reduced in vaccinated infants (OR=0.87 (0.50-1.54)). To further investigate this discrepancy, we analysed if antigenic differences between distinct G1P[8] lineages could lead to certain G1P[8] strains able to evade vaccine induced immune responses. This analysis revealed several amino acid substitutions in known antigenic sites, between circulating G1P[8] strains and vaccine strains in both genes.

Conclusion: The high incidence of G2P[4] strains can be attributed both to the vaccine introduction and/or to natural genotype fluctuations. Although no statistical association was found between vaccination status and G1P[8] lineages, we demonstrate a biologically plausible model for lineage selection as a result of vaccine pressure.

P708

REPORT OF 38 CASES OF HERPES ZOSTER (HZ) FOLLOWED UP IN A UNIVERSITY HOSPITAL IN RIO DE JANEIRO, BRAZIL

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Background and aims: The varicella zoster virus causes two distinct diseases: varicella (chickenpox), more common in children, and herpes zoster (HZ), more common in elderly. We aimed to describe predisposing causes, clinical presentations and outcome of HZ in children under care in a University Hospital.

Methods: A series of cases of HZ observed between September/1996 and December/2007, using the review of clinical data and a questionnaire. We defined situations of emotional stress: death in the family, parental illness, situation of conflict, and death of esteem animals. Patients with known HIV infection were excluded. Requested laboratory exams were: complete blood count, erythrocyte sedimentation rate, HIV serology.

Results: Thirty-eight children from 1 month to 13 years were followed. The most affected dermatomes were: lower limbs (37%), thoracic (32%) and trigeminal (16%). Twenty-one children (55.2%) related pain during the illness and three after resolution. Twenty (52.6%) related pruritus. Previous history of uncomplicated varicella was observed in 22 children (58%). Use of corticoid in immunosuppressant dosage was present in two children and stressing situations in 11 children. Two children had HIV infection diagnostic made. Treatment with acyclovir in 20 children (52.6%) was indicated. Clinical improvement occurred within 5 to 48 days. Complications occurred in 8 (21%) children: secondary infection (6), keloid (1), ocular sequels (1).

Conclusion: Although a benign disease, HZ can be associated with diseases that compromise the immunity and these must routinely be investigated. Stress situations as triggering factor of HZ must also be considered.

P709

GENOMIC DIVERSITY OF GROUP A ROTAVIRUS STRAINS AND IN-VITRO AFFECT OF VARIOUS COMPOUNDS ON ROTAVIRUS INFECTIVITY

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Background and aims: Group A rotavirus is the major cause of severe diarrhoea and dehydration in children worldwide. In developing countries, rotavirus diarrhoea is a major cause of childhood death and is responsible for half a million deaths per year. The objectives of the study were to provide information of the circulating rotavirus genotypes and access the *in-vitro* affect of various compounds on rotavirus infectivity.

Methods: In a Cross-sectional study, the prevalence of rotavirus G-P types were studied in 412 patients, aged 1-36 months, admitted with acute watery diarrhoea. Embryonic rhesus monkey kidney (MA-104) cells were used for rotavirus cultivation and assessment of various compounds on its infectivity. Cellular morphologic alterations for each compound were observed at varied concentrations. Inhibition of rotavirus infectivity in the presence of each compound was assessed by the reduction of virus titers using TCID50 determinations.

Results: Rotavirus was identified in 19.2% (79/412) cases using ELISA and PAGE. The genotypes identified were G1 (38.0%), G2 (15.2%), G3 (16.5%), G9 (10.9%) and G4 (5.1%) and mixed G type infections (10.1%). Effect of heparin, dalteparin and benzylGalNAc were negligible whereas heparinase, Tunicamycin, Zn^{++}, Ba++ and Mg^{++} were found to decrease the rotavirus infectivity.

Conclusions: A high degree of strain diversity of rotavirus G and P types were detected. Along with successful implementation of rotavirus vaccine other compounds that can play a role in its infectivity needs to be explored.

P710

MORPHOLOGICAL CHARACTERISTIC OF VIRAL HEPATITIS LETHAL CASES AT CHILDREN

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Background and aim: To study the pathomorphological changes of organs and tissues at children deceased from viral hepatitis (VH).

Methods: Pathomorphological research of organs and tissues was conducted at 13 children which died from VH. VHB was diagnosed in 21,3%, VHC - 7,7%, VHB+C - 7,7%, VH unspecified etiology - 38,4%, VH with liver cirrhosis - 21,3%.

Results: The first y.o. children die the most frequent (61,5%), giant cell hepatitis developed in them, the deep necrotic and dystrophic changes prevail in liver with activating pathogenic induced apoptosis, early chronization with development of considerable killing and fibrogenesis.

It is set, that at high activity of necrotic, dystrophic and sclerotic processes in liver at all children, the considerable pathomorphological changes emerges in other organs. In intestine, except for catarrhal inflammation, takes place phlegmogangrenous process; in lungs - atelectasis, vasculitis, congestion with widespread hemorrhages; in kidneys - glomerular collapse, dystrophy or necrosis of tubular epithelium; brain edema; thymus involution. These changes create unfavorable conditions for VH course and sometimes are the direct reason for death.

Conclusions:

1. Giant cell hepatitis can develop at the first y.o. children, the necrotic and dystrophic changes in liver are characterized by expressed high activity, on a background of which the signs of inflammatory process chronization appear early.

2. VH at children is multiple organ pathology. Outhepatic pathological processes in the internal organs create unfavorable conditions for VH course and can cause lethal outcome.

P711

HERPES ZOSTER IN INFANTS

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Background and aims: Herpes zoster (HZ) is disease caused by varicella- zoster virus due to the reactivation of latent virus lying dominant from previous disease caused by varicella. According to the possible way transmition of the virus, a history of chickenpox or contact with chickenpox during the pregnancy enables childs intrauterine exposure to the virus (varicella or herpes zoster) with further transfer of transplacental maternal antibodies that cen modifay clinical features of the disease into subclinic or mild and difficult to recognize. Reduced connatal immunity aids the manifestation of HZ disease as primary manifestation of the infection. We present a case of an infant with HZ.

Methods: The baby was male, 7 month old and his data were collected from the medical documentation.

Results: The boy was born spontaneously in a regular term, as a second child in the family. Actual disease had started with clear-fluid blistering and vesiculose herpetifoirm eruption on erythematous background on the left upper extremity and left part of the back, without febrillity and good general condition. The boy was exposed to chickenpox from another child. A diagnosis was made clinically. The infant was treated with antiviral agents, vitamins and topical antiseptics.

Conclusions: We conclude that clinical features of HZ among infants and small children are similar to that of adults, except for the milder appearance and rapid healing, rare complications and mild or absent subjective symptoms.

P712

EXPLORING THE IMPACT OF EXPOSURE TO PRIMARY VARICELLA IN CHILDREN ON VARICELLA-ZOSTER VIRUS IMMUNITY OF PARENTS

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Background and aims: Infection with varicella-zoster virus (VZV) initially causes primary varicella (chickenpox) and may reactivate - possibly due to waning immunity - at a later stage giving rise to herpes zoster (HZ). Epidemiological evidence indicates that the probability of herpes zoster is reduced after contact with primary varicella cases. However, immunological evidence to this effect is scarce, and in view of expected changes to European VZV vaccination policies, we further explored this hypothesis of exogenous boosting.

Methods: Blood samples were taken of parents (n= 24) whose children had clinical signs of primary varicella in the previous 1 to 9 days, with subsequent samples taken at 3 time points over a one year period. Controls consisted of subjects with similar demographic characteristics (G1, n=9) and recently unexposed subjects older than 50 years (G2, n=25). We analysed the antibody titers against VZV using linear mixed models taking the intra-individual correlation into account.

Results: We found no significant difference in humoral immunity between the control groups (G1, G2) and the group of exposed parents. Within both control groups we observed an overall interaction effect of age and gender. Women tended to have a higher antibody titer at a younger age which declined over time, whereas the men's lower antibody titer tended to remain constant.

Conclusions: Prospective follow-up of varicella-immune parents whose children had primary varicella at the start of follow-up showed no boosting effect on humoral immunity. Research focusing on cellular immunity is ongoing.

P713

CRANIAL CT FEATURES PROVIDE INSIGHTS INTO THE PATHOGENIC MECHANISMS FOR INFORMED MANAGEMENT DECISIONS IN CHILDHOOD NEW ONSET FEBRILE STATUS EPILEPTICUS

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Background/purpose: The management of Acute Status epilepticus challenges Intensivists. Its aetiology may not always be straight forward making definitive diagnosis imperative, infective aetiology especially from viruses have been implicated in some of these cases.Appropriate management is contingent on determining the exact aetiology. Acyclovir would be indicated in Herpes Simplex encephalitis /Steroids in Acute Disseminated encephalomyelitis.

CT will support a working diagnosis or could clarify an enigma.

Cerebral oedema is common. In appropriate settings Reyes Syndrome should be considered. A structured approach to its evaluation will be rewarding. A series of cases where this strategy was used to achieve plausible working diagnosis is described.

Imaging findings: Reviews of CTs, undertaken, evaluated, interpreted /reported in a standardized manner by Neurologist/Radiologist of 15 cases below 15 years, males 8, and females 7. Patients were encephalopathic. Cases with definite Cerebral Malarias, Bacterial meningitis, hypoglycaemic, chronic neuropathologies and remote symptomatic cryptogenic seizures were excluded.

Interventions: Anticonvulsants, supplemental oxygen, antibiotics, dexamethasone, mannitol, acyclovir, acetazolamide, appropriate fluid management.

Males 8, females 5.

Imaging features. normal 1, poor grey/white matter differentiation 9, decreased subarachnoid spaces 11, cisternal effacement 9.decreased ventricular diameter 7.

Conclusion/importance: CT features intimates that ADEM a parainfectious phenomenon could be implicated in most of these cases. CT offers a rapidly reproducible diagnostic guide in indeterminate new onset SE depicting radiologic features that may suggest plausible aetio pathogenic mechanisms, complementing non invasive modalities like TCD, MRS in supporting reconstructed ICP figures, directing progressions to more invasive definitive imaging modalities such as Interventricular foramen of Munro cathetheralization, subarachnoid bolt insertion offering treatment options/ directing research.

P714

CHEST ROENTGENGRAPHIC FEATURES IN PAEDIATRIC CLINICAL MEASLES, AND ITS IMPLICATIONS ON NOMENCLATURE, MANAGEMENT AND OUTCOME(MORBIDITY AND MORTALITY) IN THE TROPICS

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Background/purpose: The complication of measles with most significance is pneumonia in 80% of cases, causing 25% of deaths.

Anecdotally measles pneumonia is interstitial, bacterial pneumonia is a post measles phenomenon. Cultures/immunological tests may not always be rapidly achievable, routine antibiotic in measles uninfluenced progression to pneumonia, undertaking radiographs could offer an easily reproducible option for demonstrating features giving clues to the aetiology of a pneumonia based on recognized patterns.

Method/interventions: A prospective review of cases that presented during an outbreak in January-December 2000 of measles / post measles phenomena. Radiographs were undertaken, evaluated, interpreted, validated/reported in a standardized way.

Results: 107 cases , 47males/ 32 females, aged 3/4 to 15 years. Immunized 81, typical rashes 88 /desquamating rashes 21, cough 100, tachypnoea 45, wheeze 9, stridor 3, RD 36, fever 29, PEM 4, cyanosis 2, contact 24, AOM 1, encephalitis 3, death 1, anaemia 4, neutrophilia 16, lymphocytosis 12, Staphylococcal aureus 3/ Strep. Pneumonia 10, high ESR 7, TB 1, air bronchograms13, bilateral perihilar infiltrates 71, effusions 5, central opacities12, patchy opacities 7, diffuse opacities12, perihilar opacities 13, lobar opacities 2 , right apical opacity 1, normal features 34. In the post measles phenomena patchy/diffuse opacities, lobar consolidation/effusions were the principal associated features, in the active measles phenomena, bilateral perihilar infiltrates were predominantly featured. All the positive blood cultures were confined to the former group.

Interventions: Antipyretics, Vitamin A, oxygen/antibiotics.

Conclusion/importance: Radiographs complement other modalities in descriptive epidemiological studies, definition of unusual presentations & complications in clinical measles by offering a rapidly reliable clue to the probable aetiology of the pneumonia.

P715

PHYLOGENETIC ANALYSIS OF PREDOMINANT ENTEROVIRUS SEROTYPES IN MINSK REGION IN 2003-2007

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The aim of the study was to determine phylogenetic relationship and levels of genetic diversity among isolates of ECHO30, ECHO6 and Coxsackie B5 - prevalent serotypes of enterovirus in Minsk region in 2003-2007.

Between 2003 and 2007, 23 isolates of ECHO30, ECHO6 and CoxsackieB5 were obtained from patients with different forms of enteroviral infection. Fragments within VP1-gene were amplified and sequenced, nucleotide sequences were multiple aligned. A calculation of pairwise genetic distances and a phylogenetic reconstruction were carried out with MEGA 3.1. software.

The results showed a lack of genetic diversity in ECHO 30 viruses recovered from patients in 2003-2004. All of them belonged to the same genetic lineage and formed a common monophyletic claster in the dendrogram. This lineage emerged in 2003, during a large-scale outbreak of enteroviral infection, and continued circulation in 2004. Phylogenetic reconstruction of ECHO6 and Coxsackie B5 revealed a considerable genetic diversity of these serotypes. Viruses of ECHO6 formed 4 and Coxsackie B5 - 3 monophyletic clusters, reflecting an existence of various genetic lineages within serotypes. Simultaneous circulation of multiple lineages and prolonged circulation of the same genetic variant were registered for ECHO 6 but not Coxsackie B5. Viruses Coxsackie B5 showed the consecutive replacement of genetic lineages.

Despite considerable similarity of biological properties, different enterovirus serotypes display various molecular epidemiology patterns of infection and their elucidation provides an additional tool in epidemiologic surveillance.

P716

CARDIAC COMPLICATIONS OF INFECTIOUS MONONUCLEOSIS IN CHILDREN

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Background and aims: Cardiac complications have been rarely reported among children suffering from infectious mononucleosis (IM). The aim of the study was to describe the cardiac complications in IM patients and to correlate them with biochemical and immunological parameters, as well as with ultrasound findings.

Methods: Twenty-five children, 15 boys/10 girls, aged 1-11 years (median 4.48±2.6 years) suffering from IM, were studied. Cardiac evaluation comprised of electrocardiogram, echocardiogram, as well as CPK, CPK-MB and troponin levels. Transaminases, amylase, CD4+/CD8+ ratio measurement, ultrasound scanning of the spleen and viral investigation were carried out during the acute phase and 3-6 months thereafter.

Results: Electrocardiogram was normal in all patients. Echocardiography revealed mild pericardial effusion in 52% of patients, but none presented myocarditis. All children had spleen enlargement and normal amylase values. Ten out of the 21 children with EBV and 3/4 children with CMV infection presented pericardial effusion. Four out of these 13 patients also had markedly elevated liver enzymes (AST and ALT>100 IU/l, normal values < 48 and < 37 IU/l respectively), 11/13 had significant splenomegaly and 13/13 presented very low CD4+/CD8+ ratio (< 0.5). Repeated laboratory tests 3-6 months post-discharge detected mild pericardial effusion in 5/13 patients, along with mild splenomegaly in 3/5 and low CD4+/CD8+ ratio in 1/5.

Conclusions: Cardiac involvement consisting of a mild, asymptomatic and self-limiting pericardial effusion was found in 52% of children suffering from infectious mononucleosis, which persisted during follow-up in 38% of patients. Pericardial effusion demonstrated a statistically significant correlation solely with a low CD4+/CD8+ ratio ($p < 0.001$).

P717

CHILDREN UNDER SEVERE STRESS: IS THERE ANY EVIDENCE OF SUBCLINICAL REACTIVATION OF VZV?

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Background: Herpes zoster is caused by reactivation of latent varicella-zoster virus (VZV). Studies in astronauts during and after space flights showed that subclinical reactivation of VZV may occur as both VZV-DNA and infectious virus were detected in their saliva. This might be explained by their decreased cell-mediated immunity due to severe stress. Whether subclinical VZV reactivation may occur in other stressful situations has not been studied.

Aim: To examine whether children under severe stress might have subclinical reactivation of VZV. Furthermore, to investigate whether there is a difference between children post chickenpox and vaccination.

Methods: Children admitted in the ICU unit were included and stratified in three groups according to their VZV status; Group A: children post natural varicella, Group B: children vaccinated against varicella and Group C: children not exposed to VZV (controls). Whole blood and saliva samples were collected on days: 1, 5, 7, 10 post admission. Real time PCR for VZV DNA was carried out in whole blood and saliva.

Results: We recruited 19 patients 1.5-16 years old. Fourteen children had history of chickenpox confirmed by serology, 3 had been vaccinated while 2 children with no history of chickenpox or vaccination (confirmed by negative serology) served as controls. All samples contained adequate DNA (b-globin positive), however, VZV was not detected in any blood or saliva sample examined.

Conclusions: We were not able to detect any subclinical reactivation of VZV in children under severe stress. However, stress related reactivation may occur at a later time point in children.

P718

AFEBRILE SEIZURES IN CHILDREN WITH GASTROENTERITIS

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Background and aims: Afebrile seizures in children with gastroenteritis are a rare entity, usually related to rotaviral gastroenteritis and mostly described in Asia. Recent discoveries about viremia in rotaviral gastroenteritis support their potential for extraintestinal manifestations. Just a few cases of afebrile seizures in caliciviral gastroenteritis are described in the literature.

Methods: Out of 1066 records of children aged < 15 years with diagnosis of gastroenteritis hospitalized at our department from January 2008 to January 2009 we retrospectively reviewed those with concomitant diagnosis of afebrile seizures.

Results: 9 children, all < 5 years, were treated for afebrile seizures and gastroenteritis. Rotaviruses were found in 4 stool samples and noroviruses in 3. Except in one case convulsions were in all children repetitive tonic-clonic, one presented with status epilepticus. In 3 children anticonvulsants other than diazepam were needed to stop convulsions. Gastroenteritis in all children was accompanied by moderate dehydration, low CRP values, normal leukocyte counts and normal electrolytes. Lumbar puncture (done in 5 cases), CT scan (in 6 cases) and EEG (in 8 cases) were all normal except in one case where EEG showed suspicious epileptiform activity. In 3 cases of rotaviral gastroenteritis PCR for rotaviral RNA from cerebrospinal fluid was done and proved negative. All children had no consequences at discharge.

Conclusion: In our report afebrile seizures were related to rotaviral and unexpectedly also to noroviral gastroenteritis. More studies with wider diagnostic work-up are needed to better evaluate the etiology of seizures presenting in children with gastroenteritis.

P719

EVALUATION OF THE COMMON CAUSES OF MENINGO-ENCEPHALITIS AND TO QUANTIFY THE USE OF ACYCLOVIR: A TWO YEAR RETROSPECTIVE STUDY

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Background and aims: Early recognition and treatment of Meningo-encephalitis is important. Acyclovir is the drug of choice for HSV meningo-encephalitis, use being gaurded by its toxicity.

Methods:

• Retrospective Audit over a 2 yr period

• All paediatric admissions with initial diagnosis of meningitis or meningo-encephalitis

• Telephonic survey of paediatric tertiary care centres

Results: Meningo-encephalitis is **C**ommon in children less than 1 year, with no sex preference.

INVESTIGATION	POSITIVE	NEGATIVE
BLOOD CULTURE	6	12
CSF CULTURE	3	15
CSF PCR	10	8

The total number of patients was 18. All 6 positive blood cultures grew Meningococcus. Positive CSF PCR was divided as 6 Meningococcus, 3 Entero viruses and 1 Herpes.

AGE	DURATION OF IV USE (DAYS)	DIAGNOSIS
6 MONTHS	2	Meningococcal meningitis
7 MONTHS	2	VIRAL ILLNESS
11 YEARS	1	MIGRAINE
8 YEARS	14	Viral meningitis (Herpes)

Conclusions: Our study mirrors the worldwide quoted commonest causative agent for viral encephalitis as Enterovirus. No validated evidence or guidelines on the use of Acyclovir.

A telephonic survey of paediatric tertiary care centres showed a wide variability in practice. We recommend a lower threshold for the use of Acyclovir in patients < 1 year. **Viral meningitis:** British medical bulletin, 2005, Chadwick DR.

P720

CARDIAC TROPONIN-I AS A SCREENING TOOL FOR MYOCARDITIS IN CHILDREN HOSPITALISED FOR VIRAL INFECTION

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Background: Symptomatic myocarditis in children is a rare but serious disease with high mortality and morbidity. The incidence of myocarditis in children is uncertain because asymptomatic cases are not diagnosed. We hypothesised that screening all children hospitalised for an acute infection with troponin- I (TnI) would reveal myocarditis cases and performed a prospective screening study.

Methods: Between October 2005 and July 2008 a blood sample for TnI measurement was taken every time a sample for C-reactive protein measurement was drawn. The children were taken care as clinically indicated. If TnI value was above the screening limit (0.06 µg/l) electrocardiogram and cardiac ultrasound were performed. TnI measurements were repeated until at normal level.

Results: Altogether 1009 children were screened during the 33 months. TnI was above the screening limit (0.06 µg/l) in six children. None of them had any signs of myocarditis in Ecg or cardiac ultrasound. Five of those six children were younger than 30 days. All had a respiratory infection as a cause for hospitalisation, three caused by RSV. In four children, all younger than 30 days, TnI levels remained high (>0.37 µg/l) for two months but decreased after that to normal levels.

Conclusion: We screened 1009 indiscriminate children hospitalised for an acute infectious disease with TnI and found no cases consistent with any myocardial affision. The significance of the prolonged increase in TnI values in five neonates remains unclear. We conclude that the incidence of myocarditis is low and routine TnI testing for asymptomatic myocarditis is unnecessary.

P721

CONVENTIONAL VIRAL CULTURE VERSUS MOLECULAR AMPLIFICATION TECHNIQUES IN RESPIRATORY INFECTIONS IN BELGIAN PAEDIATRIC PATIENTS

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Background: Virus isolation in cell culture has long served as the "gold standard" for virus detection because of the ability to isolate and identify a wide range of viruses. Viral growth indicates the presence of an infectious, viable and replicating competent virus, a finding which is unattainable using other technologies such as antigen or nucleic acid detection. Unfortunately, cell culture requires several days to weeks, optimal transport conditions are crucial to prevent false negative results and the risk of missing viruses in mixed infections is prevalent.

Methods: Between 1/09/2007 and 31/08/2008, all respiratory samples from children with severe respiratory symptoms attending the emergency department of two university hospitals were examined by multiple real-time PCR assays. These results were compared with routine cell culture using 3 cell lines.

Results: Among the 750 children studied, 219 (29.2%) showed viral mono-infection by cell culture, whereas PCR techniques revealed a viral etiology in 348 patients, of whom 13.7% double infection, 1% triple infection and 1 sample was coinfected with 4 viruses. Contrary to culture methods, molecular techniques were able to discriminate between several viral subtypes; which may be of clinical importance.

Virus	hMPV	hBoca	Coronaviruses	Rhinoviruses	Adenoviruses	Parainfluenza-virusses	RSV	Influenza A	Influenza B
Cell culture +	0.33%	not cultivable	practically no growth	3.95%	5.27%	4.27%	9.36%	3.57%	2.49%
Real-time PCR +	2.60%	5.60%	Cor229E:0.92%; CorNL63:4.90%; CorOC43:2.50%	10.16%	8.22%	PIV1:1.76%; PIV2:0.83%; PIV3:3.21%, PIV4:2.23%	RSV A:7.43% RSV B:1.98%	7.30%	3.04%

Conclusion: Molecular amplification tests improve the sensitivity of diagnosis, especially for rhinoviruses and other difficult to culture viruses (hMPV, human coronaviruses, PIV4), and obligatory for those impossible to cultivate such as human bocavirus.

P722

PREVALENCE OF HUMAN METAPNEUMOVIRUS, BOCAVIRUS, CORONAVIRUSES AND VIRAL COINFECTION IN RESPIRATORY SAMPLES OF FEBRILE PAEDIATRIC PATIENTS IN BELGIUM

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Aim: To determine the prevalence of infection with hMPV, Coronaviruses 229E, NL63, OC43, bocavirus and of mixed viral infections in children with fever(> 38.5°C) and upper or lower respiratory tract infection; and to describe the clinical characteristics of these viral coinfections.

Material and methods: This is a prospective study conducted in 407 febrile infants (56% male) under 7 years of age admitted for 416 acute respiratory infectious episodes in two university hospitals between January and March 2008, for which an initial rapid virological screening for Influenza A/B, RSV and Adenovirus by immunochromatography didn't reveal a causal agent. The 341 nasopharyngeal aspirates, 36 nasopharyngeal flocked swabs and 39 tracheobroncheal aspirates underwent a direct immunofluoresceny for hMPV and cell culture; followed by nucleic acid extraction for the molecular research for 16 respiratory viruses by multiple in-house multiplex real-time PCR assays: adenovirus, bocavirus, influenza A & B, RSV A & B, hMPV, rhinoviruses, coronaviruses OC43, NL63 and 229E, parainfluenzaviruses 1-4 and enteroviruses.

Results: HMPV was found in 16 children (3.8%), coronaviruses NL63, OC43 and E229 in respectively 7.7%, 4.6% and 1.9% of samples, and bocavirus in 8.9% of samples. Overall, a viral etiology was determined in 268 specimens (64.4% of the samples), of which 67 presented viral coinfection.

Conclusion: Two-thirds of children suffered from a viral infection. 25% of them were coinfections with as main clinical symptom bronchopneumonia followed by wheezing. Still 35 adenoviruses, 62 influenzaviruses and 24 RSV were detected despite negative antigen detection pointing to the weak sensitivities of rapid antigen-tests.

P723

PRIMARY HERPES ZOSTER DURING CHILDHOOD AFTER PERINATAL EXPOSURE TO VARICELLA-ZOSTER VIRUS: A CASE SERIES

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Background and aims: Herpes Zoster (HZ), a painful vesicular dermatomal eruption, is the result of reactivation of the varicella-zoster virus (VZV) from infected sensory ganglia. Classically, it is considered and adult disease, in contrast to primary infection with VZV, chickenpox, which usually occurs mainly in children.

Methods: Retrospective case series.

Results: Ten cases (aged 5-60 months; 7 boys) are reported. Intrauterine exposure was documented in 3 patients, while postnatal exposure from siblings occurred in 4 children; time of exposure was unknown for the rest. Facial and lower limb dermatomes were affected in 4 and 6 cases, respectively; in the former, keratitis was always ruled out. Clinical features included: pruritus/irritability (10 patients), fever (5), and lymphadenopathy (2). Microbiological diagnoses was confirmed by means of Tzanck smear, high or rising VZV serologic titers, and/or VZV polymerase chain reaction technique. Concurrent bacterial infection of the herpetic lesions occurred in 6 patients. A 7 to 10 day regimen of acyclovir was used in most patients, with complete resolution in all cases. Residual scars in 3 children were the only sequelae. Immune status was found normal in 9 patients; vertically-transmitted HIV infection was already known in the tenth case. To date, no recurrence of HZ has been observed.

Conclusions: Our small series confirms that HZ can develop in young healthy children, its male predominance and the benign course in most cases. HZ should be included in the differential diagnoses of vesicular eruptions in pediatric patients.

P724

IDENTIFYING ONYCHOMADESIS ETIOLOGY'S IN CHILDREN

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Background and aims: An Onychomadesis outbreak started in Valencia City (Spain) on June 2008. Epidemic climb reach more than 400 cases. No previous references were founded in international medical papers.

Our aim is introducing a classic outbreak epidemiologic study showing the relation ship between HFMD and Onychomadesis.

Methods: A retrospective study was carrying out. 311 Onychomadesis cases were collected from care health services and 83 non affected individuals that were living with affected cases. 221 (71.06%) were documented, from 83 non affected individuals 77 (92.77%) accepted participating in the study. Eating habits, sweets consumption, animals and pets exposure, hygiene products and previous diseases were investigated. Stool and blood samples were collected from cases and exposed children. Dates were processed by SPSS+ for simple and stratified analysis.

Results: Only a previous diagnosis of HFMD was established as only one exposure factor with significance. Odds Ratio for those relation reach 12.62 (CI95%: 6.10-26.09; $p< 0.05$). Stratified analysis showed an O-R for any previous disease and HFMD of 4.94 ($p< 0.05$) and crude O-R for isolated factor HFMD of 17.85 (CI95%: 7.59-41.92; $p=0.001$). Qualitative analysis for Gig Enterovirus was 3 times more frequent among HMFD exposed ($p=0.028$). Molecular study identified Coxsackie virus in 34% affected of Onychomadesis in front of 14% of HFMD exposed.

Conclusions: Association measure and its accuracy and time sequence allow us to affirm that since April to June of 2008 an Onychomadesis outbreak took place in the city of Valencia consequence of an infection of CVA10 that caused FHMD.

P725

INFECTIOUS MONONUCLEOSIS IN AN HIV INFECTED GIRL AND RESPONSE TO VALACYCLOVIR

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There have been no reports of response of EBV to valacyclovir in HIV infected children. In our patient, cytopenias and fever responded to valacyclovir following which EBV VCA IgM antigen also became negative signaling latency of EBV in the child.

Case report: An 8 years old girl with HIV infection presented with fever for 1 month, cough and ear discharge for 15 days. She is on antiretroviral therapy (ART) since past 1 year consisting of Zidovudine (AZT), Lamivudine (3TC) and Efavirenz (EFV). On examination, she was febrile, had axillary and cervical insignificant lymphadenopathy, splenomegaly and oral thrush. Other systems were normal. Her hemogram showed a trend of gradual pancytopenia USG Abdomen showed hepatosplenomegaly and bone marrow examination showed hypocellular marrow with early fibrosis. Her CD4 count was 406 (27.6%) with CD4:CD8 ratio of 1.63 and HIV viral load was undetectable. Her EBV viral capsid antigen (VCA) IgM was negative (0.61 Index). On Day 40 of her fever developed large cervical and axillary lymphadenopathy. A lymph node biopsy was done which was suggestive of necrotizing lymphadenopathy. In view of persistent fever, pancytopenia and lymphadenopathy, she was suspected to infectious mononucleosis and her CMV IgM was done which was negative while her EBV viral capsid antigen IgM on repeating again after 15 days was positive (1.12 Index). She was then treated with valacyclovir (10mg/kg/dose BD) for 12 days till EBV VCA became negative. Her fever subsided within 5 days of therapy and hemogram normalized within a week.

P726

SERUM ADENOSINE DEAMINASE LEVELS IN CHILDREN AND ADOLESCENTS PATIENTS WITH HEPATITIS B VIRUS INFECTION IN ZAHEDAN, SOUTHEASTERN IRAN

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Background/aim: Adenosine deaminase (ADA) is an important and essential enzyme for the proliferation and differentiation of T lymphocytes and also the monocyte-macrophage systems. In present study, total serum ADA level was measured and compared between the children and adolescent patients with HBV infection and healthy blood donors.

Material and methods: During 8 months in 2006, ninety- one subjects were enrolled in our study : 41 patients with HBV infection and 50 healthy blood donors. Serum ADA level was measured by Chem-enzymes Kit in patients with HBV and then compared with the donors. A normal range of serum ADA was considered between 5-35 IU/l. Serum ADA levels were also compared with ALT level.

Results: We evaluated 41 patients (29 male, 12 female) with age range 11-20 years and 50 donors with age range 18-22 years(43 male, 7 female) .There was no significant difference between patients and donors in ADA level (35.45 ± 8.19 IU/l and 29.5 ± 7.3 IU/l, respectively) (P >0.05). We did not find any correlation between the serum ADA activity and ALT level in our patients.

Conclusion: The is no correlation between serum ADA level and HBV infectivity and ALT level.

P727

MULTICENTER OPEN-LABEL TRIAL OF PEGINTERFERON ALFA-2A AND RIBAVIRIN (PEGASYS/COPEGUS, ROCHE) FOR PAEDIATRIC CHRONIC HEPATITIS C

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This study aimed to prospectively evaluate the safety and efficacy of a genotype-based Peginterferon alfa-2a/Ribavirin therapy in treatment-naïve hepatitis C virus (HCV) infected children.

Sixty-five children with positive HCV serology and quantifiable HCV RNA, were assigned to 100 µg/m^2 bsa of Peginterferon once weekly and Ribavirin (15 mg/kg/d). Genotypes 2 & 3 patients (group 1) received treatment for 24 weeks, and genotypes 1, 4, 5 & 6 patients (group 2) for 48 weeks.

Response was defined as normalization of serum transaminases with HCV RNA < 600 IU/ml.

Basal ALT values were normal in 46.2% of patients. Low initial viral load was observed in 55% of group 1 patients (vs 27.6% in group 2)($p < 0.05$).

Nine patients stopped prematurely the treatment, 1 for acute hepatitis, and 8 because of no virologic response at week 24. Peginterferon/Ribavirin dose was adjusted in 15 patients, 11 for neutropenia, and 3 patients, for anemia, respectively. Four serious adverse events were recorded. Frequent adverse events included flu like symptoms (64.6%), digestive complaint (41.5%), thyroid disease (10.8%) and dermatitis (41.5%).

Early response at week 12 was observed in 94% of group 1 patients and in 59% in group 2. End of treatment response was achieved in 100% of group 1 patients and 59% in group 2. Sustained virologic response (SVR) at 24 weeks follow-up was maintained in 94% of group 1 patients and 59% in group 2.

In this cohort, Peginterferon alfa-2a/Ribavirin produced SVR in 68% of treated patients, reaching 94% for genotypes 2 and 3.

P728

ASSESSMENT OF PAEDIATRIC CASES WITH VARICELLA AND ZONA REQUIRING HOSPITALIZATION

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Background and aims: Varicella Zoster and Zona are benign virus infections. However in immunocompromised individuals including patients with malignancy, infection may cause severe complications and mortality.

Methods: In this study, a total of 175 patients [88 male, 82 female] between ages of 1.5 and 18 (median: 5.8) years who were followed up between the years 1986 and 2008 were retrospectively evaluated.

Results: Of all patients, 143 (82%) had varicella zoster infection and 32(18%) had zona. 58 patients with varicella zoster infection and 31 patients with zona were immunocompromised. Complications were occurred in 107 (62%) cases. 73 (68%) of these 107 patients were immunocompetent and 34 (32%) patients were immunocompromised. The complications were as follows: cerebellitis or encephalitis [n=37 (34%)], pneumonia [n=30 (28%)], secondary bacterial skin infections [n=18 (17%)], varicella gangrenosum [n=5], disseminated intravascular coagulopathy [n=3], purpura fulminans [n=3], hemophagocytic syndrome [n=2], myocarditis [n=2 (2%)] and transverse myelitis [n=1]. Severe hemolytic anemia concomitant with infection developed in a case of autoimmune lymphoproliferative disease. Concomitant pneumonia and skin infection and concomitant encephalitis and pneumonia developed in 4 and 3 cases, respectively. In another patient, concomitant encephalitis and skin infection was also noted. Parenteral acyclovir treatment was administered to patients with malignancy or encephalitis and patients under steroid treatment. During the follow up period, 3 patients died. Three patients who developed encephalitis survived with neurological sequela.

Conclusion: Varicella Zoster infection which is known as a benign disease may cause severe complications and mortality in immunocompetent pediatric patients as well as immunocompromised ones.

P729

PREVALENCE OF HEPATITIS B VIRUS INFECTION IN B-THALASSEMIC PATIENTS IN JAHROM, 2008

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Background and aims & Introduction and objectives: Thalassemic patients are high risk group to hepatitis B virus (HBV) infection due to repeated transfusion. To determine the incidence of HBV infection in thalassemic patients of Jahrom.

Methods: This study was carried out on all 109 thalassemic patients of Jahrom referring to thalassemia center of Jahrom, on May 2008.

Results: No cases of HBV were found. The prevalence of HBV infection in the thalassemic patients of Jahrom was 0%.

Conclusion: It seems that the prevalence of HBV infection in thalassemic patients of Jahrom is lesser than the prevalence of HBV infection in the in thalassemic patients in the most of other cities of IRAN and in other countries.

P730

SEROPREVALENCE OF HEPATITIS C VIRUS INFECTION IN THALASSEMICS CHILDREN

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Background and aims: Chronic posttransfusion hepatitis C is a progressive disease and dramatically increases morbidity and mortality rate among thalassemics due to liver failure or hepatocellular carcinoma. To determine the incidence of HCV infection by measuring anti-hepatitis C antibody (anti-HCV Ab) in thalassemics patients of Jahrom, IRAN-2006.

Methods: This study was carried out on all 109 thalassemics patients of Jahrom and 954 blood donors referring to Transfusion center of Jahrom, on May 2006.

Results: The prevalence of anti-HCV Ab in the thalassemics patients and blood donors were 7.3% and 1.36% respectively.

Conclusions: In Jahrom, it seems that the prevalence of HCV in thalassemics patients is less than the prevalence of HCV in the patients in most of the other countries.

P731

ZINC AN INHIBITOR OF INFLUENZA A VIRUS INDUCED PROGRAMMED CELL DEATH

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Background and aims: Programmed cell death a hallmark observed upon infection with many viral pathogens, including Influenza virus. Zinc is known as an inhibitor of apoptosis. However, effect of zinc on influenza A virus induced apoptotic death is not well established.

Methods: HeLa cells infected with Influenza A (A/Udorn/317/72H3N2) virus. Cells treated with 0.1, 0.15 and 0.20 mM zinc at various time intervals. DNA fragmentation and Caspase-3 activity was examined. The morphological changes and ultrastructural changes were studied using Haematoxylin-Eosin and TEM respectively. Annexin V assayed to analyze phosphatidylserine externalization. Phagocytic index determined by incubating infected cells with adherant mouse peritoneal macrophages.

Results: DNA fragmentation observed in virus infected cells by 24h post-infection. Caspase-3 activity was maximum at 4h post-infection after that it reached to plateau. It was observed that when the infected HeLa cells incubated with adherent macrophages, efficient phagocytosis occurred and the release of virus into the culture medium completely inhibited. Furthermore, TEM analysis detected phagosome-like structures within macrophages, which coexisted with the peak of phosphatidylserine externalization i.e. 9-12h. Treatment of cells with 0.15mM zinc inhibited DNA fragmentation till 8h of post infection and caspase 3 activity decreased significantly up to 2h post-infection.

Conclusion: These results suggest that the influenza A virus induces apoptosis in cell culture; thus apoptosis may represent general mechanism of cell death in infected host cells. Zinc has its inhibitory effect on caspase 3 and endonucleases both. Therefore, zinc modulated apoptosis in a time and dose dependent manner by inhibiting caspase3 and endonucleases.

P732

DISTINCT CHARACTERISTICS OF CHILDHOOD TICK-BORNE ENCEPHALITIS CASES IN POLAND

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Introduction: The clinical course and diagnosis of tick-borne encephalitis cases differs in paediatric cases. Children have usually milder outcome, and are diagnosed less frequently, compared to adults. The aim of the present paper was to compare TBE paediatric with adult cases reported to the surveillance system in Poland.

Materials and methods: Individual surveillance forms on TBE from 1993 to 2006 were used in the study. Cases < 18 years were described, and compared with adult cases in terms of clinical course and outcomes. Categorical variables were compared using chi-square test, continuous variables - using Wilcoxon test.

Results: A total of 3,064 cases were reported in 1993-2006, of which 92 (3.0%) were < 10 years old, 141 (4.6%) were 10-14 years old, and 223 (7.3%) were 15-18 years old. Children were reporting less commonly tick bites, compared to adults (59.4% vs 66.0%, p=0.007). The following symptoms of CNS involvement were less common in paediatric cases, compared to adults: meningeal symptoms (68.6% vs 76.3%, p=0.0006); loss of consciousness (9.1% vs 14.7%, p=0.002), focal symptoms of brain involvement (2.7% vs 6.1%, p=0.005). The incubation period was slightly shorter in children (22,99 days vs 23,43 days), but the difference was not significant.

Conclusions: As described elsewhere, paediatric TBE cases do not occur frequently and have milder outcomes, compared to adults. It is however important to properly diagnose TBE cases also in younger age groups, as long-term sequelae can be expected.

P733

ENTEROVIRUS MENINGITIS: CLINIC, DIAGNOSTICS, TEATMENT

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Currently growth of the enterovirus diseases reported in many countries of the World. Aseptic meningitis is the most common hospitalization cause among all enterovirus diseases. During last 5 years in Saratov Region increase of aseptic meningitis cases is detected in Summer-Fall season. Diagnosis "enteroviral meningitis" is established after enterovirus detection in CSF using PCR method or using cultural method in CSF, nasopharynx mucus and faeces.

Where were 88 patients with enterovirus meningitis under our supervision. The majority of ill children were accepted during first days of disease (2,75±1,53 days). In 100% of cases there was acute onset of disease. At the acceptance the intoxication syndrome and hypertension syndrome were predominated. Meningeal syndrome could be characterized by dissociation of features: in 7.5% of cases there were no meningeal signs, and in 11% of cases the signs were doubtful. The most constant sign was muscular rigidity of back of the head (80%), Kernig symptom (32,5%) and far less often - Brudzinsky symptom (12,5 %). Local symptomatology was detected primarily for younger patients. To diagnose meningitis, lumbar puncture was performed. CSF was clear, colorless, drained under pressure. Pleocytosis was characterized by 2-3 digit numbers of mixed type with lymphocytes predominance. However, 33,7% of cases had neutrophil predominance. For those patients controlling lumbar puncture performed on 3-4 day indicated 100% lymphocyte CSF type.

In the case of neutrophil or mixed pleocytosis for exclusion bacterial disease etiology we used following express-methods: procalcitonin detection in blood serum, C-reactive protein detection, and lactoferrine detection in CSF.

P734

PROCALCITONIN DETECTION AS EXPRESS DIAGNOSTICS FOR VIRUS AND ASEPTIC CHILDREN MENINGITIS

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Recently in Russia seasonal increase of aseptic meningitis cases of enterovirus etiology is registered. However, during onset of disease, neutrophil number in CSF may prevail, which can lead to wrong diagnosis “aseptic meningitis”.

The purpose of this study is to improve early differential diagnostics of children meningitis of different etiology.

We have had 52 patients under our supervision. All patients were accepted in neuroinfection department in 2008 with preliminary diagnosis “meningitis”. All patients at acceptance had mixed pleocytosys, in 38,4% (20 cases) with prevail of neutrophils. All children were tested with all main laboratory tests with the aim to exclude bacterial etiology of meningitis. During the first hours in the hospital immunochromographical test was performed to detect procalcitonin in serum. 41 patients had negative test result (PCT< 0.5 ng/l) - 1st group of patients, 9 had positive result (PCT > 2ng/l) - 2 group.

For the group 1, by clinical picture, negative PCR test and negative results of CSF microscopy for bacteria, in spite of neutrophil prevail, “virus meningitis of unknown etiology” was established. Treatment of this group was performed with antiviral treatment. Due to therapy, patient's condition improved to day 3-5, and CSF normalization occurred on day 14-17 of disease.

Group 2 of patients with positive PCR in serum had diagnosis “Aseptic meningitis” and received proper antibiotics.

Thus, immunechromographical test for PCT detection in serum can be used as additional method for determine hypothetic etiologic agent (virus or bacteria) during meningitis development in the first hours of hospitalization.

P735

CHROMOSOMAL INTERGRATION OF HUMAN HERPES VIRUS TYP 6 (CIHHV-6) - DIAGNOSTIC APPROACHES

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Background: Chromosomal integration of the HHV-6 (CIHHV-6) into the human genome occurs in 1-2% of healthy individuals leading to persistent high levels of HHV-6 PCR copy numbers in blood and tissue. Consequently, this may be interpreted as persistent active HHV-6 infection. CIHHV-6 is inherited from one parent or is transmitted by stem cell or bone marrow transplantation (BMT). In the latter case the CIHHV-6 is found in blood cells only. The pathophysiological impact of CIHHV-6 is under discussion.

CIHHV-6 can be proven by fluorescence-in-situ-hybridisation (FISH) of the HHV-6-DNA in the human genome.

Methods: We show diagnostic results in individuals with proven CIHHV-6 allowing the diagnosis without FISH-analysis.

Results:

Pat.Nr.	1	2	3	4
age	5a	43a	15a	18a
sex	female	male	female	female
disease	dilated cardiomyopathy	healthy father of pat. 1	AML, BMT	chron. parotitis
variant	B	B	A	A
neg. PCR results (blood)	no	no	prior to BMT	no
PCR blood (copies/ml)	$2,8 * 10^3$ to $2,1 * 10^6$	$1,2 * 10^5$	after BMT $1,0 - 8,0 * 10^5$	$2,5 * 10^4$ to $2,0 * 10^5$
pos. results range	5 years	6 months	5 years	1 year
PCR Hair follikle	pos.	pos.	neg.	pos.
PCR newborn-screening card	pos.	n.d.	n.d.	n.d.
transmission	father (pat. 2) PCR pos.	daughter (pat. 1) PCR pos.	stored donorlymphocytes PCR pos.	mother PCR pos.
serology IgG/IgM	neg./neg.	neg./neg.	pos./neg.	neg./neg.
chromosome localisation	9p ter	9p ter	17p ter	17p ter

[Table I]

Discussion:

Results indicating CIHHV-6:

- High amount of DNA-copies: Despite integration in every nucleic cell, the copy numbers in whole blood may be below the number of white blood cells (according to laboratory techniques). Generally at least 10^3 copies/ml serum and 10^5 copies/ml whole blood are expected.

- pos. HHV-6 PCR before onset of disease (e.g. newborn-screeningcard)

- persistent pos. HHV-6 PCR: CIHHV-6 is ruled out by a single negative PCR-result (exception: neg. results prior to BMT in BMT-transmitted CIHHV-6)

- pos. HHV-6 PCR in any somatic cell (e.g. hair follicle, exception: BMT-transmitted CIHHV-6)

- pos. HHV-6 PCR in first-degree relatives (or stem cell donor).

P736

EPIDEMIOLOGICAL STUDY OF ACUTE LARYNGITIS IN HOSPITALIZED PEDIATRIC PATIENTS

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Background and aims: Acute laryngitis, an acute disease of viral cause of the upper respiratory, is one of the most common causes of hospitalization in early childhood. The aim of our study was the recording of cases with acute laryngitis that were hospitalized in the Pediatric Clinic of G.H.Kalamata during the last 5years.

Methods: This study is retrospective, concerning the years 2004-2008. The data collected from the patients' files involved :number, gender, age of the patients and seasonal distribution of the cases.

Results: The study included 337 children (236 boys, 101 girls) aged 2 months- 14 years, most in the preinfant and infant age(57%). 3 cases < 3 months and 1 >12 years old, were recorded. Most cases were hospitalized during winter (33,2%) and spring (30,6%), whereas in the autumn and summer the percentiles were 27,3% and 8,9% respectively. The yearly distribution analysis showed that between 2004-2005 the cases were increased by 39,2%. In the following years, there was a decline reaching 57% in the year 2008.

Conclusions: Acute laryngitis remains one of the most common causes of hospitalization in the Pediatric Clinic, especially for the boys and during winter and spring. Despite the decline observed up to 2008, it still remains a problem during childhood.

P737

GENETIC ANALYSIS OF INFLUENZA A (H3N2) VIRUSES FROM INDEX PATIENTS AND FAMILY CONTACTS

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Background/aims: Influenza hemagglutinin (HA) is a highly evolving surface glycoprotein responsible for viral attachment and entry. Mutational HA drift among circulating human viruses during the 2007/08 season prompted a change in HA proteins used in the current 2008/09 vaccine. Analysis of influenza genes from index patients and family contacts were performed to:

1) evaluate genetic homology to vaccine strains, and

2) determine the extent of genetic mutation in confirmed family transmissions.

Methods: Genetic analysis of the influenza HA1 hemagglutinin and matrix genes (MA) were performed on viruses obtained from seven families, including an index patient and at least one influenza-positive household family contact.

Results: All index and transmission strains were genetically more similar to the 2008/09 vaccine strain, A/Brisbane/10/2007 compared to previous H3N2 vaccine strains. HA analysis of viral strains revealed 100% protein homology from index patient to family contact in four of seven families. Of the three families with HA1 sequence variation, two exhibited one amino acid change, and one family revealed 5 amino acid changes compared to the index strain. The MA and M2 ectodomain were highly conserved among family transmissions, and all strains contained the mutation conferring resistance to adamantane drugs.

Conclusions: Genetic analysis reveals that all family strains from this cohort are similar to the current A/Brisbane/10/2007 vaccine strain compared to last season's A/Wisconsin/67/2005 strain. HA changes were observed between families and within family transmissions. The results of this study suggest that the HA protein is highly evolving and can drift within a single human transmission.

P738

REAL-TIME PCR FOR RESPIRATORY VIRUSES DOES NOT IMPACT ANTIBIOTIC USE FOR VENTILATED CHILDREN WITH LOWER RESPIRATORY TRACT INFECTION

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Background and aims: Real-time (q)PCR at the pediatric intensive care unit (PICU) is much more sensitive to detect respiratory viruses than conventional immunofluorescence testing (DIF). We investigate the impact of qPCR additional to DIF on antibiotic prescription in young PICU patients with lower respiratory tract infection (LRTI).

Methods: Ventilated PICU patients (≤ 5 years) with LRTI were tested for respiratory viruses by DIF and qPCR shortly after admission. Patient care was left at the discretion of the attending physician and DIF results were reported the same day, as usual. The next day, the investigator questioned the attending physician about antibiotic treatment before revealing the qPCR result. Subsequently, the qPCR result was given to the PICU physician and antibiotic use was evaluated again one hour later.

Results: Thirty-eight children were included. Nineteen patients had a positive DIF result (all RSV), and 9 of these (47%) were treated with antibiotics before revealing the PCR result. QPCR detected 7 additional viruses in 6 of these patients. The qPCR result did not change antibiotic use in this group (as expected). Additionally, 19 patients had a negative DIF result. Twelve (63%) of these patients were treated with antibiotics before revealing the PCR result. QPCR detected 20 viruses in 16 of these patients; however in none of the patients antibiotics were discontinued.

Conclusions: QPCR, in addition to DIF, does not have an impact on antibiotic prescription in young PICU patients with LRTI.

P739

CHILDREN AND HPV INFECTION. EXPLORING MODES OF TRANSMISSION

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The purpose of this reference is to inform about the investigation of the mode of transmission of anogenital warts of children.

1st incident: Female 3.5 years submitted because dysuria and retention of urine .The examination detected intense redness of vulva and anus area and presence of anogenital warts in the same areas.From family environment paternal grandfather, who was the person childcare, had similar damage to reproductive region.Laboratory testing for other STD has been negative.The effects of indirect laryngoskopisi were negative also.

2nd incident: Female 12 years referred from dermatologist because of the presence of anogenital warts.Objective examination detected presence of multiple lesions in upper areas and also limited mental maturity likely due to family environment . During the case history the patient was admitted having sex since the last year. The other STD control, showed the presence of Trichomonas Vaginalis in the culture of vaginal coating.

Results: In both cases, biopsy of skin lesions showed HPV type 6.Despite the organized efforts of skilled stuff it wasn't possible the proof of sexual abuse.The suspicion of lechery in the first case was not confirmed but remains strong.

Conclusion: In every such case special attention must be given in the clearance of the conditions of HPV trtansmission in children even if most times it is not possible to help in essence this children that have such a need.

ZOONOSIS, PARASITIC INFECTIONS AND INFECTIONS IN MIGRANTS AND TRAVELERS

P740

CEREBRAL MALARIA IN CHILDREN WITH SICKLE CELL HAEMOGLOBINOPATHIES

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Introduction: Over one million people die from malaria annually, of which 90% are children less than 5 years of age. The haemoglobin S gene is the single most common inherited genetic disorder in West Africa. The gene is present in 25% of the population and is present in its deleterious homozygous form in 3% of the population. The Haemoglobin S gene has a selective advantage for survival in its heterozygous form in the malaria regions of sub Saharan Africa.

Methodology: Seventy, (70)children with cerebral malaria presenting to the emergency room of the Lagos University Teaching Hospital, Nigeria were recruited into a study investigating them for concomitant bacterial infections.They had haemoglobin electrophoresis performed along with malaria parasite counts, FBC, UE, LFT's, blood cultures, urine cultures and chest Xrays.

Results: Male:Female 1:1.06 for the 70 children. Age range: 3.5months-10.8 years, mean 5.26years+/-3years.The overall mortality in the study was 20%. Of the 70 children: 62 HbAA, 4 HbSS, 2 HbAS and 2 HbAC. One of the children with HbSS died accounting for a mortality of 25%. Two of the children with HbSS had concomitant bacterial infections and both survived: salmonella typhi bacteraemia and lobar pneumonia. All 4 children with the S or C trait survived and had no concomitant bacterial infections.

Conclusion: Children with the homozygous form of sickle cell disease who develop cerebral malaria have a high mortality although not markedly different from those with HbAA. All the children with the HbS or C trait who developed cerebral malaria survived.

P741

INCIDENCE OF LYME MENINGITIS (LM) IN SLOVENIAN CHILDREN WITH SYNDROME OF ACUTE LYMPHOCYTIC MENINGITIS (ALM)

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Objective: To determine the incidence of LM in children with ALM and to compare demographic, clinical and laboratory findings in children with LM and non-LM.

Methods: During 2004-2005, 122 children fulfilled the inclusion criteria of this prospective clinical study: age < 15 years, meningitis (≥ 5 leukocytes x 10^6/l CFS), no typical clinical signs for Lyme borreliosis on admission. In blood and CSF IFA antibody titres to B. burgdorferi sensu lato (Bb) were determined and isolation of Bb was performed. LM was confirmed by isolation of Bb from blood and/or CSF and/or seroconversion to Bb antigens and/or demonstration of Bb intrathecal antibody production and/or erythema migrans four months prior to the onset of meningitis. LM was probable in patients with positive but unchanging Bb serum antibody titres.

Results: LM (83% confirmed, 17% probable) was established in 34% of patients. There were no differences regarding demographic features between the patients with LM and those with non-LM. Fever was more common in non-LM (p=0.0030) and inappetence in LM (p=0.0093). Clinical and neurologic findings were comparable between the two groups. Peripheral leukocytosis was more common in non-LM (p=0.0327) and lymphocytic pleocytosis in LM (p=0.0073). Bb serum IgM and/or IgG were found in 24%, seroconversion to Bb antigens in 39%, Bb IgG intrathecal antobody production in 5% and isolation of Bb from CSF and blood in 41% and 22% of patients, respectively. In 8% Bb was isolated simultaneously from blood and CSF.

Conclusions: In Slovenia LM was found in 34% of children with ALM.

P742

MOLECULAR EPIDEMIOLOGY OF BLASTOCYSTIS IN STOOL SAMPLES FROM PATIENTS FROM BRUSSELS, BELGIUM

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Background and aims: Blastocystis is the most commonly observed intestinal protozoan parasite in humans. Blastocystis is commonly regarded as a non-pathogen but several studies suggest pathogenicity, especially in the paediatric population.

Until recently Blastocystis in humans was regarded as a single species. However, new molecular genetic insights proved that Blastocystis encompasses nine different species, which at present are called Blastocystis subtypes. Pathogenic differences between these subtypes may explain the discrepancies in literature about pathogenic potential of Blatocystis in humans. The aim of the present study was to establish the presence of different Blastocystis subtypes in stools of patients submitted for routine parasitological examination at Saint-Pierre University Hospital located in Brussels, Belgium, between August 2007 and July 2008.

Methods: 1030 faeces samples were microscopically screened for Blastocystis. On DNA isolated from Blastocystis positive samples, PCR and sequence analysis of the 18S rDNA locus was performed.

Results: 152/1030 (14.8%) faecal samples were microscopically positive for Blastocystis species. For 144/152 samples a sequence was obtained that allowed subtyping. Five different subtypes were observed: subtype 3 was the most abundant (n=63, 44%), followed by subtypes 1 (n=41, 28%), 2 (n=20, 14%), 4 (n=19, 13%) and a single subtype 6 isolate (1%).

Conclusions: In this first report on the distribution Blastocystis subtypes in Belgian patients, a surprising heterogeneity of subtypes was observed. Application of these new diagnostic techniques enables further studies towards pathogenicity of different Blastocystis subtypes.

P743

USEFULLNESS OF REC P-29 PROTEIN AS NEW MARKER FOR POST-SURGICAL FOLLOW UP OF HUMAN CYSTIC ECHINOCOCCOSIS IN YOUNG PATIENTS

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One of the key characters of cystic echinococcosis (CE) is the occurrence of relapses after surgery. A post- operative follow up is necessary to detect newly growing or relapsing cysts as early as possible. New antigen markers that allow detection of postoperative development of disease are highly demanded. It is the aim of the present work to characterize new antigen (s) marker (s) for CE follow up.

ELISA and Western-Blotting serological tests was carried out on 540 sera of follow- up. These sera were taken from 94 children affected by CE during a follow-up period ranging between 7 days and 5 years post-surgery. Based on the clinical course and imaging findings, patients were either classified into cured (CCE) (n=62) or non-cured (NCCE) (n=32) CE patients.

Western-Blotting based on protoscolex-native antigen yielded an interesting immunoreactive double band of 27 and 28 kDa that exhibited in case of cure a rapid decrease and subsequent disappearance of respective antibody reactivities.

Proteomic characterization by MS/MS sequencing, showed that 27 corresponded to P 29 protein. Corresponding cDNA (s) was subsequently cloned and expressed in *E.coli*. Purified recombinant p-29 protein (recP-29) was tested for its prognostic serological value. RecP29- Western-Blotting yielded seronegativity in 73% cured patients, compared to 27% when using the conventional Hydatid fluid (CHF) antigen. Likewise, ELISA-recP-29 preliminary results showed seronegativity in 85% cured patients compared to only 10% in CHF-ELISA.

Rec P29 protein appears prognostically useful for monitoring post-surgical follow-ups of human CE in young patients.

P744

DETECTION AND IDENTIFICATION OF LEISHMANIA IN INFANTILE VISCERAL LEISHMANIASIS CASES IN TUNISIA

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As in most Mediterranean countries, Visceral leishmaniasis (VL) affects in Tunisia children between 1 and 5 years in almost 90% of cases. Moreover, a new state of VL takes place due to the North-to-South extension and the increase of cases' number. The aim of this study is the evaluation of classic (*in vitro* culture) and molecular methods (PCR) in the detection of *Leishmania* in one hand, and that of isoenzymatic and molecular (PCR-SSCP) methods in the identification of this parasite in the other hand. Our study was conducted on blood samples of children aged between 1 and 12 years. PCR was found more sensitive than *in vitro* culture in the detection of *Leishmania*. However, the *in vitro* culture permits the isolation of the parasite strain. For identification of *Leishmania*, we found that both isoenzymatic and molecular method have identified the parasite as *Leishmania infantum* in all samples. Nevertheless, the isoenzymatic method has the advantage to be more polymorphic within *L. infantum* complex. In deed, two taxa (zymodemes) were found 91% of strains were belonging to zymodeme MON-1, and 9% to MON-24. In the other hand, the PCR-SSCP method has the advantage to be easy and can be applied directly on clinical samples without need to the isolation of *Leishmania*. In fact, *Leishmania* have been successfully identified only by molecular method from many clinical samples.

P745

IMPORTED MALARIA IN NORTHERN FRANCE: INCIDENCE AND RISK FACTORS FOR SEVERE DISEASE IN CHILDREN

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The epidemiology of imported malaria in Western countries is not well known, based on estimations.

Objectives: Main objective: to determine the incidence of imported malaria in children in Northern France. Secondary objectives: to determine the frequency of a delayed diagnosis and risk factors for severe malaria.

Methods: A retrospective descriptive multicenter cohort study was performed in all hospitals with paediatrics or infectious diseases units in Northern France from 2000 to 2006. Any children with a positive blood smear test or rapid diagnostic test was included. The incidence of imported malaria among the population of children < 18 years of age was determined, as well as the threshold of a delayed diagnosis, the frequency of a delayed diagnosis and risk factors for severe malaria after univariate and multivariate analyses.

Results: 133 children were identified. The mean incidence of imported malaria was at 1.9/100 000 children < 18 years of age. Data of 120 children were available (mean age=8.8 years, range=3 months-17.9 years; sex ratio=1.5). *Plasmodium falciparum* was responsible of the malarial access in 83% of cases. Severe malaria occurred in 19% of malaria cases. A diagnostic delay (≥1 day after the first medical advice) was identified in 31% of cases. This diagnostic delay (OR=3.2; 95% CI=1.2-8.8; p=0.02) was identified as the only independent risk factor for severe imported malaria in children.

Conclusion: Imported malaria is not so rare in Northern France. It should be systematically evoked in children returning from endemic area to avoid the risk of a severe presentation.

For Hospital Network for Evaluating the Management of Common Childhood Diseases, Lille, France

P746

PERSON-TO-PERSON TRANSMISSION OF *STRONGYLOIDES STERCORALIS* IN AN IMMUNOCOMPROMISED PATIENT

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Background and aims: *Strongyloides stercoralis*, an intestinal nematode, is endemic in tropical and subtropical regions and infects humans (the definitive hosts) who walk barefoot in areas contaminated by human feces containing the infectious larvae. *S. stercoralis* also can autoinfect the human host by invading the intestinal wall or peri-anal skin and establish latent infection which can persist for years. Person-to-person transmission has only rarely been described.

Although usually asymptomatic, *Strongyloides stercoralis* infection can become dissiminated in immunocompromised patients, which can be fatal.

Methods: We report the case of a 3-year-old boy who underwent combined liver-intestinal transplantation at the age of 8 months for congenital short bowel and TPN-induced liver failure. Maintenance immunosuppression consisted of tacrolimus only. 23 months posttransplant, the boy presented failure to thrive, cheilitis and brown pigmented oral mucosa with strikingly high IgE levels (20000 kU/L) and intermittent eosinophilia.

Results: Stools were examined (with the Baermann concentration method) and showed larvae of *Strongyloides stercoralis*. ELISA confirmed this diagnosis. Our patient nor the donor had ever been in an endemic region for the infection. Both parents (originating from the Caribbean Islands) were screened and the father tested positive for *Strongyloides*. Treatment with Ivermectin was initiated for the patient and his father.

Conclusions: This case illustrates that *Strongyloides stercoralis* can be acquired through person-to-person transmission without foreign travel. Immunocompromised hosts might be more susceptible to this alternative infection route.

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P747

POST-TRAUMATIC HYDATID CYST LEAKAGE CAUSES ANAPHYLACTIC SHOCK

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Background and aims: Echinococcosis is caused by infection with the metacestode stage of the tapeworm Echinococcus.

E. granulosis is most common and tends to form hydatidosis in liver or lung. Humans acquire echinococcosis by ingesting viable parasite eggs with their food. The parasite eggs are distributed via local environmental contamination by the faeces of tapeworm-infected canines.

Clinical case: A 14-year old boy of Turkish origine, presents with syncope after a minor abdominal trauma. During transfer to the hospital, he develops an anaphylactic shock. Laboratory shows elevated total gE, eosinophilia, elevated bilirubin (conjugated and unconjugated), elevated AST and a high LDH level. Consequently he develops fever with rash, swollen joints and respiratory distress syndrome. Laboratory results show elevated erythrocyte sedimentation rate and C-reactive protein, and leukocytosis.

Ultrasound of the abdomen reveals a liver mass with septae, Computed tomography is pathognomonic (water-lily sign) for hydatidosis.

Albendazole, an anti-helmenthic drug, is started. Because of systemic inflammatory syndrome, surgical removement is decided. Microscopic investigation of the cyst reveals an Echinococcus species. Serology is positive for Echinococcus.

Conclusion: Hydatide cysts can remain asymptomatic during many years. Symptoms are due to mass effect of the enlarging cyst in a confined space. Cyst leakage may be associated with anaphylaxis to parasite antigens. Serology can confirm suspected infection based on imaging studies.

Treatment consists of medical therapy with Albendazole, combined with Percutaneus Aspiration, Instillation of protoscolicidal agent and Reaspiration (PAIR procedure), or surgery.

To reduce the risk of secondary hydatidosis, therapy should be continued one month following surgery.

P748

ATOVAQUONE-PROGUANIL TREATMENT FAILURE OF PLASMODIUM FALCIPARUM MALARIA

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Background and aims: The combination of atovaquone and proguanil has showed high efficacy against *Plasmodium falciparum* with only mild side effects. There have been several reports of treatment failures, which have been attributed to suboptimal dosage, reinfections or point mutations in the cytochrome b gene.

Methods: A 17-month-old boy presented to the emergency department with fever the day after returning from a two-month journey to Guinea to visit his family. The child had been born in Spain and had not travelled previously. He had received no chemoprofilaxis.

Results: On admission, the patient showed a 3-cm splenomegaly. Rest of physical examination was normal. A CBC revealed a WBC of 11.000/ml, hemoglobin 10,9 g/dl, and platelets 82.000/ml. Significant serum laboratory tests values were: GOT 72 U/L, GPT 40 U/L, total bilirrubin 1,5 mg/dl. A blood smear was positive for *P. falciparum* (0,3% infected erythrocytes). He was admitted to hospital and treated with atovaquone-proguanil. However, high fever persisted and hemoglobin descended progressively. On day 3, the parasitaemia was 0,2%. Treatment was changed to quinine plus clyndamicin, which was successful. On day 5 and 28 he was asymptomatic and blood smears were negative. Atovaquone-proguanil dosage was the appropriate for the child's weight and was well tolerated. The cause of treatment failure could not be established because there are no laboratories in Madrid that measure drug concentrations and analyse citochrome b mutations.

Conclusions: Drug-resistant malaria is a growing public health problem. Continuous monitoring of atovaquone-proguanil resistant *Plasmodium falciparum* is important for the rationale use of this drug.

P749

COMPARATIVE EVALUATION OF DAT, IFAT, PCR AND BONE MARROW ASPIRATION METHODS FOR DIAGNOSIS OF MEDITERRANEAN VISCERAL LEISHMANIASIS

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This study was undertaken to compare direct agglutination test (DAT), indirect immunofluorescent antibody test (IFAT), polymerase chain reaction (PCR) and bone marrow aspiration as established diagnostic methods for Mediterranean visceral leishmaniasis (MVL). Blood samples were collected from 107 patients, suspected to MVL and 47 patients with other diseases such as malaria, tuberculosis, hydatid cyst, toxoplasmosis and leukemia in Nemazee Hospital in Shiraz, southwestern Iran. 67 out of 107 patients suspected to MVL were confirmed to have MVL. The most frequency of MVL patients (44.8%) was belonged to less than 2 years old group. The highest sensitive (85.1%) diagnostic method was IFAT while the lowest (42.8%) related to Bone marrow aspiration. The specificity (100%) of DAT was higher than that of IFAT (80.8%, CI=66.3% to 90.4%). The highest degree of agreement (agreement= 71.6%, Kappa= 0.13) was observed between IFAT and DAT. In addition, using IFAT and PCR (with sensitivity: 82.1% and specificity: 100%) (agreement= 69.1%, Kappa= - 0.09), the minimum numbers of false negative results (1 out of 55 MVL patients) were seen. In conclusion, these results suggests that IFAT together with PCR method must be performed in endemic areas of visceral leishmaniasis for early and accurate diagnosis of MVL as well as avoidance of misdiagnosis.

P750

A CASE OF COMPLICATED CEREBRAL TOXOCARIASIS IN 4 YEARS OLD CHILD

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We report the case of a 4 years old boy suffering from a cerebral form of toxocariasis. High serum titres of anti-Toxocara antibodies indicated that the primary infection was induced by a high number of Toxocara eggs and that the larvae did not penetrate the blood brain barier into the cerebrospinal fluid. Magnetic resonance image of the brain showed multiple focal lesions spread diffusely in almost all parts of the brain, predominantly paraventricularly. These might be eosinophil-rich granulomatousus infiltrates enclosing larvae. Extensive morphological changes were the cause of serious neurological symptoms, most of them being reversible after therapy. Radiology proved to be useful diagnostic method, but the specific serological assessment had a key role for the final diagnosis. In conclusion, diagnosis of this patient was intracranial primary Toxocara infection with central quadruparesis and parainfective myocarditis.

P751

LEPROSY: A CASE REPORT

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Background: In 2004 the World Health Organization reported 407.791 new cases of Leprosy and currently it is endemic only in some tropical and subtropical regions.

Methods: A 14-year-old adopted Brazilian male, who lived in Brazil from birth to 2002, was admitted to our Department of Pediatrics, University of Milan, Italy, due to an onset of erythematous and papular lesions on the face, nose and ears, erythematous macules on the arms, oedema of the wrists and on the dorsum of the hands with pain, movement impairment and papular necrotic lesions symmetrically distributed on extremities. Lesions appeared 4 months prior to the admission and initially they were present only on legs. Three months later, the patient started to present fever and a weight loss of 4 kilograms approximately. At the admission, the patient presented dry skin, bilateral cervical and inguinal lymphadenopathy, hyperaemia of the pharynx, left epitasis and oedema of the nasal mucosa associated with a subjective sensation of nasal stuffiness. Haematological and cultural examinations, chest radiography, abdominal ultrasonography, chest and abdomen tomography, that were performed during the admission, turned out to be negative. A skin biopsy, which resulted positive for Mycobacterium Leprae, allowed diagnosing Lepromatous Leprosys.

Conclusions: Leprosy, also known as Hansen disease, is a slowly progressive, chronic granulomatous disease, principally affecting skin and peripheral nerves, caused by Mycobacterium Leprae.

The diagnosis of Leprosy can be particularly difficult in no endemic regions: epidemiological, clinical and histological data are essential to make the diagnosis.

P752

STRONGYLOIDES STERCORALIS RELATED PICA

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Background: Pica is an eating disorder which can occur in patients who chronically lack certain minerals, especially iron, leading to anaemia. Patients who suffer from Pica usually eat non-nutritive substances. Strongyloidiasis is a cause of anaemia in (sub)tropical countries but to our knowledge Pica was never described in this condition.

Clinical case: We report the case of a 13-year-old Ecuadorean girl who presented with fatigue and Pica. Since a few months, she was eating plaster on the walls of her house. Her general practitioner performed a blood test which showed hypereosinophilia (10.410/µl). She was then referred to our department. The past history revealed that she spends every summer in Ecuador.We found out that she was suffering from iron-deficiency anaemia. A stool examination was positive for Strongyloides Stercoralis. This parasite was responsible for hypereosinophilia, anaemia and Pica.

Our patient was successfully treated by ivermectin and iron supplementation. The eosinophil count came back to normal. Pica has resolved.

Conclusion: Strongyloidiasis should be considered and stool examination for parasites performed in children presenting hypereosinophilia, iron-deficiency anaemia or Pica.

P753

INTERNATIONALLY ADOPTED CHILDREN FROM ETHIOPIA

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Introduction: Little is known about internationally adopted children and their associated infectious diseases. The aim of this study is to evaluate the health of this population.

Methods: Prospective, cross-sectional study. A cohort of two hundred and twenty two internationally adopted children from Ethiopia were evaluated. Epidemiological characteristics were determined like age and sex. Clinical items were evaluated: Weight, height, Cranial Perimeter and any other anomaly found on physical examination. Charts from OMS (published on 2007) were used to determine weight percentil. Blood tests were performed: white blood count, hemoglobin, AST, ALT, bilirrubin, creatinin, serology to virus hepatitis B, virus hepatitis C, HIV (even polimerase chain reaction when positive serology was obtained) and syphilis.

Results: Median age: 7 months (Range 1-120).Any abnormality was found on physical examination in 52,7%. Clinical and official age diferred in 2.7%. 90% of children were less than 5 year-old. 50% of children were under the third percentile of weight. Ophtalmic evaluation was abnormal in 1,8%, hearing difficulties in 0.9%, cardiac abnormalities in 2.3%. Hepatomegaly in 3.7%. Splenomegaly in 2.3%. Skin diseases in 50,2%. 6,4% had been circumcised. Leucocitosis was observed in 13.4%. Elevated liver enzymes in 10.2%. HIV serology positive in 4.5%. Positive PCR -VIH 0.9%. Nobody was infected by virus hepatitis B (surface antigen negative). Positive non-treponemic test in 0.5%.

Conclusions: Low weight was the main finding in this population. Infectious diseases in this group should be sistematically ruled out, even with the use of PCR when needed to rule out HIV infection in this group.

P754

CONSEQUENCES OF CONCOMITANT INFECTION WITH P. FALCIPARUM, SCHISTOSOMES AND SOIL TRANSMITTED HELMINTHS ON ANAEMIA AMONG PRIMARY SCHOOL CHILDREN IN ZIMBABWE

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In order to investigate the effect of concomitant infection with schistosomes, Plasmodium falciparum and soil transmitted helminths (STHs) on anaemia, a cross sectional study was carried out on 609 Zimbabwean primary school children. P. falciparum, haemoglobin levels and serum ferritin were determined from venous blood. Kato-Katz, formal ether concentration and urine filtration techniques were used to assess prevalence of S. mansoni, STHs and S. haematobium infections. The prevalence of S. haematobium, S. mansoni, P. falciparum, hookworm, Trichuris trichiura and Ascaris lumbricoides were 52.3%, 22.7%, 27.9%, 23.7%, 2.3% and 2.1% respectively. The overall prevalence of anaemia and iron deficiency anaemia (IDA) were 48.4% and 40.0%. Mean Hb levels were significantly lower among children who had P. falciparum, S. haematobium and hookworm infection compared to their corresponding negative individuals, $p < 0.001$, $p < 0.001$ and $p = 0.030$ respectively. Among 487children who had complete parasitological and haematological results, 22.8%, 45.2% and 32.0% had no infection, single and co-infections respectively. The prevalence of anaemia and IDA in co-infections was almost double that in single infection. Children with P. falciparum/STHs co-infections recorded the highest prevalence of anaemia and IDA (87.5% and 57.1% respectively) compared to other combinations, $p < 001$ and $p = 001$ respectively. Multiple regression analysis revealed that, P. falciparum, S. haematobium, hookworm infection and age were associated with anaemia. Integrated school based de-worming and malaria control could reduce the burden of anaemia and malaria.

P755

IMPORTED SEVERE MALARIA IN CHILDREN IN FRANCE. A RETROSPECTIVE STUDY (1996 - 2005)

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Background: Data on imported severe malaria in children are scarce.

Objectives:

(i) To investigate for factors associated with the occurrence of a severe form;

(ii) among severe cases hospitalized in the most declaring hospitals, to assess specific predictors for severity and to study the relevance of WHO criteria, using the need for major therapeutic interventions (MTIs) or admission to an intensive care unit, since no deaths were declared within this period.

Patients and methods: We conducted a retrospective study from the National Reference Center for malaria data base in children hospitalized with *falciparum* malaria from 1996 to 2005. Severe malaria was defined according to the 2000 WHO criteria.

Results: Among 4,150 children (3,200 uncomplicated and 851 severe forms), predictors for the occurrence of a severe form were age < 2 y or travel in the Sahelian region. Among 421 severe cases hospitalized in the most declaring hospitals, need for both MTIs and stay in intensive care were significantly more frequent in children travelling in the Sahel, without chemoprophylaxis or with thrombocytopenia< 100,000/mm^3 at admission ; children aged< 2 y had a significantly more frequent need for MTIs. The WHO criteria predicting the need for MTIs or stay in intensive care were: severe anaemia, coma, prostration, seizures, impaired consciousness or respiratory distress. Uncomplicated hyperparasitaemia ≥4% had no prognostic value, whereas the threshold of 8% had the best sensitivity/specificity ratio to predict severity in our study.

Conclusions: This study provides important data to improve knowledge and the management of imported severe malaria in children.

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TREATMENT OF KALA-AZAR IN PEDIATRICS

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Background and aims: We retrospectively evaluated 430 infants and children with visceral leishmaniasis at hospitals affiliated to Shiraz University of Medical Sciences in Fars Province (located in the southwestern part of Iran).

Methods: Inclusion criteria were: a positive serological test result(indirect immunofluorescence antibody [IFA] test and samples>1/128)/or the presence of leishmania in the bone marrow aspiration.Patients were treated with 20mg/kg sodium glucantim daily for 21 days. Responses were assessed by defervescence, improvement of general condition, weight and anaemia and regression of organomegaly. Drug side-effects also were reviewed.

Results: Patients responded well to glucantim therapy with a cure rate of 95% .

Conclusions: Glucantim is the first-choice treatment and the side-effects were very low.

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SE ROEPIDEMIOLOGICAL SURVEY FOR TOXOPLASMOSIS AMONG SCHOOLCHILDREN OF THE PUBLIC SCHOOLS OF THE URBAN AREAS OF THE SARI, NORTHERN IRAN

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Objectives: Toxoplasmosis is one of the more common parasite zoonosis world-wide.

Methods: Se roepidemiological survey for toxoplasmosis among schoolchildren of the public schools of the urban areas of the Sari city, Mazandaran province, Iran, was carried out from September 2006 to March 2007 .A total of 1209 serum samples (686 males, 523 females) were examined for the IgG antibodies by ELISA. Questionnaires (with age and risk information) were completed for all of participants.

Results: Concerning >10 IU/ml as positive, the infection coefficient (IC) was 266 (22 %), of which 161 were male (IC=23.5) and 105 females (IC=20.1) (p=0.15). No age-antibody association was detected, although a gradual increase in positivity with increasing age was observed, reaching 23.1% in the oldest group (p=0.84). A significant association was observed with the presence of cat, contact with soil, washing hands before meals and eating raw or undercooked meat.

Conclusion: An improvement in personal hygienic condition and behavioral characteristics such as eating cooked meat is important in reducing the rate of toxoplasma infection.

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CONJUNCTIVITIS, CALF-TENDERNESS AND ACUTE RENAL FAILURE IN ADOLESCENTS: DON'T FORGET LEPTOSPIROSIS (WEIL'S DISEASE)

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Background: Leptospirosis is a worldwide zoonosis. The spectrum of severity is broad, ranging from sub-clinical seroconversion, self-limiting febrile illness or severe multisystem illness with jaundice and renal failure (Weil's disease). Weil's disease carries a mortality of between 5%-40%. Leptospirosis is a nationally notifiable disease in Ireland. We present 2 cases of Weil's disease presenting in adolescents.

Case 1: A 14 year-old Polish boy presented with fever, headache, postural hypotension, jaundice and anuria. Examination was notable for conjunctivitis and severe calf-tenderness. A detailed history revealed a summer job laying rat-traps in a granary. Treatment with IV Cefotaxime was complicated by a Jarisch-Herxheimer reaction.

Case 2: A 14 year-old Irish boy presented with fever, headache, vomiting, generalized myalgia, hypotension and acute renal failure. Examination was again notable for conjunctivitis and severe calf-tenderness. He was anicteric. Further questioning revealed recent exposure to freshwater whilst wading in a river. He was treated empirically with IV Cefotaxime and Clindamycin. Both cases made a full and uneventful recovery. Clinical suspiscion of Weil's disease was confirmed by strongly positive IgM ELISA specific for leptospires.

Conclusion: In Ireland, from January to October 2008, 18 cases of Leptospirosis were reported nationally compared to 11 cases for 2007 (63% increase). This suggests that Leptospirosis may be re-emerging in Ireland. Climate change with increased rainfall and flooding are postulated as possible causes. Conjunctivitis and muscle tenderness, particularly in the calf, are considered characteristic physical findings in Leptospirosis and should prompt detailed enquiry for direct animal or indirect water exposure.

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THE FIRST CASE OF CONGENITAL LEISHMANIASIS IN A FEMALE INFANT IN GREECE

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Background: The most frequent mode of transmission of leishmaniasis is by vectors like the Phlebotomus species. Other exceptional modes include blood transfusion, organ transplantation, inoculation of cultures as well as vertical transmission from mother to child.

Objectives: We report the first case of congenital leishmaniasis in an 11-month-old female infant in Greece.

Case report: The child was admitted with a 15-day history of fever, paleness, gingival bleeding and weight loss. The physical examination revealed hepatosplenomegaly, lymphadenopathy and the laboratory tests showed pancytopenia (Hb: 4.3g/dl, WBC: 4600/mm^3, PLT: 27000/ mm^3), hypergammaglobulinemia (IgG 2250 IU/ml) and elevated liver function tests. The confirmation of the congenital leishmaniasis was based on the positive titer of Leishmania antibodies (IFA 1:640) and the recovery of the promastigote form of the parasite in the bone marrow and the positive history of her mother during pregnancy. Treatment with liposomal Amphotericin B was given in 6 days with repetitive doses in days 14 and 21. After 8 days clinical manifestations disappeared and in a 5 weeks period the blood cell counts reached its normal values.

Conclusions: In endemic areas congenital leishmaniasis should be considered in infants presenting fever, pancytopenia and hepatosplenomegaly. Although the treatment success rates of congenital leishmaniasis with antimonial compounds are high, we believe that LAmB represents a safer treatment and should therefore be adopted as a first line regimen in cases of congenital leishmaniasis.

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ZOONOTIC INFECTIONS AS THE PAEDIATRIC PROBLEM IN RUSSIA

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Background and aims: Because of diverse ecological and epidemiological conditions in Russia, many zoonotic diseases are widespread. The aim was to estimate their relative importance in paediatric practice.

Methods: The analysis of official medical statistics collected in 2006-2007 by the Ministry of Health. Three age groups were considered: 142,792,000 individuals of all ages (whole population), 1,460,000 children < 1 year of age, and 9,583,000 children < 7 years amounting 6.7% of whole population.

Results: Three epidemiologically different types of zoonoses are observed. For first type the annual infection rate in the whole population (IRWP) and the infection rate in children < 7 years of age (IR< 7) are approximately the same. These infections are transmitted by tick bite during leisure activity in gardens, parks, and forests: ixodal tick-borne borreliosis, encephalitis, and rickettsiosis of North Asia (Table). IRWP is tenfold higher than IR< 7 for second type; these zoonoses are related to the farm work: hantaviral infection, leptospirosis, Crimean-Congo hemorrhagic fever, and brucellosis. Finally, IR< 7 is significantly higher than IRWP for zoonoses caused by bacteria using fecal-oral route: Salmonella, Yersinia, Campylobacter, etc. Rabies and anthrax are extremely rare in children in Russia. Less than ten annual children deaths are caused by zoonosis, mainly by tick-borne encephalitis and salmonellosis.

Conclusion: Most important paediatric zoonoses in Russia are food-borne and vector-borne infections.

Infection	Total number of cases, whole population	Infection rate per 100,000 individuals of all ages	Total number of cases, children < 1 year of age	Infection rate per 100,000 children < 1 year	Total number of cases, children < 7 years of age	Infection rate per 100,000 children < 7 years	Percentage of cases in children < 7 years
Tick-borne borreliosis	7349	5.15	4	0.28	329	3.43	4.5%
Tick-borne viral encephalitis	3316	2.32	3	0.21	131	1.36	3.9%
North Asian rickettsiosis	1799	1.26	8	0.55	221	2.30	12.3%
Hemorrhagic fever with renal syndrome (hantaviral infection)	6174	4.33	0	0.00	13	0.14	0.21%
Leptospirosis	672	0.47	0	0.00	4	0.04	0.52%
Crimean-Congo hemorrhagic fever	236	0.17	1	0.04	1	0.01	0.21%
Salmonellosis	44923	31.5	2957	202	15389	161	34%
Pseudotuberculosis	4657	3.26	44	2.98	1777	18.5	38%
Acute Y. enterocolitica infection	2836	1.99	51	3.46	692	7.22	24%

[Prevalence of zoonotic diseases in Russia]

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TICK-BORNE MIXED INFECTION IN ENDEMIC REGION OF WESTERN SIBERIA

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Tick-borne infections are of the most widespread diseases with natural focality in Western Siberia. Vector (taiga tick Ixodes Persulkatus) can be simultaneously infected by several agents and mixed infections are greatly frequent.Clinical manifestations of tick-borne mixed infection in children in Kemerovo region - tick-borne encephalitis (TBE), tick-borne borreliosis (TBB), human monocytic ehrlichiosis (HME) and human granulocytic anaplasmosis (HGA) were researched.We evaluated clinical and laboratory findings in 182 patients 1-14 years old who was seeking care with febrile illness, meningitis and meningoencephalitis and other clinical manifestations caused by different serologically confirmed variants of mixed infection.Mixed-infection of HGA and HME was diagnosed in 3 (4.3%) patients; TBB and HME in 4 (5.8%); TBB and HGA - in 7 (10.1%); TBE and TBB - in 28 (40.6%); TBE and HGA - in 12 (17.4%); TBE and HME - in 7 (10.1%); TBE, TBB and HGA - in 4 (5.8%); TBE, HGA and HME - in 2 (2.9%), TBE, TBB and HME - in 2 (2.9). Disease may progressed in a febrile (63.8%), meningeal (23.2%) or focal form (13.0%). Acute general infection syndrome was the most frequent manifestation (36.6%). Meningitis was in 31.0%. Mixed infection in the meningoencephalitic form (2.1%) was characterized by the severest and longest progression. Mixed infections manifested more severe progression of clinical symptoms and absence of specific for mono-infections symptoms. The results lead to the conclusion that children in Siberian region have been at high risk of mixed-infection and of developing the most complicated clinical forms.

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VISCERAL LEISHMANIASIS: 14 YEAR EXPERIENCE IN A SPANISH PUBLIC HOSPITAL

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Background and aims: To analyze the clinical and epidemiological characteristics of cases of visceral leishmaniasis (VL), to evaluate the diagnostic techniques tested and the safety and efficacy of treatments used.

Methods: We retrospectively reviewed the medical records of children diagnosed with VL between January 1994 and December 2007 in a public Hospital in Madrid. The diagnosis of VL was based on visualization of *Leishmania* sp in bone marrow aspirate (BMA) or culture or positive PCR analysis of the BMA.

Results: Eleven immunocompetent children were identified. Median age was 21 months. Fever was present in all cases, and hepatomegaly and splenomegaly in 10 (91%). Anemia was the most frequent haematological finding (100%). A BMA was obtained in all cases. *Leishmania* amastigotes were observed in 8 (73%) cases. *Leishmania* DNA in the BMA was detected in 6 out of 6 (100%) patients. Positive IFAT analysis was observed in 63% of cases tested. Urinary antigen detection test was positive in 4 out of 6 (67%) children. Treatment consisted of meglumine antimoniate in 3 patients and liposomal amphotericin B (LAB) in 8 (73%) patients. All children had an early clinical response. Only one child treated with LAB relapsed. No severe adverse events were observed with treatment.

Conclusions: VL is a common disease in our area. PCR analysis of the BMA was more sensitive than traditional diagnostic techniques. Non-invasive diagnostic techniques may be used as an aid in the diagnosis of VL . Short course treatment of VL with LAB has been safe and effective.

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FILARIASIS. A PEDIATRIC EMERGENT TROPICAL DISEASE WITH HIGH IMPACT IN PUBLIC HEALTH

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Background and aims: Filariasis is a parasitic infection produced by nematodes. WHO estimates a prevalence up to 17.5 million worldwide and an incidence of 600 000 cases/year. Central and Southamerica, Africa and some areas in The Pacific are considered endemic.

Methods: A retrospective study was performed, revising clinical records of patients diagnosed with filariasis between 1995 and 2007 in our Tropical Diseases Pediatric Unit. Variables studied were: origin, age, clinical signs, absolute eosinophilia count, other parasites, coinfections, treatment and evolution. Filariasis diagnosis was considered when clinical and analytical signs and one of the following were present:

1) Microfilaremia;
2) Epidermic biopsy visualization;
3) filaria observation through conjunctive tissue;
4) Positive Mazzotti test;
5) highly positive serology.

Results: All the 14 patients came from Ecuatorial Guinea. Medium age: 12.1 years (3-15). Results are presented in table 1.

Clinical signs	n = 14	*Filaria*	n = 14
•Itch	10		
•Dermatosis	6	•*Oncocerca volvulus*	5
•Edema	3	•*Mansonella perstans*	8
•Eye disturbances	2	•*Loa loa*	2
•Oncocercoma	1		
•Gastrointestinal discomfort	2		
Eosinophilia cel/mm3)		*Coinfection/other parasites*	
		•*P.falciparum*	4
		•*A.lumbricoides*	8
		•*T. trichura*	5
•Mild (450-1500)	1	•*G. lamblia*	4
•Moderate(1500-5000)	6	•*E. hystolitica*	3
•Severe (>5000)	5	•*Other intestinal parasites*	4
		•*VIH/VHB/TBC*	1/1/1
Diagnosis		Evolution after treatment	
			4
•Microfilaria in blood	8	•complete recovery	1
•Conjunctive direct visualization	2	•persistence of clinical signs	3
•Epidermic biopsy	5	•persistence of microfilaremia	2
		•persistence of eosinophilia*	

[Table 1]
*Two patients presented persistent eosinophilia; one of them transitory and the other because of Oncocerca coparasitization resolved after retreatment.

Conclusions: Filariasis must be suspected in children with eosinophilia from endemic areas even lacking clinical signs. Sometimes empirical treatment needs to be performed if suspected, and other parasitization ruled out. Ivermectin is nowadays the first choice therapy in children. Diagnosis and treatment of filariasis are important public health interventions in order to prevent an established disease with serious complications (elephantiasis, blindness).

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NEUROCYSTICERCOSIS: A TWELVE-YEAR EXPERIENCE

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Background and aims: Neurocysticercosis is the most common parasitic infection of the Central Nervous System. Although it is an endemic disease of the developing countries, it can also be found in nonendemic areas, mostly due to immigration. The aim of the study was to review and evaluate the outcome of patients with neurocysticercosis in our department.

Methods: A retrospective review of children with neurocysticercosis admitted to the Pediatric Department of Fernando Fonseca Hospital between July 1996 and December 2008 was conducted. The parameters analysed were: demographic, epidemiological and clinical data, laboratory and imaging alteration, treatment, evolution and household screening.

Results: Eighteen children were studied with a median age of 11.5 years. Thirteen (72%) were female, fifteen (83%) were from Africa and all were from a low social-economical class. A seizure was the first manifestation in 89% of cases. Neuroimaging showed an active lesion in 72% of cases, mainly in the left parietal lobe. Serology was negative or inconclusive in seven (39%) patients. Therapeutics was made with anticonvulsive drugs. At follow-up, the cysticercal lesion disappeared in five (36%) patients and three (19%) children with multiple lesions had recurrent seizures. Household screening was positive in 6 relatives.

Conclusion: In our study, almost all children with neurocysticercosis were from Africa, where this disease is endemic and a negative serology didn't exclude the diagnosis, as described in literature. Neurocysticercosis was well managed with anti-epileptic medication alone and the prognosis was good.

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KIDS BOTULISM IN BOSNIA- MIMICS PROBLEMS AND DIFFICULTIES IN DIFFERENTIAL DIAGNOSIS

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Introduction: In infant botulism , paralysis is descending and there are no sensory abnormalities. Tick paralysis typically affects children but rarely infants and early manifestations and parasthesis and leg weakness followed by ascending paralysis.

Methods: Everything are analysed by Sigmastat Statistic Programme during twenty years 1988-2008 from history documents at children with differential diagnosis botulism in Bosnia and Herzegovina.

Results: Retrospective study was conducted of 19 children for twenty years from documents in Infectious Clinic, Pediatrics Clinic or General Hospital Sarajevo who were evaluated in Sarajevo during period 1988-2008 and a case-matched study was conducted of a subgroup of suspection in 300 children (6.33% true diagnosis) in age 0-19 years.

Discussion: These mimics include infectious disorders (septicemia, meningitis, poliomyelitis, encephalitis); biochemical or metabolic disorders (dehydratation, electrolyte imbalance, genetic metabolic disorders, Leigh disease); endocrinologic disorders (hypothyroidism); neorologic conditions (myasthenia gravis, infantile polyneuropathy, Guillain Baree syndrome, Werding Hoffman disease, congenital myopathy, tick paralysis); and drug or chemical poisoning.

Conclusion: Several disorders can mimic infant botulism superficially. The constellation of findings of infant botulism in setting age, feeding history, and exposures is usually classic, and the possibility of another diagnosis is remote.

Keywords: Botulism, Kids, Therapy, Complications.

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DENGUE FEVER: SITUATION IN THE CZECH REPUBLIC AND CASE REPORT OF AN 18-YEAR-OLD BOY

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Background: Dengue fever (DF) is a common febrile illness in travellers returning from tropical countries. In the Czech Republic there were 49 reported cases (adults and children) of DF in the national surveillance system since January 2000 but this number probably does not represent all cases. Since December 2004 there were diagnosed 17 cases of acute dengue infection at the Department of Infectious Diseases of Bulovka University Hospital in Prague.

Methods: We are presenting case report of an 18-year old boy who was admitted to a hospital care with fever after having returned from 3-month stay in Vietnam in August 2008.

Results: The patient presented with fever (39.5 °C), headache, arthralgia, myalgia, maculopapular rash. Laboratory findings were: significant leukocytopenia (2.7×10^9/l) with relative lymfocytosis, thrombocytopenia (66×10^9/l), hypokalemia (3,35 mmol/l), elevated aminotransferases AST (2.36 µkat/l) and ALT (2.65 µkat/l) and low CRP level (11.6 mg/l). Acute dengue infection was confirmed by serological methods based on positivity of anti-Dengue IgM and seroconversion of anti-Dengue IgG antibodies. Prolonged coagulation times were observed but the patient did not fulfil the criteria of dengue shock syndrome and the clinical course was uncomplicated. The patient was discharged from hospital care after 13 days and followed in ambulatory care.

Conclusion: Infections caused by dengue virus range among emerging in the tropical countries and may lead to life-threatening conditions. Therefore there is a need for improvement of the diagnostic approach to febrile patients returning from tropical countries and for appropriate and prompt case management.

OTHERS

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LONGTERM OUTCOME OF FEBRILE CYTOPENIA IN CHILDHOOD

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Aim of the study was to identify the association of acquired cytopenias with febrile infections in healthy children and to assess their course and outcome in a one and two years time.

Material/methods: 117 children, 4.0±3.8 y old (range:0-14), were admitted to a Pediatric Ward because of febrile cytopenia during a 3y period and were investigated with indices of infection, cultures of body fluids and serological tests.

Results: 66/117 (56.4%) children, aged 3.3±3.8y, presented with neutropenia/leucopenia, 19/117 (16.2%), 5.0±3.4y with thrombocytopenia, while 32/117 (27.4%) 4.8±4.0y had 2 or 3 cell lines affected. In 85/117(72.4%) children, cytopenia recovered within 2 mo, in 11/117 (9.4%) lasted 2-6 mo (transient cytopenia, TC), while in 21/117 (17.9%) lasted for >6 mo (chronic cytopenia, CC).

TC was associated mostly with viral infections. Among the 21 cases who evolved in CC (11 girls/10 boys), 14 (66,7%) had neutro/leucopenia, 4(19%) thrombocytopenia, in 3(14,3%) 2-3 cell lines were affected and an infectious agent was identified in 5/21(23,8%). 4 had autoimmune neutropenia,1 had SLE and 3 had hematological malignancies.

We re-evaluated 114 children in one and two years. Children with postinfectious cytopenia recovered within one year (87,2%).

At 2 years, only 7 cases (42,8%) were still cytopenic (2 autoimmune neutropenia,3 chonic ITP and 2 chronic neutropenia). In none of these 7 patients an infectious agent was identified.

Conclusion: Postinfectious cytopenias following bacterial/viral infections were in the majority transient and fully recovered within one year. In two years time very few cases still remained cytopenic.

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META-ANALYSIS ON DENGUE NS ANTIGEN AS A RELIABLE ROUTINE DIAGNOSTIC KIT

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Dengue, a mosquito-borne disease, poses threat to many subtropical and tropical countries these days. Two classical pictures of dengue include dengue fever and dengue haemorrhagic fever, with the latter being relatively more life-threatening.Clinical symptoms of dengue fever can sometimes be indistinguishable from other viral infection. Thus, a rapid laboratory diagnosis is needed in diagnosis of dengue fever. In recent years, detection of virus antigen through its non-structural protein, Dengue NS1 antigen has gained more attention in clinical laboratories. A meta-analysis study is performed based on studies reported in the literature to assess the reliability of this new detection method.

Objective: A meta-analysis is performed to assess the sensitivity, specificity and diagnostic accuracy of Dengue NS1 antigen.

Method: Literature search was performed in MEDLINE, PUBMED and scientific journals for evaluation studies reported on Dengue NS1 antigen.

Result: A total 7 studies were included in this meta analysis. A total of 3 tables summarizing the sensitivity, specificity, negative predictive value and positive predictive value and other details are presented.

Conclusion: This method of Dengue antigen detection has high level of:

Pooled Sensitivity; Pooled Specificity; Negative Predictive Value; and Positive Predictive Value

This makes this method reliable and highly recommended for routine testing.

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COST-EFFECTIVENSS ANALYSIS OF THE NEW 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN-D CONJUGATE VACCINE (PHID-CV) IN VARIOUS ENVIRONMENTS

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Background and aims: To evaluate the cost-effectiveness of routine pneumococcal vaccination with PHiD-CV compared with the currently available PCV-7 in Finland and Canada, two countries with comparable healthcare systems but in different continents.

Methods: A steady-state, age-compartmental, deterministic population model that simulates the vaccine impact for one year was calibrated with either Finnish or Canadian demography, epidemiology and cost data. The effect of childhood vaccination, assuming 100% coverage and 4-doses (3+1), was estimated by calculating the reduction in incidence and clinical outcomes associated with invasive pneumococcal disease (IPD), pneumonia, acute otitis media (AOM). Herd protection against invasive disease, cross-protection (serotype 6A) and serotype replacement are included. The clinical outcomes include the number of cases, hospitalizations, ambulatory cases, deaths, and Quality Adjusted Life Years (QALYs) gained. The economic outcomes include incremental cost per life-year gained and cost per QALY gained from the healthcare perspective.

Results: Per year across the whole population, compared against PCV-7, PHiD-CV is predicted to reduce IPD by an additional 59 cases and 384 cases; pneumonia by 69 cases and 457 cases; tympanostomies by 2624 events and 9830 events; AOM by 48808 and 170951 GP visits in Finland and Canada, respectively. Compared with PCV-7, PHiD-CV is expected to result in cost savings of 8.8M€ in Finland and CAD23.5M (14.6M€) in Canada. PHiD-CV was predicted to be the dominant strategy in Finland and Canada.

Conclusions: With country-specific demography, serotype distribution, disease epidemiology and disease management, PHiD-CV vaccination is cost-saving in both countries compared with PCV-7 at price parity.

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TUBERCULOSIS IN INFANTS: A TWENTY-YEAR REVIEW

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Background and aims: Despite the increasing global burden of tuberculosis, there are few series in infants under 1 year. Our aim is to describe epidemiological, clinical, radiological and microbiological features in these patients.

Methods: We reviewed the clinical records of the patients under 1 year diagnosed with tuberculosis between January 1988 and January 2008 at Hospital La Paz (Spain).

Results: A total of 30 cases were identified, with a mean age of 7.6 months. There were three patients under 3 months; one of them had confirmed congenital tuberculosis. The disease was diagnosed in 60% of the cases through clinical signs and symptoms (66% respiratory, 50% fever, 30% constitutional) and in 40% after case contact investigation. The source of infection was identified in 66% of cases. The most frequent radiographic finding was parenchymal consolidation (46%), whereas only 18% showed isolated hilar adenopathy. Three patients presented with miliary pattern and two as lung masses. There were four cases with extrapulmonary disease (3 meningitis and 1 arthritis). Gastric aspirate smears were positive in 10% of the patients and culture in 66%. No drug-resistant strains were isolated. Thirty-six per cent received corticosteroids, mainly due to extrinsic airway compression. Infants with pulmonary tuberculosis recovered fully. All patients with meningitis developed sequelae (seizures, mental retardation).

Conclusions: Tuberculosis in infants frequently presents with parenchymal involvement, severe or disseminated forms. Most patients are symptomatic at the time of diagnosis. Gastric aspirate smears and cultures yield positive results more frequently than in older children.

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RENAL TUBULAR ACIDOSIS TYPE II DIAGNOSED DUE TO ACUTE ROTAVIRAL DIARRHEA- CASE REPORT

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Background: Renal tubular acidosis is a rare disorder at newborn that may appear as a single isolated identity or may accompany other tubular defects.

Aim of the study: Case report of a female newborn admitted for acute diarrhea that masked proximal tubular renal acidosis.

Patient and method: Case report of a newborn girl admitted for cough, nasal obstruction, watery stools, vomiting, and failure to thrive.

Results: Lab exam revealed leukocytosis 15,900mm3 and thrombocytosis 588,000, sever nutritional anemia Hg 8,4g/dl, ESR of 38mm/h, CRP of 1.41mg/dl, persistent sever hypokalemia with a K of 2.2 mEq/l, hypocalcemia Ca= 7.6mg/dl. Sever metabolic acidosis ph=7.21 to 7.27 for 14 days, urine culture, blood culture, pharyngeal and nasal swab were negative, stool culture rotavirus. The diagnosis of proximal tubular acidosis type II was established.

Ultrasound showed fetal lobulation of the kidney. Therapy was started and the toddler received for 14 days NaHCO3 iv then orally, ceftazidime and gentamicin, supportive therapy.

After 28 days of hospitalization was discharged on oral alkali therapy. After 4 weeks was readmitted for the same complains the first time. K levels arouse after 6 days of i.v. fluid therapy. She was discharged with oral alkali therapy and underwent constant monthly follow up.

Conclusion: Proximal tubular acidosis is a rare disease that may appear in common diseases such as diarrhea or part of complex syndromes. In newborns it may express renal immaturity.

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ASSESSMENT OF POTENTIAL RISK FACTORS FOR POSTTRANSPLANT LYMPHOPROLYPHERATIVE DISORDER IN PEDIATRIC SMALL BOWEL RECIPIENTS

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Small bowel transplantation (SBTx) is an evolving field. We sought to characterize the incidence and risk factors associated with posttransplant lymphoprolypherative disorder (PTLD) after SBTx.

Methods: Between January 2003 and December 2007, 98 patients underwent 110 isolated small bowel or multivisceral transplants. Induction therapy (thymoglobulin, basiliximab) and tacrolimus-based immunosuppression were standard of care. We investigated risk factors for PTLD by logistic regression analysis; due the rarity of the outcome we reported as potential risk factors those with OR>1.50.

Results: Median age at transplantation was 1.6 years. PTLD developed in 20/98 patients (20.4%) at a median age of 1.83 years. PTLD diagnosis was made in 10 patients (50%) within 6 months and 15 (75%) in the first year post-SBTx. Potential risk factor for PTLD development were: EBV D+ compared with EBV D- (OR 2.31, 95CI 0.26, 111.26, p=0.77), and CMV D+/R- status compared with CMV D-/R- (OR 2.24 , 95CI 0.60, 8.34, p=0.23). Each HLA mismatch increased the risk of developing PTLD by 50% (OR=1.5, 95CI 0.9, 2.63, p=0.13) and mismatches at HLA-DR loci conferred a greater risk (OR 2.57, 95CI 0.9, 7.38; p=0.08). 95% (19/20) of the PTLDs developed after the first transplantation. Age, sex, type of transplantation (isolated small bowel vs multivisceral), type of induction therapy, rejection, re-transplantation did not appear to be associated with PTLD.

Conclusions: Potential risk factors for PTLD development in our pediatric SBTx population included: EBV+ organs, CMV D+/R- sero-status mismatch, number of HLA mismatches, HLA-DR mismatch donor-recipient. These factors deserve further investigation.

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PERIPHERAL FACIAL PALSY AS THE ONLY PRESENTATION OF BORRELIOSIS

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Background: Borreliosis is correlated with neurological symptoms in 10-20% of affected children. The most common symptom of neuroborreliosis in children is motor dysfunction and Peripheral Facial Palsy (PFP) may be the only sign.

Methods: We describe the case of a 3-year-old male born and grown up in Milan, who showed sudden onset of PFP.

A mountain holiday, three months before symptoms, is the only relevant anamnestic data.

A First ELISA serological test, performed when patient was admitted at the onset of the symptom, showed positive IgM (40.60 UA) and IgG (21.1UA) versus Borrelia. No other symptoms consistent with Borreliosis were observed.

Although the PFP abated spontaneously within 15 days, oral treatment with Amoxicillin 50 mg/kg/day began when serological diagnosis was made and confirmed using Western Blot procedure (WB). Pharmacological therapy was therefore continued with oral Amoxicillin Clavulanate for 21 days; no further signs or symptoms consistent with Borreliosis were observed. Serological ELISA test, carried on one month after therapy´s end, attested previous infection (IgM 0.5 UA/ml; IgG 39.5 UA/ml).

Conclusion: Treatment with antibiotics does not seem to influence the prognosis of PFP. However, a prompt treatment is always recommended to prevent a late onset of the disease.

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VALIDATION OF A CLINICAL DECISION RULE TO REDUCE ANTIBIOTIC USE FOR PHARYNGITIS TREATMENT IN LOW-INCOME SETTINGS

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Background: Systematic antibiotic treatment of pharyngitis is common in developing countries since microbiological diagnosis for Group A Streptococcus (GAS) is rarely available and rheumatic fever is very prevalent. A clinical score was developed to be used in Brazil that had the potential to reduce antibiotic prescription by 40 to 55% (Smeesters, Pediatrics 2006).

Aims: To prospectively validate the accuracy of this clinical score in a similar Brazilian paediatric population.

Methods: Children (0 to 15 years) with pharyngitis were prospectively enrolled in 3 paediatric hospital practices of Brasilia during 17 months in 2007-2008. The clinical score was compared to a rapid GAS antigen diagnostic test (RADT).

Results: 357 children were enrolled. 238 (66%) had a negative RADT. The application of this score would have reduced the antibiotic prescription by 69%. However, the specificity was 66% indicating that the use of this score would lead to a risk of no treating 34% of patients presenting a positive RADT. 75% of these potentially untreated children were however less than 5 years old suggesting that a substantial proportion of them were probably asymptomatic carriers. Sequential serologies could unfortunately not be performed to confirm this hypothesis.

Conclusions: The use of this score would have allowed for a substantial reduction (69%) of antibiotic prescription in pharyngitis in public hospitals from Brasilia. However, the low specificity observed in real settings, especially for children under 5 years old, precludes his use in its current version.

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KAWASAKI DISEASE RECURRENCE AND PERIPHERAL BLOOD EOSINOPHILIA

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Background and aims: Although eosinophilia in peripheral blood of patients with Kawasaki disease (KD) was first described by Kawasaki *et al* in 1967, little is known about the presence of eosinophilia in different stages of KD. Recently, it has been demonstrated that eosinophilia after intravenous immunoglobulin (IVIG) treatment has an inverse correlation to KD children with IVIG treatment resistance.

Methods: We present the case of a 3 year-old child who was re-admitted to our Department with KD recurrence 12 days after the initial diagnosis of KD and IVIG treatment.

Results: On his first admission he received a single dose of IVIG (2g/kg) and he was commenced on aspirin at a dose of 90mg/kg/day. The percentages of eosinophils in peripheral blood were 19% before IVIG treatment and 3% one day after IVIG treatment. On his second admission a second dose of IVIG (2g/kg) was administered. The percentages of eosinophils were 12% before IVIG treatment and 16% 4 days after IVIG treatment. He responded well and he continued aspirin for one week at a dose of 90mg/kg/day, which was reduced to 5mg/kg/day for 6 weeks. Ten days, 2 months and 3 months after his second admission the percentages of eosinophils were 20%, 34% and 15%, respectively.

Conclusions: In our case recurrence of KD was followed by a marked increase in eosinophils, especially 2 months after IVIG treatment. Further research is required to investigate the role of eosinophils in the pathogenesis of KD and the correlation of eosinophilia with IVIG treatment resistance.

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TERREIN REDUCED LPS-INDUCED LUNG INFLAMMATION IN HUMAN LUNG CELLS

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Adhesion molecules, intracellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), are expressed on several tissues in response to various inflammatory stimuli and contribute to the recruitment of inflammatory cells and transmigration. Recently many researches have focused on the down regulation of cell adhesion molecules for the treatment of lung inflammation. Fungi have provided medicine with a wide variety of valuable substances and terrein is one of the bioactive fungal metabolite. The purpose of this study is to determine the effects of terrein on lipopolysaccharide (LPS)-induced expression of ICAM-1 and VCAM-1 in human lung cell line, as well determine the mechanism of the observed effects. LPS-induced expression of ICAM-1 and VCAM-1 were inhibited by terrein in both a time and dose dependent manner. LPS-stimulated translocation of nuclear factor kappa B (NF-kB) into the nucleus, which was blocked by inhibitors of amino kinase terminal (AKT; LY294002), extracellular signal regulated kinase 1/2 (ERK 1/2; PD98059), p38 (SB203580) and c-jun NH2-terminal kinase (JNK; SP600125) or terrein. In addition, above inhibitors and terrein also reduced the level of ICAM-1 and VCAM-1 expression in LPS-induced inflammation of pulp cells. Terrein suppressed NF-kB activation by blocking the activation of Akt. These results strongly suggest the potential role of terrein as an anti-inflammatory modulator in inflammation.

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A RETROSPECTIVE ANALYSIS OF MICROBIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERN IN A DEVELOPING COUNTRY TERTIARY CARE PEDIATRIC CARDIAC ICU

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Background and aims: To evaluate the microbiological profile in a pediatric cardiac ICU.

Methods: A retrospective study was undertaken over duration of one year and included 302 preoperative and postoperative cases admitted to the pediatric cardiac intensive care unit (PCICU) in a tertiary care centre for all forms of complex cardiac heart diseases. The indications for sending cultures included, clinical signs of sepsis including core temperature >38.5°C or < 36°C, total leucocyte count elevated or depressed for age, any preexisting chest, urine or systemic infection or additional risk factors like poor nutritional status, open chest after surgery, prolonged ventilation, low output state or if the patient required ECMO.

Results: Of total 971 cultures sent, 224 were positive. Number of cultures positive were blood 120/533 (22.51%), tracheal 35/128 (27.34%), triple lumen tip 29/110 (26.36%), urine culture 17/82 (20.73%), arterial line tip 7/34 (20.59%), chest wound swab 14/35 (40%) and one each in PD fluid and abdominal wound swab. The common organisms isolated were Klebsiella, Pseudomonas, Enterobacter, Acinetobacter, Enteroccocus and Stenotrophomonas maltophilia. Candida species and gram positive organisms isolated only rarely. The predominant antibiotic sensitivity included Carbapenem, Piperacillin Tazobactum, and Colistin for gram negative, while gram positive organisms were sensitive to Vancomycin, Teicoplanin and Linezolid. In patients in whom more than 3 cultures were sent due to prolonged PCICU stay the positivity rate was 166/644 (25.93%).

Conclusion: Gram negative pathogens continue to be a bane in Pediatric cardiac ICU and contribute significantly to ICU related morbidity with decreasing levels of antibiotic sensitivity.

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CLINICAL FEATURES OF SEVERE BACTERIAL INFECTIONS OF CHILDREN IN A COMMUNITY HOSPITAL IN RURAL TAIWAN

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Background and aims: To evaluate the disease burden of severe bacterial infections of Taiwanese children in a rural county.

Methods: We retrospectively collected the culture reports from the Clinical Microbiology Laboratory in 2005-2008.

Results: We recruited 48 children with positive cultures from sterile sites in 2005-2008. The male to female rate was 1.53 (29/19) and the median age was 17 month (0-148 months). The cultured sites and organisms were listed in Table 1. *Streptococcus pneumoniae* (N=12, 25%), *Escherichia coli* (N=11, 23%) and Salmonella species (N=8, 17%) ranked among the most prevalent pathogens. Twelve (25%) children required intensive care unit admission. Mortality rate was the highest among two infants with *Streptococcus agalactiae* infection (100%). Among the 12 *Streptococcus pneuminiae* isolates, 7 were serotyped and only 4 could be covered by the PCV7.

	Organism	Site
Gram-positive	Streptococcus pyogenes (1), S. agalactiae (2) and group D streptococcus (2)	Blood
	Streptococcus pneumoniae (12)	Blood (10), Blood/CSF (1), pyomyositis (1)
	Staphylococcus aureus (4) including oxacillin-sensitive (OSSA)(4) and oxacillin-resistant (1)	Blood (4), Deep neck infection (1)
	OSSA and Streptococcus group D (1)	Blood
Gram-negative	Escherichia coli (11)	Blood (8), Blood/CSF (2), CSF (1)
	Salmonella species (8)	Blood
	Haemophilus influenzae (3) type b (2) and not-typed (1)	Blood
	Klebsiella pneumoniae (2)	Blood
	Morganella morganii (1)	Blood

Conclusions: *Streptococcus pneumoniae* remained the most important pathogen in children of this region.

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INCOMPLETE KAWASAKI DISEASE - CASE REPORT

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Background: Kawasaki disease (KD) is the 2nd vasculitic illness of childhood (after Henoch Schonlein purpura) and the commonest cause of heart disease in childrenDiagnosis is based on clinical criteria, sustaining by the laboratory finding and echocardiography and the exclusion of other diseases, primary sepsis. Along with classical forms of the disease there were described incomplete forms, especially in infants.The management, therapeutic approach and follow up of each patient are based by the risk stratification of coronary complication severity.

Methods: We report a case of 7 month infant, admitted in our hospital with diagnosis of aseptic acute meningitis, prolonged fever, palms and soles descuamation, angular keilitis. The diagnosis was sustained on: history of the disease, clinical and laboratory findings.

Results: Laboratory findings showed the presence of an high inflammatory syndrome (ESR, CRP) and coronary ECHO-dopller reveled coronary vasculitis suggesting Kawasaki disease in early stage and illustrated the insert difficulties of the patients with incomplete forms of KD. A very important role on establishing the earlier and long term therapeutic approach has been the risk stratification.

Conclusions: Propose of this paper is facilitating of recognition of incomplete KD, who appear especially in infants which, in absence or late diagnostic, could evolutes through the severe stage in presence of cardiovascular involvement. We also consider, the efficacy of standard treatment even in late diagnosed cases (subacute phase).

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ANTIBIOTIC PRESCRIBING FOR CHILDREN IN THE EMERGENCY ROOM (ER)

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Background: Judicious use of antibiotics can slow the spread of antimicrobial resistance. The ER frequently represents the site for initiating antimicrobial therapy and is usually an important source of inappropriate or unjustified prescribing. The aim was to study patterns of antibiotic use.

Material and methods: Analysis of the medical records of children seen at the ER in 2008, during 2 days a month, randomly selected. Final diagnosis and the prescribed antibiotic were analysed. Dose regimens and length of treatment were not evaluated.

Results: During this period, 2863 children were observed (119/day). Oral antibiotics were prescribed in 404 children (14%): amoxycilin (67%), amoxycilin-clavulanate (13%), flucloxacilin (8%), macrolides (6%) and second generation cephalosporins (5%).

Amoxycillin was prescribed mainly for respiratory infections and fever of unknown origin, amoxycilin-clavulanate and second generation cephalosporins for urinary tract infections, flucloxacillin for soft/skin tissue infections and macrolides for pneumonia.

Prescription occurred in 79% of the acute otitis media (AOM) cases, 7% of the fevers of unknown origin, 4.7% of the upper respiratory tract infections, 0.9% of the bronchiolitis and 0.6% of the acute gastroenteritis. AOM accounted for 24.5% of all prescriptions and in 91,9% amoxycilin was the choice.

In the following seven days, we have not noticed any unfavourable therapeutic outcome.

Conclusions: AOM was the most frequent reason for antibiotic prescription and substantial reduction in prescription could probably be possible by an expectant attitude in more cases. The limited number of prescriptions in conditions that are primarily viral is of note. Broad-spectrum agents were not used.

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FOLLOW UP OF CHILDREN WITH LATENT TB OR HILAR TB ADENOPATHY WITH QUANTIFERON ASSAY

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Introduction: Quantiferon assay (QA) is a method for diagnosis of TB infection. Limited data exist about whether QA becomes negative after treatment or if it has any value for following up patients.

Methods: We performed QA and PPD in 63 children who have been followed up in a TB clinic. Children with the diagnosis of latent TB (LTB) (46) took chemoprophylaxis with isoniazid and those with hilar TB adenopathy (TBA) (17) took therapy with isoniazid, rifampicin and pyrazinamide.

Results: No child had TB disease in the years following therapy. Children with LTB or TBA were followed up for a median time 8,76 (min-max: 1,13-14,81) and 14,69 (5,11-15,87) years respectively.

Regarding children with LTB the QA was positive in 18 out of 46 (39,1%) , whereas PPD was >15mm in 16 (34,8%). Correlation of QA was found with last PPD >15mm (p=0.02), higher values of initial and last PPD (p=0,04 and p=0,03 respectively) and a negative correlation with age at diagnosis (p=0,019) and BCG positivity (p=0,003).

Regarding children with TBA the QA was positive in 9 out of 17 (52,9%) whereas PPD was >15mm in 6 (35,3%). There was correlation of QA with positive environment for TB (p=0.02) and a negative correlation with age at diagnosis (P=0.02), years after treatment (P=0.04) and age at QA (P=0.02).

Conclusions: QA is becoming negative in a proportion of patients who took chemoprophylaxis or therapy for TB. The interpretation of positivity of QA for following up patients needs to be elucidated in prospective studies.

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AILING TODDLERS - IS THERE A RELATION BETWEEN BEHAVIOUR AND HEALTH?

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Background and aims: We studied the differences between ailing toddlers and healthy children in objective parameters to try to uncloud the phenomenon of ailing toddlers.

Methods: This cross-sectional research is conducted with the help of a questionnaire that was developed by the authors. With this questionnaire we collected information on health, food, television & hobby, sleeping patterns and other topics.

The ailing toddlers consisted of children aged 1 to 4 years with recurrent infections (>1/month) that cannot be explained by physical abnormalities. The control group consisted of healthy children aged 1 to 4 years without recurrent infections.

Results: Ailing toddlers used antibiotics more often ($p < 0,01$). Parents of control children are healthier compared to parents of ailing toddlers ($p < 0,05$).

Parents of children in the control group more often determine the size of the meal the child eats compared to parents of ailing toddlers ($p < 0,05$). Ailing toddlers eat less vegetables and beef ($p < 0,05$). Parents of ailing toddlers are less inclined to correct difficult behaviour of their child ($p < 0,05$).

No differences are found in sleeping patterns or favourite pastimes.

Conclusions: There is a difference in behaviour of children and parents in both groups. Parents of ailing toddlers utilize fewer rules in areas that directly influence the health status. Their parents are more submissive when it comes to difficult situations during meals.

A possible interpretation could be found in psychoneuroimmunology.

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ORALLY TAKEN PHAGES APPEAR IN THE URINE AND FECES OF PEDIATRIC PATIENTS

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Background and aims: Despite extensive experience in implementing phage therapy, particularly in East-European countries, the pharmacokinetics of phages in the infected human organism are not yet sufficiently investigated. The aim of the present study was to determine the extent to which phages taken orally by pediatric patients during the course of treatment are found in urine and feces.

Methods: 62 infants and children with different bacterial infections whose bacterial samples responded in vitro to a commercially available phage cocktail were included in the study. On day 3-5 of the phage therapy, the presence of phage in urine and feces was determined. The samples were titrated on the commercial phage host strains *Staphylococcus aureus, Pseudomonas aeruginosa, Proteus mirabilis* and *Escherichia coli* to separately determine the level of each kind of phage.

Results: At least one component of the oral phage ingested was detected in feces in 47/56 samples and in urine in 32/38 samples. [Not all kinds of samples were available for all 62 patients]. In feces, the highest prevalence and titer was for *P. aeruginosa* phages (76.8 %, geometric mean $5.9 \cdot 10^2$ pfu/mL), in urine - E. coli (65.7% and $4.7 \cdot 10^3$). Detection of phage in urine indicates that orally taken phages pass into the blood too. While employing the phage therapy, no adverse reactions were observed.

Conclusions: Our data indicate that phage can be safely taken orally for the treatment of intestinal, systemic and urinary tract infections in infants and children.

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LEMIERRE'S SYNDROME PRESENTING WITH SPINAL EXTRA-DURAL COLLECTIONS AND UNUSUAL PATTERN OF CRANIAL NEUROPATHY

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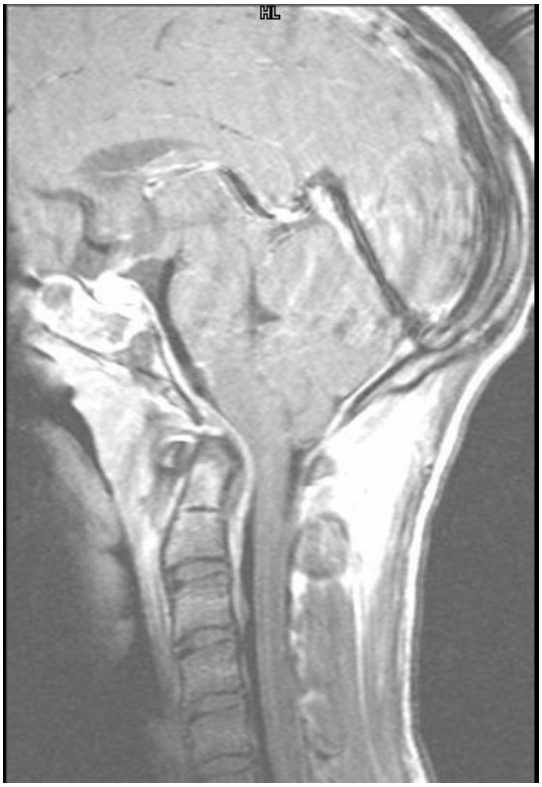
Background: Lemierre´s syndrome is a rare clinical condition, in which, oro-pharyngeal infection caused by Fusobacterium leads to internal jugular vein thrombosis and metastatic infections.

Methods: We highlight this with a case of Lemierre´s syndrome with spinal extradural abscess. A previously healthy fourteen-year-old boy was admitted with a 5 day history of sore throat, headache, neck stiffness and fever. Tonsils were severely inflamed. Antibiotic therapy was commenced for presumed meningoencephalitis. He subsequently developed acute renal failure and paralysis of right sixth and twelfth cranial nerves. He was transferresd to our tertiary centre. MRI scan demonstrated extensive leptomeningitis with left sigmoid sinus and internal jugular vein thrombosis. There was fluid collection in the extra-dural space in the upper cervical spine (pic_01) which enlarged after a few days, without causing medullary compression. Given the site of the collection, it was elected to treat this conservatively. *Fusobacterium necrophorum* was isolated on blood culture. Appropriate antimicrobial therapy was continued. Anticoagulation was commenced. His symptoms improved but cranial nerve palsies persisted.

Discussion: Lemierre´s syndrome has a high mortality rate. Thus prompt recognition of the characteristic presenting features is vital. The occurrence of multiple septic emboli leads to protean manifestations as the illness evolves. Our case illustrates this with a clival pattern of cranial nerve palsies and the unusual feature of spinal extradural collection.



[Extradural collection extending from clivus to C3]

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CORRELATION BETWEEN HAEMOGLOBIN LEVEL AND SERUM NEOPTERIN CONCENTRATION IN HEALTHY AND INFECTED CHILDREN

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Background and aims: According to the international classification system neopterin belongs to the class of pteridines -it is pyrazino-[2,3-d]-pyrimidine compounds. Neopterin is a small molecule. The half-life of neopterin is fully dependent on the renal clearance; it is eliminated by the kidneys in unchanged form.

Serum neopterin level may reflect the intensity of human cellular immune response as it correlates with cytotoxic activity of macrophages. Monocyte/macrophages (and production of neopterin) are stimulated by IFN-γ, which is secreted by stimulated Th1 lymphocytes.

Increased serum neopterin concentration is observed in many pathologies of cell mediated immune system: viral and intracellular bacterial infections, autoimmune and malignant diseases.

Aim of the study was to determine correlation of the serum neopterin concentration with haemoglobin level in healthy and infected children.

Patients and methods: A total of 381 children: 172 girls (45.1%) and 209 boys (54.9%) participated in this study. The mean age was 8.4 ± 6.4 [SD] , ranged from 0.08 to 17.99 years.

They were divided into three group depending on their conditions: 127 children with acute illnesses: diarrhea (viral or bacterial) and urinary tract infections; 149 children with chronic diseases: inflammatory bowel disease and juvenile idiopathic arthritis, and 105 healthy children.

The serum neopterin concentration was evaluated using the immunosorbent assay method (ELISA) with coated plates technique.

Results: There was statistically significant, although weak, negative correlation between neopterin values and haemoglobin level in whole analysed population (N=381, Rs= -0.15, p=0.002).

Conclusions: Serum neopterin concentration negatively correlates with the haemoglobin level.

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THE INFLAMMATORY PSEUDOTUMOR (IPT) - AN IMPORTANT DIFFERENTIAL DIAGNOSIS IN FEVER OF UNKNOWN ORIGIN

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Background: Inflammatory pseudotumors are rare and benign tumors of the soft tissue. An increased secretion of cytokines leads to unspecific symptoms such as tiredness, weight loss, fever, lymphadenopathy and increased markers of inflammation.

Methods: Between 2002 and 2008 two girls admitted to the university children's hospital in Munich with long-lasting non-specific inflammatory findings were finally diagnosed as IPT.

Results: The two girls, aged 13 and 14 years, presented with fever and weight loss, one of them with exanthema and arthralgia of the knee. Inflammation markers were highly increased, excessive serological, microbiological and immunological exams as well as “routine” medical imaging were normal. FDG-PET and MRI demonstrated tumors at the porta hepatis and in the left axilla. Therapeutic approaches with antibiotics, methotrexate, anakinra, indometacin, colchicine and tonsillectomy were not successful, prednisolone led to an intermittent partial remission. After excision of the tumors both patients were free of symptoms and inflammation markers returned to normal within few days. No relapses were reported after 6 months and 2.5 years. Histology showed nodular areas with spindled cells, immunohistochemically positive for actin and CD30. HHV8 was negative.

Conclusion: The diagnosis of IPT is difficult due to unspecific symptoms. It seems to be an important differential diagnosis to autoimmune disease, malignant tumors and mainly fever of unknown origin. FDG-PET plays an essential role in localization; histology and immunohistochemistry confirm the diagnosis. Surgical excision can be curative.

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DEVELOPMENT OF AN ELISA KIT FOR DETECTION OF HBSAG IN HUMAN SERUM

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Objectives: Hepatitis B virus, the cause of serum hepatitis, is classified as a hepadnavirus. HBV have various antigens, the important of which is surface antigen or HBsAg. The particles containing HBsAg are antigenically complex. Each contains a group - specific antigen "a" in addition to two pairs of mutually exclusive subdeterminants, d/y and w/r. HBsAg is an important diagnostic marker of an active hepatitis B infection. Therefore, numerous methods have been developed for detection ofHBsAg, from all of which RIA and ELISA are the most sensitive and specific techniques. ELISA´s simplicity, speed, precision and sensitivity makes it the preferred technique among all other approaches. The emphasis of this study is to develop a direct sandwich ELISA method for detection of HBsAg in the serum.

Methods: In summary, the surface of well of microplate was coated by mouse monoclonal anti-HBs, then serum or plasma sample added to the wells of microplate after they had been saturated by BSA. Then, diluted anti-HBs-HRP was added to each well which was able to connect to the trapped HBsAg. The final colorometric detection of HBsAg is performed by adding a solution of substrate of peroxidase enzyme to each well. The color intensity is directly proportional to the concentration of HBsAg in serum.

Results: The sensitivity and specificity of the developed method was studied on 1350 serum samples. The results indicated a 96% sensitivity and 98.8% specificity. The precision of this method was determined by the %CV for inter-assay and intra-assay.

P788

INFECTIOUS COMPLICATIONS IN A PEDIATRIC BURN UNIT IN ARGENTINA

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Objective: To evaluate the epidemiological, clinical, microbiological characteristics and outcome of burned pediatric patients.

A prospective chart review of pediatric patients admitted in our tertiary burn unit was performed In the study period, 51 patients were included. The mean age of the patients was 48 months (m) (r: 3-241 m) , 36 p (70%) were male. The burn surface was between 1% and 80%. (median 25%). Full thickness was present in 41p (80%). Inhalatory injury was present in 27 p (53%). In 51 patients were diagnosed 116 infections. Burn wound sepsis was the most frequent focus in 53 cases (46%). In 19cases (16%) burn wound infection without sepsis. Bacteremia related with intravascular catheter was found in 15 cases (13%) and only bacteremia in 2 p (2%) Pneumonia in 7 cases, (6%) osteomyelitis in other 3 (2%) and urinary tract infection in 8 cases (7%) and in 9 cases (8%) other infections Forty two infections (36%) were caused by *P aeruginosa spp* and 11 (10%) by *Acinetobacter spp* only susceptibles to colistin. Fungal infections were detected in 22 cases (19%). The median time of hospitalization was 42 days (r: 8-139 d). Ten patients (20%) died for reasons related with infection.

Conclusion:

- Infections play an important role in burned children.

- Burn wound infections with and without sepsis were the most frequent.

- Multi - resistant Gram negatives bacteria were the most common.

- Mortality was related with infections.

P789

POINT PREVALENCE SURVEY OF ANTIBIOTIC USE IN PEDIATRIC POPULATION AMONG PRIMARY CARE PHYSICIANS IN SLOVENIA

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Background and aims: In Slovenia, the prescription rate of antibiotics is high compared to some other European countries, particularly in the age group of 1-4 years. The aim of our study was to assess the antibiotic prescription habits among the primary care physicians working with pediatric population.

Methods: A point prevalence survey conducted among the primary care physicians on the European Antibiotic Awareness Day 2008. Information on the total number of examined patients, number of those who were prescribed antibiotic therapy, their age, sex, duration of symptoms, diagnosis and treatment was collected.

Results: Of 256 questionnaires sent to the members of the Pediatric Society of Slovenia, 80 were collected (response rate 31.3%). Of those, only 56 were adequately completed and could be used in analysis. Responding 56 primary care physicians received 1944 patients (34.7 patients per physician). Of those, 212 (10.9%) were prescribed an antibiotic, most, 84 (39.6%), in the age group of 1-5 years. The most common diagnosis treated with antibiotic was acute tonsillitis - 81 (38.2%), followed by acute otitis media - 59 (27.8%) and UTI - 16 (7.55%). The most commonly prescribed antibiotic was penicillin V - 77 (36.3%), followed by amoxicillin - 55 (25.9%) and macrolides - 20 (9.43%).

Conclusions: The most common infection, treated with antibiotics was acute tonsillitis and penicillin V was the most widely used antibiotic. Relatively low overall prescription rate of antibiotics was found. More extensive surveys are planned to delineate our results.

P790

BEDSIDE TESTING OF TETANUS IMMUNITY IN THE PAEDIATRIC EMERGENCY DEPARTMENT

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Aim: Tetanus is an acute, often fatal illness caused by a toxin produced by the anaerobic, bacillus, Clostridium tetani. It is vaccine preventable but knowing the immune status of a patient is a familiar problem in the Emergency Department. Protetanus is a rapid bedside test for tetanus immunity. Two large scale studies on adult patients recommended its use but as yet its usefulness has not been assessed in children.

Method: In a prospective cross-sectional study, 128 children presenting to the paediatric emergency department requiring a blood test were consented for additional testing of tetanus immunity with Protetanus and ELISA antibody levels. A complete vaccination history was taken at the time.

Results: 117 children were included in the study, with an age range of 7 months to 15 years. Compared with ELISA, Protetanus testing has a positive predictive value of 82% (95%CI 71-89), negative predictive value of 40% (95%CI 24-58), sensitivity of 76% (95%CI 66-89) and specificity of 48% (95%CI 30-67). When vaccination history was compared with ELISA, the positive predictive value was 76% (95%CI 66-83), negative predictive value of 33% (95%CI 6-76), sensitivity of 95% (95%CI 89-99) and specificity of 7% (95%CI 1-24).

Conclusion: For predicting Tetanus immunity, Protetanus is no more accurate than a careful vaccination history. The use of this test in the paediatric emergency department would not convey any obvious benefits to patient management.

P791

KAWASAKI DISEASE IN A TWO MONTHS OLD INFANT: CASE REPORT

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Kawasaki disease (KD), a systemic vasculitis of unknown etiology, is rare in patients aged less than 3 months, who are at increased risk for the formation of coronary artery aneurysm. We present a case of KD in a very young infant, who developed anemia, generalized oedema and cardiac insufficiency and responded to intravenous immunoglobulin (IVIG) treatment.

Description: A two months old boy presented with irritability, diarrhea and fever. On admission the patient's temperature was 38.5°C, erythrocyte sedimentation rate (ESR) 85 mm hourly, haemoglobin 9.6 g/dl, white blood cell (WBC) count 10,400/mm^3, and platelet count 351,000/mm^3. Urinanalysis revealed 25 leukocytes per high power field, CSF examination revealed pleocytosis with normal glucose and protein values. His blood, CSF and urine cultures were reported as negative.On sixth day of his admission a generalized macular rash on his trunk and oedema of extremities appeared. Hypoalbuminemia, anemia and leukocytosis were also detected. The next day generalized oedema developed. On 12^{th} day of his fever, physical examination revealed tachycardia with an S3 gallop rhythm. Red fissured lips, desquamation of fingers, thrombocytosis and perianal dermatitis accompanied to other findings. His echocardiography demonstrated left coronary artery dilatatation and KD was considered as a final diagnosis. High-dose IVIG and aspirin were administered but his fever subsided only after a second dose of IVIG. All his other complaints also resolved during the following days but a repeat echocardiogram pointed out coronary artery aneurysm formation.

Comments: KD should be considered in differential diagnosis of unexplained fever even in very young children.

P792

THE TYPE OF CARE THAT THE PARENTS SEEK FOR FEBRILE CHILDREN

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In order to treat febrile illnesses the parents seek care into Private Pediatricians (PP), Hospital Emergency Rooms (ER) and specialized physicians. We evaluate the type of care that the parents seek.

Patients/methods: 85 questionnaires were answered in a ER. The type of care that the parents seek for febrile conditions was recorded according to their residency and maternal education.

Results: Elementary school education had 44% of mothers and University graduates were 21%. In rural areas were living 19%, in a town 26% and 45% in a city. A PP had 61% of the patients. 65.8% of the patients were visited ER when the PP was not available and 72.9% when the clinical condition was severe. The patients were visited pulmonologists (12.9%), ENT doctors (47%), internists (8.2%) and general practitioners (GP) (8.2%). The parents (36.4%) ask advises from their pharmacists. The visits to the ER ($p=0.026$) and the GP ($p=0.0002$) were significantly associated with maternal education. The residency was significantly associated with the visits to GP ($p=0.01$), internists ($p=0.01$) and pulmonologists ($p=0.01$).The maternal education ($p< 0.0001$) and residency ($p=0.0001$) were significantly related with the contact to pharmacists. No associations were reported between the maternal education and the visits to other specialized physicians.

Conclusions: Most of the children visit the PP for febrile conditions and the ER for more severe illnesses. 1/3 of the parents seek advises from their pharmacists and the ENT doctors. The maternal education and the residency affect the parental decision to visit other specialized physicians.

P793

PATHWAY-BASED APPROACH LEADS TO IDENTIFICATION OF BIOLOGICAL PATHWAYS ASSOCIATED WITH KAWASAKI DISEASE

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Background and aims: The aetiology of Kawasaki disease (KD), an acute systemic vasculitis, is unknown. However it may arise from an excessive or uncontrolled inflammatory response to infectious stimuli occurring in genetically predisposed individuals. We postulated that polymorphic variation in genes within inflammatory pathways may play a role in the disease.

Methods: Using a pathway-based analysis we analyzed the genotypic data from a genome-wide study of 250,000 SNPs typed on the Affymetrix™ 250K NSP chip in 119 Dutch Caucasian KD cases and 136 ethnically matched controls. Well-defined biological pathways controlling inflammation and cellular function were assessed using a novel pathway statistic. We identified those SNPs and genes within significant pathways using a variable selection process with the program HyperLasso.

Results: Growth factor signaling and lymphocyte signaling pathways were significantly associated in KD. 147 SNPs from 117 genes were found to contribute to the overall genetic effect.

Conclusions: Using a pathway-based analysis, multiple genes interacting in pathways are associated with KD. The pathways identified provide new information on the biological processes involved in the pathophysiology of the disease.

P794

EVALUATING THE USEFULNESS OF DIFFERENT INFLAMMATION MARKERS AT CHILDREN

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Background: There are several studies that show the usefulness of inflammatory markers for distinguishing between viral and bacterial infection at children.

Aim of the study: To evaluate the usefulness of leukocytes, CRP and ESR as markers of infection in children.

Patients and method: We have prospectively evaluated 114 patients divided into two groups:

1) group A with 74 patients having viral infections and

2) group B with bacterial infections comprised of 40 patients, through a score made of leucocytes over 16000, granulocytes over 12000, ESR > 50mm/h and CRP> 2.4 mg/dl.

Results: Mean values related to age for both groups were not significantly different (p=0.78) using the ANOVA test. Mean values for leucocytes was significantly different (p< 0.001) for viral infection 9210 ±2755 versus 15789 ± 5856 for bacterial one.

Mean ESR for viral infection was 19.73 ± 12.29 versus 44.93 ± 33.48 for bacterial infections. Mean CRP for viral infection was 9.19mg/dl ± 6.77 versus 61.39 mg/dl ± 55.81 for bacterial one.

The analysis of ROC curves shows in what degree inflammatory tests may distinguish between the two groups. This suggests that the quality of separation between the two groups was 0.846 for CRP, 0.841 for leucocytes, 0.830 for granulocytes and 0.750 for ESR with a probability p< 0.001.

Conclusion: We consider that CRP, ESR, leucocytes and granulocytes is a good clinical score in evaluating the risk of bacterial versus viral infection in children.

P795

DO WE NEED TO MONITOR GENTAMICIN DRUG LEVELS IN NEONATES, INFANTS AND CHILDREN?

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Objectives: To evaluated the need for routine serum gentamicin trough concentrations (SGTC), and to determine the predictors of an elevated (greater than or equal to1-2µg/mL) SGTC in pediatric patients.

Patients and methods: SGTC were studied retrospectively in all the children who were hospitalized in one pediatric ward between June 2003 and July 2008 and who were treated with once-daily gentamicin dose of 4-5 mg/Kg intravenously.

SGTC was measured using a fluorescence polarization immunoassay (Cobas Integra 700 - Roche, Holliston, MS, USA).

Serum was collected on day 3 of therapy, 30 minutes before the third dose.

The data was extracted from computerized laboratory information management software (Autolab, Softov Ltd, Israel).

Characteristics of patients with high SGTC were analyzed.

Results: Two hundred and nineteen infants and children with a median age of 25 days (mean 412.30, range 7-5988 days) were studied.

Mean serum level was 0.44±0.205µg/mL, lowest and highest values were 0.1 and 2.66µg/mL respectively. Five patients (2.3%) had gentamicin trough levels >1.5µg/mL and only 1 patient (0.4%) had >2µg/mL. However, 158 patients (72%) had levels below 0.5µg/mL.

SGTC had inverse relationship to patient´s age, with mean concentration of 0.51, 0.37 and 0.28 at mean ages of 0-1, 1-3 and above 3 months respectively.

We could not find any predictors or risk factors for high SGTC.

Conclusions: Our data do not support the routine monitoring of gentamicin concentrations in pediatric patients who are receiving appropriate standard doses of gentamicin and have normal renal function.