O001

THE NEED FOR IMPROVED INFLUENZA VACCINES IN CHILDREN

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Influenza is a serious infectious disease and places a significant burden on children, who have high rates of infection and illness. An estimated 20-30% of children (< 14 years of age) attract influenza A and B infections each year. During influenza epidemics, children (< 5 years of age) have the highest rate of medically attended illness and the second highest rate of hospitalization. Furthermore, the rate of influenza mortality in children is highest in the very young (< 1 year of age). Children are key transmitters of influenza and amplify community outbreaks due to prolonged virus shedding. Thus, vaccinating children can protect them directly, and the population, indirectly. The serious burden of influenza in children is reflected in recommendations for influenza childhood immunization programs in many countries, including the US, Canada, Austria, Finland and most South American countries.

As young children have a naive immune system, their responses to conventional trivalent influenza vaccines (TIVs) can be suboptimal. Estimates from clinical trials suggest that in younger children conventional TIVs have an efficacy of 40-60%, compared with 70-90% in healthy adults, potentially leaving children with limited protection against influenza. Efficacy is further compromised by the risk of eventual mismatches of the vaccine composition to strains circulating during the current influenza season.

To ensure sufficient protection, especially of young children, broader and more potent immune responses against influenza are required. Therefore, the development of more efficacious influenza vaccines for children, engaging innovative techniques to improve immunogenicity, will address an important unmet medical need.

O002

INSIGHTS ON ATTITUDES TOWARDS PEDIATRIC SEASONAL FLU VACCINATION

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Children have high rates of seasonal influenza infection and amplify community viral transmission due to prolonged virus shedding. Therefore, several countries introduced annual influenza vaccination recommendations for children, particularly for those with chronic conditions.

Uptake of vaccination by pediatric risk groups is relatively low, with rates estimated to be 41.2% in the US, and 20% to 52% in European countries, leaving many children at risk from infection.

As the attitudes of parents and health care professionals towards pediatric influenza vaccination do influence vaccination coverage, it is important to understand them in order to optimize strategies to improve the effectiveness of future vaccination campaigns. We have conducted a quantitative online survey among 250 Paediatricians, 250 General Practitioners, and 250 mothers of young children in Germany, Italy, Mexico, S. Korea and USA, to identify attitudes and beliefs towards pediatric influenza vaccination. Individuals were questioned on their perception of the risk and consequences of influenza in children as well as on their understanding, expectations and concerns of flu vaccination and vaccines. Results provide pragmatic insights that may support more effective future vaccination campaigns.

O003

CLINICAL PROFILE OF FLUAD® IN CHILDREN - IMMUNOGENICITY AND SAFETY

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The burden of influenza and the limited efficacy of conventional trivalent inactivated influenza vaccines (TIVs) in children are well known; therefore influenza vaccines that offer improved immune responses will address an important unmet medical need. An MF59®-adjuvanted seasonal influenza vaccine was developed for the vaccination of children based on FLUAD, an influenza vaccine licensed in older adults (≥65 years of age) since 1997.

The immunogenicity and safety and tolerability profile of FLUAD in children has been assessed in a clinical development program. Post-vaccination antibody titers against all 3 vaccine strains, including influenza B, were significantly higher with FLUAD than observed for conventional TIVs in young children 6 to < 60 months of age ($p < 0.001$). Seroprotection rates against influenza A were also significantly higher with FLUAD than conventional TIVs after a single dose ($p < 0.001$) and the enhanced immunogenicity observed with FLUAD persisted for at least 6 months post-vaccination ($p < 0.001$). In children, FLUAD also induced a significantly broader immune response against drifted strains compared with conventional TIVs ($p < 0.05$). FLUAD demonstrated a comparable safety and tolerability profile to conventional TIVs in children, with most reactions being mild-to-moderate and transient in nature.

In young children, FLUAD induces a superior immune response compared with conventional TIVs, and has an acceptable safety and tolerability profile. These data support a potential role for FLUAD in the vaccination of young children against influenza.

O004

CRITICAL APPRAISAL OF INTERVENTION STUDIES

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A detailed appraisal of any randomized trial requires a thorough assessment of the validity of the trial as well as the importance and applicability of its results. Using examples from the published literature, the speakers will describe the key features of a well-designed randomized trial, focussing on the method of treatment allocation, follow-up of patients, and assessments of outcome. Appropriate statistical methods will be described for different types of endpoints along with the correct presentation of any analyses performed (including estimation of treatment effects and confidence intervals). Finally, the speakers will discuss the interpretation of trial results, and their applicability to clinical care, with emphasis on the difference between clinical relevance and statistical significance, as well as the generalisability of the trial findings to local clinic populations.

O005

COMPARATIVE EFFICACY OF FLUAD® AND CONVENTIONAL INFLUENZA VACCINES IN CHILDREN

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The burden of influenza in young children emphasizes the need to vaccinate this age-group against influenza. However, the efficacy of conventional trivalent influenza vaccines (TIV) in children is limited. An MF59®-adjuvanted influenza vaccine, based on FLUAD (licensed for use in older adults), was shown to be highly immunogenic in 6 to < 36 month-old children and was subsequently tested for clinical efficacy. Data from the first comparative efficacy study of FLUAD and conventional TIVs in children (6 to < 72 months of age) will be presented. Vaccine-naive children received 2 age-appropriate doses of FLUAD, conventional TIV or non-influenza control vaccines during the 2007/08 and 2008/09 influenza seasons. The absolute and relative vaccine efficacy (VE) against polymerase chain reaction (PCR)-confirmed influenza-like illness (ILI) was assessed.

In children, the VE of FLUAD against all ILI across both seasons was 86% and was maintained throughout the influenza season. The VE for TIV was 43% and the relative VE of FLUAD in children compared with conventional TIV was 76%. The vaccine efficacies of FLUAD against vaccine-matched strains were 81% and 96% for children 6 to < 36 and 36 to < 72 month old, respectively. Seroprotective titers (≥40) against homologous (2008/09 vaccine strains) and heterologous (2007/08) influenza A subtypes were achieved already following one dose of FLUAD. The majority of adverse reactions were mild to moderate in severity and frequencies of serious AEs were similar in all vaccine groups. In young children, FLUAD demonstrated greater efficacy against PCR-confirmed ILI than conventional TIVs, supporting its use in pediatric vaccination.

O006

INFLUENZA VACCINATION OF VULNERABLE GROUPS - TRANSLATING THE CLINICAL DATA INTO POTENTIAL ECONOMIC BENEFITS

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Due to the disease burden of Influenza, vaccination of children is currently recommended by six countries in Europe, the USA, Canada, and many countries in South America. Although limited, data from some countries suggest that vaccinating children against influenza may be cost-effective. An MF59®-adjuvanted influenza vaccine, based on FLUAD® used in older adults, is the first vaccine to demonstrate greater efficacy against vaccine-like and mismatched influenza strains in young children (6 months to 6 years of age) than conventional trivalent inactivated vaccines (TIVs). The health economic implications of vaccinating children with this vaccine and conventional TIVs require further clarification.

We have used the comparative efficacy data from a Phase III trial in young children to model the economic and public health implications of the positive clinical benefits (i.e. enhanced protection against influenza) of vaccinating young children with FLUAD. Using these data, our model predicts that, compared with conventional TIVs, vaccinating children with FLUAD will have positive economic benefits for society, in terms of reduced direct and indirect medical costs of influenza. In addition, we predict that vaccinating children with FLUAD will benefit the wider community in terms of greater herd immunity, leading to lower levels of virus transmission, as well as reduced numbers of influenza-related deaths. In conjunction with the clinical benefits, our data demonstrate the wider societal benefits of vaccinating children with FLUAD and support vaccination of this vulnerable group against influenza.

O007

SUSTAINABILITY OF PROTECTION AGAINST MENINGOCOCCAL DISEASE IN THE NETHERLANDS: STRATEGIES TO MAINTAIN PROTECTION OVER TIME

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In 2002 a MenC conjugate (MenCC) vaccination was introduced at the age of 14 months and a mass catch-up campaign was performed targeting individuals aged between 1 and 18 years. We determined age-related immune responses before and after introduction of the MenCC vaccine.

In two population-based studies, established in pre- and post-vaccination periods, polysaccharide-specific IgG, IgG subclasses and avidity were determined by a multiplex immunoassay. In addition, in a subset of sera MenC-specific serum bactericidal antibody titers were determined.

Overall SBA seroprevalence was 22% and 45% in the pre- and post-vaccination period, respectively. SBA titers and PS-specific IgG show an age-specific trend, with the highest antibody persistence in the oldest vaccinated age-groups. SBA seroprevalence is not significantly different between the pre- and post-vaccination periods in unvaccinated adult groups, whereas the MenC PS-specific antibodies are. In all immunized age-groups higher levels of IgG1 compared to IgG2 were observed, while naturally derived immunity was mainly restricted to the IgG2 subclass. Noteworthy, the increase in IgG2 correlated with a reduced IgG-avidity with age.

MenCC vaccination induced higher IgG levels compared to natural exposure, but only older vaccinated age-groups seem to benefit from antibody persistence. Due to mass vaccination, MenC circulation probably decreased, resulting in lower IgG titers in the unvaccinated older age-groups, posing them at risk if MenC starts re-circulating. To maintain the present herd immunity and to offer better protection in the younger age cohorts a study to define the proper age for a booster vaccination will be conducted in 2011.

O008

OPTIMISING THE UK INFANT MENINGOCOCCAL SEROGROUP C VACCINE SCHEDULE; CAN THE SCHEDULE BE REDUCED?

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Since 2006 the UK infant immunisation schedule has incorporated two priming doses of monovalent meningococcal serogroup C conjugate (MCC) vaccine at three and four months of age and a booster of combined MCC/*Haemophilus influenzae* type b (GSK) at 12 months. Studies completed for the optimisation of this 2+1 schedule, suggested that certain MCC vaccines may be suitable for use as a single priming dose in infancy. Consequently, we undertook a randomised trial in 146 infants of a single dose of either MCC-CRM197 (Novartis) or MCC-TT (Baxter) at three months of age in conjunction with a booster dose of MCC-Hib at 12 months. The serum bacterial antibody (SBA) geometric mean titre (GMT) one month following a single dose of MCC-TT or MCC-CRM197 was 214.7 (95% CI 156.8-294.0) and 100.6 (95% CI 70.4-143.7) with 100% and 96% of infants attaining protective SBA titres, respectively. At 12 months of age, antibody levels had significantly declined but one month post- MCC-Hib booster, SBA GMTs increased to 2251.0 (95% CI 1546.2-3276.9) and 399.1 (95% CI 263.8-603.9) for toddlers primed with MCC-TT and MCC-CRM197, respectively. The serum bactericidal antibody (SBA) geometric mean titre (GMT) one month following a single dose of MCC These data suggest that a 1+1 schedule may provide a feasible alternative to the current 2+1 infant schedule. The choice of vaccine(s) in a 1+1 schedule and combination between those used for priming and boost may be of paramount importance. A 1+1 schedule could allow the "move" of one of the priming doses to be used as a further booster dose, later in life.

O009

THE PANDEMIC H1N1 VACCINATION CAMPAIGN IN JERSEY 2009-2010

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Jersey is a small Island of approximately 92,000 people (including 18,000 children). The H1N1 pandemic posed particular challenges for our community. We anticipated a single rapid wave but had limited acute healthcare capacity to respond (and no paediatric intensive care facility). Reducing the potential impact of the pandemic was vital.

We used a strategy of extended containment measures until vaccine became available, followed by urgent vaccination of key groups. An extensive public information campaign aimed to optimise uptake. GPs vaccinated people with underlying medical conditions whilst mobile teams of nurse immunisers offered vaccination to pregnant women, healthcare workers, all pre-school and school children (aged six months to 18 years).

Uptake was high amongst healthcare workers (80%) and at-risk patients (75%). We vaccinated over 12,500 nursery and school children in 6 days (83% coverage). Vaccine efficacy among children was 100% (95%CI: 70%-100%)1. No schools were closed as a result of influenza outbreaks. Vaccine reaction rates were low. No attributable serious adverse reactions occurred. Hospital admissions with confirmed pandemic influenza totalled seven patients (no deaths occurred).

To protect our island population, it was important to deliver the vaccination campaign as efficiently as possible. We achieved high coverage in a short time frame. We believe the immunisation of children was key to protecting our population. We would employ a similar model in the event of future pandemics.

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O010

TICK BORNE ENCEPHALITIS (TBE) IN CHILDREN AND KEY STUDIES OF A PEDIATRIC TBE VACCINE

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Tick-borne encephalitis (TBE) virus, one of the major human pathogenic flaviviruses, is transmitted by Ixodes ticks in a vast geographical area reaching from Western Europe throughout Asia, with more than 10.000 severe cases recorded annually. Case numbers in endemic areas are on the rise and areas in which TBE is reported are expanding. Consequently, TBE is becoming an international public health issue. Climate change, outdoor leisure activities, as well as improved diagnostics and surveillance are factors considered to contribute to increased incidence.

TBE causes acute meningo-encephalitis, with or without myelitis. Morbidity is age dependent, with meningitis predominantly occurring in children and adolescents, and more than half of adults developing encephalitis. Many patients are left with long term sequelae such as cognitive and neuropsychiatric complaints, dysphasia, hearing disorders and spinal paralysis.

The seriousness of TBE and the lack of causal therapy emphasize the need for effective prophylaxis. Inactivated whole-virion vaccines against TBE are widely used across Europe. Here we report on the clinical development of a pediatric formulation of a TBE vaccine. Phase 1/2 dose-finding studies identified a 1.2µg viral protein dose as optimal with respect to tolerability and immunogenicity. Safety of the vaccine was confirmed in a large-scale phase 3 study with local and systemic adverse reactions being mostly mild and short in duration. Equivalent neutralization of European, Far-Eastern and Siberian TBE virus strains was recently demonstrated. Field effectiveness studies in Austria estimate the effectiveness of TBE vaccination to be above 96% in children 1 to 15 years of age.

O011

IMPACT OF HUMAN ROTAVIRUS VACCINATION AND ELEMENTS TO HELP IMPROVE PROTECTION

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Rotavirus (RV) causes considerable global morbidity and mortality as the single most common cause of severe dehydrating diarrhoea in children aged ≤5 years.[1] Rotavirus accounts for up to 56% of hospitalisations and 33% of emergency room visits due to community-acquired acute gastroenteritis (GE) in children < 5 years of age in Europe.[2] The cost of treating these cases places a substantial economic burden on health-care providers in developed countries.[3,4]

Children are vulnerable to rotavirus infection from an early age with about 16% (Europe) and 27% (USA) of community-acquired RVGE occurring in infants < 6 months of age.[2,5] Therefore there is a need for early protection that can be provided by a two-dose human rotavirus vaccine.

In clinical trials the human rotavirus vaccine has been shown highly effective (85% to 100%, depending on the setting) in preventing severe RVGE in Europe, Asia and Latin America.[6-8] In clinical trials vaccine efficacy has been shown to be sustained for at least three years (Asia) and protection was observed against the five most common circulating RV genotypes, accounting for more than 90% of all RVGE worldwide.[7,9]

Placebo-controlled clinical studies have demonstrated that the human rotavirus vaccine has a clinically acceptable safety profile and is generally well-tolerated and immunogenic when co-administered with other common paediatric vaccines, including for premature infants and HIV-infected children.[10,11] Data from post-marketing studies suggest a small increased risk of intussusception after the first dose of rotavirus vaccination.[12,13] The benefits of rotavirus vaccines continue to outweigh the small increased intussusception risk identified to date.[12,13]

Effectiveness data from Europe and Latin America demonstrate the impact vaccination can have on rotavirus disease burden. The introduction of the human rotavirus vaccine into the national child immunisation programme of Austria led to a substantial decrease in hospitalisations due to RVGE, and rotavirus-positive diagnoses in Belgium were more than halved in the post-vaccine period when compared to pre-vaccine records.[14-16]

In conclusion, sustained and broad protection by human rotavirus vaccines, administered early in life, has the potential to reduce significantly the health and cost burden of RVGE in Europe.

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O012

PERTUSSIS GUIDELINES - HELPING TO CONTROL THE BURDEN OF PERTUSSIS FROM INFANCY TO ADULTHOOD

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Despite widespread use of pertussis vaccines, pertussis infection remains endemic in Europe. While the overall incidence of pertussis infection substantially decreased following vaccine introduction in early childhood, in recent years several European countries have reported resurgence, particularly in older children and adults.[1-3]

Outbreaks have been reported in many European countries including Ireland,[4] France[5] and the United Kingdom.[6] Infants younger than 6 months of age in particular are at high risk of developing complications due to pertussis infection, accounting for the majority of hospitalisations and deaths.[7]

Protective immunity is estimated to last for 4-12 years following pertussis vaccination and 4-20 years following pertussis infection.[8] Pertussis infections in adolescence and adulthood may occur due to waning immunity or due to genetic variation and natural adaptations of *Bordetella pertussis*.[9-10] Although a chronic cough may persist for weeks, sometimes accompanied by vomiting, these cases often go undiagnosed as the typical whoop is mostly absent and physicians typically do not consider pertussis as a differential diagnosis in adults.

To date most European countries offer a booster dose for preschool children aged 4-6 years, while adolescent booster doses are recommended in only seven countries including Austria, France, Germany and Luxembourg.[11] At this time only Belgium, France and Germany also recommend dTpa booster doses for all adults who received their last pertussis vaccine more than 10 years ago.

Recent data demonstrate that administration of a dTpa vaccine given ten years after a preceding dTpa dose is immunogenic and generally well tolerated in adolescents and adults.[12-13] In consequence, decennial booster vaccination could help provide continued protection throughout life.[12-13] The Consensus On Pertussis booster vaccination in Europe (COPE) panel of European experts proposes that the existing dT booster dose for adolescents (10-18 years) and adults (≥19 years) be replaced by a dTpa vaccine, and adults should continue to receive a dTpa booster dose at 10 year intervals to maintain protective immunity.[14] The COPE panel recognises that vaccine implementation will depend on raising disease awareness and creating opportunities for vaccine delivery.

The identification of adolescents and adults as a source of pertussis transmission to unprotected infants highlights an additional need for an effective pertussis booster vaccination programme in older age groups.[15] The COPE panel recommends a further 'cocooning' strategy, involving the selective vaccination of close contacts of newborns such as parents, until sufficient adult herd protection is established to eliminate transmission to vulnerable infants.[14] Protection against pertussis can now be achieved from infancy to childhood and onwards into adolescence and adulthood. Using a booster dose for pertussis in older age groups will additionally create herd immunity that will help protect the unprotected.[1]

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O013

EXPERIENCE OF VACCINATION AGAINST CERVICAL CANCER - FROM CLINICAL TRIAL DATA TO CLINICAL PRACTICE

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In developed countries effective screening programmes have substantially reduced cervical cancer mortality by detecting pre-cancerous lesions and cancer at an early stage. Treatment to remove cervical lesions carries a risk of complications, and is at high cost to health care services.[1]

HPV-16 and 18 are responsible for 71% of the cervical cancer worldwide.[2] Final analysis of a large Phase III trial recently showed that the bivalent HPV vaccine substantially reduced cervical pre-cancerous lesions (CIN3+) by 87% in an HPV-naive population.[3]

The bivalent HPV vaccine has shown sustained high level of antibodies for HPV-16 and 18, 8.4 years after vaccination.[4] The bivalent HPV vaccine can be co-administered with other vaccines such as dTpa-IPV, hepatitis B and a combined hepatitis A and hepatitis B vaccine.[5] The bivalent HPV vaccine is generally well tolerated and more than 15 million doses have been distributed worldwide.

To impact on the burden of cervical cancer and pre-cancerous cervical lesions, cervical cancer vaccine coverage will need to be high and include catch-up programmes for adolescents and young women. Vaccine acceptance and uptake will depend on increasing patient awareness of the causal link of HPV and cervical cancer and the protection afforded by timely vaccination. HPV vaccination against high-risk HPV types in combination with regular cervical screening will provide European women with two important tools to help protect themselves from cervical cancer.

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O014

RECENT ADVANCES IN EPIDEMIOLOGY OF INVASIVE DISEASE, BACTERIAL RESPIRATORY TRACT INFECTIONS AND ACUTE OTITIS MEDIA

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The understanding of epidemiology of invasive disease, pneumonia and acute otitis media (AOM) is constantly evolving. Recently, a substantial amount of new information on the burden of disease, risk factors, intervention effectiveness, natural and vaccine-induced fluctuations in the relative prevalence of *Streptococcal pneumoniae* serotypes and patterns of antibiotic resistance has been generated. Several large ongoing projects and initiatives, such as the new international Global Burden of Disease (GBD) effort, the work of the Child Health Epidemiology Reference Group (CHERG), the Lives Saved Tool (LiST), PneumoADIP, Pneumonia Etiology Research for Child Health (PERCH) and Global Action Plan for Pneumonia (GAPP), are expected to produce the most accurate estimates on the epidemiology and aetiology of these diseases to date. A wealth of new information, including influx of novel vaccine efficacy and impact data, continues to challenge the established understanding of these diseases, offering new approaches to their prevention and treatment. The aim of this presentation is to review and discuss the main areas of progress.

The GBD and CHERG projects have recently revised the epidemiological estimates of morbidity, severe morbidity, mortality and sequelae from childhood respiratory tract infections and AOM, exposing several key findings. First, the burden of pneumonia decreases more rapidly than the overall under-five mortality, due to ongoing vaccination efforts championed by the Global Alliance for Vaccines and Immunization (GAVI) and improved access to antibiotics and care-seeking behaviour in low-income countries.[1-3] Second, the burden of pneumonia sequelae, such as empyema, and of AOM has generally been underestimated, not only in developing but also in developed countries, where the information on these conditions is surprisingly sparse and needs to be addressed.[4] And finally, though rarely life-threatening, untreated AOM can lead to sequelae such as mastoiditis, meningitis and chronic suppurative otitis media (CSOM), an important cause of hearing loss.[5]

The study of disease aetiology has also generated new insights. Increased recognition of the importance of bacterial pathogen with increased severity of disease implies an underestimated effectiveness of vaccines on reduction of mortality and severe morbidity in published trials.[6-9] The interplay between viral and bacterial pathogens, interaction of different bacterial pathogens and time sequence in which mixed infections develop seem to be important for disease severity and prognosis, with protection against bacterial superinfection required, particularly after some viral infections or opportunistic bacterial infections.[10] Several studies raised concerns about the issue of serotype replacement following the vaccination roll-out.[11]

S. pneumoniae has been confirmed as the leading cause of meningitis, sepsis and severe forms of pneumonia. *S. pneumoniae* and non-typeable *Haemophilus influenzae* (NTHi) are the two most common pathogens in AOM, and there is growing evidence on the involvement of NTHi in respiratory tract infections.[12] The first licensed paediatric pneumococcal conjugate vaccine (PCV), PCV-7, aimed to eliminate invasive pneumococcal disease (IPD) in children by the inclusion of seven prevalent causative serotypes. Indeed, overall IPD incidence declined following vaccine introduction, subject to some regional variation, and PCV vaccination afforded additional protection to unvaccinated populations through herd

immunity.[13] An increased proportion of disease caused by non-vaccine serotypes has since been observed and it is uncertain to what extent serotype replacement will erode the benefits of PCV.[11] PCVs initially focused on invasive disease, but the interplay between aetiological agents and a demonstrated decrease in pneumonia and AOM in the post-PCV-7 period both imply an extended impact of PCV vaccines in the spectrum of respiratory tract infections beyond pneumococcal pneumonia to all-cause pneumonia hospitalisation and death.[10, 13-16]

All the recently emerging evidence and information on the role of bacterial pathogens in invasive disease and respiratory infections suggest that vaccination remains the most effective measure to prevent this spectrum of infectious diseases. In addition, vaccination effects on severe forms of the disease and mortality reduction have likely been underestimated in published trials, and additional benefits of pneumococcal conjugate vaccines aimed at multiple pathogens should be expected.

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O015

NOT ALL CONJUGATES ARE THE SAME - WHAT WE'VE LEARNED ABOUT PNEUMOCOCCAL CONJUGATE VACCINES ALONG THE WAY

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Since introduction of the heptavalent pneumococcal conjugate vaccine (PCV-7) in 2000, two additional pneumococcal conjugate formulations have been licensed: 10-valent pneumococcal *Haemophilus influenzae* protein D conjugate vaccine, PHiD-CV, and PCV-13. The collective immunological and clinical experience with these vaccines and other vaccine candidates suggests that, besides serotype content, differences in conjugation methodology and vaccine formulation play an important role in determining vaccine efficacy.[1] These factors will have varying impact on the efficacy of the vaccines against different serotypes and against different diseases.

In two African studies, a 9-valent version of PCV-7 (including serotypes 1 and 5) yielded equivocal efficacy results against serotype 1 disease. The relatively low anti-serotype 1 opsonophagocytic activity (OPA) responses in multiple conjugate formulations and late onset of most serotype 1 IPD cases suggests a booster dose might be of great value.[2-5]

Several serotype 3 conjugate formulations tested to date have failed to show consistent boosting (measured by ELISA), and no clinical efficacy has been observed with the only serotype 3 formulation yet evaluated; polysaccharide-based protection against serotype 3 may be intrinsically difficult.[6-8]

Similar OPA responses elicited by the serotype 6B-containing conjugate vaccines (PCV-7 and PHiD-CV) against the closely related serotype 6A, and the near elimination of IPD caused by serotype 6A in children in the USA and elsewhere by PCV-7, imply these vaccines are sufficient to control 6A disease.[5,9]

Evidence suggests that disease caused by serotype 19A may be preventable by 19F-containing conjugate vaccines, but OPA differences elicited by structurally different serotype 19F formulations suggest the level of cross-protection varies according to the conjugation chemistry.[10]

In randomised clinical studies three different vaccine candidates provided virtually identical protection against vaccine-type pneumococcal AOM, but gave very different estimates of overall AOM clinical impact. While variability in trial design, setting, and local epidemiology undoubtedly form part of the explanation, intrinsic vaccine differences are also likely to contribute.[11-14]

Four different efficacy trials with 7 to 11-valent conjugate vaccines prevented 25-35% of alveolar consolidated pneumonia, despite differences in vaccine formulations and settings.[15]

More efficacy and effectiveness data are needed to improve and refine our understanding of the disease-preventing potential of pneumococcal conjugate vaccines.

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O016

NOVEL VIRUS INFECTONS IN HUMANS AND ANIMALS

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In the past century, pandemic outbreaks of influenza and AIDS have cost the lives of tens of millions of people. These events were all caused by multiple introductions of animal viruses - influenza A viruses and SIV of birds and non-human primates respectively - into the human population. Besides these introductions causing major pandemics in humans, a large number of other virus infections have spilled over from animal reservoirs to humans or other susceptible species, resulting in considerable morbidity and mortality as “virgin soil” epidemics. The most recent examples in humans are the introduction of SARS coronavirus and influenza A viruses (H5N1 and H7N7) from the animal world, which caused global concern about their potential to be at the origin of new pandemics. Over the last decades there seems to be a dramatic increase in the emergence or re-emergence of virus threats in humans and animals worldwide. A long list of exotic names like Ebola, Lassa, Rift-Valley, Crimea-Congo, Hendra, Nipah and West-Nile is the illustration of names of just some of the places associated with the origin of viruses that crossed the species boundary to humans, with dramatic consequences in the last ten years alone. Similarly, recent mass mortalities among wild aquatic and terrestrial mammals caused by previously known and newly discovered morbilliviruses, as well as outbreaks of hog cholera, foot-and-mouth disease and fowl plague among domestic animals, highlight this trend.

Although improved detection and surveillance techniques, as well as increased media attention may have contributed to our perception of an increase in the incidence of outbreaks of virus infections, it is becoming more and more clear that major changes in our modern society increasingly create new opportunities for virus infections to emerge: a complex mix of changes in social environments, medical and agricultural technologies and ecosystems continues to create new niches for viruses to cross species boundaries and to rapidly adapt to new species. In combating this global threat, we should make optimal use of the new tools provided by the unprecedented advances made in the research areas of molecular biology, epidemiology, genomics and bioinformatics. Especially the role of early warning systems based on state of the art virus detection and discovery techniques, as well as targeted intervention strategies based on data on the mutual virus-host interaction, obtained from modern genomics studies, have already shown to make the difference in dealing with recent viral threats like SARS and avian influenza.

O017

UNIVERSAL SCREENING AND TREATMENT OF CONGENITAL CYTOMEGALOVIRUS: WHERE ARE WE NOW AND HOW DO WE MOVE FORWARD?

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Congenital cytomegalovirus (CMV) infection can result in clinically apparent (symptomatic) disease at birth, or in clinically inapparent (asymptomatic) infection. Data on the treatment of congenital CMV infection are only available for babies in the former group. Among neonates with symptomatic congenital CMV disease, administration of six weeks of intravenous ganciclovir protects against hearing deterioration over at least the first two years of life, and may lead to improved neurodevelopmental outcomes as well. The dose of oral valganciclovir which produces similar blood concentrations of ganciclovir as does intravenous ganciclovir has been identified. A multicenter study being conducted in the United States and the United Kingdom by the NIAID Collaborative Antiviral Study Group is now evaluating whether six months of oral valganciclovir therapy results in better hearing and neurodevelopmental outcomes than six weeks of oral valganciclovir therapy. The trial is almost completely accrued, and efficacy data will be forthcoming over the next several months.

The main toxicity of ganciclovir or valganciclovir is neutropenia; with oral valganciclovir and intravenous ganciclovir, 25-68% of treated babies develop neutropenia during a six week course of therapy. In animal models, ganciclovir is carcinogenic and gonadotoxic, although these toxicities have not been seen in humans. Before consideration can be given to evaluating treatment of babies with asymptomatic congenital CMV infection with valganciclovir, technologies to universally screen all newborn babies for CMV infection need to be evaluated and, ideally, biomarkers for patients at higher risk of subsequent hearing impairment need to be identified. The NICHD CHIMES network has screened approximately 90,000 newborns for congenital CMV infection at seven academic medical centers across the United States, and is identifying methodologies which are sensitive as well as scalable (that is, expandable to a mass-screening level) which ultimately may be used to evaluate all babies born for congenital CMV infection.

At the current time, only symptomatic babies with central nervous system involvement should be considered for antiviral therapy. Either intravenous ganciclovir or oral valganciclovir may be used, and the duration of treatment should be six weeks. Patients should be monitored for neutropenia at least weekly throughout the treatment period.

O018

DAVID AND GOLIATH: HOW DO SMALL ANTIBIOTICS PARALYZE THE GIANT RIBOSOME?

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Ribosomes are the universal cellular machines that translate the genetic code into proteins. Composed of proteins and RNA, among which the RNA moieties perform almost all functional tasks, they posses spectacular architecture accompanied by inherent mobility that facilitate their smooth performance in decoding, peptide bond formation and nascent protein elongation.

Owing to their fundamental role, ribosomes are targeted by many antibiotics that paralyze the ribosomes by binding to their functional sites. Their binding modes, inhibitory action and synergism pathways, will be demonstrated. Issues concerning their ability to differentiate between patients and pathogens, and mechanism leading to bacterial resistance to antibiotics will be discussed.

O019

PHARMACOGENOMICS AND ANTIMICROBIAL AGENTS

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Infectious diseases continue to account for a significant amount of morbidity and mortality worldwide, disproportionally affecting marginalised and resource-poor populations. The greatest disease burden is associated with HIV, malaria and tuberculosis. Genomic biomarkers for response to therapy for HIV coinfections such as hepatitis C are also emerging. Following ingestion of standard doses of most medications, inter-individual variation in both desired and toxic effects is often observed. Factors contributing to this variability include age, sex, ethnicity, body mass index, physiologic status, co-morbidity, dietary factors and co-prescribed medication. The contribution of genetic variation to inter-individual variability has been reported to range between 20 to 95%. In infectious diseases, the most commonly studied variants are SNPs in genes implicated in drug absorption, distribution, metabolism and excretion pathways. The financial impact of standardised prescribing mainly through hospitalisations resulting from therapeutic failure or adverse drug events is increasingly being recognised. Hospitalisations secondary to adverse events are expensive and are estimated to cost ~6000 Euro per hospital bed per year in mainland Europe. Pharmacogenetics aims to individualise therapies so that therapeutic benefits are maximised and toxic side effects are minimised. Recent advances in our knowledge of genomic biomarkers for infectious disease drug exposure and response will be discussed.

O020

RESEARCH AND FUNDING IN PAEDIATRIC AND NEONATAL RESEARCH: CURRENT CHALLENGES, FUTURE PERSPECTIVES, OPPORTUNITIES IN EUROPE: TINN AND GRIP

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The licensing process was introduced in order to ensure that medicines are safe, effective and of high quality. However, over 50% of children admitted to hospital in Europe will receive an unlicensed or off-label medicine and off-label prescription is the rule in neonates for most therapeutic classes. To improve such situation, both the US and the EU have introduced Paediatric Regulations that facilitate participation of children in research and pharmaceutical innovation. The objectives are to improve the health of children in Europe by facilitating the development and availability of medicines for chilfren aged 0 to 17 years, by ensuring that medicines are of high quality, ethically researched and authorized appropriately, by improving the availability of information on the use of medicines for children without subjecting children to unnecessary trials or delaying the authorization of medicines for use in adults. Indeed, the Paediatric Regulation requires that all marketing authorizations for adults submitted to EMA (European Medicines Agency) include a paediatric investigations plan (PIP), with the objective to ensure that médecines for use in children are evaluated and authorized appropriately in all paediatric age groups, including neonates, when appropriate. In addition, the EMA issues the inventory of paediatric / neonatal needs within the EMA Priority list and guidelines to optimize drug evaluation in the paediatric population.

There are major issues in relation to studying medecines in the vulnerable group of preterm and term neonates, including the need to perform juvenile animal studies, the need for adapted formulations suitable for use in young patients to avoid medication errors from multiple dilution or presentation of excessive quantities of drug. The marked differences in the behaviour of most drugs between neonates, children and adults require a pharmacokinetic evaluation usually based on an initial pilot study aiming at informing posology and a complementary population pharmacokinetic design with an optimum sampling strategy to analyze variability. In addition numerical modelling and simulation by *in silico* investigations, are new approaches taking into account all the available evidence on drug physiopathology, efficacy and safety to optimize evaluation. Suitable methodological approaches for clinical trials are required to study the different paediatric age groups, to develop highly sensitive analytical methods and obtain relevant informations on adverse effects on child development. There are also major ethical issues in relation to studying medicines in this high risk population.

Therefore, drug evaluation in neonates is a major challenge. The neonatal population is characterized by unique diseases, including respiratory distress syndrome, patent ductus arteriosus or primary pulmonary hypertension.. and unique susceptibilities, particularly if premature, including necrotizing enterocolitis, Intraventricular hemorrhage or retinopathy of prematurity.. In addition, the potential for neuro-developmental or growth toxicities should be investigated. Neonates represent only a small part of the population as compared to older children and adults, the number of neonates with comparable diseases is limited and the variation of specific types of diseases in this young subpopulation is higher than in the paediatric counterpart. Adverse drug reactions may only become apparent many years after the initial exposure, which requires a specific long-term follow-up programme. It is essential, therefore, to recruit neonates with similar diseases from various regions in Europe in order to

obtain a critical sample size of sufficient magnitude and to conduct scientific sound studies. All these goals can only be achieved by organising clinical trials and monitoring of selected drugs at the European level, in a collaborative project.

In this context, the European Commission promotes collaborative researches, bringing down barriers between countries, between organisations (universities, research centres, SMEs..) and between disciplines. The main policy drivers of the collaborative research in the health theme are improving health of European citizens, increasing competitiveness of European health-related industries and businesses, addressing global health issues, including emerging epidemics. Child health was a EC priority. The Topics for the first calls of FP7 included Paediatric medicinal products: Adapting off-patent medicines to te specific needs of the paediatric populations. Among others, the following programs were funded in order to evaluate antiinfective drugs in neonates:

TINN (Treat Infections in Neonates, coordinators : Professor Evelyne Jacqz-Aigrain Paris France and Professor Imti Choonara, Derby, UK- Management : Jerome Weinbach Inserm Transfert), aiming to evaluate ciprofloxacin and fluconazole prescribed off label to prevent and/or treat neonatal infections.

TINN2 (Treat Infections in Neonates 2, coordinators : Professor Evelyne Jacqz-Aigrain Paris France and Professot Sailesh Kocheta (Cradiff - UK)- Azithromycin is a macrolid antibiotic with anti-inflammatory properties active against Ureaplasma, It might be effective in reducing the severity of chronic lung disease, a multifactor disease in which Ureaplasma infection and inflammation play a role.

GRIP (Global Research in Paediatrics - Coordinator Carlo Giaquinto, Italy). The main aim of GRIP is to implement an infrastructure matrix to stimulate and facilitate the development and safe use of medicine in children. This implementation entails active coordination of knowledge management efforts and integrated use of existing research capacity both in EU and US, whilst reducing the fragmentation and duplication of activities. GRIP mobilizes researchers across Europe, the US and Asia. The integration of the WHO, EMEA and the NICHD associated networks, including the FDA, will be a major asset for the rapid translation of GRIP deliverables into practice. This partnership will work closely with families to provide children with safe and effective medicines.

As there is inadequate critical mass of investigators in any single European country these neonatal projects (including the neonatal part of GRIP) will allow to set up a European network for drug evaluation in neonates, based on the collaboration of trained investigators with expertise in neonatal clinical trials, adequate methodologies adapted to neonates for drug evaluation and drug monitoring programmes.

O021

ANTIFUNGAL THERAPY IN THE IMMUNOCOMPROMISED CHILD

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Posaconazole is a drug with excellent properties to be used as prophylactic agent (good tolerability, limited drug-drug interactions, and a broad antifungal spectrum). Clinical studies using posaconazole oral therapy support the efficacy of posaconazole in the treatment of invasive fungal infections in severely immunocompromised adult patients, either to prevent (prophylaxis) or as salvage therapy (after failure of other therapies). Although mechanistically similar to the other azole antifungal agents and structurally similar to itraconazole, posaconazole is more potent and effective against various types of yeasts and moulds, including those that are refractory to other antifungal agents. Especially the activity of posaconazole against *Fusarium* spp. and Zygomycetes, distinguishes it from the antifungal spectrum of voriconazole and itraconazole. Posaconazole is not officially licensed for the use in children younger than 18 years of age, although its use in children is described in literature. Posaconazole oral solution has shown to be relative safe and well tolerated in children with dosing up to 800 mg/day and seems to be a promising antifungal agent for prophylaxis as well as treatment of invasive mould infections in pediatric patients.

Micafungin is the most well-studied agent in prospective clinical trials for antifungal prophylaxis in stem cell transplantation and treatment of invasive fungal infections. Within the pediatric population only 1 randomized controlled antifungal trial has been performed. In this trial micafungin was compared with liposomal amphotericin B for the treatment of invasive candidiasis or candidemia in both neonates and children without any difference in outcome. Caspofungin has been studied prospectively for febrile neutropenia and treatment of invasive fungal infections, but most published data are from retrospective reviews or case reports. It is not yet clear what the clinical consequences are of the observed decreased susceptibility of *C. parapsilosis* to the echinocandins. The role of echinocandins in the management of invasive pediatric fungal infections has expanded but dosing issues still exists. Dosing has been well established for caspofungin only in children 3 months of age and above. Pediatric pharmacokinetics has been evaluated with all 3 echinocandins but is limited with anidulafungin. Anidulafungin should be avoided in children until more pharmacokinetic and clinical data become available.

During this interactive session an overview will be presented focussed on the newer antifungals and its value in the treatment of invasive fungal infections in immunocompromised children. The relevance to identify the causative fungus by invasive diagnostic procedures to direct antifungal therapy will be shown. Knowledge of the local epidemiology, susceptibility patterns, and the pharmacokinetics in children are indispensable to initiate antifungal therapy with a specific antifungal in the correct dose.

O022

ANTIFUNGAL THERAPY IN THE IMMUNOCOMPROMISED CHILD

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Invasive fungal diseases (IFDs) are an escalating problem among immunocompromised children. *Candida, Cryptococcus* and *Aspergillus* species are the leading causes of these diseases in paediatric patients. Other more rare fungi include members of Zygomycetes, *Trichosporon, Fusarium* and *Scedosporium* spp. Invasive diseases due to these organisms are associated with significant morbidity and mortality and early therapy has been found to improve survival. While novel antifungal agents (echinocandins and second generation triazoles) as well as treatment strategies based on surrogate markers (galactomannan and beta-D glucan) have established utility in treating immunocompromised adults, limited data are available when managing immunocompromised children with IFDs. The collective findings of the up-to-date data show that treatment recommendations are similar for paediatric and adult patients. Options for first-line therapy of invasive candidiasis for all pediatric age groups include liposomal amphotericin B, fluconazole, caspofungin and micafungin. Criteria for selecting the initial treatment include the clinical status of the patient, organ impairment, concomitant medications, pretreatment with antifungal agents, the *Candida* species isolated and its resistance pattern. Similar to adults, central venous catheters should be removed promptly if feasible. Neutropenic patients should receive colony-stimulating factors (G-CSF or GM-CSF, respectively), and in patients on immunosuppressive therapy, steroids should be reduced, discontinued or replaced. The recommended duration of therapy for uncomplicated candidemia is 14 days after the clearance of the bloodstream and resolution of all symptoms. Following clearance of the bloodstream and clinical stabilization, oral consolidation with fluconazole is feasible for susceptible isolates. Fundoscopy is mandatory prior to end of treatment to rule out endophthalmitis. Options for first-line therapy of invasive aspergillosis include voriconazole and liposomal amphotericin B. Criteria for selecting one of these agents include organ impairment, concomitant medications, the type of preceding antifungal treatment, and the local epidemiology. In settings with a high frequency of zygomycosis, voriconazole may not be a choice for pre-emptive therapy. Progress has been made in describing pharmacokinetics and safety of voriconazole and echinocandins, respectively; while further efficacy, safety and pharmacokinetic trials are ongoing. The current guidelines proposed, mainly for adults with IFDs, are likely applicable also to paediatric patients, but prior to making definitive recommendations more pharmacokinetic and Phase III trials are needed. Similar to adults, adjunctive surgical interventions need consideration in skin and soft tissue infections, sinus infections, impeding erosion of pulmonary arteries, and in operable CNS- and lung lesions. G-CSF or GM-CSF, respectively, are indicated in neutropenic patients, and reduction, discontinuation or replacement of steroids in immunosuppressed patients. Treatment of infections by more rare fungal pathogens needs to be individualized based on the patient's presentation and response to treatment. For empirical antifungal therapy in hemato-oncological patients with prolonged neutropenia and refractory or new fever in pediatric patients liposomal amphotericin B and caspofungin are recommended. Prophylactic fluconazole remains a standard in antifungal prophylaxis post allogeneic HSCT due to its marked effect on long-term outcome. Posaconazole may be given to children with high risk hematological malignancies or augmented immunosuppression for GVHD >12 years of age, and voriconazole in younger children.

O023

RECOGNITION OF PID IN CHILDREN

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Textbook PID descriptions are not helpful as children do not appear with a diagnosis but rather a pattern of infections and other features. Infections are common in young children and most do not have a PID. Pattern recognition is the key to diagnosis. A positive family history is an important clue, and non-immunological features can be very helpful. Ask: is this infection of unusual severity, type, frequency or site? All part of the puzzle solving that makes infection and immunity so fascinating!

The NIH “10 warning signs for primary immunodeficiency”, are also useful:-

1. 8 or more new ear infections within 1 year.

2. 2 or more serious sinus infections within 1 year.

3. 2 or more months on antibiotics with little effect.

4. 2 or more episodes of pneumonia within 1 year.

5. Failure of an infant to gain weight or grow normally.

6. Recurrent deep skin or organ abscesses.

7. Persistent superficial candidiasis after age 1 year.

8. Need for intravenous antibiotics to clear infections.

9. 2 or more deep-seated infections e.g. sepsis, meningitis.

10. A family history of PID.

However, in a recent study of their use, only failure to thrive, need for IV antibiotics and a family history of PID were significantly associated with diagnosing PID.

In general, 2 major invasive infections, 1 major infection with frequent minor infections, or recurrent infections at different sites warrant investigation. The earlier the onset of infection the more severe the PID.

Respiratory infection is a common presentation of PID. Persistent bronchiolitis due to RSV or parainfluenza virus suggests SCID. Interstitial pneumonitis due to PCP suggests SCID, CD40 Ligand deficiency or ICF syndrome, whereas Aspergillus suggests CGD, and CMV a T cell PID. Pneumatocoeles (usually due to Staphylococcus aureus) are pathognomonic of Hyper IgE syndrome. Recurrent pneumonia with organisms such as S.pneumoniae, S.aureus and Pseudomonas species is typically seen in antibody deficient patients. After time bronchiectasis often develops. Pneumonia associated with extension into adjacent bone and soft tissue is highly suggestive of Aspergillus infection and CGD. CGD is also associated with subtly progressive lung fibrosis.

Gastrointestinal infection is also common in PID. Cryptosporidium is seen in CD40 Ligand and CD40 deficiencies as well as combined immunodeficiency such as MHC II, whilst Giardia is seen in antibody deficiencies. Chronic viral enteritis strongly suggests SCID or a severe T cell immune deficiency.

Persistent superficial candida infection is the hallmark of APECED and the associated AIRE gene defects.

Bacterial infections, especially Staphylococcal and Pseudomonas of skin and soft tissue are seen in neutrophil and antibody deficiency; Staphylococcal and Streptococcal infections are seen in IRAK and NEMO defects, suppurative Staphylococcal lymphadenitis in CGD. Recurrent Streptococcal pneumoniae and Haemophilus influenzae infections are seen in defects of the early components of the classical complement pathway, whilst recurrent meningococcal disease is seen in defects of the alternate and late pathways.

Disseminated Mycobacterial infection is an important clue. Babies with disseminated BCG almost always have SCID, whereas non-tuberculous Mycobacterial infection in older children suggests a defect in the IL-12 / IFNg pathogen or a NEMO defect

Human Herpes virus infections are difficult to control and persistent or severe infections uncover a further group of PIDs; HSV1 in Unc deficiency, VZV in CHH, EBV in XLP or XIAP, HHV6 in other CIDs, often with CD4 lymphopenia.

O024

ANTIVIRAL THERAPY IN STEM CELL TRANSPLANTATION

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During this meet-the-the professor meeting we will focus on viral infections after hematopoietic stem cell transplantation (HSCT) and the current opinions regarding antiviral therapy and management.

Viral infections are an important cause of morbidity and mortality in severely immunocompromised children, i.e. patients post allogeneic hematopoietic stem cell transplantation. Infections with human herpes viruses occur most frequently, but also infections with adeno, BK, respiratory and influenza viruses can be encountered. Diagnosis is based on frequent monitoring and detection of viral DNA or RNA using molecular techniques like PCR. Antiviral therapy is useful in controlling viral infections temporarily but ultimately immune reconstitution of virus-specific immunity is required to cure the infections.

Different therapeutic strategies can be used to prevent or treat virus infections, namely anti-viral prophylaxis, pre-emptive or symptomatic treatment. Furthermore, antiviral immunity can be improved by withdrawing immunosuppressive therapy, by infusions of virus-specific donor lymphocyte, or by specific antiviral antibodies. These strategies all have their advantages and disadvantages. The choice for a specific strategy will be guided by factors such as access to frequent laboratory testing, cost of laboratory testing, the risk of antiviral resistance, therapy compliance, side-effects, drug interactions and immunosuppressive regimes. Cell therapeutic options require advanced GMP laboratory facilities.

Using different case-reports we will try to offer you tools for optimal antiviral patient management.

Key learning facts

- define goal of antiviral treatment

- decide on optimal antiviral strategy

- learn about different antiviral drugs and their (side-)effects

Key open issues

- long-term adverse events

- impact on antiviral resistance development

O025

STREPTOCOCCUS PNEUMONIAE: SURFACE MOLECULES AND IMMUNE EVASION STRATEGIES

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Surface-exposed bacterial structures are involved in pivotal biological functions of pathogens, such as binding to host cellular receptors or interactions with proteins of the extracellular matrix. These interactions can trigger attachment to and uptake by host cells, which represent important steps in the process of disease. Colonization of, and translocation across, the mucosal barrier eventually leads to dissemination within the host. Once disseminated, the pathogen then requires strategies to circumvent host immunity.

Streptococcus pneumoniae is a commensal of the human respiratory tract. However, in addition to colonization, pneumococci cause mucosal infections such as otitis media and sinusitis, as well as life threatening infections such as pneumonia, sepsis and meningitis. The pneumococcus is considered to be an extracellular pathogen. However, the dynamic process of adherence to mammalian cells is accompanied by cell-specific internalization mechanisms.

Our knowledge of the function of Streptococcus pneumoniae cell-surface structures, and the basic mechanisms underlying their interaction with host receptor molecules has significantly increased. In particular, choline-binding proteins have received considerable attention because of their versatility, and their sophisticated role in the interaction with host proteins. Interestingly, subversion of host protein functions to facilitate host invasion and immune evasion has been attributed to both surface-exposed and intracellular proteins of the pathogen.

Recent progress in our understanding how pneumococcal adherence molecules interact directly with host proteins will be discussed in an interactive manner, with specific emphasis on immune-evasion strategies of the pathogen.

O026

BACTERIAL-VIRAL CO-INFECTIONS

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The upper respiratory tract is the ecological niche of many commensals and potential pathogens like Streptococcus pneumoniae, Staphylococcus aureus and Haemophilus influenzae. The composition of this microflora is constantly altered due to microbial interactions and environmental influences. Imbalance of the microflora is considered crucial in pathogenesis of respiratory and invasive diseases. Viral infections predispose to bacterial super-infections, which is thought to occur through diverse mechanisms, including disruption of the epithelial barrier, virus-induced immunomodulation and production of viral chemicals. However, respiratory viruses can also 'infect' the host without causing any symptoms, which suggests more triggers are needed to induce a full-blown respiratory infection. Other factors in this complex interplay we might consider are host-, environmental and ecological factors.

Much of what we “know” about the etiology of pneumonia in children is wrong. There is considerable overlap in the clinical and radiological features of pneumonia caused by viruses, pyogenic bacteria and “atypical” bacteria such as mycoplasma. Furthermore, recent studies employing molecular diagnostics indicate that co-infection is very common in children with pneumonia: this includes co-infection with more than one virus, a virus and a bacterium, or even two bacteria! Bacterial pneumonia complicating influenza is of particular concern because of its increased severity, poor response to antimicrobial therapy, and reported association with many or most fatal cases of influenza infection. An animal model of post-influenzal pneumococcal pneumonia offers some insights into the pathogenesis of this potentially life-threatening condition and suggests alternative therapeutic approaches.

In this session, we will discuss the current knowledge on role of the bacterial microflora and respiratory viruses as well as the host immune response in the pathogenesis of respiratory infections and discuss the clinical implications of bacterial pneumonia complicating respiratory viral infections

O027

EPIDEMIOLOGICAL ASPECTS OF COAGULASE-NEGATIVE STAPHYLOCOCCI IN A NEONATAL INTENSIVE CARE UNIT

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Gram-positive coagulase-negative staphylococci (CoNS) are a subgroup of staphylococci, which distinguish themselves from *Staphylococcus aureus* by their lack of ability to produce coagulase. Being commensal bacteria, CoNS were long thought to be non-pathogenic and were regarded as contaminants when found in specimens of human origin. Nowadays, CoNS are the most frequent cause of late-onset sepsis (LOS) in neonatal intensive care units (NICU) worldwide. Incidences of up to 66% have been reported.

Important risk factors for LOS in intensive care neonates are immaturity of the immune system and invasive procedures like prolonged intravascular catheterization. An additional risk factor is poor infection control. LOS by CoNS also contributes to a significant morbidity and increased health care costs, mainly because of prolonged hospitalization.

An increasing antibiotic resistance and its ability to form biofilms cause the success of CoNS. Biofilm formation is mediated by several factors, such as surface proteins and the polysaccharide intercellular adhesin (PIA). PIA is regulated by the *ica* operon, and the presence of the *ica* genes has been shown to be a predictor for biofilm formation of *Staphylococcus epidemidis*. Many strategies are being developed to prevent CoNS LOS, including measurements to prevent biofilm formation by blocking molecular mechanisms of biofilm formation or impregnating catheters with antimicrobial agents and immune enhancement strategies. Most of these strategies are still under development; however measurements like catheter lock techniques and hygiene measurements have proven to decrease CoNS LOS.

Infecting CoNS strains are usually highly antibiotic resistant. The antibiotic resistance in CoNS isolated from the skin of neonates increases during admission.

Infecting strains of these commensal bacteria may originate from NICU personnel. CoNS carried by NICU personnel differ from those in the general population. *MecA*, *icaA* and penicillin, oxacillin and gentamicin resistance are significantly more prevalent in CoNS strains from personnel than in community isolates. We also studied the epidemiological effects of CoNS carriage of NICU personnel after a period of absence. The antibiotic resistance of CoNS decreased when strains were compared with personnel before and after vacation. NICU personnel are a likely cause for cross-contamination of virulent CoNS that originate from the NICU to patients.

We conclude that CoNS are the most important cause of bloodstream infection in neonates. NICU CoNS are more virulent than population CoNS.

O028

MEET THE PROFESSOR SESSION: VALUE OF ALARMING SIGNS AND SYMPTOMS IN CHILDREN WITH FEVER

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The diagnostic approach to a feverish child is a sequential stepwise process, starting with their symptoms and signs, and then considering the added value of further testing. There is a large body of research on identification of serious infection in children, but a relatively small proportion is directly relevant to the challenges faced by front-line clinical staff. During this session we will highlight the key findings from the most recent systematic reviews which have identified which symptoms, physical signs, and laboratory markers are most useful in acute paediatric care settings for identifying children with serious infection. The focus will be on first contact care, where most children present, and where the prevalence of serious infection can be low. Clinical prediction rules present a more formal process for combining independent alarming signs and symptoms to assess the risk of a serious infection. After deriving a prediction rule, it is important to validate the rule in different settings, and finally to assess the impact of the decision rules with predefined cut-offs for the different diagnostic or treatment strategies. Some of the challenges and problems in prediction research in children with fever are due to differences in patient population (low prevalence and high prevalence setting, inclusion on presenting problems and not based on diagnosis), low prevalence of serious infection, heterogeneous outcome (e.g. pneumonia, urinary tract infection, meningitis and sepsis), lack of reference test to confirm bacterial origin for all cases, wide range of possible predictors in rules and low prevalence of alarming signs, lack of validation and impact studies. During the session we will identify which clinical prediction rules for children with serious infection seem to be most useful for paediatricians. This session will be interactive, and we encourage participants to present their own clinical challenges and questions in the diagnosis of febrile children.

O029

CLINICAL PREDICTION OF SERIOUS INFECTIONS 1030-1050 ESPID PARALLEL SESSION 1

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Predicting which child presenting to primary care paediatric settings is most likely to have a serious infection is a common clinical challenge. Most invasive bacterial infections have become less frequent due to vaccination in developed nations, and most clinicians now consider pneumonia, UTI, and complications of viral illnesses as serious infections which need prompt recognition and appropriate therapy. However, in most frontline clinical settings, serious infections such as these are still uncommon, and differentiating the child who may have serious infection from the vast majority presenting with other acute illnesses can be a diagnostic challenge. As part of a European collaboration between paediatric and primary care researchers in The Netherlands, UK, and Belgium we have recently systematically reviewed diagnostic studies which assessed the value of clinical features and laboratory tests for identifying children with serious infection in paediatric primary care and emergency department settings. This identified several clinical features which are useful to increase or decrease the probability that a child has a serious infection. However, none were sufficient on their own to substantially raise or lower the risk of serious infection. Inflammatory markers were used in several studies, where we found that C-reactive protein and procalcitonin had similar diagnostic characteristics, and both were superior to white cell counts. Clearly some clinical features and and inflammatory markers are highly specific (“red flags”), so when they present should prompt a more thorough or repeated assessment. However, even in children with a serious infection, red flags will occur infrequently and unfortunately their absence does not lower the risk. Clinicians seem to fill this diagnostic gap by using their clinical “gut-feeling” and providing an opportunity for further repeat consultations (“safety-netting”). Clinical prediction rules provide a more formal way of assessing children with acute infection, and we identified several rules from the literature. However, few of the prediction rules are suitable for widespread implementation without further research.

O030

OUTPATIENT MANAGEMENT OF FEBRILE INFANTS UNDER 3 MONTHS WITH LOW RISK CRITERIA WITHOUT SYSTEMATIC LUMBAR PUNCTURE OR EMPIRICAL ANTIBIOTIC

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Objectives: To study the evolution of infants under 3 months with fever without source (FWS) attended in a Pediatric Emergency Department (PED) and discharged without performing a lumbar puncture (LP) and without antibiotic therapy.

Methods: Prospective seven-years study (September 2003 to August 2010) including all infants under 3 months with FWS attended in our PED. Those not admitted to the ward were followed by phone or, if not possible, reviewing subsequent reports.

Results: 1575 infants were included (serious bacterial infection -SBI- rate: 19.7%; positive blood culture rate: 1.9%).

Among the 988 initially diagnosed with FWS, 599 (60.6%) had low-risk clinical and laboratory criteria. Among them, 449 (74.9%) were discharged without performing a lumbar puncture or administering antibiotics.

After arriving the culture results, 17 of 449 (3.7%) were diagnosed with a SBI: 16 urinary tract infections and 2 occult bacteraemias (0.4%, one by *E. coli* and one by *E. faecalis*).

Fifty infants returned to the PED (38 unscheduled visits - 8.4%). Four (0.8%) were diagnosed with lymphocytic meningitis (one with a positive enteroviral culture). None of them was diagnosed with bacterial meningitis. Ten infants (2.2%) were admitted to the ward.

Of those 401 infants who did not return to the PED, 8% did not visit their primary care paediatrician after being discharged.

All did well.

Conclusions: In infants younger than 3 months with FWS and low-risk clinical and laboratory criteria, outpatient management without systematic LP or empirical antibiotic is adequate if parents understand physician's instructions and proper medical follow-up is guaranteed.

O031

CLINICAL PREDICTORS OF INFLUENZA IN YOUNG CHILDREN: THE LIMITATIONS OF 'INFLUENZA-LIKE ILLNESS'

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Background and aims: Definitions of influenza-like illness (ILI) have been studied infrequently in young children. Using data from observational studies designed to measure vaccine efficacy, we assessed the clinical predictors of influenza infection in children < 5 years old and constructed age-specific ILI definitions.

Methods: Children 6-59 months old with a history of fever and symptoms of acute respiratory infection were recruited in the Western Australia Influenza Vaccine Effectiveness (WAIVE) study. Clinical data and nasal swabs were obtained from each child. Logistic regression analysis identified significant predictors of influenza infection. Sensitivity, specificity, positive and negative predictive values (PPV, NPV) of different ILI definitions were determined. Parental opinion was also assessed.

Results: 944 children were recruited (2008-2009 influenza seasons). Of the 919 eligible, 179(19.5%) had laboratory-confirmed influenza infection. Predictors of infection included increasing age; lack of influenza vaccination; lower birth-weight; fever; presence of cough; and absence of wheeze. An ILI definition comprising cough and absence of wheeze had 60% sensitivity (95%CI:52-68), 59% specificity (95%CI:55-63), 26% PPV (95%CI:21-30) and 86% NPV (95%CI:83-93). Parental opinion had 77% sensitivity (95%CI:67-84), 47% specificity (95%CI:40-54), 29% PPV (95%CI:22-37) and 86% NPV (95%CI:79-92). Both compared favourably with definitions of ILI currently used. The addition of fever to ILI definition had little impact.

Conclusions: ILI is a poor predictor of laboratory-confirmed influenza infection in young children but can be improved using age-specific data. Parental prediction of influenza infection compares favourably to ILI definitions. Incorporating age-specific ILI definitions and/or diagnostic testing into influenza surveillance systems should be considered.

O032

PREVALENCE AND PREDICTIVE FACTORS FOR PULMONARY BACTERIAL CO-INFECTION IN INFANTS WITH SEVERE VIRAL BRONCHIOLITIS

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Background: Recent studies show a high incidence of pulmonary bacterial co-infection(PBCo-I)in children with severe viral bronchiolitis(VB),and the importance of quantitative tracheal aspirate(TA)on the diagnosis of PBCo-I.

Aims: To evaluate the prevalence of PBCo-I in infants mechanically ventilated for VB according to quantitative TA and blood cultures(BC),and analyze the clinical/laboratory features that may be predictive of PBCo-I.

Methods: Retrospective 3years study of children 1-24months who underwent mechanical ventilation(MV)for VB, and had a semi-quantitative TA specimen collected within the first 48hours of MV.Patients were classified as: No co-infection(negative TA and BC); Possible co-infection(negative BC and positive qualitative or < 10^5cfu/mL TA), and Confirmed co-infection(positive BC and/or>10^5cfu/mLTA).

Results: 102 patients,62(60,7%) were male. Viral etiology was: VSR 9 0(88,2%), Adenovirus7(6,8%), ParainfluenzaIII 4(4%)and Influenza A1(1%).The most frequent bacterial isolates were:*H. influenzae(*17/27,4%) *S.pneumoniae*(16/25,8%),*S.viridans*(10/16%)and *S.aureus*(10/12,9%).Clinical/laboratory data are shown in Table1.

	No co-infection (n=41)	Possible co-infection (n=41)	Confirmed co-infection (n=20)	p
Age(months)	4.92+/-4.02	5.07+/-4.43	4.1+/-3.83	0.567
PRISM II	7.03+/-3.78	8.17+/-4.29	7.5+/-2.66	0.301
RSV	33(80.5%)	38(92.7%)	19(75%)	0.133
Prior antibiotic	20(48.7%)	20(48.7%)	7(35%)	0.541
WBC/Neutrophil	9858/5554	10925/6297	10065/5149	0.689
CRP(mg/dL)	40.6+/-43	34.2+/-30	31.1+/-29.7	0.575
Fever/hypotermia	26(63.4%)	26(65%)	14(70%)	0.885
MV(days)	4.9+/-3.05	5.5+/-3.04	4.75+/-1.97	0.601
ICU stay(days)	8.6+/-5.5	9.2+/-4.9	7.9+/-2.3	0.609

[Table 1]

Conclusion: In this series,PBCo-I could be excluded in only 40% patients.None of the clinical/laboratory data were predictive of PBCo-I.Additional tests are necessary for early diagnosis of PBCo-I in severeVB.

O033

INNATE LYMPHOCYTES FREQUENCY AND GENE EXPRESSION OF INNATE CYTOKINES PREDICTS DISEASE SEVERITY IN VIRAL BRONCHIOLITIS

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Background and aims: Bronchiolitis is an infection of the lower airways caused by respiratory viruses, most commonly RSV. Disease severity varies from asymptomatic/mild infection to respiratory failure and death. We hypothesized that severe bronchiolitis results from an inadequate innate immune response. We aimed to compare frequencies of innate lymphocytes and innate cytokine gene expression in children with viral bronchiolitis.

Methods: We enrolled 3 distinct groups of children; children requiring hospital admission with viral bronchiolitis (n=15), children with severe viral bronchiolitis (n=10) admitted to Paediatric Intensive Care Unit (PICU), and age-matched healthy controls (n=15). All infants were below the age of 18 months at enrolment. Respiratory viruses were detected in respiratory samples by DFA or Taqman real time PCR. Lymphocyte subset composition was determined on peripheral blood mononuclear cells (PBMC) by flow cytometry. Quantitative PCR was used to measure gene expression of the following cytokines in PBMC; IL-2, IL-7, IL-10, IL-15, IFN-γ and TNF-α.

Results: Viral bronchiolitis requiring hospital admission was characterized by increased mRNA levels of IL-10 and TNF-α ($p < 0.0001$). IL-15 mRNA levels were significantly raised in children hospitalized with bronchiolitis ($p < 0.0002$), but not in the subgroup requiring PICU admission. Flow cytometry revealed a significant reduction in the relative number of natural killer cells ($p < 0.005$) and γδ-T cells ($p < 0.003$) among children admitted with bronchiolitis.

Conclusion: Bronchiolitis is associated with changes in innate lymphocyte frequencies and innate cytokine gene expression. These findings suggest that deficiencies of the innate immune system may underlie susceptibility to severe bronchiolitis.

O034

INTERLEUKIN-8 AND RANTES PLASMA CONCENTRATIONS IN COMBINATION WITH CD4 T-CELL COUNTS DISCRIMINATES DISEASE SEVERITY IN CHILDREN WITH RSV INFECTIONS

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Background: Current tools to predict severity of RSV infection are mainly based on clinical signs that present in an advanced stage of clinical deterioration. These tools might be improved by including immunological parameters.

Objective: We hypothesized that the combination of inflammatory markers will differentiate between children with severe RSV infection and those with mild symptoms.

Methods: Blood and nasopharyngeal samples from 52 children younger than 2 years of age with RSV bronchiolitis were prospectively collected during acute infection and after recovery. Patients were categorized in 3 groups based on disease severity: mild (no supportive treatment), moderate (supplemental oxygen and/or nasogastric feeding) and severe (mechanical ventilation). Clinical data, viral etiology, flow-defined leukocytes subsets cell counts and cytokine concentrations were compared.

Results: Children with severe RSV infection were characterized by young age, lymphopenia, increased IL-8, G-CSF and IL-6 plasma concentrations, and decreased RANTES plasma concentrations. The combination of IL-8, RANTES plasma levels and CD4 T-cell counts with cut-off values of 67 pg/ml, 13 ng/ml and 2.0*10E6/ml, respectively, discriminated severe from mild RSV infection with 93% sensitivity and 96% specificity.

Conclusion: This study demonstrates that IL-8 and RANTES plasma concentrations in combination with CD4 T-cell counts correlate with disease severity in pediatric RSV infection. In addition to clinical features, these immunological markers may be a useful tool to predict severity of RSV infection and guide clinical management in an early phase of disease.

O035

EXTERNAL VALIDATION OF A MODEL PREDICTING HEARING LOSS AFTER CHILDHOOD BACTERIAL MENINGITIS IN THE NETHERLANDS

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Background and aims: Bacterial meningitis (BM) is a serious infectious disease responsible for high mortality and a high incidence of short and long term sequelae. Previously a prediction model identifying children at risk of hearing loss after BM was developed. This study performed external validation of the model in a new cohort of Dutch school aged BM survivors.

Methods: In 2006 a new cohort of 117 BM survivors was constructed and the presence of sensorineural hearing loss (>25 dB), based on information from questionnaires and medical records, was determined. The presence of potential risk factors for hearing loss was obtained from medical records. External validation was performed by application of the model on the new cohort followed by determination of the discriminative ability and testing of the goodness of fit.

Results: The discriminative ability (Area Under the Curve, AUC) of the model was 0.84 in the original cohort and 0.78 in the new cohort. The Hosmer-Lemeshow test for goodness of fit was not significant (p>0,05). The distribution of patient characteristics and risk factors of the two cohorts were comparable. Applying the model on the combined cohorts resulted in a AUC of 0.82, Hosmer-Lemeshow test was not significant (p>0,05).

Conclusions: Performance of the model appeared to be stable in a new cohort of school aged BM survivors. The model seems to be implementable in Dutch pediatric practice.

O036

ANTIBIOTICS INCREASE THE RISK OF DEVELOPING INFLAMMATORY BOWEL DISEASE: A PEDIATRIC POPULATION-BASED COHORT STUDY

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Background and aims: Alterations in gut flora are hypothesized to contribute to the pathogenesis of inflammatory bowel disease (IBD). Antibiotic exposure is known to alter gut flora. We examined whether exposure to antibiotics is associated with IBD development during childhood.

Methods: We performed a retrospective cohort study using a United Kingdom electronic General Practice research database, The Health Improvement Network (THIN). Children followed for >2 years were included; those with prior IBD were excluded. All antibiotic prescriptions were captured. An antibiotic course was defined as a new antibiotic prescription >3 days after completion of a prior prescription. The outcome of interest was first diagnosis of IBD. Participants were censored at development of IBD, practice de-registration, death, or 19 years of age. We used an adjusted Cox Proportional Hazards model for analysis.

Results: The cohort included 1,072,444 children, of whom 766 developed IBD. The median latency period between first visit for IBD symptoms and first IBD diagnosis was 3.6 months (inter-quartile range, 0.4-17.3). Excluding antibiotic courses between the median latency period and censorship from the cohort, the Hazard Ratio for the association between each course of antibiotics and developing IBD was 1.05 (95% Confidence Interval, 1.03-1.07, $p< 0.001$). Sensitivity analyses of other exposure measures (e.g., ever- versus never-exposed to antibiotics) and different latency periods yielded similar results.

Conclusions: We found that children have a 5% increased risk of developing IBD for every course of antibiotics received. Reductions in inappropriate courses of antibiotics may reduce the risk of developing IBD among children.

O037

THE INFLAMMASOME AT THE SURFACE BETWEEN MICROBIAL COLONIZATION OR INVASION OF THE MUCOSAL SURFACES

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One of the most intriguing processes during the interaction between the human host and the microbial flora colonizing the skin and the mucosae is represented by the tolerance towards the colonizing microorganisms by the mucosal host defense, yet the induction of potent defense mechanisms as soon as invasion of the tissue takes place. This discrimination is important for both bacterial flora, as well as colonization with fungi such as *Candida albicans*. *C. albicans* colonizes 30% of individuals in a population at any given moment, and lack of proper recognition is associated with invasion and disseminated disease in case of defective immune defenses (e.g. chronic mucocutaneous candidiasis patients), and has been proposed to contribute to autoinflammation if overwhelming stimulation takes place in patients with Crohn's disease.

Mucosal or alveolar macrophages are in continuous contact with the bacterial and fungal flora, yet it is not known how they can discriminate between colonizing and invading microorganisms. The mucosal immune mechanism responsible for the activation of antifungal defense during tissue invasion is the Th17 response. The differential induction of Th17 responses by colonizing yeasts (no induction) and invading hyphae (potent induction of Th17) represents the immune mechanism discriminating between *Candida* colonization and invasion. The mechanism behind this process is represented by differential activation of the inflammasome:

- germination from yeasts into hyphae is crucial for the Th17 induction.

- inflammasome activation during germination is the discriminating step during production of IL-1b, and the subsequent IL-17 induction.

- Dectin-1/Syk recognition of b-glucans is an essential component of inflamamsome activation and IL-1b release, and this step is defective in patients with dectin-1 deficiency.

These in-vitro data have been complemented by data in mice defective in components of the inflammasome, including caspase-1-/-, ASC-/- and Nalp3-/- mice. These mice show defective caspase-1 activation and IL-1beta production, accompanied by an increased susceptibility to candidiasis.

The description of the mechanisms responsible for the discrimination between *Candida* colonization and invasion has additional important consequences. Firstly, the proper discrimination of these two states is crucial for avoiding inappropriate inflammation, yet reacting properly in case of invasion. Secondly, this model of tissue recognition of invasion is likely to be important for other colonizing microorganisms: in case of bacteria, the second signal needed to trigger inflammasome activation and Th17 responses is likely represented by ATP, released from dead cells during the process of tissue invasion. Finally, these findings may impact the mechanisms through which tolerance may be lost during inflammatory bowel disease such as Crohn's disease in which specific anti-*Candida* antibodies (ASCA) have been described, and genetic variant in the inflammasome component Nlrp3 predispose to disease.

O038

TRANSCELLULAR MIGRATION OF NEUTROPHIL GRANULOCYTES THROUGH THE BLOOD-CEREBROSPINAL-FLUID BARRIER AFTER INFECTION WITH *STREPTOCOCCUS SUIS*

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Background: A critical point during the course of bacterial meningitis is the excessive influx of polymorphnuclear neutrophils (PMN) from the blood into the brain. Both paracellular and transcellular routes of leukocyte transmigration through the blood-brain-barrier have been described in CNS diseases so far.

Methods: In an “inverted” Transwell culture model of the blood-CSF barrier the zoonotic agent Streptococcus suis (S. suis) was used to stimulate porcine choroid plexus epithelial cells (PCPEC) specifically from the physiologically relevant basolateral side. Barrier function was analyzed by measuring TEER and inulin-flux, tight junction morphology was investigated by immunofluorescence. Route and mechanism of PMN transmigration were determined by immunofluorescence, electron microscopy and FACS analysis.

Results: Here, we show that the transmigration of PMN through PCPEC was significantly higher after stimulation with TNFa or infection with S. suis strain 10 compared to its non-encapsulated mutant. Most strikingly, PMN preferentially migrated across PCPEC via the transcellular route. Extensive sequential analyses of the PMN transmigration process with Apotome®-imaging and electron microscopy revealed a stop of paracellular migrating PMN just before tight junctions. Interestingly, PMN subsequently appear to proceed by trancellular migration via funnel-like structures developing from the apical membrane. Noteworthy, some PMN contained bacteria during the transmigration process. Flow cytometric and transmigration inhibition studies with integrin-specific antibodies showed that PMN traversal is dependent on CD11b/CD18.

Conclusion: Our data underline the relevance of the blood-CSF barrier as a gate for leukocyte entry into the CNS and suggest a novel transcellular migration step during the pathogenesis of bacterial meningitis.

O039

IMPACT OF TOLL-LIKE RECEPTOR 3 POLYMORPHISM ON SEVERITY OF INFLUENZA

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Background and aims: To limit the effects of annual epidemics and prevent the consequences of a pandemic, the possible host immunogenetic factors conditioning the severity of influenza require to be investigated with the aim of identifying the subjects who are more likely to suffer a negative course. The aim of this study was to assess whether the susceptibility and severity of influenza was related to polymorphisms of toll-like receptors (TLR) 2, 3, and 4.

Methods: Samples of nasopharyngeal secretions and blood were obtained from 272 otherwise healthy subjects with influenza-like illness (ILI) and 164 healthy controls. The nasopharyngeal swabs were assayed for influenza viruses using molecular biology methods and blood was examined for the presence of polymorphisms of genes TLR-2, TLR-3, and TLR-4. Any association between the clinical and socio-economic impact of influenza and the genetic polymorphisms was evaluated.

Results: A total of 51 children (18.7%) showed A/H1N1v infection and 18 of these children were hospitalized for pneumonia. In patients with influenza A/H1N1v and pneumonia, TLR3 rs5743313 heterozygous CT polymorphism was significantly more common than in patients with influenza but absence of pneumonia (100% vs 9.1%; $p< 0.0001$) and was also associated with an higher viral load (17.1 ± 3.4 vs 16.0 ± 2.8 $\log_{10}$ cp/mL; $p< 0.05$). No other association with influenza severity and no relationship between frequency of different TLRs polymorphisms and influenza susceptibility was observed.

Conclusions: Otherwise healthy subjects with TLR3 rs5743313 heterozygous CT polymorphism appear at greater risk of developing severe influenza A/H1N1v with respiratory complications.

O040

NOVEL IMMUNOLOGICAL MARKERS FOR THE DIAGNOSIS OF TUBERCULOSIS - CYTOKINE PROFILES IN WHOLE BLOOD ASSAYS FOLLOWING STIMULATION WITH RD1 ANTIGENS

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Background and aims: Existing diagnostic tests for tuberculosis (TB) have considerable limitations. The tuberculin skin test (TST) has limited specificity. Interferon-gamma (IFN-γ) release assays (IGRA), relying on the detection of IFN-γ produced in response to *in vitro* stimulation with RD1 antigens, may have greater specificity but perform less well in children compared to adults. This study aimed to find novel immunological markers that have the potential to identify individuals with *Mycobacterium tuberculosis* infection.

Methods: Children < 18y were screened for latent TB infection (LTBI) or active TB by TST and QuantiFERON-TB-Gold-In-Tube. In addition, whole-blood samples were incubated overnight with the RD1 antigens ESAT-6 and CFP-10. Concentrations of 17 cytokines in supernatants were determined using xMAP technology (*Milliplex* bead-based assays; *Luminex*-platform). Results were background-corrected before statistical comparisons using Kruskal-Wallis and Mann-Whitney-*U* tests.

Results: Six children had active TB (symptomatic/TST >10mm/positive IGRA), 15 had LTBI (asymptomatic/TST >10mm/positive IGRA) and 15 were uninfected (asymptomatic; negative TST and IGRA). Median concentrations of seven cytokines (IFN-γ, IL-1ra, IL-2, IL-13, IP-10, TNF-α, MIP-1β) were significantly higher in children with active TB and those with LTBI compared to uninfected children. Concentrations of three cytokines (IL-1ra, IL-13, TNF-α) were significantly higher in children with active TB compared to those with LTBI. No significant differences were found for: IL-6, IL-8, IL-10, IL-12(p40), IL-15, IL-17, GM-CSF, MCP-1, MCP-3, RANTES.

Conclusions: A range of cytokines with the potential to distinguish between *M. tuberculosis*-infected and uninfected individuals were identified. Incorporating these immunological markers into future diagnostic assays may improve their performance.

O041

SEVERE INFLUENZA H1N1/09 IS CHARACTERISED BY A DISTINCT HOST TRANSCRIPTOMIC AND CYTOKINE RESPONSE

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Background: Children presenting to our hospital with influenza H1N1/09 were at a higher risk of shock and mortality than seasonal flu patients from 2004-2009. Our *Immunopathology of Respiratory Infection Study* (IRIS) aims to understand how the host inflammatory response to H1N1/09 infection differs from other acute childhood infections, using enhanced pathogen diagnosis, genome-wide RNA expression profiling and multiplex cytokine analysis.

Methods: Febrile children were enrolled at presentation to St Mary's Hospital London, during winter 2009-10. A detailed virological diagnosis was made using nested PCR. Blood was collected for 11-plex cytokine measurement using Mesoscale Discovery and for gene expression profiling with Illumina HumanHT-12 microarrays. Patients were characterised by severity according to cardiovascular and respiratory criteria.

Results: Recruitment included 180 children with respiratory infection and 50 age-matched controls. A viral pathogen diagnosis was made in 80%, of whom 20% had multiple pathogens. Rhinovirus, influenza H1N1/09 and RSV were the most frequently detected. Shocked patients with influenza H1N1/09 showed a distinct pattern of cytokine expression typified by raised interleukin 6; this was correlated with their transcriptomic profile. We also identified distinct subsets of genes differentially expressed between cases and controls in all pathogen groups. In addition, an H1N1/09-specific signature was detected that discriminated between bacterial and other viral infections. Interestingly this signature contained genes related to non-immune pathways as well as interferon signalling.

Conclusions: Our combined transcriptomic and proteomic approach demonstrates a unique H1N1/09 profile and provides insight into immunopathogenic mechanisms that may guide the introduction of immunomodulatory treatments.

O042

GROUP B STREPTOCOCCUS-INDUCED SURVIVAL SIGNALING IN MACROPHAGES IS INDEPENDENT OF TLR SENSING AND PHAGOLYSOSOMAL PROCESSING

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Background and aims: Group B streptococcus (GBS) is both a common mucocutaneous colonizer and a leading cause of neonatal sepsis and meningitis. It was recently shown that the macrophage inflammatory response towards GBS requires recognition of bacterial single stranded RNA through the Toll-like receptor (TLR) adapter Myeloid Differentiation factor (MyD)88. Furthermore, this inflammatory response requires lysosomal acidification. We previously found GBS particles elicit an anti-apoptotic response in macrophages, which does not require the expression of single TLRs. Here we investigated the role of GBS nucleic acids and the requirement of the TLR system and phagolysosomal acidification in GBS-induced anti-apoptosis.

Methods: Immortalized bone marrow-derived macrophages from wild-type, iNOS- and MyD88/TRIF-deficient mice were co-incubated with various apoptosis-inducing agents (Actinomycin D, Staurosporine) and fixed whole GBS organisms for 24h. GBS organisms were additionally treated with RNAse A, RNAse H, RNAse III or DNAse. In single experiments, lysosomal acidification was blocked with chloroquine. Apoptosis was assessed by FACS analysis of Propidium Iodide-stained cells and active-caspase-3 staining.

Results: We found that, in contrast to the inflammatory response, anti-apoptosis in macrophages occurs independently of GBS single stranded RNA or other bacterial nucleic acid species. On the host side, both signaling through the TLR system and phagolysosomal processing are dispensable, as determined by inhibiting lysosomal acidification with chloroquine and by usage of iNOS- and MyD88/TRIF-deficient macrophages.

Conclusions: GBS induced anti-apoptosis in macrophages is not mediated by recognition via the TLR system or particle modification by lysosomal acidification.

O043

TOWARD A FUNCTIONAL CLASSIFICATION OF GROUP A STREPTOCOCCUS M PROTEIN?

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Background and aims: Group A Streptococcus (GAS) M protein is a major virulence factor, a target for vaccine development and constitutes the basis for molecular typing (M-typing). This gold standard typing relies on a small N-terminal portion (around 10%) of the M protein, while the entire molecule interacts with diverse host proteins and thereby possesses multiple virulence properties. We aim to evaluate the genetic diversity of the complete sequence of the 200 M-proteins described so far worldwide to provide novel typing based on functional characteristics and to define vaccine strategies.

Methods: Representative GAS isolates recovered worldwide during the two last decades were included. *emm*-typing and complete *emm* sequencing were performed in the two coordinating laboratories (ULB-Belgium and QIMR-Australia). Phylogenetic analyses were performed using the muscle and neighbour joining algorithms.

Results: The amino acid sequences of 1088 GAS isolates belonging to 176 M proteins and recovered from 31 countries represent the first global description of this protein. The M-type was predictive of the full amino acid sequence independent of geography and clinical association although half of them presented size variants. A neighbour joining tree defined thirty-three clusters of similar M-types. The three biggest clusters encompass 53, 33 and 20 different M-types respectively indicating that numerous M-types present highly related sequences. Theoretical efficacy and design of M protein vaccine would benefit from this classification.

Conclusions: Based on a large dataset, 33 clusters of similar *emm*-types were defined. These clusters may represent a functional classification and should help in vaccine design.

O044

LPS AND R848 INDUCE BYSTANDER T CELL ACTIVATION THAT CORRELATES WITH IFN GAMMA PRODUCTION BY NK CELLS

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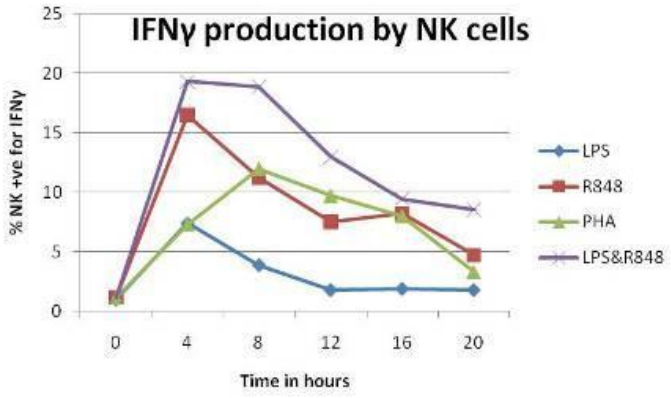
Introduction: Bystander T cell activation may occur following TLR engagement. We report that in human whole blood cultures, the extent of bystander T cell activation correlates with the Interferon gamma (IFNG) production from NK cells, exceeding that produced directly from T cells.

Methods: Short term cultures (4-20 hours) were set up on healthy controls (n=5). Flow cytometric analysis of intracellular IFNG and surface expression of CD69 in T and NK populations following activation with LPS, R848 or mitogen was undertaken.

Results: CD69 expression by T cells was induced by LPS (mean=17.9%, n=5), R848 (mean=26.5%, n=5) and PMA (mean=99% n=5) after 4 hours incubations. IFNG production by NK and T cells at 4hours is summarised in Table1 , identifying NK cells as the main IFNG producing subset. Maximal IFNG $^{+ve}$ NK cells were present at 4 hours, for both TLR ligands (Fig1). T cells also showed similar kinetics for both ligands. A strong correlation was found between the percentage of IFNG producing NK cells and the percentage of activated T cells (R^2=0.79).

	Number of IFNG+ve T cells/105 Lymph				Number of IFNG+ve NK cells/105 Lymph			
	Control	LPS	R848	PHA	Control	LPS	R848	PHA
Mean (2SD)	82 (66)	308* (242)	525* (186)	3643 (1915)	175 (125)	1351* (1134)	3278* (2668)	1246 (943)
*P <0.001 for LPS and R848 induced IFNG+ve T and NK cells by paired-sample Wilcoxon Signed Rank Test								

[IFNG production by T and NK cells at 4 hours]



[IFNG production by NK cells over time]

Conclusion: Ex vivo human whole blood culture with TLR ligands leads to robust IFNG production 4 hours, dominated by NK cells. A significant correlation exists between T cell activation and NK cell IFNG production, suggesting that this is an important interaction for the early IFNG response.

O045

RECENT ADVANCES IN THE EXPERIMENTAL TREATMENT AND PREVENTION OF INFLUENZA

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Influenza virus poses epidemic, zoonotic and pandemic threats to humans. The past decade has witnessed remarkable advances in treatment and prevention strategies against influenza. M2 ion channel blockers and neuraminidase inhibitors are currently available anti-influenza drugs. A new compound, nucleozin, shows effective inhibition of influenza virus by entrapping viral nucleoprotein (NP) in cytosol, suggesting the potential of NP as another valid antiviral target (Nat Biotechnol 2010). However, the continuing influenza mutation limits the effectiveness of drugs targeting viral components, which drives the search for alternative options. The potential molecules acting on host cellular proteins may hold promise in bypassing viral resistance. Cellular Raf/MEK/ERK signaling cascade is required for influenza ribonucleoprotein export from the nucleus. Inhibition of this signaling pathway results in nuclear retention of viral NP and therefore the impairment of viral propagation, showing a good example of cellular factor as an ideal drug target (Nat Cell Biol 2001). DAS181, a sialidase fusion protein, demonstrates broad-spectrum anti-influenza activity through removing viral receptor from the target cells (PLoS One 2009). Recently, RNAi high-throughput screening has revealed hundreds of human genes that are required for influenza life cycle. Some of them may emerge as novel drug targets (Nature 2010; Nature 2010). Apart from these chemical compounds, convalescent plasma harvested from influenza patients effectively reduces the viral load, suggesting a place in influenza treatment (NEJM 2007; CID 2011). In addition, supplementing immunomodulators to antivirals provides additional benefit to decrease mortality in H5N1 influenza (PNAS 2008).

Current influenza vaccine strategy provides sterilizing immunity to antigenically specific virus. Recently, several groups identified broadly neutralizing antibodies that cross-react with distinct subtypes of influenza viruses by targeting conserved regions in hemagglutinin (HA) stem and blocking viral fusion (Science 2009; Nat Struct Mol Biol 2009). Vaccination with plasmid DNA priming plus seasonal or vector vaccine boosting stimulates the production of neutralizing antibodies targeting HA conserved stem region, conferring protection against divergent H1N1 viruses (Science 2010). A synthetic HA peptide vaccine also induces cross-neutralizing antibodies and provides broad protection against distinct subtype viruses (PNAS 2010). Moreover, the broadly neutralizing antibodies against epitopes in HA stalk were further identified in humans with pandemic H1N1 (JEM 2011). Compared with HA, matrix (M) protein and NP are relatively conserved. A conformational M2 epitope highly conserved in nearly all influenza strains elicits broadly cross-reactive antibodies in humans (PNAS 2010). Unlike antibody-inducing vaccines, CTL-based vaccine mainly targets conserved internal proteins and seems to be an attractive strategy to induce cross-protective responses. A recent phase I clinical trial yielded encouraging data, where a vector-based vaccine encoding NP and M1 protein induces remarkably strong CD8 T cell response (CID 2011). In addition to the adaptive responses, manipulating host innate immunity, such as enhancing gamma delta T (JID 2009) and NK cells (JV 2009; JV 2010), also appears to be an effective approach for influenza therapy.

O046

ANTI-LIPOTEICHOIC ACID (LTA) MONOCLONAL ANTIBODY (PAGIBAXIMAB) ADJUNCT THERAPY IMPROVES OUTCOME FOR METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) SEPSIS IN SUCKLING MICE

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Background: MRSA sepsis treatment in infants is not optimal. Pagibaximab, which targets staphylococcal cell wall LTA, is in a large phase 3 clinical trial to determine efficacy in preventing staphylococcal sepsis.

Aim: We sought to determine if pagibaximab treatment added to vancomycin could improve the outcome of MRSA sepsis in suckling mice.

Methods: The MIC of vancomycin was determined in-vitro using CLSI methods. Pagibaximab binding and bacterial killing were determined using standard methods. Three day old suckling FVB mice were infected with 300 cfu of MRSA strain USA 300 subcutaneously. Pharmacokinetics of vancomycin and pagibaximab were determined. At 1 hr and 24 hrs after infection, pups received intraperitoneal either: vancomycin 20 mg/kg/dose twice daily for 5 days, pagibaximab 100 mg/kg/dose once daily for two days, saline, or vancomycin with pagibaximab, Survival and time to death (d) were determined daily. Standard comparison of means and proportions were used and results reported as % or mean (±) SEM.

Results: The MIC of vancomycin was 0.25 ug/ml and pagibaximab binding and neutrophil mediated bacterial killing occurred at < 0.001 and < 0.6 ug/ml respectively. Peak and trough serum vancomycin levels were 5.17 (0.90) and 1.38 (0.68) ug/ml respectively. Pagibaximab serum level was > 400 ug/ml. Vancomycin with pagibaximab improved survival ($p=0.02$) and increased time to death ($p=0.059$) compared to vancomycin alone.

Conclusion: The addition of pagibaximab to vancomycin for MRSA sepsis treatment significantly improved outcome after a fatal infection. Clinical studies are warranted to determine pagibaximab safety and efficacy in treating MRSA sepsis.

O047

ANTENATAL SCREENING FOR T.PALLIDUM; YIELD AND NEONATAL OUTCOMES

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Prevalence of T.pallidum is increasing in Europe. Universal antenatal screening with comprehensive follow up algorithms are in place in Ireland. We aimed to evaluate adherence to comprehensive neonatal follow up algorithms in at risk pregnancies.

Positive T.pallidum serology was identified from laboratory surveillance data (2006-2010). False positive serology, mothers not returning for delivery and spontaneous miscarriages / neonatal deaths not attributable to syphilis were excluded. A retrospective chart review was carried out to obtain relevant maternal and infant data.

58 positive maternal serological results were identified. 41 pregnancies met inclusion criteria. 2 were Irish, and 56 were first generation immigrants. Infant evaluation and follow up is assigned to one of three algorithm arms depending on maternal history. 18 had adequate, documented maternal treatment prior to this pregnancy (arm 1), 9 had been inadequately treated or were at risk of re-infection (arm 2) and 14 required and received adequate treatment in the current pregnancy (arm 3). 22 infants were incompletely evaluated. Inappropriate algorithm interpretation was the most common cause(18). Where expert advice was sought (n=6), follow up was complete. Communication difficulty was documented in 6 cases, none of which completed follow up. All 17 infants who received post natal treatment were completely evaluated.

Infants at risk of syphilis identified by antenatal screening are often inadequately followed up. Misinterpretation of treatment algorithms is the most common cause. Seeking expert advice improved algorithm completion. Positive maternal serology was associated strongly with first generation immigrant status, a vulnerable group in terms of health access.

O048

IMPACT OF NEONATAL INFECTION ON 5-YEAR NEURODEVELOPMENTAL OUTCOMES OF VERY PRETERM INFANTS: THE EPIPAGE STUDY

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Background and aims: To determine if neonatal infections are associated with increased risks of adverse neurodevelopment at 5 years of age in a population-based cohort of very preterm children.

Methods: We included all live births between 22 and 32 weeks of gestation from 9 regions in France in 1997 (EPIPAGE study). Of the 2193 survivors eligible for follow-up evaluation at 5 years of age, 1769 had a medical examination and 1495 a cognitive assessment. Neurodevelopmental outcomes (cerebral palsy and cognitive impairment), were studied according to early onset sepsis (EOS) and late onset sepsis (LOS) after adjustment for potential confounding variables using multivariate models.

Results: In total, 372 (14%) of the 2665 live births included had an EOS alone (without LOS associated), 645 (24%) a LOS alone (without EOS associated) and 171 (6%) EOS and LOS associated. At 5 years of age, the rate of cerebral palsy was 9% (157/1769) and cognitive impairment 12% (177/1495). Compared with uninfected infants, cerebral palsy was significantly increased in the group of EOS alone (OR = 1.82, 95% CI: 1.05-3.16), and this risk was increased further when a LOS was associated (OR = 2.57, 95% CI: 1.35-4.91). There was no association between neonatal infection and cognitive impairment.

Conclusions: Neonatal infections among very preterm infants are associated with an increased risk of cerebral palsy at 5 years of age, particularly when EOS and LOS are cumulative. This is the first study to assess respective impact of EOS and LOS on 5-year neurodevelopmental outcomes.

O049

CONGENITAL CYTOMEGALOVIRUS (CMV) INFECTION IN THE NETHERLANDS: BIRTH PREVALENCE AND RISK FACTORS

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Congenital cytomegalovirus (CMV) infection is the most common congenital viral infection worldwide. The most frequently encountered sequela is hearing impairment, affecting approximately one out of five congenitally infected infants. Data on the birth prevalence and risk factors of congenital CMV infection in the Netherlands are scarce. The aim of this study was to determine the birth prevalence of congenital CMV in the Netherlands. A sample of 6500 dried blood spots (DBS) from infants born in the Netherlands was tested anonymously for CMV DNA. The sample was stratified by the number of live births in different regions of the Netherlands of the year 2007. Additionally, on a regional level, risk factors for congenital CMV were analyzed. The birth prevalence of congenital CMV in the Netherlands was 0.54% (35/6433, 95%CI 0.36-0.72). Congenital CMV infection was significantly higher in regions with more than 15% young children (0-5 years) compared with regions with a lower proportion of young children (OR 5.9, 95%CI 1.4-25.2). Furthermore, congenital CMV infection was significantly higher in regions with more than 30% immigrants compared with regions with a lower proportion of immigrants (OR 2.2, 95%CI 1.1-4.6). This association was strongest for regions with more than 30% non-Western immigrants (OR 3.3, 95%CI 1.5-7.5). Based on the knowledge of the natural history of congenital CMV infection, approximately 1000 children are born with congenital CMV infection in the Netherlands annually, of whom eventually approximately 180 children will be affected by long term sequelae, with hearing loss being the most frequently encountered symptom.

O050

VALGANCICLOVIR (VGC) FOR SYMPTOMATIC CONGENITAL CYTOMEGALOVIRUS (CMV) INFECTION: A MULTICENTRIC SPANISH STUDY

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Background and aims: Congenital CMV is the leading cause of nonhereditary sensorineural hearing loss in children. Intravenous ganciclovir prevents hearing deterioration, but 6-weeks' treatment may not achieve a sustained effect. Long-term treatment with oral VGC could lead to a better auditory outcome.

Methods: Multicentric retrospective case series of infants with congenital CMV infection with CNS involvement treated with oral VCG for at least 6 weeks from 2005 to 2010.

Results: Fifty-five infants (16 premature) were identified, (35% mycrocephaly, 31% abnormal neurological examination, 76% altered neuroimaging studies). Nine patients were diagnosed retrospectively by PCR in dried blood spots.

Thirty-seven infants received ganciclovir prior to VGC therapy; in the rest (33%), VGC was administered as initial treatment. VCG median treatment duration was 6 months (1.4-18 months), being well tolerated without serious adverse events. Twenty-nine patients (53%) developed neutropenia, but only six required G-CSF. Hearing was tested by brainstem auditory evoked response (BAER) at birth (51 patients), 6 months (46) and 12 months (39). Before treatment, 61% had hypoacusia (26% mild, 32% moderate, 42% severe). At the 6/12 month BAER-controls, 74%/74% patients remained stable, 21%/23% improved and 4%/3% worsened. Only 1 patient out of 13 (8%) with severe hearing loss at baseline improved, compared to 10/18 (56%) with mild or moderate hypoacusia ($p< 0.01$).

Conclusions: Long-term VCG therapy in infants with congenital CMV infection with CNS involvement is well tolerated, neutropenia being the most common adverse event, and may preserve or improve hypoacusia in children with mild/moderate hearing loss at baseline.

O051

COMPARISON OF THE IMMUNE RESPONSE TO BCG IMMUNISATION GIVEN AT BIRTH AND 2 MONTHS OF AGE

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Background: More than 100 million doses of BCG vaccine are given each year to protect children against TB. The WHO recommends BCG to be given at birth. The immature immune system of newborns may influence the immune response and protection conferred by BCG. The few previous studies investigating the influence of age at immunisation on the immune response induced by BCG have reported conflicting results. This study aimed to comprehensively compare the immune response induced by BCG given at birth and two months of age.

Methods: Newborn infants in Melbourne were randomly allocated to be immunised with BCG-Denmark at birth or at two months of age. Ten weeks later the mycobacterial-specific immune response was measured using (i) intracellular cytokine assays with multicolour flow cytometry and (ii) concentrations of 12 cytokines in supernatants with xMAP technology (*Luminex*-platform).

Results: Data from 98 BCG-immunised infants were included in the final analysis. BCG immunisation at birth (n= 54) and at 2 months of age (n=44) induced comparable proportions of Th1 cytokine-producing CD4 and CD8 T cells and, in particular, comparable proportions of multifunctional CD4 T cells. Concentrations of all measured cytokines in supernatants were also comparable in both groups.

Conclusions: Multifunctional CD4 T cells have recently been found to correlate with protection against TB in animals. Immunisation with BCG at birth or at 2 months of age may therefore be associated with comparable protection against TB. Our data does not support delaying BCG immunisation in high prevalence TB countries for immunological reasons.

O052

HIGH SUSCEPTIBILITY FOR CYTOMEGALOVIRUS IN PREGNANT WOMEN IN FLANDERS, BELGIUM

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Background and aims: CMV IgG and IgM seroprevalence was measured in 221 women during pregnancy, at delivery and 3 months post partum (2006-2008). IgG was also measured in the respective cords.

Methods: ETI-CYTOK-G and -M Plus (Diasorin®, Saluggia, Italy) ELISA tests were used. Data were analysed with linear regression (SPSS, Chicago).

Results: The women's mean age was 29.8 years (22.2-39.9) and ¾ were primipara. Only 30% was seropositive for IgG (Table). IgG seroprevalence in women aged 22-40 years in Belgium (European ESEN 2 database (2002, not published)), was 24% (N=700).Geometric Mean Titers (GMT) of IgG differed significantly between cord and maternal serum samples at delivery (p< 0.001) confirming active transplacental transport (ratio 1.15/1). Higher maternal IgG titer (p< 0.001) and higher parity (p=0.002), but not age, were significantly associated with higher IgG seroprevalence in cord blood. Only one woman tested IgM positive, she delivered a child with congenital deafness.

Timepoint (N=available samples)	Week 36 of pregnancy (N=212)	At delivery (N=188)	Cord (N=182)	Month 3 post partum (N=212)
GMT IgG IU/mL (95% CI) (% positive)	1.48 (1.34-1.63) (64/212=30.2%)	1.44 (1.32-1.58) (53/188=28.2%)	1.66 (1.48-1.86) (51/182=28%)	1.56 (1.42-1.72) (63/212=29.7%)
GMT IgM IU/mL (95% CI) (% positive)	1.21 (1.19-1.23) (1/212=0.5%)	1.21 (1.19-1.23) (1/188=0.5%)	Not tested	1.20 (1.19-1.22) (1/212=0.5%)

[IgG and IgM GMT at different time points]

Conclusions: CMV IgG is actively transported from mother to child. However, few children in the presented population are protected by maternal antibodies since IgG seroprevalence in this pregnant population in Belgium is low. The low IgG seropositivity is in accordance with ESEN 2 data.

Therefore, prevention of intrauterine infection with CMV is of critical importance in this highly susceptible population.

O053

FUNGAL INFECTIONS IN THE IMMUNOCOMPROMISED HOST

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Congenital and acquired immunodeficiencies may be associated with increased susceptibility to invasive fungal diseases (IFDs), depending on the type of immune deficit. IFDs occur with increased frequency in patients with phagocytic and cellular immune defects but are rarely observed in those with humoral or complement deficits. Among congenital immune disorders, chronic granulomatous disease is most frequently associated with IFDs, in particular invasive aspergillosis; patients with hyper-IgE syndrome, severe combined immunodeficiency and other congenital immunodeficiencies also exhibit variable susceptibility to fungal pathogens. *Aspergillus, Candida, Cryptococcus* and members of other fungal genera are variably implicated in causing invasive diseases in these patients.

Among acquired immunodeficiencies, profound and prolonged neutropenia as well as corticosteroid treatment, as those seen in patients with acute myelogenous leukemia and hematopoietic stem cell transplants, are important risk factors for IFDs. Invasive diseases due to *Aspergillus* spp., *Candida* spp., Zygomycetes and other more rare fungi are challenging causes of increased mortality in these patients.

Non-culture methods of diagnosis, such as beta-D glucan, galactomannan and PCR have been variably tested and have limitations especially in children. Prompt diagnosis of IFDs in these patients requires a high degree of suspicion together with a knowledge of their clinical presentation and limitations of diagnostic modalities.

Antifungal prophylaxis is used in CGD patients and some types of acquired immunodeficiencies. Pharmacokinetics of antifungal agents in pediatric patients differs from that in older patients. Apart from administration of appropriate antifungal agents, successful management often requires the addition of surgical intervention. Adjunctive immunotherapy may be considered, although not systematically studied.

O054

VARICELLA ZOSTER REACTIVATION IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS: STRONG IMPACT OF PRE-TRANSPLANT CHEMOTHERAPY AND LYMPHOPENIA

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Background and aims: Varicella Zoster virus (VZV) reactivation following hematopoietic stem cell transplantation (HSCT) may cause significant morbidity. Based on a clinical observation of a significant increase in early VZV reactivation in our unit we undertook a retrospective study to determine the frequency and risk factors associated with VZV reactivation.

Patients and methods: Between 2002 and 2008, 163 children underwent a first HSCT in our unit. VZV diagnosis was based on clinical features and supported by Q-PCR and viral culture. Patient data and possible risk factors pre and post-HSCT were recorded and compared using a multivariate regression analysis.

Results: Within this cohort, forty-one (25%) patients developed VZV reactivation during the first year after transplantation at a median of 60 days post HSCT. VZV reactivation occurred more often within the subgroup of patients with acute leukemia compared to the remainder of patients (38% vs.15%, $p< 0.01$). Multivariate regression analysis showed that the use of fludarabin, a highly immunosuppressive agent as part of (re)induction chemotherapy in leukemia patients, was the most important risk factor for VZV reactivation (OR 5.0, 95% 2.0-12.4). This was associated with low pre-transplant T cell counts, especially in the CD4+ subset. No differences were found in relation to donor type, age or use of serotherapy.

Conclusion: VZV reactivation after HSCT predominates in acute leukemia patients. The use of fludarabin in chemotherapy regimens is associated with very low T cell counts and is a significant risk factor for VZV reactivation. This demonstrates the impact of pre-HSCT host immune suppression on VZV reactivation after HSCT.

O055

RISK FACTORS FOR *CANDIDA* INFECTIONS IN PEDIATRIC SMALL BOWEL TRANSPLANT (SBT) RECIPIENTS

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Background: Limited data has been published concerning risk factors for *Candida* infections is pediatric SBT.

Methods: This 1:1 matched case-control study including 26 *Candida* culture-positive patients (cases) and 26 culture-negative patients (controls). Patients characteristics were compared with Wilcoxon rank-sum, chi-square or Fisher's exact tests. McNemar test was used to assess discordance between pretransplant and posttransplant fungemia. Conditional logistic regression analysis was performed to identify risk factors.

Results: The median age of the group was 1.91 years (range 0.90-17.60); 60% were male. Within one month and 1-6 month before transplant, 7.7% and 23.08% cases had fungemia compared to 73.1% 12 months after transplant (p< 0.0001, p=0.002). The results of univariate analysis are presented:

Variables	Cases	Controls	p-value
Tacrolimus level, median	10.9	11.8	0.96
TPN, %	88.46	53.85	0.03
Renal failure, %	23.08	11.54	0.27
Central line, %	92.31	76.00	0.1
Previous antibiotic treatment, %	68.00	26.92	0.02
Steroids, %	65.38	69.23	0.71
Recent surgery, %	50.00	38.46	0.27
ICU residence, %	73.08	65.38	0.57
CMV D+/R-, %	19.23	26.92	0.53

[Table 1]

In multivariable analysis only total parenteral nutrition (TPN) remained an independent risk factor [OR10.0 (95%CI1.28,78.11),p=0.03].

Conclusions: Fungemia was significantly more frequent after SBT. The patients on TPN had 10 times higher odds of having Candida infections after SBT.

O056

PERSISTENT EBV INFECTION IN TWO SIBLINGS WITH CARTILAGE-HAIR-HYPOPLASIA - DOES THE RISK FOR LYMPHOMA JUSTIFY PREEMPTIVE STEM CELL TRANSPLANTATION?

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Background: Cartilage-Hair-Hypoplasia (CHH) is a rare autosomal-recessive disease with skeletal dysplasia and a highly variable clinical phenotype, including immunodeficiency and an augmented risk of malignancies.

Case descriptions: We report on two siblings with connatal short limb skeletal dysplasia. The clinical appearance and detection of an EBV-associated CD20 positive B-cell lymphoma in the 10 year old boy led to subsequent sequencing of the RMRP-gene in both children and established the underlying diagnosis of CHH. Both children had variable degree of B- and T-cell lymphopenia, very low naive T-cells and reduced T-cell proliferation, corresponding to the previously increased infection rate. The boy was treated according to B-NHL BFM study, including Rituximab. Under treatment, EBV-load became negative. Although in complete remission, he was considered high-risk for relapse because of the underlying CHH and hematopoietic stem cell transplantation (HSCT) was consequently undertaken. The 13 year old sister displays a continuously positive, yet unchanged EBV-load in the blood. Although she is in good health without signs of EBV-triggered lymphoproliferation, she remains under close follow up with repeated evaluation regarding preemptive HSCT because of her brother's history.

Conclusions: CHH should be taken into account as differential diagnosis in patients with skeletal dysplasia, particularly if accompanied by recurrent infections. Close monitoring of CHH-patients is required to promptly diagnose malignancies and infections, which may lead to chronic lung changes and increased mortality. In persistent EBV-infection a rising viral load or lymphoproliferation should entail further investigations. HSCT should be considered in cases with severe immunodeficiency or malignancies.

O057

DIAGNOSTIC VALUE OF GALACTOMANNAN IN BRONCHOALVEOLAR LAVAGE FOR INVASIVE PULMONARY ASPERGILLOSIS IN IMMUNOCOMPROMISED CHILDREN

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Background: Invasive pulmonary aspergillosis (IPA) is a life-threatening complication in immunocompromised patients. Early diagnosis and therapy improves outcome. Diagnosing IPA is difficult. Assessment of galactmannan (GM) in bronchoalveolar lavage (BAL) is a proposed tool to diagnose IPA. Little is known about the diagnostic value of BAL GM in children.

Aim: To evaluate the diagnostic and clinical value of BAL GM in immunocompromised children suspected of IPA.

Methods: 47 BAL GM tests from 456 bronchoscopies performed from 2002-2008 were included according to the hostfactor section of the EORTC/MSG criteria. 39 of 47 immunocompromised patients received chemotherapy prior to or at the time of BAL. A cut-off index value GM of ≥ 0.5 was used. Clinical data, chest CT-scans and BAL cultures were collected. In absence of a gold standard, patients were classified as proven, probable, possible or no IPA as indicated by the EORTC/MSG criteria.

Results: Sensitivity, specificity, PPV and NPV of BAL GM for a diagnosis of proven and probable IPA were 82.4%, 87.5%, 82.4% and 87.5% resp. (n=41). A significant relation was found for BAL GM and chest CT (P= 0.03, n=41). No significant relation was found for BAL aspergillus culture and chest CT (P= 0.656, n=47). In 10 out of 12 patients classified as possible IPA, antifungal therapy was continued or started, despite a negative BAL GM.

Conclusions: The BAL GM test had a significant diagnostic value in children suspected of IPA, but the clinical suspicion of IPA was often more important to continue or start antifungal therapy.

O058

THE IMMUNOGENICITY OF A NOVEL A (H1N1) VACCINE IN HIV-INFECTED CHILDREN

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Background: The UK DOH recommended vaccination of high-risk groups, including children with HIV with a novel, oil-in-water AS03 adjuvanted Influenza A (H1N1) vaccine (Pandemrix™).

This study evaluated the immunogenicity of 2 doses of this adjuvanted Influenza A (H1N1) vaccine in HIV-infected children and assessed the impact of vaccination on individual CD4 counts and HIV viral load.

Methods: HIV-infected children attending outpatient appointments between 01 November and 31 December 2009 were offered two doses of H1N1 vaccine three weeks apart and a blood test before and 3 weeks after the second dose of vaccine. Serum antibody responses were determined by a haemagglutination inhibition (HAI) assay using standard methods.

Results: Of the 39 children recruited for vaccination, 31 (median age 11.2, range 3.0-17.9 years) received both doses of vaccine and provided pre- and post-vaccination blood samples. Eight children (26%) had baseline HAI titers ≥1:32. After vaccination, 29 children (94 %) had HAI titers ≥1:32 (seroprotection), of whom 27 (87 %) had also had a four-fold rise in titers (seroconversion). In the univariate analysis, post-vaccination geometric mean titers (GMTs) were higher among the 21 children receiving highly-active anti-retroviral therapy compared with the 10 treatment-naïve children (GMT 406 [95% CI 218-757] vs. 128 [49-336]; P=0.035) but this was no longer statistically significant when adjusted for pre-vaccine GMTs. There was no significant impact of vaccination on CD4+ T cell count or HIV viral load.

Conclusion: The $AS03_B$ -adjuvanted pandemic Influenza A (H1N1) vaccine is highly immunogenic and appears to be safe in HIV-infected children.

O059

PAEDIATRIC ANTIBIOTIC USE IN THE NETHERLANDS BETWEEN 1996 AND 2010: AN ARPEC STUDY

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Background and aims: The ARPEC (Antibiotic Resistance and Prescribing in European Children) project aims to improve the evidence base for antibiotic prescribing in children.

Within this pilot-study we aimed to study which antibiotics were prescribed by Dutch general practitioners to children in a 15-year period.

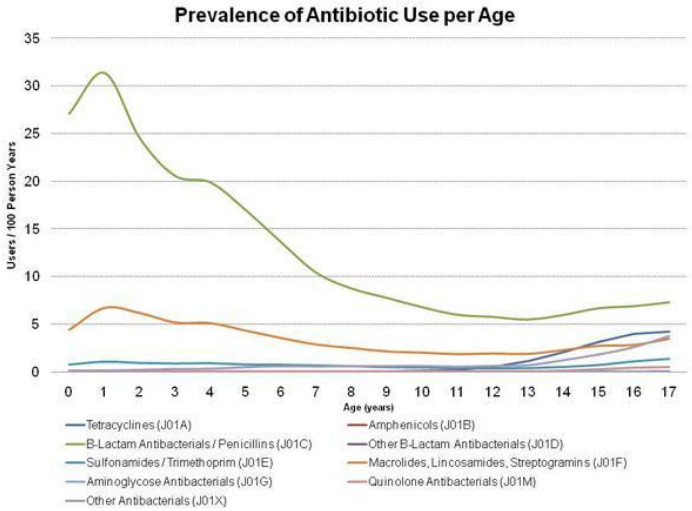
Methods: We conducted a retrospective cohort-study within the Integrated Primary Care Information (IPCI) database, an electronic medical records database in the Netherlands.

We included 293,293 children (0-18 years) with a total of 583,188 person-years (PY) of follow-up between 1996 and 2010.

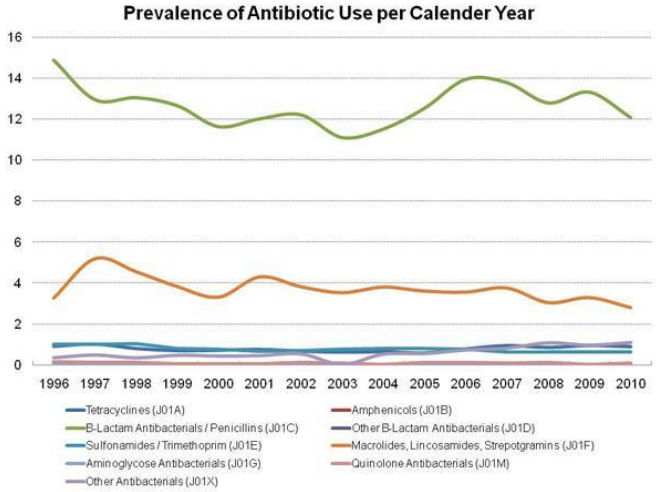
Prevalence of antibiotic prescriptions was calculated; defined as the number of children with at least one antibiotic prescription per year. Results were stratified by age and calendar-year.

Results: The yearly prevalence of antibiotic use was 17 users/100 PY, with a peak in ≤2 years (up to 35/100 PY)(fig1). Beta-lactam antibacterials and penicillins were most frequently prescribed (13/100 PY), followed by macrolides (3.4/100 PY). From puberty on, tetracyclines were prescribed (up to 4.2/100 PY). The yearly prevalence was stable over calendar time (15-19/100 PY)(fig2).

Conclusions: In the Netherlands, the yearly prevalence of antibiotic use in children varies highly by age, but stayed constant over the past 15 years. Beta-lactam antibacterials and penicillins are most frequently prescribed with a peak in ≤2 year-olds. Within the ARPEC-project further studies will be conducted to analyse the extend and types of antibiotics prescribed for common childhood infections in Europe.



[Figure 1]



[Figure 2]

O060

THE EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL DISEASE IN EUROPE, 2008 AND 2009

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The objective of this analysis was to describe the surveillance and epidemiology of invasive meningococcal disease (IMD) in Europe in 2008 and 2009.

Designated national experts from Member States (MS) reported data into the European Surveillance System (TESSy) database, following EU-wide reporting standards. Out of 27 EU and 2 EEA countries with a comprehensive and passive reporting system, 28 submitted case-based data. Case definitions varied between countries, with the majority applying the 2008 EU case definition.

In 2008 and 2009, a total number of 9615 cases of IMD were reported with an overall notification rate of 0.99/100,000 in 2008 and 0.92/100,000 in 2009. The highest notification rates were reported by Ireland (3.68/100,000 in 2008 and 3.37/100,000 in 2009) and the United Kingdom (2.29/100000 in 2008 and 2.02/100000 in 2009). The highest age-specific rates were notified in infants younger than 1 year (18.3/100,000 in 2008 and 15.9/100,000 in 2009). Serogroup B accounted for the largest proportion of cases (71%), followed by serogroup C (13%). In countries with MenC vaccination (MCC), the serogroup C incidences in 2009 were lower in age groups targeted by vaccination (< 1 year: 0.54/100000; 1-4 year: 0, 22/100000), compared with countries without MCC vaccination (< 1year: 1.01/100000; 1-4 year: 0.45/100000).

The overall case fatality was 8.5% (422 deaths) in 2008 and 7.4% in 2009 (340 deaths). Multilocus sequence typing (11% data completeness) showed that the bacterial population was highly diverse with 26.1% of isolates (n=256) belonging to CC ST-41 complex.

O061

PERTUSSIS RISK IN CHILDREN AS A FUNCTION OF TIME SINCE RECEIPT OF THE 5TH DOSE OF ACELLULAR PERTUSSIS VACCINE

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Background and aims: In the United States, children receive 5 doses of diphtheria, tetanus, and acellular pertussis (DTaP) vaccine before age 6. To better understand the effectiveness of the 5th DTaP dose, we assessed the risk of pertussis relative to time since the 5th DTaP in the setting of a large pertussis outbreak in California.

Methods: We conducted a case-control study within Northern California Kaiser Permanente (NCKP) among members vaccinated with DTaP between ages 45 and 84 months from December 2005 through December 2010. Confirmed pertussis polymerase chain reaction (PCR)-positive cases were compared with two age- and sex-matched populations with regard to time since 5th dose of DTaP (pertussis PCR-negative controls [group 1] and random sample of NCKP members matched 5:1 [group 2]). We excluded all individuals who received pertussis-containing vaccines subsequent to their 5th DTaP.

Results: A total of 305 pertussis-positive cases were compared to 3220 individuals in control group 1 and 1529 individuals in control group 2. The majority of cases (61%) were between ages 4 and 11 years. Cases were significantly more likely to have received the 5th dose of DTaP earlier in time than control group 1 (odds ratio [OR] per 365 days since receipt of the 5th dose 1.19; 95% CI: 1.08, 1.31) and control group 2 (OR 1.42; 95% CI: 1.03, 1.97).

Conclusions: Increasing time since receipt of a 5th DTaP dose is associated with elevated risk of pertussis. Effectiveness of the 5th DTaP dose against pertussis appears to wane over time.

O062

DETECTION OF *MYCOPLASMA PNEUMONIAE* IN HEALTHY CHILDREN BY REAL TIME PCR - PRELIMINARY DATA FROM THE MYMIC STUDY

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Background and aims: *Mycoplasma pneumoniae (Mpn)* is a common cause of respiratory tract infections (RTIs) in children. In the past decade, PCR has become a widely used tool to detect *Mpn* with the general assumption that a positive result always indicates infection. However, if asymptomatic carriage exists, treatment of all *Mpn* PCR-positive patients will lead to unnecessary antibiotic treatment and risk of development of antibiotic resistance. In this study we aim to improve diagnosis of *Mpn* RTIs in children by investigating the existence of asymptomatic carriage.

Methods: From June 2008 until December 2010 267 children with an RTI and 300 healthy children were enrolled in the study. For each child with RTI, clinical symptoms and signs were registered and from all children (naso)pharyngeal samples and serum were collected and tested for *Mpn*, other bacteria and viruses.

Results: Thus far, real-time PCR for *Mpn* and standard bacterial cultures have been performed for 523 participants. *Mpn* DNA was detected 14% of the 236 children with RTI versus 17,1% of the 287 healthy children. In addition, there was no significant difference in *Mpn* load between the two groups.

Conclusions: Our data indicate that real- time PCR, as a diagnostic test for *Mpn,* should be interpreted carefully, since positive results could also represent cases of carriage. Nevertheless, the existence of true carriage still needs to be determined. A positive PCR could also indicate recovery from an infection or represent the start of an infection. We are currently addressing this issue by sampling longitudinally.

O063

DEFINITION OF A CORRELATE OF PROTECTION FOR INACTIVATED INFLUENZA VACCINES IN CHILDREN LESS THAN FIVE YEARS OF AGE

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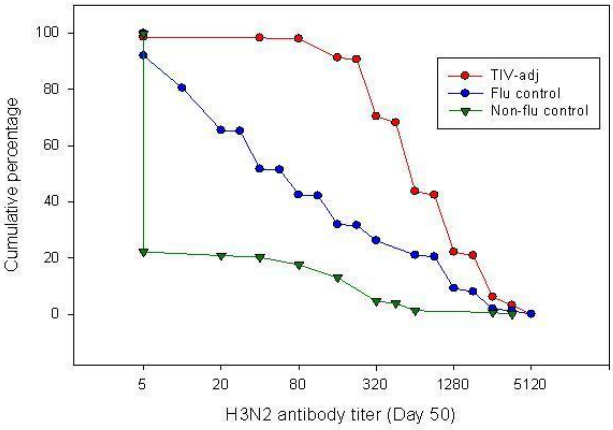
Background: Although an HAI titer of 1:40 has been recognized as an immunologic correlate corresponding to a 50% reduction in the risk of contracting influenza in adult populations, this relationship has not been evaluated in children.
Methods: 4707 influenza vaccine naive children 6-72 mo old were randomized 2:2:1 to MF-59 adjuvanted influenza vaccine (Novartis), subunit TIV (control, GSK) or placebo during the 2007-8 and 2008-9 influenza seasons. Cases identified by active surveillance were confirmed by RT-PCR. Immunogenicity at day 50 (21 days after dose two) was evaluated in a subset of 777 children.
Results: H3N2 Immunogenicity and efficacy results were evaluated against the Prentice criteria which confirmed that the immunogenicity data warranted estimation of an immunologic correlate. The Dunning model fitting H3N2 antibody titers and cases observed in the immunogenicit subset revealed that a cut-off titer of 1:110 was associated with the conventional 50% clinical protection rate whereas titers of 1:215, 1:330 and 1:629 predicted protection rates of 70%, 80% and 90% respectively. The conventional adult 1:40 HAI titer was only associated with 22% protection.



[Reverse Cummulative Distributions]

Conclusion: The use of the conventional 1:40 HAI correlate of protection derived from adult challenge studies is not appropriate when evaluating influenza vaccines in children. Although a cut-off of 1:110 may be used to predict the conventional 50% clinical protection rate, a titer of 1:330 would predict an 80% protective level which would seem to be more desirable from a public health perspective.

O064

DETERMINING THE QUALITY OF CARE FOR ACUTE RESPIRATORY INFECTIONS IN MALAWIAN CHILDREN

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Background: Acute respiratory infections (ARI) are the leading cause of global child mortality. Integrated Management of Childhood Illnesses (IMCI) are case-management guidelines validated to improve patient outcomes in resource-poor settings. Although Malawian ARI guidelines are IMCI-based, little is known about the quality of ARI care. Thus, we aimed to evaluate the quality of pediatric ARI care delivered by Malawian clinical officers (COs).

Methods: Provider knowledge of ARI guidelines was assessed with a written questionnaire. An ARI-trained pediatrician observed 695 evaluations of children by unsupervised COs at a government clinic in Malawi. From each evaluation, 25 elements (e.g. history, physical examination, diagnosis, and treatment) were analyzed by multivariate logistic regression to identify factors that predict a correct ARI “assessment” (classification and treatment).

Result: Only 235 patients (34%) received the correct ARI assessment. Correct evaluation of chest indrawing predicted a correct ARI assessment (OR, 4.4; CI, 1.9-10.0) as did a CO's ARI care knowledge (OR, 2.3; CI, 1.4-3.9), based on $\geq$50% of correct responses on the questionnaire. Other positive predictive factors for a correct ARI assessment were encounters on days other than Monday, eliciting ≤70% key components of a patient's history, obtaining a temperature, not obtaining pulse oximetry, and documenting chest indrawing status (regardless of accuracy).

Conclusions: Pediatric ARI care quality at this Malawian government clinic is poor and may reflect regional practices. Revision of current ARI training and supervision is likely needed to optimize the quality of pediatric respiratory care, better utilize existing human and material resources, and improve patient outcomes.

O065

IMPACT OF THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON INVASIVE PNEUMOCOCCAL DISEASE IN ALASKA NATIVE CHILDREN: RESULTS OF A CLINICAL TRIAL

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Background: Before 7-valent pneumococcal conjugate vaccine (PCV7), Alaska Native children < 5 years from Yukon Kuskokwim Delta (YKD) had invasive pneumococcal disease (IPD) rates 10-fold higher than non-Native Alaskan children (547 vs. 56 per 100,000/year). After PCV7 vaccine introduction, IPD rates in YKD children decreased to 148/100,000 in 2001-2004, but then increased to 433/100,000 in 2005-2008 due to non-vaccine serotypes. In 2009, the YK Health Corporation participated with Wyeth (Pfizer) in a clinical trial of PCV13.

Methods: Pneumococci isolated from Alaska-wide laboratory-based IPD surveillance were serotyped. Between 1/30/2009 and 3/25/2010, participating YKD children < 5 years received PCV13 vaccine while others received PCV7 vaccine. After 3/25/2010, licensed PCV13 vaccine was offered routinely to all YKD children < 5 years.

Results: 372 subjects were vaccinated with PCV13 during the clinical trial (1/2009-3/2010) and 2551 children were vaccinated after licensure (4/2010-12/2010). Fifty-two IPD cases occurred in YKD children < 5 during 2005-2008, and 8 cases occurred during 1/2009-12/2010 (139/100,000) ($p < 0.001$). Thirty-one PCV13-serotype IPD cases occurred in the pre-vaccine period (258/100,000) compared with 6 cases in the vaccine period (104/100,000) ($p=0.030$). No PCV13 serotype cases occurred among children who received PCV13 (1613 person follow-up years), while 6 occurred among children with no PCV13 (4140 person follow-up years, $p=.139$). No IPD cases occurred among YKD children < 5 years after 5/14/2010.

Conclusion: PCV13 IPD dropped significantly in YKD after PCV13 introduction. While non-PCV13 IPD also declined, absence of PCV13 IPD in children who received ≥1 dose of PCV13 suggests a protective vaccine effect.

O066

VISCERAL LEISHMANIASIS

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L. donovani complex consisting of L donovani and L infantum are the aetiologic agent for visceral leishmaniasis (VL). VL is a disseminated and potentially fatal disease.

If untreated. India, Nepal, Bangladesh, Sudan and Brazil account for 90% of VL burden, and India alone has the 50% of worlds VL patients. Though parasitological confirmation in splenic or bone-marrow smears is the gold standard for diagnosis of VL, these are invasive and risky procedures. Serodiagnosis using rK39 based rapid immunochromatographic test is highly sensitive but has several drawbacks. There is an urgent need to develop a marker for active disease. Pentavalent antimonials (Sb^v) are the treatment of choice worldwide except in developed world (Europe), where liposomal amphotericin B (L-AmB) is used for the treatment of VL. In the state of Bihar, there is widespread Sb^v unresponsiveness, all efforts to overcome by increasing the dose and duration and increasing the dose 10-12 fold ,were unsuccessful. Further, Sb^v treatment can be fatal in about 3-5% patients. Thus, in India amphotericin B deoxycholate is used as first line drug in areas with Sb^v unresponsiveness. In last decade a remarkable progress has been made in the treatment of VL. An oral drug miltefosine , an alkyl phosphocholine, became available for clinical use after extensive trials in India and is licensed in several countries for the treatment of visceral leishmaniasis. Its prolonged regimen of 28 days and teratogenic potential entailing contraception during the treatment and for further three months, are major limitations. Miltefosine has been chosen for the VL Elimination initiative in India, Nepal and Bangladesh. Second drug to be licensed recently was paromomycin. It is being manufactured in India and the cost of treatment is ~US$ 15 for treatment of an adult. Its drawback include 21 intramuscular injections. L-AmB in the only FDA approved antileishmanial drug, however, due to cost-constraints it is seldom used in developing countries. Recently WHO negotiated the price of L-AmB for resource poor countries at US$18/ 50 mg vial. This makes the drug very attractive. In several trials in India and elsewhere the drug has been found to be very safe and effective. In a recent study in India, L-AmB, in a single dose of 10 mg/kg was compared with the conventional amphotericin B deoxycholate (1 mg/kg, 15 infusions on alternate days), and the efficacy was similar and L-AmB had no safety issues, thus it was possible to reduce the duration of treatment from one month to one day. Except amphotericin B, all other antileishmanial drugs have potential for development of drug resistance, thus it is prudent that multidrug regimens should be developed. Recently in a phase 2 study followed by a phase 3 trial, an efficacy of >97% was established using single dose of L-AmB (5 mg) followed by either miltefosine for 7 days or paromomycin for 10 days. A third multidrug constituted miltefosine and paromomycin for 10 days each. These new regimens have high efficacy, cost-effective and compliance can be excellent if used as a directly observed therapy.

O067

MALARIA AND SALMONELLA CO-INFECTION: A CONFLICT BETWEEN PATHOGEN TOLERANCE AND RESISTANCE

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Background and aims: Invasive non-Typhoid Salmonella (NTS) is a common and often fatal complication of *Plasmodium falciparum* infection in children. Induction of heme oxygenase-1 (HO-1) mediates tolerance to the cytotoxic effects heme-derived reactive oxygen species (ROS) during malarial-hemolysis, promoting survival of the host without reducing parasitemia. We hypothesised that induction of HO-1 impairs resistance to NTS by limiting bactericidal ROS production, permitting increased bacterial growth.

Methods: C57BL/6 mice with *Plasmodium yoelii* 17XNL (Py17XNL) infection, or pretreated with phenyhydrazine (PHZ) or the HO-1 substrate/ inducer hemin, were infected by intraperitoneal injection of Green Fluorescent Protein expressing-*S.* Typhimurium. Bacterial burden was assessed by quantitative culture and bacterial distribution, host cell phenotypes, HO-1 expression and oxidative burst by flow-cytometry.

Results: Py17XNL, PHZ and hemin impaired resistance to S. Typhimurium infection, decreasing survival time and increasing bacterial loads compared to S. Typhimurium infection alone. S. Typhimurium localized in granulocytes, which showed normal phagocytosis but impaired killing of S. Typhimurium. Py17XNL, PHZ and hemin caused HO-1 upregulation in the granulocyte precursor compartment of bone marrow, and mobilization of granulocytes with reduced oxidative burst activity. Inhibition of HO by tin protoporphyrin (SnPP) abrogated the impairment of resistance to S. Typhimurium by Py17XNL.

Conclusions: For the first time we show that a mechanism of tolerance to one infection, malaria, impairs resistance to another, S. Typhimurium. This may explain the association of NTS bacteremia with *P. falciparum* infection. Furthermore, HO inhibitors may be useful adjunctive therapy for NTS infection in the context of malarial or sickle cell hemolysis.

O068

A NOVEL, FULLY AUTOMATED SAMPLE-TO-RESULT REAL-TIME PCR ASSAY FOR POINT-OF-CARE DETECTION OF DENGUE VIREMIA

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Introduction: Appropriate treatment of patients with dengue relies on early clinical recognition. Laboratory methods to confirm dengue virus (DENV) infection are time-consuming, labor-intensive, and require a high level of technical skill. RT-PCR, the most sensitive method for DENV detection, has been difficult to transfer to the clinical setting; the lack of integration and automation of nucleic acid tests has been one major obstacle.

Methods: We developed a fully-automated, rapid qualitative RT-PCR assay for the detection of dengue viremia based on IQuum's lab-in-a-tube (Liat™) platform, which integrates raw sample processing and detection, including target enrichment, inhibitor removal, nucleic acid extraction, reverse transcription and real-time PCR, in a single closed-tube format. We tested the assay performance using spiked normal human serum and whole blood as well as archived serum from DENV-infected patients. Assay results were compared to those using a published benchtop real-time RT-PCR method.

Results: The Liat™ Dengue Assay detected DENV in serum or whole blood samples (50-100 ml), with a turnaround time of < 40 minutes. The assay sensitivity was < 4.8 pfu/ml for all four serotypes. Testing of sera from DENV-infected patients showed that the Liat™ assay had sensitivity equal to or better than the benchtop assay with faster results and minimal personnel effort.

Conclusions: Preliminary testing of the Liat™ Dengue Assay indicated a higher sensitivity compared to traditional laboratory-based methods for detection of dengue viremia. The ease-of-use and speed of this Liat™ test allows it to be used in decentralized settings, enabling greater access to nucleic acid testing.

O069

IL-15 GENE POLYMORPHISMS ARE ASSOCIATED WITH RESISTANCE TO VISCERAL LEISHMANIASIS

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Background and aim: Protozoan parasites of the genus Leishmania infect millions of people worldwide causing a wide spectrum of diseases collectively termed leishmaniasis that vary in their clinical manifestations. There are several reports on the importance of IL-15 in the immunity against leishmaniasis. Since the production of IL-15, like other cytokines, is under control of its gene, we tried to find any relationship between kala azar and IL-15 genetic polymorphisms.

Methods: One hundred and seventeen patients with kala-azar and 146 individuals who lived in the same area as patients and didn't have any history of leishmaniasis, joined this study. DNAs extracted from samples were genotyped for IL-15 (267C/T, 367G/A, 13687C/A, and 14035A/T) polymorphisms using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method.

Results: IL-15 (267) TT and T genotype and allele were significantly higher in the patients than the controls ($P< 0.001$ and $P< 0.003$, respectively). Also IL-15 (13687) CC and C genotype and allele were less frequent in the controls than the patients ($P< 0.015$ and $P< 0.031$, respectively). Haplotype analysis showed a higher frequency of 13687C/267T/367G/14035A in the patients than the controls ($P< 0.000001$).

Conclusions: As data shown IL-15 267T allele could be considered as a susceptibility factor for kala azar. Vice versa, IL-15 13687C allele might be one of the genetic resistance factors against kala azar. In addition, we can consider the haplotype 13687C/267T/367G/14035A as a susceptibility factor for kala azar. Evaluation of IL-15 level beside genetic polymorphisms is recommended.

O070

CRYPTOSPORIDIOSIS IN KUWAITI CHILDREN: ASSOCIATION OF CLINICAL CHARACTERISTICS WITH *CRYPTOSPORIDIUM* SPECIES AND SUBTYPES

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Background and aims: To determine the association of clinical characteristics with *Cryptosporidium* types and subtypes.

Mathods: Fecal specimens from 2548 children with diarrhea were screened by microscopy for *Cryptosporidium* spp. and the positive specimens were genotyped and subtyped by PCR-restriction fragment length polymorphism.

Results: Eighty seven of 2548 (3.4%) children had cryptosporidial diarrhea by microscopy and the majority (41.4%) of the infected children were between 4-8 year-old age group. Molecular characterization showed that *C. parvum* was the most commonly identified species (72.5%) and consisted of 3 subtypes, IIa, IId were the commonest (80.2%) followed by IIc. Twenty-two (26.5%) of the children had *C. hominis* and showed three subtypes, Id was the most common (54.5%) followed by Ia (36.4%) and Ie. Associated clinical manifestations varied between *C. parvum and C. hominis*. Diarrhea associated with subtype Id, the most commonly identified *C. hominis* subtype, was more severe than that associated with other subtypes.

Conclusion: In conclusion, our study confirms a very different *Cryptosporidium* genotype and subtype distribution, with a predominance of *C. parvum* IIa and IId among the Kuwaiti children with diarrhea. In addition, subtype Id of *C. hominis* was associated with more diverse and severe clinical manifestations in infected children suggesting that parasite genetics may play an important role in the clinical manifestations of human cryptosporidiosis.

O071

VACCINE SAFETY AND PUBLIC CONFIDENCE: A VISION FOR THE NEXT DECADE

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The past sixty years has witnessed an amazing level of new vaccine development and consequent reductions or even elimination of diseases due to the major infectious scourges of humanity. Beginning with polio vaccine introduction in the 1950s, we have seen vaccines developed for hepatitis A and B, new conjugate vaccines developed for *Haemophilus influenzae* type b, and the pneumococcus, polyvalent conjugate vaccine for the meningococcus, a vaccine to prevent varicella as well as vaccines to prevent cervical cancer. Because of these vaccines, the number children and adults dying and suffering from these diseases has been reduced dramatically. However, because of this success, generations of children now are growing up without personal experience with the diseases that these vaccines have prevented. This, along with other trends, has engendered an increasing lack of public confidence in vaccines, as well as lack of confidence in the statements made by public health experts and infectious disease specialists regarding vaccine effectiveness and safety. In fact, as methods of evaluating vaccine safety have become more sophisticated, as more information has become available on vaccine safety and effectiveness both before and after vaccine licensure, public confidence in this information and vaccination programs has continued to decrease. Misinformation on vaccine safety now not only impacts vaccination programs in the US and Europe where organized vaccine disinformation programs began, but also now impact programs such as the polio eradication program in Africa and elsewhere. Additionally, attacks on the integrity of national and WHO public health officials making vaccine recommendations are making it more difficult to identify individuals willing to take on this role. Clearly the answer does not lie in merely providing more safety data. A reassessment of how we can more credibly communicate risk and benefit to the public regarding vaccines, the risks of the diseases they prevent, and any risks associated with receipt of vaccines will be a key step to improve the situation moving forward.

O072

CARING FOR INTERNATIONALLY ADOPTED CHILDREN: IMMUNIZATION AND INFECTIOUS DISEASES SCREENING

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Background: During the last years the number of international adoptions has more and more increased in Italy: in 2010 more than 4000 foreign born children were adopted from Italian families. Children involved in international adoption are at high risk of infectious diseases because of their previous life conditions; moreover they were not always adequately immunized against vaccine-preventable diseases.

Methods: From June 2007 to June 2010, 65 adopted children and adolescents (37 males, 28 females, aged from 6 month to 17 years) have been evaluated with a complete sanitary screening in the Department of Infectious Diseases - University of Pavia.

Results: In our cohort most subjects were coming from Latin America (about 33%) and East Europe (26.6%). We detect fifteen cases not fully immunized against poliomyelitis. Just 40% of the screened patients resulted vaccinated against hepatitis B but in two Asiatic children, hepatitis B surface antigen (HBsAg) was detected with impaired hepatic function. Although adequate immunity against tetanus and diphtheria resulted in more than 80% of cases, only 48% of them were fully protected against measles, mumps and rubella.

Multiple intestinal parasites were found in 40% of screened subjects with Giardia lamblia and non-pathogenic amoebae the most frequently identified protozoa; among the worms Hymenolepis nana was mostly detected.

Conclusions: Screening internationally adopted children for infectious diseases even uncommonly encountered in industrialized countries and to assess their immunization status is mandatory in order not only to promote their integration into a new social environment but also to protect the adoptive families.

O073

ALARMING SYMPTOMS FOR SERIOUS BACTERIAL INFECTIONS ARE PRESENT AS TRIAGE CRITERIA AND ASSOCIATED WITH HOSPITALISATION

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Background and aim: A recent systematic review identified alarming symptoms for serious bacterial infections (SBI) in children[1]. Eleven of these symptoms are defined in the Manchester Triage System (MTS) as triage criteria. How often are these alarming symptoms selected at triage and does their presence predict hospitalisation?

Methods: Observational study, including 1770 children with fever (0-16 years) that attended the Emergency Department (ED) of the Sophia Children's Hospital, Rotterdam, Netherlands (Jan 2008-Jul 2009). Triage by the MTS involves selection of one flowchart (major presenting problem) and linked discriminator(s) to determine the patient's urgency level. Numbers of alarming symptoms selected at triage were divided by the maximum number of alarming symptoms available per patient. These percentages were used to identify the association between alarming symptoms selected at triage and hospitalisation by logistic regression.

Results: Median age of patients was 2.2 years (IQR 0.9-4.5), median temperature 38.9°C (IQR 38.2-39.6), 58% were boys. The maximum number of alarming symptoms that could be selected at triage was 8 per patient. Twenty-six percent of patients (n=469) had at least 1 and maximum 4 alarming symptoms scored. The odds of hospitalisation increased with the percentage of alarming symptoms selected (OR 1.04; 95%CI 1.03-1.05). E.g. hospitalisation occurred twice often in children with 20% alarming symptoms selected at triage compared to those without.

Conclusion: Alarming symptoms for SBI are defined in the MTS. Presence of alarming symptoms at triage is associated with hospitalisation. This knowledge can be used to direct patientflows at the ED.

1. Van den Bruel, Lancet 2010.

O074

A NATIONAL SURVEY OF THE INCIDENCE AND EPIDEMIOLOGY OF KAWASAKI DISEASE IN IRELAND

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Background and aims: Kawasaki disease (KD) is an acute vasculitic syndrome of unknown aetiology. It is now the commonest cause of acquired cardiac disease in children in the developed world. This study aimed to determine prospectively the incidence and epidemiology of KD in Ireland between 2008 - 2009.

Methods: The Irish Paediatric Surveillance Unit issues monthly notification cards to all paediatricians. Surveillance for KD took place from January 2008 through December 2009. Paediatricians who reported a case were issued with a questionnaire seeking further information..

Results: There were 23 cases of KD recorded during the 2 year study period. 74% were under 5 years which represents an annual incidence of 2.03 /100,000 children under five years. Eleven cases (47%) were classified as incomplete or atypical KD. Average age at presentation was 3 years 2 months (median 4years 6months; range 3.5months- 8years 11months). Median duration of fever prior to therapy was 7 days (range 1 to 28 days). Four children (17%) had coronary artery abnormalities at presentation: coronary artery dilatation, 3; and coronary aneurysms, 1. Twenty cases (87%) received aspirin and IV immunoglobulin. Three cases presented after 3 weeks of symptoms and received aspirin alone.

Conclusions: The incidence of KD in this study is low by international standards. Almost half of cases were incomplete KD, which may be explained by increased awareness of atypical presentations. However, 3 children (13%) were late presenting, suggesting that awareness of KD still needs to be reinforced.

O075

VERY SEVERE CASES OF ROTAVIRUS DISEASE IN GERMANY - A PROSPECTIVE EPIDEMIOLOGICAL SURVEY

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Background: According to the German Infection Protection Act, all cases of rotavirus (RV) disease in Germany are to be reported to the authorities. There are no data concerning the severity of the disease. Aim of study was to prospectively determine the incidence and the outcome in very severe cases of RV disease.

Methods: Cases of very severe RV disease were queried through the collection unit for rare pediatric diseases in Germany (ESPED) using anonymous questionnaires. Data acquisition started in April 2009 for a planned period of two years.

Inclusion criteria were detection of RV in faeces, patient age 0 - 16 years and one or more of the following criteria: intensive care treatment, hyper- or hyponatremia (> 155 mmol/l or < 125 mmol/l), clinical signs of encephalopathy (somnolence, seizures, apnoeas), death due to complications related to RV disease.

Results: 86 cases were reported between April 2009 and December 2010 of which 61/86 questionnaires have been returned. 15/61 cases were nosocomially acquired, 12/15 were in neonatal intensive care.

46/61 cases were community acquired, their mean age was 15.7 months (0 - 83 months), mean hospital stay was 9 days (4 - 38 days). 24/46 patients needed intensive care treatment, 34/46 children had signs of encephalopathy, 24/46 cases had a hyper- or hyponatremia. One death was reported (child with syndromal disease with multiple organ anomalies).

Conclusions: This study shows that RV infections may take a life-threatening course. A substantial number of these cases were nosocomially acquired.

O076

INCIDENCE OF PERTUSSIS AMONG PATIENTS WITH PROLONGED COUGH VISITING GENERAL PRACTITIONERS IN POLAND, 2009-2010: A PROSPECTIVE ENHANCED SURVEILLANCE STUDY

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Background and aims: Each year, 1500-2000 pertussis cases are reported through routine surveillance in Poland, but the sensitivity of reporting system remains unknown. The aim of the present study was to assess the incidence of pertussis among patients with cough lasting >2 weeks in the general practitioner (GP) setting in Poland.

Methods: The study was performed from July 2009 until September 2010 in the population served by 77 randomly selected GPs (158,596 inhabitants). Inclusion criteria were: age >3 years, cough lasting 2-15 weeks, and informed consent. GPs interviewed each eligible patient, collected a blood sample, and a nasopharyngeal swab. At follow-up 30 days after the initial visit physicians collected a second blood sample and interview. Confirmed pertussis cases were defined as patients meeting the clinical criteria confirmed by laboratory (specific antibody response or PCR).

Results: During the study period, 2,724 patients with cough were admitted to participating GPs, of whom 830 met the inclusion criteria and were recruited into the study. A total of 274 cases were confirmed as pertussis, giving an overall incidence of 1.77 per 1,000 person-years. Extrapolating the present study results to the entire Polish population, we estimated the annual number of GP-referred pertussis cases at 63,742, which is 71-times higher than 896 cases reported by GPs to national surveillance during corresponding period. Underreporting factor ranged from 12 among 3-5 year olds, to 320 among 65-70 year olds.

Conclusions: The present study confirmed the high underreporting rate of pertussis cases seen by general practitioners in Poland.

O077

IMPACT OF FRENCH ANTIBIOTIC GUIDELINE FOR ACUTE RESPIRATORY TRACT INFECTIONS IN A PEDIATRIC EMERGENCY DEPARTMENT, 2005-2009

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Context: Antibiotic use leads to the emergence and the dissemination of multi-resistant bacteria. Acute Respiratory Tract Infections (ARTI) are the main reason for antibiotic prescription in children. In 2005 the French medicine agency (AFSSAPS) published new guidelines to reduce the misuse of antibiotics in ARTIs.

Objective: To determine the usefulness of the implementation of guidelines to reduce antibiotic prescriptions for ARTI in a Pediatric Emergency Department (PED).

Methods: Retrospective cohort study in a French PED from November 2005 (date of implementation of this guideline in our institution) to October 2009. We retrieved for every child diagnosed as ARTI: date of visit, age, diagnosis, antibiotic prescription.

Main outcome measures: Proportion of ARTI visits that resulted in antibiotics at discharge during and after the implementation of the French guidelines.

Results: During the study 60165 children have been diagnosed as ARTI in our PED. Antibiotic prescription at discharge in our PED was related in approximately 60% to an ARTI visits. The proportion of antibiotic prescription in ARTI visits fell from 29,8% during the first year of implementation of guideline to 19,9% at year 4 ($p< 10^{-6}$). The percentage of antibiotic prescription at discharge decreased for most ARTIs except for Acute Otitis Media and pneumonia for which the percentage remained stable. Amoxicillin/clavulanic acid and amoxicillin were the two most prescribed antibiotic and respectively accounted for 50% and 35% of antibiotic prescriptions.

Conclusions: Antibiotic prescriptions for ARTI declined significantly in our PED with the implementation of French antibiotic guidelines.

O078

DECREASE OF VARICELLA ZOSTER VIRUS - ASSOCIATED PAEDIATRIC HOSPITALISATIONS AND COMPLICATIONS IN BAVARIA AFTER RECOMMENDATION FOR ROUTINE VARICELLA VACCINATION

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Background: In 2004, routine vaccination for varicella was recommended for all children 11-14 months of age in Germany. We investigated the impact of vaccination on the frequency of paediatric hospitalisations and complications associated with varicella (VZ) or herpes zoster (HZ).

Methods: Children < 17 years of age hospitalized with an ICD-10 discharge diagnosis of VZ or HZ were captured by annual data queries in Bavarian paediatric hospitals from 2005 to 2009. Additionally, age, gender, length of stay, and accompanying diagnoses were collected.

Results: 33 (89%) out of 37 hospitals participated; 19 (51%) contributed data for all five years. In total, 1132 VZ and 340 HZ cases were reported. VZ hospitalisations (55% male, median age 3 years, IQR 1-5) lasted 3 days (median; IQR 2-6). HZ hospitalisations (56% male, median age 9 years (IQR 6-13) lasted 6 days (median; IQR 4-8). Specific complications in VZ patients were: 25 (2%) encephalitis, 13 (1%) meningitis, 27 (2%) pneumonia, 329 (29%) other complications; in HZ patients: 10 (3%) encephalitis, 7 (2%) meningitis, 9 (3%) zoster generalisatus, 107 (31%) other complications. The annual incidence estimate of VZ hospitalisations in Bavaria in children < 17 years of age was 13.3-16.8/100,000 until 2007 and decreased from 15.8/100,000 in 2007 (CI 14.2;17.6) to 10.3/100,000 (CI 8.9;11.7) in 2008 and 6.7/100,000 (CI 5.6;7.9) in 2009. For HZ hospitalisations, incidence was estimated as 3.2-4.4/100,000 from 2005 to 2009.

Conclusions: Five years after recommended vaccination, VZ-associated hospitalisations had decreased by >50%. The impact on paediatric herpes zoster hospitalisations needs long-term evaluation.

O079

EVOLUTION OF THE MENINGOCOCCAL DISEASE´S INCIDENCE ON PAEDIATRIC NAVARRE´S POPULATION (NORTH OF SPAIN)

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Introduction: The meningococcal disease is a clinical feature of low incidence but with a very important epidemiologic weight, because its high morbimortality

Objectives: - Analysis about evolution of invasive meningococcal disease´s (IMD) incidence on paediatric Navarre´s population.

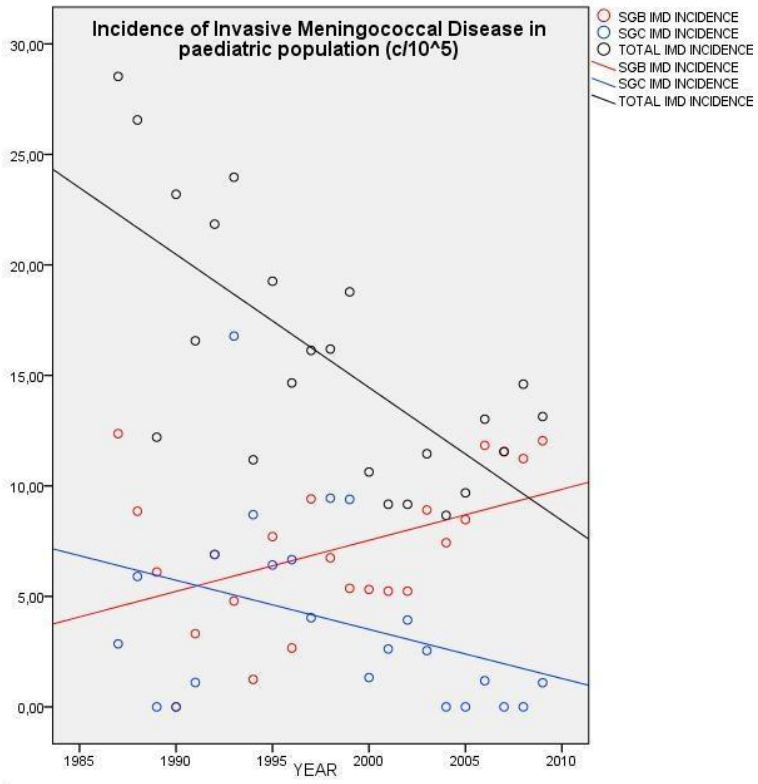
- Evaluate changes on the IMD´s incidence on after introduction of the systematic vaccination against meningococcal C at the last months on 2000 year.

Methods: Population data was obtained from Census of Navarre.

Meningococcal disease data was obtained from the Navarre´s Institute of Public Health from January of 1987 to december of 2009.

Statistical analysis: Student T test, Chi Square test and binary logistic regression.

Results: We observed a global decrease in IMD´s incidence on our population from prevaccinal period(1987-2000) to postvaccinal(2001-2009), from 18,54 to 11,16c/10^5(OR:0,594; CI95%:0,463-0,763). This fall was due to the drop in cases of serogroup C(SGC) from 5,67 to 1,26c/10^5(OR:0,221;CI95%:0,110-0,444) and in non-grouped cases. On the contrary, the cases of serogroup B(SGB) increased on the postvaccination period(from 5,76 to 9,1c/10^5;OR:1,576;CI95%:1,13-2,198). When we stratified by ages and serogroups, we observed an important decrease in SGC incidence in younger groups: 0-5years(OR:0,033;CI95%:0,004-0,237) and 5-9years(from 3.56 to 0c/10^5). In these groups there were not significant rises in SGB incidence. In the other hand SGB incidence increase in older group(10-15years:OR:4,66;CI95%:1.20-18,04) with no significant fall in SGC incidence.



[Incidence of Invasive Meningococcal disease]

Conclusions: After the introduction of vaccination, there was a decrease in IMD´s incidence on paediatric population. However, the important fall of SGC cases on little children has been disguised by the increase of SGB cases on older groups.

O080

CONSTRUCTION, EXPRESSION, AND IMMUNIZATION OF ENTEROVIRUS-71 VIRUS-LIKE PARTICLES

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Background and aims: EV71 is a cause of hand, foot and mouth disease (HMFD) combined with severe paralysis or encephalitis or possibly death in children. Numerous large outbreaks of EV71 caused HMFD have occurred recently in Asia, especially in China Mainland in 2010, 1,795,336 cases were reported in which the fatal cases were 888. So it is important to find a method for preventing infection with EV71 since there is no antiviral agent or vaccine for humans.

Methods: Transform P1-pGAPZa-A and 3CD-pGAPZa-A recombinant plasmids into SMD1168 and get the recombinant strain expressing P1 and 3CD proteins which form EV71 VLPs. Identify the expression proteins by Tricine-SDS-PAGE and Western-blot, visualize the VLPs by electronmicroscope. Further evaluate the potential of the purified VLP as a vaccine by the immunization of BALB/c mice. Total IgG and neutralization antibody were tested to evaluate humoral immunity. Lymphocyte proliferation assay and the cytokines produced by the stimulated splenocyte were tested to evaluate cytoimmunity response.

Results: The P1 protein was cleaved by 3CD prolease into VP0, VP1 and VP3 , which assembled into regular and homogeneous VLPs with diameter 20nm through the electron microscope. The VLP-immunized mice produced high total IgG and neutralization antibody titre. The splenocytes collected from the VLP-immunized mice exhibited significant cell proliferation and produced high levels of INF-γ, IL-2 and IL-4 after stimulation.

Conclusions: The EV71 VLPs could induce the mice's specific IgG and neutralization antibody and stimulate the cytoimmunity indicated that VLPs may be a valuable vaccine candidate to prevent EV71 epidemics.

O081

PHYLOGENETIC ANALYSES OF ROTAVIRUS OP354-LIKE P[8] STRAINS INDICATE A RAPID SPREAD IN THE HUMAN POPULATION

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Background and aims: Rotaviruses (RV) are the main etiological agent of gastroenteritis in young children causing approximately 600.000 cases per year. Two recently introduced life oral vaccines, Rotarix™ and RotaTeq™, have been proven highly efficacious against all major circulating genotypes in humans. OP345 is the reference strain for a recently described P[8]-lineage, which has been increasingly reported and has emerged in Africa, Asia, Europe and the Middle-East. Moreover, OP354-like P[8] RV strains have been found in combination with virtually all VP7 genotypes commonly found in humans.

Methods: OP345-like P[8] RV strains were collected from various continents and the sequence of the complete VP4 gene was determined. Phylogenetic and pairwise comparison analyses were applied to establish the evolutionary relationships among OP345-like P[8] RV strains.

Results: Phylogenetic analyses showed that OP345-like RV strains clustered close together and displayed more than 96% similarity on a nucleotide level. In contrary, OP345-like P[8] strains were only 89-90% similar to the P[8] genotypes of both Rotarix™ and RotaTeq™.

Conclusions: OP345-like P[8] RV strains have been detected on several continents. However, the limited diversity among OP345-like P[8] RV strains indicated that they have been circulating in the human population for a relatively short time span, and must have spread swiftly. The combination of i) distinct antigenic properties compared to the P[8] genotypes in vaccines and ii) the fact that they have been found with Wa-like as well as DS-1-like backbones, which are well adapted to infect humans, could make them a potential threat to future vaccine efficacy.

O082

" EFFECT OF HOME BASED CHILD CARE ON DIARREAL DEATHS IN A TRIBAL POPULATION: RESULT OF A FIELD TRIAL"

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Background: Melghat is tribal area in India with very high child mortality & malnutrition. The major causes of mortality & morbidity are infectious diseases like diarrhea due to scarcity of doctors. We developed Home Based Child Care (HBCC) model for tribal population to reduce children mortality and infectious diseases.

Aims:

1. To reduce diarrheal deaths by at least 35% in population of 14,120 of Melghat over 3 years.

2. To reduce case fatality rate of diarrhoea by at least 50% in population of 14,120 of Melghat over 3 years.

3. To reduce incidence of diarrheal diseases by 35% over 3 years.

Methods: Study-design was Randomised Control Trial . We selected 16 intervention (population 14,888) and 18 control (population 16,310) villages. Trained village health workers in intervention area treated diseases such as diarrhoea, dysentery, etc. Behaviour Change Communication programs were conducted.

Results: The incidence , number of deaths & case fatality rates due to diarrhoea in intervention area were reduced significantly from 1139 to 631 , 14 to 2, 1.23 % to 0.32% respectively ($p < 0.001$).Baseline mortality indices in control versus intervention areas were: NMR- 57.19 vs 50.93, IMR- 72.97 vs 94.9, & U5MR- 102.56 vs 143.52. After intervention NMR, IMR & U5MR were significantly decreased in intervention area to 29.2, 44.64 & 58.04 respectively($p < 0.05$).

Conclusions: HBCC resulted in significant decrease in children mortality due to diarrheal deaths & incidence of diarrhoea. Our model is replicable for reducing children mortality due to diarrhoea in other backward part of world.

O083

VIRAL ETIOLOGY, PROGNOSTIC FACTORS AND OUTCOME OF FULMINANT HEPATIC FAILURE IN CHILDREN

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Fulminant hepatic failure (FHF) is a catastrophic syndrome which may progress to death. In developing countries viral hepatitis is common etiology. Our aim is to identify the viral etiology, determine the prognostic factors and outcome of FHF

Methods: All patients with FHF with suspected viral etiology, admitted to a tertiary care hospital over a 3-year period were included. FHF due to drugs, autoimmune or metabolic liver disease were excluded. Grade of encephalopathy, viral markers, coagulation profile, liver function test and serum potassium levels were recorded.

Results: 108 children were identified with FHF due to viral hepatitis.Median age was 5 years. Forty were due to hepatitis A, 11 due to non A -G viral hepatitis, 13 due to hepatitis B,1 hepatitis E while 4 were having co-infection. 53 patients survived, 38 expired while 18 LAMA. Children with grade IV encephalopathy had 77% mortality, while those with grade 1 had 100 % survival. Delay between the first symptom and the onset of hepatic encephalopathy (within 10 days vs > 10 days), low albumin (< 2.5 g/dL), PT > 60 seconds & hypokalemia (< 3.5 mmol/dl) on admission were more likely to die.($P < 0.05$).

Conclusions: Hepatitis A and B were the most common viruses causing FHF. Children with severe coagulopathy, hypoalbuminemia and hypokalemia on admission and prolonged duration of illness before the onset of hepatic encephalopathy are more likely to die.Timely and proper vaccination against hepatitis A and hepatitis B can reduce the mortality and morbidity due to these viruses.

O084

HIGH PREVALENCE OF HUMAN G8 ROTAVIRUS STRAINS DURING 2008-09 IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Background and aims: Rotaviruses are the world's leading cause of severe rotavirus diarrhea in children < 5 years of age and form a major public health problem. However, limited regional and country specific data on rotavirus diversity is available from sub-Saharan Africa. This study aims to determine the genetic diversity of group A rotaviruses detected during 2008-2009 in the Democratic Republic of the Congo (DRC).

Methods: In this study a total of 218 fecal specimens were collected in the pediatric ward of three hospitals in Kisangani (University Hospital, General Referral Hospital of Kisangani, Village de Pédiatrie) and screened by an immunochromatographic antigen test (Rota-CIT, BioConcept, Belgium) for the presence of group A rotavirus antigen. In total, the G and P-types of 68 rotavirus-positive samples were characterized by reverse-transcription polymerase chain reaction and sequencing.

Results: The predominant G-type was G8 (detected in 37% of specimens) and the most predominant P-type was P[8] (60%). A total of 9 different G/P-combinations were found: G8P[8] (32%), G1P[8] (23%), G2P[4] (15%), G1P[6] (9%), G12P[6] (9%), G9P[8] (5%), G8P[6] (3%), G8P[4] (2%) and G2P[6] (2%).

Conclusions: The high prevalence of the G8 VP7 specificity in the DRC, which is believed to be of bovine origin, highlights the need for continued surveillance of rotavirus diversity in the DRC. Based on these data, rotavirus vaccines will be challenged with a wide variety of different RV strain types in the DRC.

O085

ENTEROVIRUS AND HUMAN PARECHOVIRUS INFECTIONS ARE A MAJOR CAUSE OF FEVER OF UNKNOWN ORIGIN IN YOUNG CHILDREN

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Background and aims: Enterovirus (EV) or Human Parechovirus (HPeV) infections in young children are usually self-limiting, but may cause serious symptoms, such as convulsions and cardiorespiratory instability. We investigated the incidence, clinical characteristics and management of EV and HPeV infections among young children with fever of unknown origin.

Methods: In 2008 345 children under 36 months of age presenting with fever of unknown origin and sepsis-like symptoms at the Juliana Children's Hospital in The Hague, the Netherlands, were evaluated in a prospective observational study. All received a sepsis work up including white cell count, CRP, blood culture and urine screening. Cerebrospinal fluid (CSF) was collected on indication. EV or HPeV DNA was detected by PCR in plasma and/or CSF. Urine cultures were performed when urine screening was positive. 115 children with urinary tract infection were excluded. Data of the remaining 230 children were analysed.

Results: EV/HPeV PCR could be performed in 163/230 children: 52 (32%) were EV positive, 31 (19%) HPeV positive, 10 (6%) had bacterial sepsis/meningitis and 70 (43%) were negative. Clinical characteristics at presentation varied only slightly between the four groups. EV and HPeV infections occurred predominantly in summertime. Bacterial infections resulted in longer hospital stays than viral infections.

Conclusion: EV and HPeV infections are a major cause of fever of unknown origin and sepsis-like symptoms in children under 36 months of age in summertime and are difficult to differentiate from bacterial infections. Early diagnosis EV and HPeV infections using PCR diagnostics reduces duration of hospital admission.

O086

GENETIC ANALYSES OF THE VP7 AND VP4 GENES OF CIRCULATING ROTAVIRUSES IN BELGIUM REVEAL ANTIGENIC DISPARITIES WITH ROTARIX™ AND ROTATEQ™

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Background and aims: Two rotavirus (RV) vaccines, Rotarix™ (G1P[8]) and RotaTeq™ (G1-G4, P[8]), have recently been successfully introduced in many countries around the world, including Belgium. The RV vaccine parental strains were isolated approximately 30 years ago in France (G4 parental strain in RotaTeq™) and the US (all other parental strains). At present, little is known about the relationship between currently circulating RV strains and vaccine strains.

Methods: In the present study, we determined the complete sequences of the RV genome segments encoding the outer capsid proteins VP7 and VP4, of currently circulating RV strains in Belgium. VP7 and VP4 both contain antigenic domains that induce neutralizing antibody responses.

Results: Several amino acid (AA) differences between wild-type RV and RV vaccine strains were observed in multiple antigenic domains for every G- and P-genotype. However, the highest variability was observed among G1P[8] RV strains and the G1 and P[8] components of both vaccines. Phylogenetically, the circulating RV strains clustered in three distinct P[8]-lineages. In particular the RV strains of the P[8]-lineage 4 (OP354-like) showed a significant number of AA differences with both vaccines mainly in VP8*. Circulating G3 RV strains were found to possess an extra N-linked glycosylation site compared to the G3 strain in RotaTeq™.

Conclusions: These results indicate that the antigenic domains of RV strains contained in the vaccines differ substantially from those of the currently circulating RV strains in Belgium. Over time this might result in selection for strains that escape the RV neutralizing-antibody pressure induced by vaccines.

O087

DURATION OF SHEDDING OF HUMAN PARECHOVIRUS IN FAECES OF YOUNG CHILDREN AFTER SYMPTOMATIC INFECTION

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Background and aims: Human parechoviruses (HPeV) are closely related to enteroviruses (EVs) and have recently been recognized as important cause of sepsis and CNS infection in infants. HPeV infections in children are very prevalent, mostly associated with mild gastrointestinal and respiratory disease. HPeV-specific real-time PCR is used for diagnosing HPeV infections. It is unknown for how long children are shedding HPeV in their faeces after clinical infection. Therefore, we determined the duration and amount of HPeV detection in faeces of children < 1 year in relation to clinical symptoms.

Methods: Faecessamples of 19 HPeV-positive children with symptomatic infection were collected every 2 weeks until termination of HPeV shedding. The HPeV viral load in faeces was quantified as Ct-value. Clinical symptoms were concurrently documented.

Results: Symptoms at presentation were fever, diarrhea and/or meningeal irritation. The initial Ct-value in faeces varied between 16,5 and 30. The viral load decreased gradually over time. The duration of HPeV shedding ranged from between 4 until 24 weeks. No clinical symptoms were reported after the first week except for one patient who was admitted 2,5 weeks after initial diagnosis with diarrhea and co-infection with adenovirus and two patients who had an episode of mild diarrhea respectively 3 and 15 weeks after initial diagnosis.

Conclusions: The duration of asymptomatic shedding of HPeV in faeces after clinical infection can be up to 6 months. The relative long duration of shedding can be an explanation for the high prevalence of HPeV infection in the first years of life.

O088

HOSPITALIZATION DUE TO VARICELLA IN THE NETHERLANDS

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Objectives: In the Netherlands, incidence of physician's consultations and hospitalizations for varicella is low compared to other countries. Better knowledge about the severity of varicella among Dutch hospitalized patients is needed.

Methods: Hospital admissions due to varicella in 2003-2006 were obtained from the National Medical Register. Retrospectively, additional data were retrieved from the medical record of patients hospitalized with varicella in 23 Dutch hospitals using a standardized form.

Results: The study population (N=296) was representative for all varicella admissions in the Netherlands (N=1,658) regarding age, sex, duration of admission and type of diagnosis. Complications were recorded in 76% of the patients (37% had at least one relatively severe complication). Bacterial super infections of skin lesions (28%), (imminent) dehydration (19%), febrile convulsions (7%), pneumonia (7%) and gastroenteritis (7%) were most frequently reported. No varicella-related death occurred within the study population and 3% of the patients had serious rest symptoms.

Conclusions: It is not likely that the severity of varicella among hospitalized patients in the Netherlands differs from other countries. A considerable part of the varicella complications among hospitalized patients was rather moderate and can be treated effectively. These data are relevant in the decision-making process regarding whether or not to introduce routine varicella vaccination in the Netherlands.

O089

MOLECULAR AND CLINICAL CHARACTERIZATION OF ROTAVIRUS FROM DIARRHEAL INFANTS ADMITTED TO PEDIATRIC EMERGENY UNITS IN FRANCE, 2006-2010

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Background and aims: Rotaviruses are the major cause of acute gastroenteritis in young children worldwide, and require careful surveillance, especially in the context of vaccination programs (current vaccination coverage is under 10% in France). Prospective surveillance is required to monitor and characterize rotavirus infections, including viral and clinical data, and to detect the emergence of potentially epidemic strains.

Methods: Between 2006 and 2010, stool samples and clinical records were collected form 2727 children under 5 years old with acute diarrhea admitted to the pediatric emergency units of 15 French large public hospitals. Rotaviruses were detected, then genotyped by RT-PCR for P (VP4) and G (VP7) types.

Results: The genotyping of 2630 rotaviruses showed that G1 strains (62.9%) were predominant, G9 (23.0%) were decreasing, G2 (9.1%) were very changing, and G3 (4.1%) and G4 (2.5%) circulated locally. Most strains were associated with P[8] (91.2%). Overall, 63 uncommon strains or possible zoonotic reassortants were detected including G12 and G8 rotaviruses, some being closely related to bovine strains. No difference in clinical presentation and severity was found among genotypes.

Conclusions: In spite of the fluctuation of G2 strains, the relative stability of rotavirus genotypes detected in France may ensure vaccine effectiveness in the short and medium terms. Moreover, the likely emergence of G12 and G8 strains should be monitored during ongoing and future vaccination programs, especially as all genotypes can cause severe infections. Special attention should be paid to the emergence of new rotavirus reassortants not included in current rotavirus vaccines.

O090

GENES ESSENTIAL FOR *MORAXELLA CATARRHALIS* SURVIVAL UNDER IRON-LIMITING CONDITIONS

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Background and aims: *Moraxella catarrhalis* is an emerging human-restricted respiratory tract pathogen that is a common cause of childhood otitis media. Successful colonization of the human respiratory tract mucosa is an important step towards infection and depends on its ability to acquire essential iron. To evaluate the role and importance of iron metabolism in *M. catarrhalis*, we used genomic array footprinting (GAF), a genome-wide negative selection screen, to identify genes essential for survival under iron-limiting conditions.

Methods: *M. catarrhalis* RH4 transposon mutant libraries of ~28,000 mutants were either grown under standard or under iron-limiting conditions. Mutants that failed to survive under iron-limiting conditions were subsequently identified by differential hybridization of mutant-specific DNA probes to microarrays. For validation, growth of directed gene deletion mutants was tested individually under iron-limiting conditions.

Results: In total, 5 genes were identified as being essential for survival under iron-limiting conditions, including genes predicted to be involved in haem biosynthesis and in RNA maturation and degradation. Known *M. catarrhalis* iron-acquisition factors were not among the identified genes, which is most likely due to the high redundancy in iron-transport mechanisms. Finally, growth of 4 directed mutants selected for validation was attenuated under iron-limiting conditions, confirming observed GAF phenotypes.

Conclusions: We have successfully applied GAF to identify genes that are essential for *M. catarrhalis* survival under in vitro iron-limiting conditions, in this way mimicking host-like stress conditions. Currently, the specific roles of the identified genes in *M. catarrhalis* iron metabolism in vitro and at mucosal surfaces are under investigation.

O091

VIRAL CO-INFECTIONS IN INFANTS WITH COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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Background and aims: Infants frequently suffer from CAP and in most of them viruses are found as etiologic agents, sometimes together with bacteria. However, whereas the relevance of bacterial and viral co-infections is quite known, information on viral co-infections is very poor. This study was planned to increase our knowledge at this regard.

Methods: Hospitalized children aged < 12 months with radiographically-confirmed CAP were enrolled. A nasopharyngeal swab was performed and analyzed for the presence of 19 viruses by the Multiplexed Luminex xMAP Assay. Data regarding history, clinical and laboratory findings, and outcome were recorded.

Results: A total of 139 infants were studied. At least one virus was found in 118 (84.9%) cases. The most frequent viruses were RSV (62, 44.6%), rhinovirus (46, 33.1%), and hMPV (17, 12.2%), with influenza viruses identified in 10 (7.1%) cases. Viral co-infections were found in 40 (28.7%) infants (2 viruses in 33 infants and 3 in 7). Bocavirus (92.8%), coronavirus (100%), adenovirus (100%) and parainfluenza viruses (100%) were almost always detected with other viruses. No increase in CAP severity was observed in patients with viral co-infections, and RSV and influenza viruses were associated with the most severe CAP cases even when alone.

Conclusions: Viral co-infections in infants with CAP are common but seem without clinical relevance. The fact that RSV and influenza have a relevant role for frequency and severity in CAP of infants strongly supports the use of the available preventive measures against these pathogens since the first months of age.

O092

VARIATION IN A SURFACE-EXPOSED REGION OF THE *MYCOPLASMA PNEUMONIAE* P40 PROTEIN AS A CONSEQUENCE OF DNA RECOMBINATION BETWEEN REPMP5 ELEMENTS

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Background and aims: *Mycoplasma pneumoniae (Mpn)* is a human pathogen that causes respiratory tract infections. The first step in infection is adherence of the bacteria to the respiratory epithelium, which is mediated by a specialized organelle containing several adherence proteins (cytadhesins). Two of these proteins are encoded by the MPN142 gene. This gene contains a repetitive DNA element, RepMP5, of which homologs are found at seven other loci within the *Mpn* genome. It has been hypothesized that these elements may provide a source of sequence variation for MPN142 by homologous DNA recombination. As this variation may give rise to amino acids changes within P40 and P90, the recombination between RepMP5 elements may constitute the basis of antigenic variation and immune evasion by *Mpn*.

Methods: To investigate the sequence variation of MPN142 in relation to inter-RepMP5 recombination, we determined the sequences of all RepMP5 elements in a collection of 25 strains isolated between 1962 and 1995. Sequences were analyzed and aligned using the application SeqManTM II (DNASTAR) and the sequence alignment program ClustalW.

Results: In two strains, the RepMP5 element within the MPN142 gene contained an aberrant sequence indicative of an inter-RepMP5 recombination event and resulting in amino acid changes in a surface-exposed part of the P40 protein.

Conclusion: This is the first time that variation in the MPN142 gene has been established. Since the proteins encoded by MPN142 are surface-exposed and highly immunogenic, homologous DNA recombination of RepMP5 could play an important role in immune evasive strategies of *Mpn*.

O093

BENEFICAL EFFECT OF LACTOBACILLI IN TIGHT JUNCTION INTEGRITY

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Background and aims: Probiotics are considered to reduce diarrhoea duration in clinical. Disruption of the epithelial barrier was affected by pathogens. We have previously shown that Lactobacilli provide anti-inflammation in vitro. The aim of this study was to investigate whether Lactobacilli may limit epithelial damage induced by lipopolysaccharide (LPS).

Methods: *Lactobacillus. rhamnosus* GG (LGG), *L. paracasei* and *L. johnsonii* were added on inflamed Caco-2 cells exposed to *Salmonella* LPS for 1, 6, or 24 hours. To identify the damage of Caco-2 cells monolayer was evaluated with epithelial permeability by transepithelial electrical resistance (TEER). The expression of tight junctional protein-1 was measured by immunofluorescence microscopy.

Results: Compared to LPS-pretreated controls, TEER of the polarized Caco-2 cell monolayers co-cultured with LGG, *L. paracasei* or *L. johnsonii* was significantly increased after 24 hours. Tight junction in control cells without any supplementation markedly curvy but the cells seemed larger after LPS exposure. The curvy junctions and the size of the cells appeared to be better preserved than in cells co-cultured with LPS alone.

Conclusions: Lactobacilli increase epithelial barrier function as measured with TEER and might reinforcing barrier of the epithelium exposed by LPS. In addition, Lactobacilli were suggested to strength disrupts epithelial tight junction structure, including tight junction protein-1 in Caco-2 cells monolayer. Therefore, Lactobacilli may stabilize tight junctions and prevent damage of the epithelial monolayer barrier function in host cell morphology.

O094

HUMAN T-CELL KINETICS FOLLOWING VACCINATION WITH THE TUBERCULOSIS VACCINE MVA85A

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Background/aims: A major effort is underway to develop new vaccines capable of generating T-cell protection against important intracellular pathogens including tuberculosis (TB), HIV and malaria. Viral-vectored prime-boost vaccine regimes can induce potent T-cell responses but little is known of the kinetics of such responses in humans or of the proliferative response *in vivo*.

Methods: 3 groups of 4 healthy Bacille Calmette-Guérin (BCG)-primed adults received a single intradermal dose of a TB vaccine candidate, MVA85A.

Group 1 volunteers underwent daily clinical assessments and interferon-γ ELISPOTs for 14 days post-vaccination.

Group 2 and 3 volunteers received a stable isotopic label (deuterated glucose) at either day 4 or 10 post-vaccination respectively. Vaccine-specific $CD4^+$ cells were separated from follow-up blood samples and gas chromatography-mass spectrometry (GC-MS) was used to estimate the fraction of labelled (and hence dividing) cells during the labelling period.

Results: MVA85A was safe and well tolerated. Immunogenicity was high: median IFNγ responses to pooled 85A peptides were 1,137 spot-forming units (sfu)/10^6 peripheral blood mononuclear cells (PBMC) at day 7 post-vaccine. IFNγ-secreting cells appeared in the blood abruptly at day 5/6 and rapidly rose to peak by ~day 7. Recently divided cells were detected at 1.8-7.8 times greater frequency amongst vaccine-specific $CD4^+$ PBMC than in non-responding $CD4^+$ cells even 4 days after labelling.

Conclusions: This study provides new data describing the cellular immune kinetics and clinical response to an MVA-vectored vaccine. Improving our understanding of the vaccine response could aid the design and evaluation of other T-cell inducing vaccine regimes.

O095

COMPARISON OF VIRULENCE TRAITS BETWEEN *ESCHERICHIA COLI* CLINICAL ISOLATES CAUSING EARLY NEONATAL SEPSIS AND THOSE COLLECTED FROM HEALTHY NEONATES

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Background and aims: Neonatal risk factors for invasive bacterial disease and its diagnosis and therapy remain an important problem for obstetricians and pediatricians being Escherichia coli and Streptococcus agalactiae the cause of major health problems in industrialized countries. The objective of the present work was to evaluate the virulence of E. coli strains causing early and late neonatal sepsis and to compare them with E. coli strains isolated from healthy neonates.

Methods: Twenty-seven E. coli strains from early neonatal sepsis and 28 from healthy neonates were studied. Detection of virulence genes was carried out by PCR. Phylogenetic group analysis was carried out by multiplex-PCR. Type 1 fimbriae expression was performed by agglutination with Saccharomyces cerevisiae. Fisher´s exact test was used for statistical analysis.

Results: Among the genes studied hly (hemolysin), cnf1 (cytotoxic necrotizing factor 1) and pap genes, all contained in a pathogenicity island, were significantly more frequent among strains causing early neonatal sepsis (p= 0.05, 0.02 and 0.04, respectively). In addition to these genes, the ibeA gene, involved in the translocation of membrane, was also significantly more frequent among strains causing early neonatal sepsis. On the other hand, type 1 expression and the papGIII allele encoding for the tip of the P-fimbria were more frequently presented in strains from healthy neonates.

Conclusions: E. coli strains causing neonatal sepsis were more virulent than the strains collected from healthy neonates and more frequently presented virulence genes contained in pathogenicity islands.

O096

SEVERITY AND MORTALITY IN "THIRD WAVE" INFLUENZA A H1N1/09 INTENSIVE CARE ADMISSIONS CONTINUE TO EXCEED THAT OF PREVIOUS SEASONAL INFLUENZA

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Background: Children admitted to intensive care (PIC) with influenza A H1N1/09 during 2009-10 had increased cardiovascular shock, duration of admission and mortality, compared to the previous 5 seasons of seasonal influenza A admissions. We studied the clinical characteristics of H1N1-infected children admitted during the "third wave" (April 2010 - March 2011) to determine whether H1N1 disease severity persisted. We also studied influenza B admissions.

Methods: We retrospectively reviewed clinical records of all children admitted to St Mary's Hospital, London, testing positive for influenza A/B.

Results: There were 27 H1N1 admissions this season (cf 43 during 2009-10). The median age decreased from 54 to 18 months. Respiratory presentations predominated. In the 6 H1N1 patients on PIC, length of stay increased: median PIC-free days at day 28 fell from 12.5 to 3. All 6 presented with shock, (cf 13 of 18), and 3 of 6 died (cf 6 out of 18). There were 20 influenza B admissions, and 22 between 2006-10. Together, 10 of 42 patients required PIC, of whom 5 had cardiovascular shock, and 3 died. Median PIC-free days at day 28 was 10.

Conclusions: This season, H1N1 admissions fell, and overall median age decreased to that of previous seasonal influenza cohorts. However for PIC patients, mortality and refractory shock remained significantly higher, worsening since last year's "first and second wave" admissions. Influenza B admissions rose this year. Severity in PIC admissions was intermediate between seasonal and H1N1 influenza A. As H1N1 evolves, ongoing surveillance of its pathogenicity remains important.

O097

SEPTIC SHOCK AND SOFT TISSUE LESIONS IN *PSEUDOMONAS AERUGINOSA* BACTERAEMIA IN PAEDIATRIC HAEMATO-/ONCOLOGIC PATIENTS - A RETROSPECTIVE ANALYSIS

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Background and aims: *Pseudomonas aeruginosa* (*Pa*) causes difficult-to-treat nosocomial infections in neutropenic patients including sepsis and soft tissue defects (ecthyma gangraenosum, necrotising fasciitis, perityphlitic abscess). We describe a single center experience of *Pa* infections, complicated by soft tissue lesions in paediatric haemato-/oncologic patients.

Methods: At the Division of Paediatric Haematology/Oncology of the Medical University of Graz, Austria, we retrospectively analysed blood cultrure (BC) results from the years 1999 through 2010. Frequency and clinical course of *Pa* bacteraeimas were analyzed.

Results: From 1999 through 2010 a total of 3376 blood cultures (BC) were drawn. In 190/3376 (5,6%) BC a pathogen was isolated. In 18/190 (9,4%) BC *Pa* was detected. 17/18 patients with *Pa* bacteriaemia developed septic shock. Five out of 18 (27,8%) patients had septic shock combined with soft tissue complications (2x ecthyma gangraenosum, 1x necrotizing fasciitis, 1x *perityphlitic abscess* , 1x inflamed hemorrhoids), of whom 4 patients required surgical interventions (1x incision and drainage combined with temporary colostomy, 1x vacuum assisted closure dressing, 1x appendectomy, 1x incision,)

Conclusions: *Pa*-associated bacteraemias are life-threatening complications in immunocompromised patients. Soft tissue lesions are dreaded complications. In addition to antibiotic therapy and G-CSF-application, surgical intervention is frequently required in complicated courses.

O098

INFECTION FOLLOWING CEREBROSPINAL FLUID SHUNT INSERTION IN THE REPUBLIC OF IRELAND: A RETROSPECTIVE AUDIT

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Background: The Irish national paediatric neurosurgical service was established in 2008. A retrospective audit of infection arising following cerebrospinal fluid (CSF) shunt insertions, 2008 - 2009, inclusive, was conducted.

Methods: A standardised data collection form was completed for each procedure. US Centers for Disease Control and Prevention (CDC) definitions of surgical site infection (SSI) were utilised.

Results: Ninety-one children underwent 130 CSF shunt insertions, 65 (50%) using clindamycin & rifampicin-impregnated catheters. At admission, 63 (69%) were ≤1 year old and 62 (68%) weighed ≤10 kg. Post-operative infection followed 27 (21%) procedures; 12 episodes of SSI (25% MRSA) and 15 episodes of meningitis (0% MRSA). Eighty-eight percent of culture-positive SSIs were due to *S. aureus* and 77% of culture-positive meningitis episodes were due to coagulase-negative staphylococci. Average length of stay for infection following CSF shunt insertion was 27 days versus 17 days without. No infection-related deaths were recorded. SSI following shunt revision or replacement following temporary external ventricular drainage (EVD) (9%) was more common than following primary shunt insertion only (5%). Post-operative meningitis occurred in 18% of shunts replaced following EVD versus primary shunt insertion only (11%). Where antimicrobial-impregnated catheters were used, post-operative infection developed in 20% versus 23% for non-antimicrobial-catheters.

Conclusions: This study highlights the persisting problem of infection following CSF shunt insertion, despite use of antimicrobial-impregnated catheters particularly in young, small children. The predominance of coagulase-negative staphylococci causing meningitis following CSF shunt insertion has implications for empiric choice of therapy when treating suspected infection.

O099

COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS INFECTIONS ACROSS EUROPE

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Background: Community-acquired, methicillin-resistant S. aureus (CA-MRSA) infections in children are increasing in the USA and in some other parts of the world. Data from Europe is unclear.

Objectives: To describe the clinical and microbiological characteristics of children presenting to Pediatric Emergency Departments across Europe with a Staphylococcus aureus infection.

Methods: We prospectively enrolled children under 16 years of age with community-acquired S. aureus infections during the month of June 2010 in different European hospitals.

Results: During the study period, 155 cases were collected from 16 centres in 10 different countries (Spain, England, Lithuania, Germany, Israel, Romania, Cyprus, Estonia, Italy and Georgia). The prevalence of CA-MRSA was 12 % in this study. The Panton-Valentine leukocidin (PVL) genes were detected in 30 % (35/117) of the isolates tested. The children had a median age of 31,5 months and 59% were male. Diagnoses included: superficial infections 56%, cellulitis or abscess 31% and deep infections 13%. 12% of the patients had one or more established risk factors for health care-associated infection. 61% of the patients were admitted to the hospital and 44% required drainage. There were no significant differences between CA-MRSA and CA-MSSA infections related to hospitalization, need for drainage or type of infection.

Conclusions: There is an emergence of CA-MRSA infections across Europe, but less than in the USA. In this study there were no significant clinical differences between CA-MRSA and CA-MSSA infections. A significant proportion of infections were caused by PVL-positive isolates.

O100

STAPHYLOCOCCUS AUREUS BACTEREMIA AMONG CHILDREN IN NORTHERN ISRAEL

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Background and aims: The epidemiology of pediatric staphylococcal bacteremia (PSAB), particularly community-acquired (CA), has not been extensively studied. The epidemiology of PSAB in our region has not been described. This study was designed to evaluate the incidence and characteristics of PSAB in northern Israel.

Methods: A retrospective review, (January 2002- December 2005), in 7 medical centers serving the entire population of hospitalized children of northern Israel.

Results: The annual incidence of PSAB during the study period was 4.7 and 2.1/100,000, overall, and for CA- PSAB, respectively. 47/106 (44.3%) episodes were CA- PSAB (mean age 73 months); all CA isolates were methicillin-susceptible. 71% were male. 59 (55.7%) were hospital-acquired (HA), median age 15 months, mean 49 months, 8 (14%) had MRSA. Predispositions for HA-PSAB included intravascular catheter 31 (52.5%); neonates, 16 (27%); immune suppression 12 (11.3 %). Primary diagnoses among those with CA-PSAB included osteoarticular infection (26, 55.5%), skin infection (4, 8.5%), primary bacteremia (5, 10.6%), pneumonia (4, 8.5%), endocarditis (2, 4.3%), and isolated cases of pyelonephritis, necrotizing fasciitis, lymphadenitis, otitis, paronychia, intra-abdominal abscess. In 5 (4.6%) there was a history of staphylococcal infection in a family member. Average duration of total antibiotic treatment was 24.6 days. There were no deaths directly related to staphylococcal bacteremia in the study group.

Conclusions: CA-PSAB occurs rarely and is associated with bone, joint and skin disease. CA-MRSA was not isolated during the study period. Groups at risk for HA-PSAB included mainly neonates especially post complicated delivery, immune suppressed patients, and those with intravascular lines.

O101

ACTIVE SURVEILLANCE IS NEEDED FOR AMP-C B-LACTAMASEAND ESBL-PRODUCING ORGANISMS IN CHILDREN

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Background and aims: The emergence of multi-resistant Amp-C & ESBL-producing gram-negative bacteria in the community is one of the most significant recent epidemiologic changes in infectious diseases. In the years 2007-8 laboratory had vitek1 machine which could identify extended-spectrum β-lactamases (ESBLs) from isolates which were cefpodoxime (used as a marker) resistant. In an audit done from January 2007 to June 2008, 17 ESBLs were isolated from children. A method which can identify Amp-C β-lactamase and ESBL producing bacteria was adopted and evaluated for active surveillance.

Methods: Laboratory in the hospital adopted the five disc diffusion method on a single plate in the last quarter of 2008. Evaluation was done over a period of from 1st July 2009 to 31st December 2010.Type of specimen, location where specimen was collected; age of the patient was recorded.

Results: 72 children were identified with Amp C producers and 33 with ESBLs aged 2days to 16 years. 53(74%) Amp-C isolates & 31(94%) ESBLs were obtained from urine, while the others from a cough swab, pus, eye, ears and umbilicus (no bacteraemia). 57(79%) Amp-C isolates & 29(88%) ESBLs were obtained from the community specimens.

Conclusions: Thus Amp-C & ESBL-producing organisms are reported with increasing incidence in the children and the number increased manifold with active surveillance which was sought as they are potentially serious pathogens. It is important to look for these multi-resistant infections so as maintain high standard of quality of children care and best management of children's illness episodes in the hospitals & community.

O102

HOW TO MODEL VITAL SIGNS IN THE PREDICTION OF SERIOUS BACTERIAL INFECTIONS? COMPARING DIFFERENT MODELLING STRATEGIES

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Background and aims: Vital signs are frequently used in the assessment of the febrile child. Clinical preference to use dichotomized parameters contrasts with methodological preference to analyse variables continuously. In this study we compare strategies of modelling vital signs in predicting serious bacterial infections in febrile children.

Methods: Patients' characteristics were retrieved from 1750 febrile children aged < 16 years, visiting the emergency department of the Erasmus MC - Sophia Children's Hospital; 13% serious bacterial infections (n=222). Tachycardia and tachypnea were defined using thresholds for upper limit values of heart rate (HR) and respiratory rate (RR) for age. The association of HR and RR with the presence of SBI was studied using logistic regression models. Four strategies to model HR were compared: the dichotomous variable tachycardia, a normalised continuous value of HR, a continuous value of HR (either linear or transformed) and a model including age and HR and the interaction of age and HR. Performance of models was assessed with the area under the receiver operating characteristic curve (ROC area). The same strategies were applied to RR.

Results: The dichotomised vital signs showed similar predictive ability as the continuous vital signs, either linear or transformed (ROC-area 0.53 (HR) and 0.55 (RR)). A model that also included age performed substantially better (ROC area 0.60 (HR) and 0.63 (RR)), with 8-13% better classification of absence or presence of SBI.

Conclusion: Clinical preferred use of dichotomized vital signs results in information loss, and relatively low predictive ability for the presence of SBI.

O103

SEVERE STREPTOCOCCAL GROUP A DISEASE IN CHILDREN WITH OR WITHOUT RISK FACTORS OF INVASIVE INFECTION: CLINICAL FEATURES AND *EMM*-TYPES DISTRIBUTION

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Background and aims: The molecular characterization of Group A streptococcus (GAS) leading to invasive infection in children is poorly described. We aimed to assess the clinical, microbiological and molecular characteristics of invasive GAS infections in 65 children hospitalized between 2000 and 2009 in 7 French Pediatric tertiary care centers.

Methods: Emm-typing and determination of the main virulence factors: SpeA, SpeB, SpeC, SmeZ-1, Ssa, SIC et Sil was performed to characterized molecularly the GAS isolates.

Results: The median age of the children was 2,8 years. Osteoarticular infection and pulmonary infection were the main clinical manifestations (38.5% and 37% respectfully). 31/65 children had at least one of the following risk factors of invasive GAS infection: use of non steroidal anti-inflammatory drugs or corticosteroids, varicella, surgical intervention, underlying chronic disease or immunodepression. Emm 1, emm 3, emm 4 and emm 12 accounted for 70% of the isolates and SpeA and SmeZ-1 were present in more than half of the isolates. No significant correlation was found between emm type and clinical manifestations. However, patients without risk factor (n=34) were younger than those presenting risk factors (1.7 *versus* 3.6 years, p=0.03) and a larger variability of emm-type was found in these patients without risk factors compare to patients with risk factors (18 *versus* 9 different emm-types).

Conclusion: In patients without risk factors of invasive GAS infection, young age and large variability of emm-types might suggest a role of host immunity in the pathogenesis of severe infection.

O104

INVASIVE GROUP A STREPTOCOCCAL INFECTIONS IN THE VARICELLA VACCINE ERA

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Background: Varicella is an important risk factor for Invasive Group A Streptococcal Infection (IGASI). We aimed to describe IGASI before and after inclusion, in January 2006, of varicella vaccine (VV) in Quebec's routine immunization schedule.

Methods: We retrospectively reviewed medical charts of all patients (0-18 years) admitted at a tertiary care center in Quebec, for whom Group A *Streptococcus* strains were isolated from normally sterile biologic sites between January 1998 and December 2010.

Results: IGASI was diagnosed in 126 children. Median age was 50.5 months (range, 1-207). Eighty-five IGASI were identified prior to inclusion of VV in the immunization schedule and 41 cases after. The mean number of IGASI cases hospitalized per year was 10.6 (SD 8.0) prior to VV inclusion, and 8.2 (SD 5.0) post inclusion (p=0.5, mean difference 2.4;, 95%CI: -5.5-10.4). Post VV inclusion, patients with IGASI were significantly less likely to have had recent chickenpox (OR 0.2;, 95%CI: 0.03-0.7).

The mean number of skin and soft tissue infections (SSTI), including necrotizing fasciitis and bacteriemic cellulitis, decreased significantly from 5.2 cases per year (SD 3.9) to 1.0 (SD 1.7) following VV inclusion (p=0.02, mean difference 4.2, 95%CI: 0.7-7.8). Pneumonia and osteo-articular infections represented 18.8% and 16.5% of IGASI before VV inclusion, and 24.2% and 24.2% afterwards, respectively.

Conclusion: At a single center, IGASI were not significantly decreased after VV inclusion in a routine immunization schedule, but SSTIs were. The direct impact of VV on individual risk of IGASI has to be explored.

O105

AETIOLOGY AND RISK FACTORS FOR HOSPITAL-ACQUIRED BACTERAEMIA IN CHILDREN ADMITTED TO A LONDON TERTIARY REFERRAL HOSPITAL

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Background: Hospital-acquired infections are associated with significant morbidity and mortality because they are often caused by multi-resistant pathogens and usually affect children with serious underlying medical conditions. This study aimed to describe the aetiology and risk factors for hospital-acquired bacteraemia among children aged < 16 years admitted to a London tertiary hospital between 2001 and 2009.

Methods: A standard pro-forma is used by clinical microbiologists at St. George's Hospital, London, to document the management of all clinically significant bacteraemia. Bacteraemia was considered to be hospital-acquired if the blood culture was taken at least 72 hours after hospital admission in a child with clinical symptoms, signs and/or laboratory markers consistent with infection.

Results: There were 478 episodes of hospital-acquired bacteraemia over the 9-year period, with venous catheters being the main foci in 279 episodes (58%). Gram-positive cocci were responsible for 385 episodes (81%) and were mainly due to coagulase-negative staphylococci (63%). Overall, 45% of 33 *S. aureus* isolates were methicillin-resistant, but none exhibited reduced vancomycin susceptibility. Five (15%) of 34 enterococcal isolates tested for ampicillin were resistant and 2/29 (7%) isolates tested for vancomycin were resistant. Of the enteric Gram-negative rods, 20% (9/44 isolates) were resistant to cefotaxime (mainly *Enterobacter* spp.), 27% (12/44 isolates) to piperacillin/tazobactam and 13% (9/72 isolates) to gentamicin, but none produced extended-spectrum beta-lactamases.

Conclusions: Hospital-acquired bacteraemia in children are mainly due to venous catheter infections and caused by Gram-positive organisms. Antimicrobial resistance rates remain low compared to other countries and multi-resistant organisms are rare**.**

O106

ANTIMICROBIAL RESISTANCE OF *ESCHERICHIA COLI* CLINICAL ISOLATES CAUSING NEONATAL SEPSIS

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Background and aims: Neonatal meningitis and septicemia caused by Escherichia coli and Streptococcus agalactiae are still major health problems in industrialized countries. The objective of the present work was to evaluate the antimicrobial resistance of E. coli strains causing early and late neonatal sepsis and to compare them with E. coli strains isolated from healthy neonates.

Methods: Twenty-seven E. coli strains from early neonatal sepsis, 40 from late neonatal sepsis and 28 from healthy neonates were studied. Minimal inhibitory concentrations were determined using the NM37 Panel (Siemens). Detection and characterization of determinants of resistance, integrons, and gyrA and parC mutations were carried out by PCR and sequencing.

Results: No differences were found in the resistance to the antimicrobial agents used to treat late neonatal sepsis (amikacin, ceftazidime and imipenem). However, resistance to chloramphenicol and piperacillin was significantly more frequent among strains collected from septic than from healthy neonates (p=0.05 and 0.0004, respectively). Two strains from neonatal sepsis presented BLEAS (CTX-M14 and CTX-M15, respectively). Twenty strains (30%) presented class-1 integrons with different combination of gene cassettes. Finally, four strains presented mutations in the amino acid codons Ser83Leu and Asp87Asn from the gyrA gene, two only Ser83Leu and one Asp87Lys. Of these, five also presented the Ser80Ile mutation and one the Gly84Val mutation in the parC gene.

Conclusions: E. coli strains causing neonatal sepsis were more resistant to the antimicrobial agents studied than the strains collected from healthy neonates except in those related to ciprofloxacin and gentamycin resistance.

O107

NITRIC OXIDE INDUCES DISPERSAL OF MULTISPECIES CYSTIC FIBROSIS BIOFILMS AND ENHANCES ANTIBIOTIC SENSITIVITY OF PSEUDOMONAS AERUGINOSA

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Background and aims: The presence of bacterial biofilms in the lower airways and their recalcitrance towards antimicrobials is important in the progression of patients with cystic fibrosis (CF). Recently, a key role for nitric oxide (NO) in the natural process of dispersal in biofilms has been described. As such, the application of NO to CF biofilms represents a potentially novel adjunctive therapy to conventional antibiotics.

Methods: *Ex vivo* multispecies biofilms were isolated from the sputum of CF patients undergoing an exacerbation. Clinical isolates of *P. aeruginosa* were obtained from patient sputum samples and biofilms cultured *in vitro*. Dispersal and antibiotic sensitivity was assessed by a combination of suspension optical density measurements, Syto 9/Propidium Iodide fluorescent staining combined with confocal laser scanning microscopy and viable cell counts.

Results: *Ex vivo* patient biofilms from a range of opportunistic CF pathogens were dispersed upon treatment with nano-molar concentrations of NO. With focus on *P. aeruginosa* as a pathogen of interest, the data demonstrates that the extent of biofilm dispersal is NO concentration dependent and accompanied by a removal of surface-bound biofilm into the planktonic suspension. Moreover, biofilm dispersal was accompanied by an increased susceptibility of *P. aeruginosa* to clinically relevant antibiotics such as Tobramycin and Ceftazadime, both *in vitro* and *ex vivo*.

Conclusion: NO-mediated dispersal subverts *P. aeruginosa* antibiotic resistance mechanisms associated with biofilm structure. An NIHR Respiratory Biomedical Unit funded proof-of-principle clinical trial is ongoing assessing the application of NO as adjunctive therapy in CF teenagers and young adults (EudraCT 2010-023529-39).

O108

CLINICAL CHARACTERISTICS AND ANTIBIOTIC RESISTANCE OF SHIGELLA GASTROENTERITIS IN CENTRAL TURKEY: COMPARISON OF THE YEARS 1987-1994, 1995-2002 AND 2003-2009

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Background: Shigella epidemiology and antibiotic susceptibility changes over years. It´s necessary to trace the changes for good clinical management. In this study it's aimed to define epidemiologic, clinical and antibiotic susceptibility patterns of shigellosis cases between years 2003-2009 and compare it with the years 1987-2002.

Methods: The files of the children who admitted to Hacettepe University Children's Hospital Diarrheal Diseases Training and Treatment Unit between 2003 and 2009 (n=238) were reviewed. The clinical characteristics and antibiotic susceptibility results of Shigella species were recorded. The results were compared with the results of the two previous period (1987-1994 n=618; 1995-2002 n=218).

Results: The predominant species is S. Sonnei in all periods with increasing predominancy within periods (64.0%, 71.5% and 87.8%, respectively, p< 0.001). The prevalence of bloody diarrhea is not changing however the prevalence of dehydration shows an increasing trend (11.0%, 20.6% and 28.6% respectively, p< 0.001). During the 2003-2009 period 69.9 % of shigella cases were resistant to trimetoprim/sulfamethoxazole, 35.8% to ampicillin and 4.7% to nalidixic acid. No case resistant to ciprofloxacin was detected. This resistant pattern was comparable to the previous periods. Multidrug resistance was also found to be similar within the last two periods (24% vs. 28.1 % respectively, p=0.13).

Conclusion: In this setting there is both a microbiologic and clinic change of childhood shigellosis cases over the 12 years. Antibiotic resistance pattern seems to be stable for the last two periods. There is a need to resurge the criteria and clinical management guidelines for suspected shigellosis cases.

O109

THE ECDC *PILOT* POINT PREVALENCE SURVEY OF HEALTHCARE ASSOCIATED INFECTIONS AND ANTIMICROBIAL USE: PAEDIATRIC DATA

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Background and aims: Previous prevalence surveys did not have standardized identical protocols or objectives. The aims of the 'pilot ECDC point-prevalence survey (PPS) on antimicrobial use and Healthcare-associated-infections (HAI)' (ECDC-PPS) were to: provide a standardized methodology for European Union (EU) Member States; estimate the prevalence of HAI and antimicrobial use in EU acute-care hospitals and; describe patients, invasive procedures, infections and antimicrobials prescribed.

Methods: The pilot ECDC-PPS used two data collection protocols, a patient-based protocol where denominator data including demographics and risk factors were collected for each patient and a unit-based protocol aggregating denominator data at ward level. Thus, for this analysis only children (≤15 years) from hospitals using the patient-based protocol could be included.

Results: From a total of 14,329 patients 1,406 (9.8%) were ≤15 years old. 465 (33.1%) had antimicrobials whilst 89 (6.3%) HAI. Differences in use and infection rate for various risk factors are shown in table.

Conclusions: The full-scale representative European PPS, planned for 2011-2012, will provide reliable, standardised European, national and local hospital data on HAI and antimicrobial use. The patient-based protocol (more detailed information) is preferred to the unit-based protocol allowing better data analysis (e.g., prevalence amongst paediatric patients).

Risk Factor	(%) of patients with Prescription (without:with) risk factor	p value	(%) of patients with Healthcare associated infection (without:with) risk factor	p value	Statistical Test
Surgery since admission	28.69%:49.47%	<0.0001	4.83%:12.46%	<0.0001	Z test
Central vascular catheter	27.97%:73.08%	<0.0001	3.96%:24.36%	<0.0001	Z test
Mechanical ventilation	30.78%:75.34%	<0.0001	4.36%:42.47%	<0.0001	Z test
McCabe Score	Non-Fatal 29.38%:Ultimately-Fatal 59.20%:Rapidly-Fatal 69.23%	<0.0001	Non-Fatal 4.16%: Ultimately-Fatal 20.80%: Rapidly-Fatal 8.46%	<0.0001	Chi-Squared

[Effect of risk factors on HAI & Presciptions]

O110

POTENTIALLY TOXIC EXCIPIENTS ARE FOUND IN ORAL ANTIMICROBIAL AGENTS USED IN UK NEONATAL UNITS

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Background: Excipients are used to facilitate the manufacture of dosage forms and maintain the stability of medications in the face of chemical and microbial challenges. Some excipients have been associated with mortality and significant morbidity in neonates but the extent of exposure to excipients related to antimicrobials used in neonates has not been reported.

Methods: A survey of UK neonatal units was conducted using the NIHR MCRN Neonatal Network. Units were asked to report the number of babies who received medicines in a two week period of their choice. The excipient content of each medicine was determined from material in the public domain and by contacting manufacturers.

Results: 31 units responded to the survey reporting a total of 642 prescriptions for enteral medications. Excipient content could be identified in 64 unique products 16 of which (25%) were antimicrobials. 30 taste enhancers or colourants were included in antimicrobial formulations and 10 agents to modify chemical or physical properties of the formulation. 9 excipients known to be harmful in neonates, or potentially harmful (since they are metabolised by pathways known to be immature in neonates) were found in a total of 12 antimicrobials.

Discussion: Three quarters of enteral antimicrobial preparations used in UK neonatal units contain additives that are potentially toxic. Further study of the extent of excipient use among neonates is required, including clinical work to define the extent of excipient exposure and identify whether reformulation is required.

O111

EVIDENCE BASED EMPIRIC ANTIBIOTIC CHOICES FOR PAEDIATRIC BACTERAEMIA: NATIONAL SUSCEPTIBILITY PROFILES OF GRAM-POSITIVE AND GRAM-NEGATIVE BACTERAEMIA IN ENGLAND AND WALES

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Background and aims: To compare the activity of combinations of antibiotics recommended for empirical treatment of paediatric sepsis by the British National Formulary guidelines for Children (BNF-C). The guidelines recommend: gentamicin+amoxicillin, or cefotaxime/ceftriaxone alone or aminoglycoside+anti-pseudomonal beta-lactam if pseudomonas suspected, or flucloxacillin or vancomycin if Gram-positive infection suspected.

Methods: The Health Protection Agency's national surveillance database was interrogated to determine the 10 commonest pathogens causing bacteraemia in children (1 month - 18yrs) and their antimicrobial susceptibility. Data were aggregated to capture resistance rates for the time period July 2008-June 2010 in England and Wales.

Results: The 10 commonest pathogen groups (accounting for ~80% of reported paediatric bacteraemias) comprised coagulase-negative staphylococci (CoNS) (28%), *Staphylococcus aureus* (10%), non-pyogenic streptococci (9%), *Streptococcus pneumoniae* (7%), *Enterococcus* spp. (7%), *Escherichia coli* (5%), *Neisseria meningitidis* (5%), *Klebsiella* spp. (4%), *Enterobacter* spp. (3%) and *Pseudomonas aeruginosa* (2%). For Gram-positives, resistance to gentamicin+amoxicillin was ≤1% apart from CoNS (28%); the corresponding figures for Gram-negatives were 3-9%. Resistance to cefotaxime/ceftriaxone varied with species (0-12%) but was not commonly reported for staphylococci. Staphylococci remained fully-susceptible to gentamicin+vancomycin. *Pseudomonas* spp. remained susceptible (>96%) to anti-pseudomonal combinations.

Conclusions: The susceptibility results show that for each organism, at least one of the recommended antibiotic therapies was appropriate. However, this study does highlight the need for regular and timely surveillance of antimicrobial susceptibility of bacteria causing invasive disease in children to allow objective assessment of the continued appropriateness of national treatment guidelines.

O112

AETIOLOGY AND RESISTANCE OF CHILDHOOD BACTERIAL ENTEROPATHOGENS IN CRETE

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Aim: To investigate the long-term trends in prevalence and antimicrobial resistance of bacterial enteropathogens among children in a well-defined geographical area.

Methods: All children younger than 14 years treated as inpatients or outpatients for enteritis at the University General Hospital at Heraklion, Crete, Greece during the 18-year period January 1993 to December 2010 were included. Stool specimens were examined by the standards methods for enteropathogenic *Escherichia coli* (EPEC), *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*, and *Aeromonas* species.

Results: Of a total of 33,032 stool samples processed, 1,315 yielded a bacterial pathogen in adults and 1,597 in children. Among childhood pathogens, *S. enterica* was the most common (42.3%), followed by *Campylobacter* spp. (33.6%), EPEC (17.4%), *Y. enterocolitica* (5.82%), *A. hydrophila* (0.44%), and *Shigella* spp. (0.38%). A summer peak was principally attributed to *Salmonella* infections. *Salmonella* was the leading cause of bacterial enteritis all during the study with increasing prevalence ($p< 0.0001$). *Campylobacter* prevalence increased through the study period ($p=0.0008$ by chi-square for trend), but EPEC prevalence decreased ($p< 0.0001$ by chi-square for trend). The last *S. typhi* was observed in 1996. The overall rates of resistance to amoxicillin, imipenem, gentamicin, tetracycline, cotrimoxazole and cirpofloxacin were 40.4, 0.06, 1.17, 30.2, 32.9 and 17.0%, respectively.

Conclusions: In the study area bacterial enteritis continues to be principally caused by nontyphoidal Salmonellae. Considerable changes in the long-term morbidity of specific pathogens call for ongoing surveillance and tailored management.

O113

PREVALENCE OF COMMUNITY-ACQUIRED METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS AMONG CHILDREN WITH SKIN AND SOFT TISSUE INFECTIONS IN BROOKLYN, NEW YORK

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Background: The prevalence of community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) infections among the pediatric population has been gradually increasing over the years leading to a large burden to the health system.

Objectives: To determine the prevalence and sensitivity pattern in accordance with D-Test of CA-MRSA among skin and soft tissue infections in our community. We also describe and analysis the most common diagnosis, days of hospitalization and chosen antibiotics with CA-MRSA.

Methods: We retrospectively reviewed medical records of patients under 18 years of age with the diagnosis of skin or soft tissue infections from January 2008 to august 2010. Only those cultures positive for MRSA meeting criteria of community acquired infection were included and analyzed.

Results: 603 were reviewed. Culture was obtained in181 patients. 126 of them were positive for Staphylococcus aureus, of which 76(60.3%) were CA-MRSA. 97.3% of the isolates were sensitive to co-trimoxazole, 88.1% to clindamycin and only 7.8% to erythromycin. Inducible resistance was detected in only 2% of strains. The main diagnosis associated with CA-MRSA was gluteal abscess (34.2%), leg cellulitis and knee abscess (11.8%). 57.8% of the CA-MRSA required hospitalization (mean 3.3±2.5 days). Clindamycin was the preferred drug in hospitalized patients (65.1%). Cephalexin (40.2%) followed by clindamycin (28.5%) were the favorites initial drugs prescribed for outpatient cases.

Conclusions: The prevalence of CA-MRSA is high (41.9%) in our children community. The sensitivity of CA-MRSA to co-trimoxazole and clindamycin is still favorably high, and the presence of clindamycin inducible resistance among the strains is very low in our community.

O114

IDENTIFICATION OF ROTATEQ® VACCINE IN PAEDIATRIC PATIENTS WITH ACUTE GASTROENTERITIS FOLLOWING ROUTINE VACCINATION

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Background and aims: Rotavirus is the predominant cause of acute gastroenteritis in young children worldwide. Two live-attenuated vaccines were introduced into the Australian National Immunisation Program in July 2007. Rotarix® is a monovalent vaccine containing a human G1P[8] strain. RotaTeq® is a pentavalent vaccine containing five human-bovine reassortant strains: G1P[5], G2P[5], G3P[5], G4P[5] and G6P[8].

The aim of this study was to identify and characterise rotavirus strains isolated from children recently vaccinated with RotaTeq® who were subsequently admitted to the Royal Children's Hospital, Melbourne, Australia with symptoms of acute gastroenteritis.

Methods: Rotavirus was detected using a gene-specific RT-PCR which amplified regions of the genes encoding the capsid proteins VP4, VP6 and VP7. Amplicons were sequenced and compared to the reference sequences for RotaTeq® and wild-type rotavirus strains.

Results: Of the 79 faecal samples collected between 1/7/2007 to 1/7/2010 from recently vaccinated children who developed acute gastroenteritis, 13 samples were identified as containing RotaTeq® vaccine. Nine of the thirteen vaccine associated samples contained at least two of the five RotaTeq® vaccine strains. In four samples, a G1P[8] strain was detected that was derived via reassortment between two RotaTeq® vaccine strains G1P[5] and G6P[8]. Eighteen samples were identified as wild-type rotavirus strains and the remaining 48 samples tested negative for the presence of rotavirus.

Conclusion: This study shows that reassortment between the five component strains of the RotaTeq® vaccine does occur and this event may result in a strain with increased virulence. Thus, continued monitoring of rotavirus associated acute gastroenteritis is required.

O115

VACCINE EFFECTIVENESS AGAINST COMMUNITY-ACQUIRED SEVERE ROTAVIRUS GASTROENTERITIS AMONG YOUNG CHILDREN, IN BELGIUM: A HOSPITAL-BASED, PROSPECTIVE, CASE CONTROL STUDY

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Background and aims: In Belgium, 2 rotavirus (RV) vaccines are licensed (Rotarix™ and RotaTeq™); vaccination is recommended since October 2006 and reimbursed since November 2006. This study evaluates direct vaccine effectiveness (VE) against severe rotavirus gastroenteritis (RVGE) among young children.

Methods: Case-control study in 39 Belgian hospitals between FEB2008 and JUN2010. Confirmed cases were children hospitalized with PCR-confirmed RVGE and age-eligible (>=14 weeks of age and born after 01OCT2006) to be vaccinated against RV. For each case, at least one age and hospital-matched control without GE was enrolled. VE was calculated as (1-matched odds ratio of vaccination) x 100, using condition logistic regression with 95% confidence intervals (CI).

Results: The VE analysis included 213 confirmed cases and 276 matched controls and showed no significant differences between groups in terms of previous hospitalisations due to GE, or medical history. Cases were significantly more frequently formula-fed, had a larger household size and their mother had lower educational level than controls. Forty-eight % of cases and 91% of controls had received any RV vaccination.

The VE against RVGE of Rotarix™ full-series-vaccination compared to unvaccinated children was 90.2% [95% CI: 81.0-94.9%]. VE was 91.0% [95% CI: 74.5-96.8%] in children aged 3-11 months and 89.6% [95% CI: 75.5-95.6%] in children aged >=12 months. G2P[4]-specific VE was 85.0% [95% CI: 64.7-93.8%].

Conclusions: RV vaccination proves highly effective for prevention of RVGE hospitalizations in young children in Belgium. The significant differences between cases and controls suggest tackling health inequalities as a priority for further RV prevention.

O116

HOSPITAL-BASED SURVEILLANCE OF ROTAVIRUS ACUTE GASTROENTERITIS IN CHILDREN AFTER INTRODUCTION OF ROUTINE ROTAVIRUS VACCINATION IN FINLAND WITH PENTAVALENT ROTAVIRUS VACCINE

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Background and aims: Rotavirus (RV) is the leading cause of severe dehydrating diarrhoea in children under-five and is associated with direct costs for medical care and indirect costs for family. RV vaccine was included in the Finnish National Vaccination Programme starting from September 2009. All infants aged 2 months would have received 3 doses of live attenuated pentavalent vaccine (RV5) free of charge. The aim of the study is to assess the incidence of children hospitalized with RV positive AGE (RV+AGE) during the RV seasons 2009/2010 and 2010/2011 in conjunction with increasing RV vaccination coverage.

Methods: Since December 2009 a prospective observational hospital-based surveillance study has been conducted in two paediatric hospitals in Finland (Oulu and Tampere). All children under-16 years-old, permanent residents and admitted for an acute gastroenteritis (AGE) were eligible for inclusion in the study. RVs were detected in stool samples by ELISA and RT-PCR.

Results: The results of the first season´s surveillance (December 2009- mid-June 2010) showed a low overall number of RV+AGE (total of 65 cases of RV+AGE; 20 in Tampere and 45 in Oulu). The season lasted from January to June with no peak. The vaccine coverage estimated in each area rapidly reached approximately 90%. No child fully vaccinated with RV5 was hospitalized for RV+AGE.

Conclusion: Compared to three previous RV seasons 2006-2009 in Finland, the number of RV+AGE hospitalizations was lower during this first season of routine rotavirus vaccination, very likely associated with the high RV vaccination coverage and high efficacy of RV5.

O117

ACUTE GASTROENTERITIS HOSPITALIZATIONS BEFORE AND AFTER ROTAVIRUS VACCINE INTRODUCTION IN NORTH-WEST SPAIN (GALICIA)

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Background and aims: Rotavirus vaccines were licensed in Spain between late 2006 and early 2007. Rotavirus vaccination was recommended but not reimbursed by the Spanish National Health System. The significant coverage rates reached in some areas allowed describing variations in severe acute gastroenteritis (AGE) incidence in young children before and after vaccine introduction.

Methods: Hospital discharge data was obtained from the National Surveillance System of Hospital Data of the Region of Galicia. Rotavirus vaccination estimated coverage increased from 12% in period July2006-June2007 to 51% between July2008-June2009. The annual hospitalization rates before and after rotavirus vaccine introduction for children ≤2 years of age for all-cause AGE and rotavirus-AGE admissions were calculated.

Results: In the 3-yearly periods pre-vaccination, July2004-June2007, the median all-cause AGE hospitalization rate was of 892,8 per 100.000 children ≤2years. Rates in the post-vaccination periods (excluding the transition period 2007-2008) July2008-Jun2009 and July2009-June2010 decreased by 32% (606,9 per 100.000) and 51% (436.2 per 100.000), respectively. Considering rotavirus-AGE, hospitalizations rates decreased by 24% in 2008-2009 (372.03 per 100.000) and 52% in 2009-2010 (233.4 per 100.000) compared to the median rate for the pre-vaccination period (487.9 per 100.000).

Conclusions: Compared to pre-vaccination years, a decrease in all-cause and rotavirus AGE hospitalization rates was observed. The greater decline in period 2009-2010 vs 2008-2009 and the linear increase in vaccine uptake since vaccine introduction, could lead to the hypothesis that non-systematic vaccination has significant impact on severe AGE, although this should be confirmed by continued surveillance given the variability in rotavirus trends over time.

O118

THIRD YEAR POST-ROTAVIRUS VACCINATION IN BELGIUM: IMPACT ON ROTAVIRUS-POSITIVE STOOL SAMPLES IN HOSPITALIZED CHILDREN

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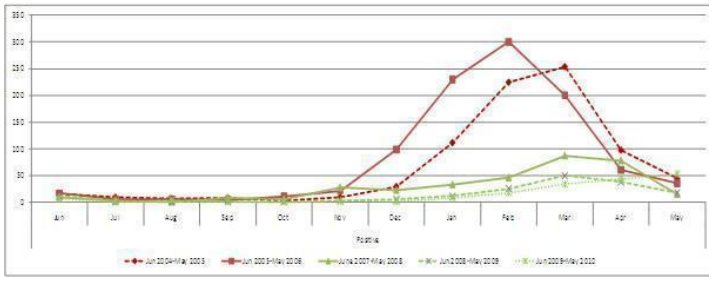
Background and aims: Rotavirus vaccination has been reimbursed in Belgium since November 2006. This study is the third year follow-up of previously reported impact of vaccination on rotavirus-positive stool samples in 9 pediatric centers across Belgium (rotavirus vaccine coverage (> 85%)).

Methods: Stool samples for rotavirus detection were collected from ≤ 5y old hospitalized children, within the same centers. Pre- (01/06/2004-31/05/2006) and post-vaccination periods (01/06/2007-31/05/2010) were compared. Absolute numbers and % reduction (95 % CI) are reported per year post-vaccination considering the average of the pre-vaccination period as a reference.

Results: The number of rotavirus-positive stool tests in children aged ≤5 years decreased from an average of 881 pre-vaccination to 368 (-58%) in the 1st year post-vaccination, to 202 (-77%) in the 2nd year and to 180 (-80%) in the 3rd year. In children aged between 2-24 months the percentage reductions were 64% (95% CI: 61-68), 81% (95% CI: 78-84) and 82% (95% CI: 79-84) in the 1st, 2nd and 3rd years respectively, compared with pre-vaccination. In addition an overall decline (-44%) in all-cause acute-gastroenteritis related hospital admissions was observed from 1700 per year pre-vaccination to 950 per year 3rd year post-vaccination.

Conclusion: Significant annual decline in number of rotavirus positive stool samples and in all cause acute GE related hospital admissions has been seen in young children after several years of vaccination in Belgium.

Figure 1: Monthly distribution of the number of rotavirus positive stool tests in hospitalized children age[s]d between 2 months and 24 months.



[Figure 1]

O119

IMPACT OF A ROTAVIRUS VACCINATION CAMPAIGN ON HOSPITALISATIONS IN FRANCE: THIRD-YEAR SURVEY OF THE IVANHOE STUDY

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Objective: To determine the real-world impact of rotavirus vaccination, controlling for epidemic-to-epidemic variation in disease burden.

Methods: An active hospital-based surveillance system initiated 5 years before vaccine introduction (May 2007) enabled the occurrence of acute rotavirus diarrhoea (ARD) to be modelled. Inclusion in a poisson regression model of an indicator variable for vaccination quantified the impact of a vaccination campaign with Rotateq$^{\grave{O}}$ offered to all children born in Brest by paediatricians, mother and child health centres and general practitioners from the Brest Urban Community (BUC). The principal endpoint was the number of hospitalisations for ARD in infants under 3 years old living in the BUC during 2009/2010 epidemic season.

Results: More than 7150 infants received at least one dose. Vaccine coverage was 55% and 51% for one and 3 doses respectively. Timely administration of doses 1 and 3 was respected in 97% of cases.

Modelling allows estimating that number of hospitalizations for ARD has been divided by 2,8 (95% CI: 2,2 - 3,5) during the last epidemic season (2009/2010). The observed number of cases was 40 whereas the expected number was 110. Comparatively, in the previous 2008/2009 season the number of hospitalizations has been divided by 1,8 (95% CI: 1,5-2,2).

Relative risk reduction for ARD hospitalization was 95% (95% CI: 87% - 98%).

Conclusion: We observed an increasing impact of rotavirus vaccination on hospitalization in the third year survey on this vaccination campaign.

O120

COMPLETE GENETIC CHARACTERIZATION OF HUMAN G2P[6] AND G3P[6] ROTAVIRUS STRAINS

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Background and aims: Human rotavirus (HRV) strains bearing genotype P[6], in association with a variety of G-types, have been detected in Africa. However, the relative frequency of P[6] HRV strains outside Africa is low. Recently, a number of P[6] HRV strains in combination with G3 have been isolated for the first time during the 2008-2009 rotavirus season in Belgium and a G2P[6] was isolated in the United States in 2006. This study aims to describe complete genomes (11 segments) of these recent P[6] HRV strains isolated outside Africa and analyze their relationship to other known RV strains.

Methods: To investigate the evolutionary relationships of these strains, we sequenced the complete genomes of 3 P[6] HRV strains, 2 strains isolated in Belgium and 1 strain in the United States, and compared them with the genomes of other RV strains.

Results: Our genetic analysis revealed that most of the 11 gene segments of these 3 strains belonged to genotype 2 (DS-1-like). The genomic comparison of the 2 Belgian G3P[6] strains revealed that all 11 segments were identical. The American G2P[6] strain was phylogenetically closely related to the Belgian P[6] strains and to other recently isolated HRV strains.

Conclusions: These data suggest that reassortment(s) involving VP7 have occurred recently. The rise of the P[6] genotype needs to be closely monitored especially because this genotype is not included in the currently available RV vaccines.

O121

THE BURDEN OF ROTAVIRUS DISEASE IN DENMARK 2009-2010

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Background: This study sought to determine the incidence and the burden of severe diarrheal disease in Denmark with emphasis on rotavirus disease.

Methods: This study was designed as a national prospective disease surveillance of children< 5 years of age hospitalized for acute gastroenteritis in Denmark during March 2009 to April 2010, using rapid rotavirus and adenovirus antigen detection.

Results: A total of 3100 hospitalizations annually among Danish children < 5 years can be attributed to acute gastroenteritis and 1210 (39%) of these to rotavirus disease. The majority of RV-associated hospitalizations occur among children ≤24 months of age (RV-associated hospitalization rate: 7.7/1000 children ≤24 months-of-age and 3.8/1000 children< 5 years-of-age). Although the well-known seasonal pattern of rotavirus was evident with a peak during the spring months of March to April, our active surveillance demonstrated RV-associated hospitalizations throughout the year. Genotyping of a subset of RV-samples demonstrated high frequency of G1 (39%) and G4 (32%). Adenovirus was detected in 350 AGE-associated hospitalizations (11.2%).

Conclusion: In conclusion, of the 3100 annual AGE-associated hospitalizations among Danish children < 5 years, 1200 are RV-associated (39%). Rotavirus is indeed ubiquitous in the population; despite a marked seasonality it is associated with hospitalizations year round and can be considered a major health burden among young Danish children.

O122

IMMUNOGENICITY AND PROTECTIVITY OF *STAPHYLOCOCCUS AUREUS* AND *STREPTOCOCCUS PNEUMONIAE* PROTEINS IN RELATION TO NASOPHARYNGEAL COLONIZATION AND VACCINATION

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Background: Colonization rates of *S. pneumoniae* and *S. aureus* are inversely correlated and seem to shift after pneumococcal conjugate vaccination (PCV-7). We decided to study the natural humoral response against pneumococcal and staphylococcal surface proteins in relation to carriage with both pathogens in PCV-7 immunized and non-immunized children.

Methods: During a RCT(NCT00189020), we obtained nasopharyngeal samples at 6, 12, 18 and 24 months and sera at 12 and 24 months of age. We analyzed IgG against 40 staphylococcal and 18 pneumococcal proteins using flow cytometry (n~130 per group) and studied immunogenicity and protectivity of these antibodies.

Results: In children previously colonized with *S. aureus* IgG levels were significantly higher against the proteins ClfA, Efb, SCIN, SEH and SSL_5 ($p < 0.01$), whereas in children previously colonized with pneumococci IgG levels were higher against all proteins when compared to non-colonized individuals ($p < 0.001$).Increasing age was associated with a higher response against almost all pneumococcal proteins and a lower response against more than half the staphylococcal proteins ($p < 0.01$), which correlates with colonization dynamics. None of the pneumococcal or staphylococcal antibodies seemed to protect against colonization with the homologous or heterologous species in the following year. Finally, there were no differences between vaccinated and non-vaccinated children in antibody levels.

Conclusions: Pneumococcal and staphylococcal proteins appear immunogenic in infants. Unfortunately, at 12 months of age neither of the anti-protein antibodies showed to be protective nor cross-protective against pneumococcal and staphylococcal colonization, respectively. No effect of PCV-7was observed on natural immunity against both pathogens.

O123

A PREDICTION TOOL FOR THE NET EFFECTIVENESS OF PNEUMOCOCCAL VACCINATION UNDER SEROTYPE REPLACEMENT

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Background and aims: Serotype replacement and herd immunity are the ever-intriguing issues in developing mathematical models for pneumococcal epidemiology and control efforts. Recently, increasing attention has been paid to the possibility of these two types of indirect effects having opposite effects on the population level effectiveness of a vaccination program. We propose using tools built on relatively simple probabilistic models to demonstrate potential effects of serotype replacement on the projected outcome of alternative pneumococcal vaccination programs.

Methods: Under a scenario of a complete elimination of the vaccine-types in carriage and their replacement by non-vaccine types, the projected effectiveness of a vaccination program is a function of two key serotype-specific quantities, the incidence rate of carriage and case-to-carrier ratio for invasive disease (IPD).

Results: Using data from Finland, we demonstrate that each of the three current pneumococcal conjugate vaccines (with 7, 10 or 13 serotypes) may be expected to decrease the IPD incidence among children < 5 years of age, with larger improved effectiveness with higher valency of the vaccine. However, in the population at large the reduction in IPD is much more moderate, and among the elderly the replacement may entirely erode the reduction in vaccine-type IPD.

Conclusions: These results highlight the importance of the interplay between the two quantities, the incidence of carriage and the case-to-carrier ratios among the groups of vaccine and non-vaccine serotypes. In particular, the comparison of the effectiveness of alternative vaccination programs should not be based on either of the quantities alone.

O124

NATURAL ANTIBODIES AGAINST SEVERAL PNEUMOCOCCAL VIRULENCE PROTEINS IN CHILDREN IN THE PRE-PNEUMOCOCCAL VACCINE-ERA: THE GENERATION R STUDY

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Background and aims: The current pneumococcal vaccines do not protect against all serotypes of *Streptococcus pneumoniae*. A shift towards non-vaccine serotypes causing colonisation and invasive disease has occurred and studies on protein-based vaccines are undertaken. We assessed the association between specific antibodies against pneumococcal virulence proteins and colonisation and respiratory tract infections (RTI). Additionally, we assessed to what extend colonisation induces a humoral immune response.

Methods: Nasopharyngeal swabs were cultured for pneumococcus at 1.5, 6, 14 and 24 months of age. Serum samples were obtained at birth, 6, 14 and 24 months (n=57) in the pre-pneumococcal vaccine-era. IgG, IgA and IgM levels against seventeen pneumococcal protein vaccine candidates were measured using a bead based flow cytometry technique (xMAP®, Luminex Corporation). Information regarding RTI was questionnaire-derived.

Results: IgG levels to all proteins were high in cord blood, decreased in the first 6 months and increased thereafter, contrary to the course of IgA and IgM levels. Specific antibodies were induced upon colonisation. Increased levels of IgG against BVH-3, NanA and SP1003 at 6 months, NanA, PpmA, PsaA, SlrA, SP0189 and SP1003 at 14 months and SlrA at 24 months were associated with a decreased number of RTI in the third year of life but not with colonisation. Maternal antibodies did not protect against pneumococcal colonisation and infection.

Conclusions: Certain antibodies against pneumococcal virulence proteins, some of which are induced by colonisation, are associated with a decreased number of RTIs in children. This should be taken into account for future pneumococcal vaccine studies.

O125

IMPACT OF THE 13-VALENT PNEUMOCOCCAL VACCINE ON THE INCIDENCE OF PAEDIATRIC EMPYEMA IN THE NORTH OF ENGLAND

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Background: The incidence of paediatric empyema has increased substantially in the UK since 1995. Paediatric empyema in the UK is predominantly a pneumococcal disease and a 13-valent pneumococcal conjugate vaccine (PCV-13) replaced the seven-valent vaccine in the UK routine immunisation schedule in April 2010. The 13 valent vaccine includes antigen for serotype 1, which has been the commonest cause of paediatric empyema in the UK. The objective of this study was to investigate the impact of the introduction of PCV-13 on the incidence of paediatric empyema.

Methods: A preliminary interrupted time-series analysis was performed using clinical data from empyema admissions for children aged up to 14 years in Northern England from May 1995 to November 2010. Seasonality was accounted for by including monthly temperature measurements within the regression models. Terms for the seven-valent vaccine were also included.

Results: A total of 313 patients were included in the study. The incidence of empyema increased from a mean monthly rate of 1.1 cases per million children in 1996 to 5.2 per million in 2009 and fell in 2010 to 3.2 per million. Introduction of the PCV-13 vaccine was associated with a significant reduction in the number of monthly cases of paediatric empyema (regression co-efficient -0.26, 95% CI -0.42 ─ -0.10, p=0.002).

Conclusions: We have documented a recent reduction in the incidence of paediatric empyema in the North of England, but it would be premature to conclude a causal relationship with introduction of the PCV-13 vaccine.

O126

CONTINUING INCREASE IN 19A AND 6C SEROTYPE CARRIAGE IN CHILDREN AFTER THE INTRODUCTION OF PCV-7 IN THE NETHERLANDS

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Background: Pneumococcal conjugate vaccine (PCV-7) was implemented in the Dutch NIP in 2006. We studied the ongoing effect of PCV-7 introduction on nasopharyngeal pneumococcal carriage over time.

Methods: In follow-up of a randomized controlled trial (RCT) (NCT00189020), we performed two cross-sectional studies in 2009 and 2010 collecting nasopharyngeal swabs at 11 and 24 months of age from PCV-7 vaccinated children and from one of the parents of the latter group (n~330 per group). Swabs were cultured for *S. pneumoniae* and serotyped by Quellung.

Results: In 11-month-olds PCV-7 carriage rates were 38%, 8% and 3% in 2005, 2009 and 2010, respectively, whereas in 24-month-olds vaccine serotype carriage was 36%, 3% and 3% ($p < 0.001$ for all comparisons vs. 2005). Carriage of non-PCV-7 serotypes increased in 11-month-olds from 29% in 2005 to 39% and 50% in 2009 and 2010, respectively ($p < 0.01$ for all comparisons vs. 2005) and from 30% to 45% and 61% in 24-month-old children ($p < 0.001$: vs. 2005). A significant increase in carriage of 19A was found in 11 and 24-month-old children over time (11 months: 2%, 10% and 12%, 24 months: 3%, 6% and 14%, respectively). Moreover, the latter serotype also became the most dominant serotype. Besides, 6C carriage increased as well as other non-vaccine serotypes over time. In parents a similar shift of serotypes was seen.

Conclusions: Within 4.5 years after introduction of PCV-7, vaccine serotypes are virtually eliminated in children and their parents. However, non-PCV-7 serotypes, in particular 19A, have emerged. Pneumococcal disease surveillance remains important.

O127

PNEUMOCOCCAL CARRIAGE IN LIGURIA, ITALY, 7 YEARS AFTER PCV7 IMPLEMENTATION: ALMOST COMPLETE REPLACEMENT OF VACCINE SEROTYPES

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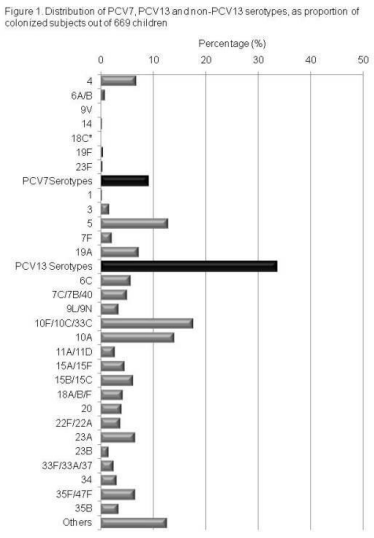
Background and aims: Since May 2003, a large-scale programme of vaccination against pneumococcus was started in Liguria, Italy. All newborns have been invited to receive PCV7 according to 3-5-11 month schedule. PCV7 uptake reached coverage of >80% and >90% in every districts since 2004 and 2007, respectively, determining an epidemiological picture infrequent in Europe. As part of the surveillance of PCV7 introduction, a cross-sectional study was performed in the autumn 2010 to determine the prevalence of carriage, the risk factors for and serotype distribution of pneumococcal carriage in 0-5 year population.

Methods: Broth enrichment, real-time PCR, conventional multiplex PCR and MLST approaches were used for pneumococcus detection, serotyping and characterization, as recently recommended by CDC. Nasopharyngeal specimens and standardized questionnaires were obtained from 669 children, that were enrolled using cluster sampling.

Results and conclusions: The overall carriage rate was 43.5% and carriage varied significantly across age groups with 22%, 48.6% and 60% of 0-12, 13-24 and 25-59 month children carrying Streptococcus pn, respectively. Distribution of PCV7, PCV13 and non-PCV13 serotypes, as proportion of colonized subjects out of 669 children is reported in figure 1. PCV7 serotypes (9.1%) were almost completely replaced; now-available PCV13 serotypes cover 33.6% of total serotypes. Among predictors of carriage, “age”, “number of brothers or sisters” “group child care” played a significant role.



[Figure1]

O128

RAPID REDUCTION IN INVASIVE PNEUMOCOCCAL DISEASE (IPD) AFTER INTRODUCTION OF PCV7 TO THE NATIONAL IMMUNIZATION PLAN (NIP) IN ISRAEL

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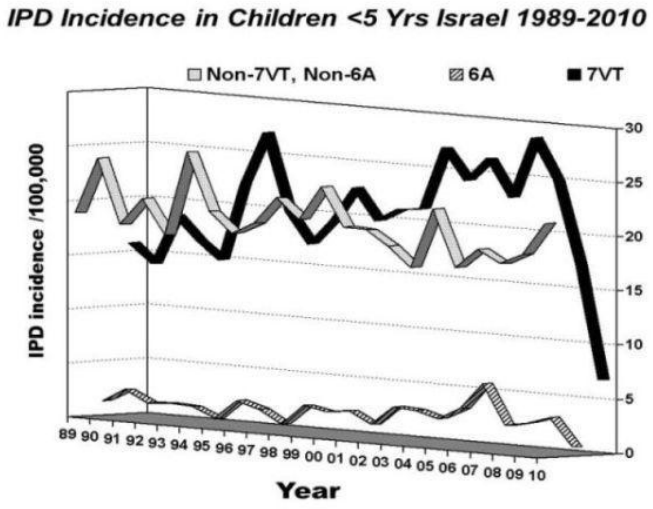
Background and aims: PCV7 was licensed in Israel in 2007, with scattered use till 2009, and was introduced to Israel NIP in July 2009, as a 2, 4, 12m schedule, with catch-up (2 doses, 2nd year). IPD nationwide active surveillance has been conducted since 1989.

Methods: All 27 medical centers performing blood cultures in Israel participated by reporting monthly all IPD cases (defined by positive blood/CSF cultures). Capture-recapture methods were used to evaluate completeness. ~50% of isolates were submitted to serotyping until recent years, and >95% since 2000. Extrapolation by year, ethnic group, age, and serogroup was conducted to insure appropriate age-specific serotype-specific incidence assessment.

Results: During 1989-2010, 5,821 cases were reported (**FIGURE**). PCV7 serotypes+6A (VT) contributed ~50% of IPD. VT incidence increased during 1989-2008, causing overall IPD increase. In 2004-8, mean IPD incidence/100,000 was 47.2 and 85.3 for < 5 and < 2 years, respectively. In 2010, VT incidence decreased by 72.9% and 78.7% compared with 2004-8 in < 5 and < 2 years respectively, (P< 0.001). The respective overall IPD reduction was 37.7% and 41.4% with no replacement so far. In 2010, 73% of isolates causing remaining IPD < 5 years were PCV13 serotypes.

Conclusions: PCV7 introduction to NIP as a 2+1 schedule with catch-up in < 2 years, showed a rapid decrease in IPD < 5 yrs. PCV7 was replaced by PCV13 in November 2010.



[Figure]

O129

IMPACT OF PNEUMOCOCCAL VACCINATION IN DENMARK DURING THE FIRST 3 YEARS AFTER PCV7 INTRODUCTION IN THE CHILDHOOD IMMUNIZATION PROGRAMME

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Background and aim: From October 1st 2007 the 7-valent pneumococcal conjugate vaccine (PCV7) was implemented in a 2+1 dose schedule in the national immunization program for infants. Vaccine coverage has reached 86%. To assess the impact of PCV7 we evaluated direct and indirect effects on incidence of invasive pneumococcal disease (IPD) and pneumococcal serotype distribution.

Method: We compared disease incidence in pre-PCV7 (years 2000-2007) and PCV7 periods (years 2008-2010) based on national surveillance data, IPD laboratory-based surveillance and vaccination registry.

Results: In the whole population the overall incidence of IPD declined from 19.4 to 17.8 cases per 100,000 persons (incidence rate ratios (IRR) 0.92; 95% confidence interval (CI) [0.84-1.02]) and vaccine serotypes incidences (VT) changed from 7.7 to 3.8 (IRR 0.49; 95%CI [0.40-0.59]) comparing pre-PCV7 and PCV7 periods. In children aged 0-2 years the overall incidence of IPD decreased from 54.8 to 25.5 (IRR 0.47; 95%CI [0.29-0.77]) cases per 100,000 and for VT from 36.7 to 4.1 (IRR 0.11;95% CI [0.06-0.22]) comparing pre-PCV7 and PCV periods. The incidence of non-vaccine serotypes (NVT) increased from 11.8 to 14.0 cases pr 100,000 in the whole population (IRR 1.18; 95%CI [1.05-1.32]) and dominant serotypes in the PCV7-period were serotypes 1 and 7F.

Conclusions: We report a marked decline in the incidence of VT IPD in both vaccinated and non-vaccinated individuals, the latter suggesting the development of herd immunity. The incidence of NVTs in the whole population seems to increase slightly with dominant serotypes that are covered by the recently introduced 13-valent vaccine.

O130

EFFECT OF AGE ON QUANTIFERON-TB GOLD-IN-TUBE (QFT-IT) ASSAY PERFORMANCE AMONG CHILDREN EVALUATED FOR LATENT TUBERCULOSIS INFECTION

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Background and aims: Limited studies have investigated the effect of age upon interferon-γ release assays (IGRAs) performance among children. The study aims were to evaluate the effect of age upon the quantitative and qualitative performance of the QFT-IT method among children and adolescents evaluated for latent tuberculosis infection (LTBI).

Methods: A cross-sectional study was conducted among 769 children (mean age±SD: 7.84±4.68years) evaluated for LTBI between 1/1/2007-1/8/2010. Participants were examined with both TST and QFT-IT and categorized into 4 age groups (infants: < 2years; young children: 2 to < 5years, children: 5 to < 10years; and, adolescents ³10yrs) to evaluate the study objectives.

Results: LTBI (QFT-IT positive) and QFT-IT indeterminate results were detected among 28.7% (n=221) and 3.0% (n=23) of study participants, respectively. QFT-IT indeterminate results occurred more frequently among young children (8.1%; p< 0.0001) and children (2.7%; p=0.025) than adolescents (0.7%). Among LTBI patients, infants had significantly higher mean(±SD) QFT-IT results than adolescents (10.42±5.21 IU/mL vs. 7.49±5.46 IU/mL; p=0.045). Moreover, mean TST size was significantly smaller among infants (11.83±4.90mm; p< 0.0002) and young children (13.45±4.20; p=0.005) than adolescents (15.81±3.50mm). Overall, multivariate logistic regression indicated that QFT-IT positive outcome was not associated with age, but only with mitogen response (OR:1.03; 95% CI:1.01-1.06) and prior BCG immunization (OR:0.46; 95% CI:0.30-0.70). Among LTBI patients, linear regression analysis indicated no association between quantitative QFT-IT result and age (p=0.054).

Conclusion: The quantitative or qualitative (positive-negative) result of the QFT-IT assay is not affected by patient age. However, indeterminate results occur more frequently among younger children.

O131

MOLECULAR TESTING OF NASOPHARYNGEAL SPECIMENS HAS POTENTIAL AS A DIAGNOSTIC TEST FOR MENINGOCOCCAL DISEASE

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Background: Molecular testing of nasopharyngeal specimens for *Neisseria meningitidis* (NM) is not widespread because of the risk of detecting asymptomatic carriage. We present our experience of testing nasopharyngeal specimens for NM using Loop Mediated Isothermal Amplification (NM LAMP).

Methods: Children presenting to our hospital with suspected meningococcal disease (MD) have a 'meningococcal pack' of investigations taken including blood for culture, Taqman PCR & NM LAMP and a throat swab for NM LAMP. We compare the results of the throat swab with laboratory confirmed meningococcal disease over a 12 month period.

Results: 160 children had a meningococcal pack completed. 14 had laboratory confirmed MD (14 PCR, 3 blood culture, 1 CSF culture positive). There was one false negative (throat swab negative; blood culture, PCR and clinical picture positive) and one false positive (throat swab positive; blood culture, PCR negative, probable nasopharyngeal carriage). This gives NM LAMP testing of nasopharyngeal specimens a sensitivity of 92.8% (95% CI: 76 to 98) and a specificity of 99.3% (95%CI: 97.7 to 99.8).

	MD	Not MD
TS LAMP +	13	1
TS LAMP -	1	145

[Throat swab result compared with final diagnosis]

Conclusions: LAMP technology is simple and inexpensive and could be applied in the near patient setting. Testing of nasopharyngeal specimens using LAMP has potential as a relatively non-invasive diagnostic test for MD. We believe the potential to diagnose this life threatening disease early outweighs the risk of detecting asymptomatic carriage.

O132

PRELIMINARY RESULTS OF THE PERFORMANCE OF IP-10 IN CHILDREN AT HIGH RISK FOR TUBERCULOSIS INFECTION

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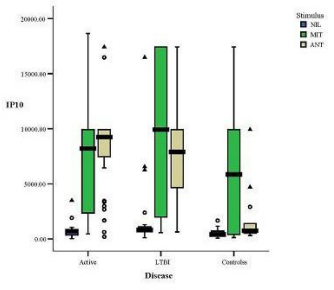
Background and Aims: The diagnosis of childhood tuberculosis (TB) remains complex. Recent, predominantly adult studies have presented the interferon-γ inducible protein 10 (IP-10) as a promising diagnostic biomarker for tuberculosis infection. This study aim to further explore the performance of CXCL10 in pediatric TB infection.
Methods: A study was conducted among 77 children (active disease n=33, LTBI n=27, controls n=17) at high risk of tuberculosis infection. IP-10 concentration was determined using ELISA, in supernatants from whole blood stimulated with Mycobacterium tuberculosis-specific antigens (ANT), mitogen (MIT) and negative control antigen (NIL) obtained from QFT-IT vaccutainer tubes.
Results: Results are illustrated in Figure 1. Stimulation with MIT (positive control) produced a significant increase in IP10 production in all the disease subgroups ($p< 0.01$ in all cases). Stimulation with TB specific antigen resulted in a significant increase in IP10 production in both active disease and LTBI groups but not in the control group (active vs. control $p< 0.001$; active vs. LTBI $p< 0.001$). No significant difference in IP-10 production after ANT stimulation was observed between active and latent infection.
Conclusion: Our results show high IP-10 responses to antigen-stimulated supernatants from children with TB infection, indicating the potential role of CXCL10 as an additional diagnostic TB biomarker. We believe that in combination with IGRAs it could be used to increase diagnostic accuracy in high risk children populations.

Figure 1



ANT; Mycobacterium tuberculosis-specific antigens, MIT; mitogen, NIL; negative control antigen

[Figure 1]

The study was supported by the 2010 ESPID Fellowship award, (fellow:

Dr Virginia Amanatidou)

O133

KINGELLA AS A CAUSE OF SEPTIC ARTHRITIS IN CHILDREN: THE BENEFIT OF MOLECULAR TECHNIQUES FOR MICROBIOLOGICAL DIAGNOSIS

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Background: Septic arthritis (SA) is a potentially severe disease in children. *Kingella* is a common cause of SA in young children, but often underdiagnosed by classical microbiological procedures. The aim of this study was to evaluate the effect of molecular techniques on the diagnosis of this infection.

Methods: We compared the clinical and diagnostic characteristics of children with SA before (retrospectively) and after (prospectively) the implementation of bacterial PCR in synovial fluid.

Results: Forty-nine children diagnosed with SA were evaluated between 2002-2010. Thirty-two were diagnosed before the PCR analysis was implemented in our hospital (2009) and 17 after that. Microbiological diagnosis was achieved in 31% during the first period vs 59% in the second period (p=0.12). *Kingella* was isolated in 7 of 10 cases in the second period but in none in the first period. Children with *Kingella* were younger (13 vs 27 months; p=0.059), had fever more often (100% vs 43%; p= 0.01), and higher ESR at admission (74 vs 50; p=0.031), but the duration of hospitalization (7 vs 11 days; p=0.06) and IV antibiotics (6 vs 10 days; p=0.01) was shorter. However, total duration of antibiotics was similar (31 vs 36 days). There were no sequelae in children with *Kingella* SA vs 20% in children with other types of SA (p=0.58).

Conclusions: *Kingella* is an important cause of SA in children that may be underdiagnosed with classical microbiological procedures. Although *Kingella* SA may be severe at presentation, it seems to respond optimally to therapy without sequelae.

O134

IMPACT OF GEN-PROBE'S AMPLIFIED MYCOBACTERIUM TUBERCULOSIS DIRECT TEST ON TUBERCULOSIS DIAGNOSIS IN CHILDREN

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Background and aims: The aim of the study was to evaluate the performance of Gen-Probe Amplified Mycobacterium tuberculosis Direct Test (AMTD, Gen-Probe, San Diego, California) for the diagnosis of tuberculosis in children, compared to conventional culture and clinical diagnosis.

Methods: We retrospectively studied 81 children (48 males; mean age 7 years; range 1-16 years) evaluated for possible active TB over a 2-year period. Respiratory samples (n=64/95;67%) examined included gastric aspirates (n=30), induced sputa (n=30), bronchial aspirates and bronho-alveolar lavages (n=4). Non-respiratory samples (n=31/95; 33%) included lymph nodes (n=20), and other sterile fluids (n=11). Specimens were examined using AFB microscopy, Gen-Probe and bacterial culture using BACTEC™ MGIT™ 960 (Becton Dickinson, USA) and Löwenstein-Jensen (LJ) media.

Results: The clinical diagnosis of TB was made in 34/81 (42%) children (29/34 with pulmonary disease). Direct smear was positive for AFB in 2/34 (6%) children; Mycobacterium tuberculosis (MTB) was recovered by culture from 13/34 (38%) and AMTD was positive in 20/34 (59%). Based on clinical diagnosis, the sensitivity, specificity, PPV and NPV of the AMTD test vs. culture were 59%, 96%, 91%, and 76% vs. 38%, 100%, 100% and 69%, respectively. For pulmonary vs. extra-pulmonary disease the performance of AMTD compared to culture was: 100%, 87%, 67%, 100% vs. 75%, 96%, 75%, and 96%, respectively.

Conclusions: Nucleic acid amplification tests are more sensitive and very specific methods for the (rapid) detection of MTB compared to culture in children with TB. The Gen-Probe technique increases TB detection in children by about 50% compared to culture.

O135

QUANTIFERON®-TB GOLD IN-TUBE PERFORMANCE FOR TUBERCULOSIS DIAGNOSIS IN 0-5 YEARS OF AGE CHILDREN

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Background and aims: Interferon-Gamma-Release Assays (IGRAs) are increasingly used for the diagnosis of tuberculosis (TB). Unknown performance in infants and controversial rate of indeterminate results in < 5 years children limit their pediatric usage.

Methods: Immunocompetent children (n=82, 0.10 to 5.6 years of-aged; median: 1.8) referred for suspected TB or TB contact and sequentially evaluated for QuantiFERON®-TB Gold In-Tube (QF-TB-IT) reactivity were included for QF-TB-IT performance evaluation.

Results: BCG vaccination rate at birth was high (91%). Fifteen children were diagnosed as active TB disease; 10 had latent TB: recent TB contact and positive Tuberculin-Skin Test (TST); 16 were healthy contacts: recent TB contact and negative TST; the 41 remaining children, with TB excluded, were used as controls. The rate of QF-TB-IT indeterminate was 5% in active TB, latent TB and healthy contact children (0% in < 2 years; n=23) while 22% in controls with irrelevant diseases. QF-TB-IT sensitivity and specificity, as determined by positivity in active TB and negativity in controls were 86% and 100% respectively (67% and 100% in < 2 years). Four out of nine children with latent TB had QF-TB-IT positivity (2/4 were < 2 years). Finally, concordance between TST and QF-TB-IT results was high only when considering TST negativity < 10mm and positivity >15mm induration diameter respectively.

Conclusions: QF-TB-IT sensitivity and specificity were high and the rate of indeterminate results was low in < 0-5 years children with TB or TB contact. QF-TB-IT appears therefore a promising tool for TB diagnosis in young immunocompetent children.

O136

IDENTIFICATION OF SERUM BIOMARKERS OF PAEDIATRIC TUBERCULOSIS USING SELDI

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Background: Improved diagnosis of tuberculosis (TB) is essential for reducing the incidence of disease in sub-Saharan Africa. Currently half of all cases of infectious TB are undiagnosed. This proportion is higher in children, as clinical features overlap those of many chronic infections and microbiological confirmation is complicated by paucibacillary load. The development of a rapid, sensitive and affordable serological diagnostic test for TB in children is urgently needed. Surface-Enhanced Laser Desorption Ionisation (SELDI) technology has been widely employed to identify serum based biomarkers in infectious diseases.

Methods: Serum samples (n=1000) were collected from children and adults (HIV-positive and HIV-negative) with active TB (culture confirmed), latent TB (IGRA+ and TST+) and controls (other infections and inflammatory conditions). Patients were recruited from two regions of sub-Saharan Africa with differing patterns of HIV, TB and malarial infection to ensure that the biomarker candidates would not be population specific. Serum proteomic profiles were obtained by SELDI using cation capture (CM10; pH 4.0 and 6.0), anion capture (Q10; pH 7.5 and 9.5) and immobilized metal affinity (IMAC30; Cu) ProteinChip™ arrays.

Results: SELDI analysis generated over 6000 serum protein profiles. Specific proteins were identified as statistically significant ($P < 0.001$) in distinguishing children with active TB from those with latent TB infection regardless of HIV status. Several of these potential biomarkers were observed in both children and adults.

Conclusions: A series of serum proteins have been found that will potentially enhance the diagnosis of TB in children. These are currently being identified at the molecular level.

O137

VALUE OF MOLECULAR DIAGNOSTIC TOOLS IN VIRAL RESPIRATORY ILLNESS IN HOSPITALIZED CHILDREN

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Background and aim: With the development of multiplex nucleic acid testing panels, the number of detectable respiratory viruses has expanded. The value of molecular tools for the diagnostic process is not yet well established because of a current lack of relating clinical and epidemiologic data.Here we present potential benefits of molecular diagnostics in the detection and identification of viral causes of respiratory illness in hospitalized children.

Methods: As part of a prospective study into viral respiratory tract infections in hospitalized children, we collected clinical data of all children in whom respiratory samples were taken for detection of 15 respiratory viruses. We further characterized human rhinoviruses (HRVs) by sequencing the VP4/VP2 region of the HRV genome. Molecular diagnostic findings were related to clinical symptoms and patient characteristics.

Results: From September 2009 till January 2011, 1455 respiratory samples were collected from 644 patients with 904 disease episodes. In 916 samples (63.0%), one or more viruses were detected. HRV was the single respiratory virus detected in 446 samples (48.7%), relating to 254 disease episodes. HRV is associated with considerable respiratory symptoms in patients with pulmonary underlying disease. Sequence analysis revealed an upsurge of enterovirus 68 infections (which is identical to HRV87) associated with severe respiratory illness in the absence of other viral or bacterial causes of infection.

Conclusion: Molecular diagnostic tools for the detection and identification of respiratory viruses are helpful in explaining respiratory illness and may give guidance to medical care.

O138

EMERGENCE OF THE COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* CLONE USA300 AMONG CHILDREN AND YOUNG ADULTS IN ISRAELI AND PALESTINIAN POPULATIONS

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Background: Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections are epidemic in the USA and are caused mainly by a single clone, USA300. In Europe, the prevalence of CA-MRSA is low but increasing and USA300 is uncommon. Data on CA-MRSA in Israel are scarce and these bacteria are still considered to be rare. This report focuses on the appearance of USA300 clone among CA-MRSA strains that have been sent for further classification to the Israeli *S. aureus* Reference Center from various sources.

Methods: All *S. aureus* isolates were sent to the reference center during 2010. CA-MRSA strains were defined as MRSA isolated from individuals in the community or during the first 72h of hospitalization. Staphylococcal chromosome cassette *mec* (SCC*mec*) type, *arcA*, and presence of the genes for Panton-Valentine leukocidin (*pvl*+) were determined by PCR. Sequence types (ST) were assigned by multilocus sequence typing. USA300 strains were defined by pulsed-field gel electrophoresis.

Results: Twelve USA300 isolates were collected from Israeli and Palestinian children and young adults in different regions. Clinical manifestations included skin and soft tissue infections (SSTI´s) and asymptomatic colonization; only one subject had traveled to the USA. All Isolates were SCC*mec* IV, ST8, *pvl*+, and carried the arginine catabolic mobile element. Variable antimicrobial resistance patterns were evident, however all were clindamycin susceptible.

Conclusions: The CA-MRSA USA300 clone, presenting as SSTI´s or colonization, has now been documented among Israelis and Palestinians and may be more widespread in the region than previously perceived. The geographic and antimicrobial resistance variability implicates multiple infection sources.

O139

INFLUENZA SURVEILLANCE IN SÃO PAULO STATE: VIRUS DETECTED IN POST-PANDEMIC PERIOD, SP - BRAZIL, 2010

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Background and objectives: In 2009, 12,002 cases and 578 deaths were caused by Flu A H1N1 in SP state, Brazil. On Aug/2010 WHO declared a post-pandemic period, but recommended active surveillance for Flu. The aim of this study is to describe influenza circulation in SP during 2010.

Methods: There are 10 surveillance centers for Flu in SP state to monitor influenza circulation through IFI. This is a descriptive study of virus and Flu strains isolated from patients with ILI in 2010, focused on post-pandemic period, based on registered data in SIVEP-GRIPE and IAL.

Results: In 2010, ILI was responsible by 15% of medical visits, with greater impact in 0-14 y and 25-29 y age groups. Till EW 51, 1,861 samples were collected, and 238 (13%) were lab confirmed (IFI or PCR) for virus; from these, Flu was detected in about 1/3 since April (Flu A =13.5% and FluB =18.9%) B strains predominated till August, and in post-pandemic period Flu A H3 was the predominant one. RT-PCR positivity was higher (22.4%), being 66% of strains positive for Flu B, 23.4% A/H3 and 10.6% for H1N1. Only 89 cases and 15 deaths caused by H1N1 were registered in SP, mostly before the national campaign of immunization with monovalent H1N1.

Conclusions: Co-circulation of Flu B and A H3N2 was detected in SP during pandemic post-period. Influenza surveillance is very relevant to detect clusters and flu strains, and propose the most appropriated measures to control this disease, that cause substantial impact in the community.

O140

PANDEMIC A/H1N1V INFLUENZA 2009 IN CHILDREN: A MULTICENTRIC BELGIAN SURVEY

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Background and objectives: During the 2009 influenza A/H1N1v pandemic, children were identified as a particular “at risk” group. We conducted a multicentric trial to describe pattern of A/H1N1v infection among hospitalized children.

Material and methods: From 01/07/09 to 31/01/10, we prospectively collected all proven (positive H1N1v PCR) and probable (positive Influenza A antigen or culture) pediatric cases of H1N1v infections, hospitalized in four tertiary centers in Brussels.

Results: We reported 215 children hospitalized with proven/probable H1N1 infection. Median age was 31 months. 47% had ≥ one co-morbidity. Febrile respiratory illness was the most common presentation. 36% presented initial gastrointestinal symptoms and 10% neurological manifestations. 35% had pneumonia. Compared to PCR, sensitivity of antigen and culture was low (53% and 59%, respectively). Only 23% of patients received oseltamivir. 21 (10%) children had to be admitted to ICU, of whom seven suffered from ARDS. Rate of co-morbidity tended to be higher among ICU than general wards patients (62%>< 45%,p=0.1). Fatality-rate was 5/215 (2%) and concerned only children suffering from chronic neurological disorders. Children > 2 years old showed a higher propensity to be admitted to ICU (16%>< 1%,p=0.002) and a higher mortality (4%>< 0%,p=0.06). Infants ≤ 3 months showed a particularly mild pattern of infection, with few respiratory and neurological complications.

Conclusion: Although H1N1 infections were globally self-limited, pediatric burden of disease was significant. Compared to other countries experiencing different health care systems, our Belgian cohort was younger and received less frequently antiviral therapy; disease course and mortality were however similar.

O141

RETROSPECTIVE COMPARISON OF PANDEMIC INFLUENZA A/H1N1 (2009/2010) CLINICAL CHARACTERISTICS VERSUS SEASONAL INFLUENZA A (2007-2009) IN HOSPITALIZED CHILDREN IN BASEL, SWITZERLAND

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Background: 2009, pandemic influenza A/H1N1 (piA) caused significant morbidity and mortality worldwide. Here we compare clinical features and epidemiology of pandemic H1N1 infections to those of seasonal influenza A (siA) infections of the two preceding winter seasons in hospitalized children and adolescents.

Methods: Medical records of all hospitalized patients < 18 years with RT-PCR-confirmed siA (fall 2007 to spring 2009) or piA infections (April 2009 to March 2010) were analysed retrospectively.

Results: 134 patients (piA: N=55, 58% male; siA: N=79, 58% male) were identified; median age was 2.5 yrs (range 0.07-15.5) in piA patients and 1.5 yrs (range 0.04-17.5) in siA patients. Underlying chronic disease was present in 25% (piA) versus 33% (siA) patients. All patients except one had fever; most common other symptoms were cough (piA/siA: 78%/86%), rhinitis (76%/76%) and pharyngitis (67%/68%). Croup syndrome (15%/3%, p=0.02), conjunctivitis (31%/10%, p=0.002) and febrile seizures (26%/13%, p=0.05) were more frequent in piA patients. Overall, 64% (n=35) of piA and 53% (n=42) of siA patients had >1 complication: pneumonia 15%/22%, AOM 13%/11%, CNS complications 29%/18% (all p>0.05). 5 patients (3/2) were admitted to ICU; one 4.8 month old boy with underlying congenital malformations died due to secondary bacterial pneumonia, all other patients recovered without sequelae. Mean hospitalisation duration was 2.9/3.9 days (p>0.05). Influenza immunization rates were 5%/0%). None of siA but 20% of piA patients were treated with oseltamivir.

Conclusions: Although patients with piA infection presented with more febrile seizures, overall severity of disease was not different compared to siA in previous years.

O142

A NOVEL SEVERITY SCORING SYSTEM TO ASSESS SEVERITY OF DISEASE IN AUSTRALIAN CHILDREN HOSPITALISED WITH PERTUSSIS INFECTION DURING AN EPIDEMIC

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Background and aims: Pertussis is the most common vaccine preventable disease in Australia. Despite high immunisation coverage, Australia is experiencing its worst epidemic since introduction of pertussis vaccine into the national childhood immunisation program. The aim of this study was to assess the severity of disease in Australian children hospitalised with pertussis during an epidemic using an objective pertussis severity scoring system designed in Adelaide.

Methods: Variables assessed included length of hospitalisation, frequency of apnoea, level of hospitalisation required, respiratory support, presence of complications and requirement for intravenous fluids (score range 1-18).

Results: Data from 132 children hospitalised in Australia were scored using the pertussis scoring system. 60.6% of admissions scored as mild (score < 7) and 39.4% as moderate-severe (score ≥ 7). 63.6% of moderate-severe cases were in infants < 2 months. The mean severity score for infants < 2 months, 2-< 6 months and 6-12 months was 7.6 (range 2-18), 4.6 (range 2-11) and 7.3 (range 2-16) respectively. For infants < 2 months, 56.9% were assessed as moderate-severe compared to 23.5% in 2-6 month old infants. 55% of Indigenous children scored moderate-severe disease (score ≥7) compared to 38% of non-Indigenous children.

Conclusions: The majority of severe disease occurs in very young infants although severe disease also occurred frequently in children to 12 months of age and Indigenous children. A universal objective scoring system can aid in assessing the impact of pertussis, identifying risk factors for severe disease in children and predicting health resource requirements during an epidemic.

O143

INCREASED INCIDENCE OF PERTUSSIS IN A TERTIARY CARE HOSPITAL IN MADRID (SPAIN) 2010. EPIDEMIOLOGICAL AND CLINICAL FEATURES OF THIS DISEASE

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Introduction: Whooping cough is a disease that generates high morbidity and mortality in young children. After universal vaccination was introduced, a decrease of this entity was observed. The aim of this study is to describe the incidence of this disease over the last years.

Material and methods: Epidemiological, clinical and microbiological study; retrospective (2006-2009) and prospective (2010) of paediatric patients hospitalized with whooping cough in a tertiary hospital in Madrid. Diagnosis was made with DNA amplification techniques (PCR) or immunofluorescence (IF) in 2006/07.

Results: 57 patients were admitted with clinical suspicion of whooping cough. Diagnosis was confirmed in 36 patients (63%) with PCR, and no IF was positive. The median age was two months. An increase in annual incidence was observed: 3.4 cases per 100,000 pediatric emergency visits (2006), 11 (2007), 9.2 (2008), 10.2 (2009), 34.2 (2010). 72% of cases occurred in summertime (June-September). The main clinical features were cough (100%), cyanosis (58%), whoop (50%). The average hospital stay was 7 days. 12% of patients were admitted in PICU. The most frequent complication was pneumonia, with a mortality rate of 2.7%. 86.4% of the patients had received less than two doses of vaccination for pertussis. We found household contacts with symptoms consistent with pertussis in 64.8% of patients.

Conclusions: We observed a sharp increased incidence of pertussis in 2010. Most affected patients were infants under three months with incomplete vaccination, with high morbidity. Revaccination in adults should be strongly considered as they may represent important disease transmitters.

O144

A PRACTICAL APPROACH TO Q FEVER IN CHILDREN

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Since 2007, the Netherlands was confronted with the largest Q fever outbreak ever. Q fever has a wide clinical spectrum ranging from asymptomatic to fatal disease. Knowledge of Q fever has greatly expanded over the last decades, but research has mainly focused on adult disease; data in children are scarce. Available data suggest that children are less severely affected than adults. The warranted approach to pediatric Q fever is often unclear to the general pediatrician. Therefore, the Working Party for Pediatric Infectious Diseases and Immunology of the Dutch Pediatric Society has composed a practical tool for the diagnosis and treatment of Q fever in children, based on best-available evidence and expert opinion. Disease transmission occurs mainly through contaminated aerosols, or by ingestion of contaminated milk. Vertical transmission has also been described. The reference method for diagnosing Q fever is serology using an indirect immunofluorescence assay. However, significant titers may take 3-4 weeks to appear. Therefore, *Coxiella burnetii*-specific PCR of serum samples can be very useful for diagnosis in the early acute phase. Self-limiting febrile illness, gastro-intestinal symptoms such as abdominal pain, nausea and diarrhea, and skin rash are the most frequently reported symptoms in pediatric Q fever. These symptoms, or a history of exposure to *C. burnetii* in a symptomatic child, should trigger the physician to investigate the possibility of Q fever. Routine serological and PCR follow-up of neonates born from Q-fever infected mothers is also recommended. Treatment regimens depend on the age of the patient and presenting symptoms.

O145

Q FEVER IN THE NETHERLANDS IS LESS REPORTED IN CHILDREN

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Background and aims: The Q fever outbreak in the Netherlands of 2007-2009 is the largest one ever reported: 3522 notifications. *Coxiella burnetii*, that causes this zoonotic disease, is mainly transmitted to humans through aerosols. Living near contaminated farms, especially in the lambing period, is the main risk factor. In theory, the exposure risk is equal for all those living in the same area, both adults and children.

Methods: We inventoried the number of cases amongst children (0-19yr) during that period, calculated the reported incidence and compared this with adults. We reviewed the literature to inventory case reports among children.

Results: 123 children (3,6% of total notifications) were reported. The incidence in children was 0,31 per 10.000 compared to 2,65 in adults. Main reported symptoms were fever of unknown origin and gastro-intestinal symptoms. Besides 14 pneumonias, no other serious complications were reported.

We found 20 national and/or regional scientific studies reporting seroprevalences between 0-70%. In 19 articles 52 cases with a serious outcome were described. 4 children died of complications. In chronic Q fever cardiac infections were predominant.

Conclusion: With only 3,6% of notifications from 23,11% of the exposed population we conclude that infections in children are less symptomatic but also frequently overlooked. Children get infections that can present themselves with self-limiting flu-like symptoms but also as rare conditions like encephalitis, osteomyelitis, hepatitis or endocarditis. Therefore paediatricians should be aware of *Coxiella* infections in these or unexplained cases. The Dutch Society of Paediatrics (www.nvk.nl) has drafted a guideline “Advices on Q fever”.

O146

INCIDENCE OF ACUTE OTITIS MEDIA IN EUROPEAN CHILDREN UNDER 5 YEARS: RESULTS OF A PROSPECTIVE OBSERVATIONAL COHORT STUDY

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Background and aims: Acute otitis media (AOM) is one of the most frequent paediatric infections. We previously reported high incidences of AOM with large variations across five European countries in a retrospective study.[1] This prospective, observational cohort study was conducted to generate precise incidence estimates of AOM.

Methods: 5882 healthy children ≤5 years of age were randomly selected from 73 convenient medical practices in Germany, Italy, Spain, Sweden and the UK. Of these, 5764 children were followed prospectively for 12 months and episodes of AOM leading to physicians visits were recorded. The incidence of AOM was estimated, applying uniform case definitions.

Results: 1113 children experienced 1419 AOM episodes. The overall incidence of any AOM episode was 256/1000 person-years (95% CI: 243-270) ranging from 195 (171-222) in Italy to 328 (296-364) in Spain. AOM incidence was higher in 0-2-year olds than 3-5-year olds (299 [279-319] *vs* 212 [195-230]). Except for Italy, this trend was observed across all countries, being most pronounced in Sweden (344 [298-394] *vs* 174 [141-212]). 7.1% (101) of episodes were associated with perforation of the tympanic membrane, 4 episodes were associated with other complications.

Conclusions: In agreement with our previously reported retrospective study[1], these results confirm the high incidence of AOM in European children, although this is lower than reported in Finnish and US studies (700-1200/1000 person-years). Variations between countries may indicate possible differences in diagnostic and reporting procedures, as well as primary healthcare organisation and social structure.

1. Liese. WSPID 2009, Buenos Aires, Argentina

O147

NASOPHARYNGEAL BIOFILM PRODUCING RESPIRATORY PATHOGENS IN CHILDREN WITH RECURRENT ACUTE OTITIS MEDIA

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Backgrounds and aims: Differences in nasopharyngeal (NP) bacterial flora in children with nonsevere recurrent acute otitis media (RAOM) and chronic otitis media with effusion have been described. Recently bacterial biofilms, highly resistant to antibiotics, been suggested to play a role in recurrences of upper respiratory infections. Most of the studies rely on biofilm detection from specimens obtained during surgery. We assessed the nasopharyngeal carriage rate of respiratory pathogens and the presence of nasopharyngeal biofilm producing bacteria (BPB) in children with RAOM.

Methods: Nasopharyngeal swabs were obtained from 113 children (aged 10 months to 5 years), including 55 children with RAOM (≥ 3 episodes in 6 months, with or without othorrea), and 58 healthy controls. Nasopharyngeal colonization by respiratory pathogens was assessed by means of semiquantitative analysis, and the presence of BPB by means of spectrophotometric analysis.

Results: The nasopharyngeal carrier rates of respiratory pathogens and the presence of of BPB were significantly higher in children with RAOM (41.4% and 29.3%) compared to controls (14.8% and 10.9%) (p=0.01). Among children carrying BPB, H. influenzae was detected in 52.0%, S. pneumoniae in 26.1% and M. catharralis in 8.7% of cases.

Conclusions: Our results confirm the role of biofilm and of H.influenzae in recurrent middle ear infections in children, and suggest to take it into account in management of otitis-prone children. As nasopharyngeal swab could underestimate the presence of biofilm producing bacteria, these results need to be compared to those obtained on bioptic assays in children scheduled for surgery.

O148

CHARACTERISATION OF BACTERIAL PATHOGENS CAUSING SEVERE ACUTE OTITIS MEDIA (AOM) IN GERMAN CHILDREN POST-INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7)

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Background and aims: AOM is a frequent childhood disease, however, tympanocentesis is not routinely performed and swabs from perforated cases may be contaminated, limiting aetiology data. This non-interventional epidemiological study assessed aetiology and antimicrobial susceptibility of bacterial AOM pathogens in Germany.

Methods: 112 children aged ≥3-< 60 months visiting, or referred to, ENT specialists for spontaneous tympanic rupture or clinically indicated tympanocentesis were enrolled. Middle ear fluid (MEF) samples were collected by tympanocentesis or by sampling spontaneous otorrhoea directly from the perforated area of the tympanum after thoroughly cleaning the ear canal. Samples were cultured for bacterial characterisation.

Results: 100 samples were analysed from 100 children (median age 36 months) meeting inclusion criteria. The most common symptoms at presentation were ear discharge (70%) and ear pain (68%). 74 children had received ≥1 dose pneumococcal vaccine. Bacteria were cultured from 53% of samples; *Haemophilus influenzae* (Hi; 21%), *Streptococcus pyogenes* (Spyo; 13%) and *Streptococcus pneumoniae* (Spn; 10%) were most common, with 1 sample positive for both Spn and Hi. Spyo and Spn were only isolated in MEF from spontaneous otorrhoea (n=76). 86% of Hi samples were non-typeable (NTHi) and 60% of Spn samples were serotype 3. All Spn-isolates were susceptible to all antibiotics tested (except 1 with intermediate penicillin susceptibility). Hi-isolates showed some resistance to various antibiotics; notably, 10% were amoxicillin resistant.

Conclusions: NTHi was the main bacterial AOM pathogen in Germany 4-5 years post-PCV7 introduction, which should be considered when choosing antibiotics. Vaccination against Hi, Spyo and Spn may substantially reduce AOM.

O149

THE EPIDEMIOLOGY OF INVASIVE NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* (NTHI) DISEASE IN THE ERA OF ROUTINE HIB VACCINATION IN ENGLAND AND WALES

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Background: The reduction in invasive *Haemophilus influenzae* serotype b (Hib) disease following routine immunisation means that non-typeable *H. influenzae* (ntHi) are now the most common cause of invasive *H. influenzae* disease. Understanding the epidemiology of invasive ntHi disease is important because the infection may be prevented by a newly-licensed 10-valent pneumococcal conjugate vaccine that uses *H. influenzae* outer-membrane protein D as its primary carrier protein.

Methods: The Health Protection Agency Centre for Infections (CfI) conducts enhanced national surveillance of invasive *H. influenzae* disease in England and Wales through a combination of laboratory and clinical reporting schemes, and provides a national service for serotyping invasive *H. influenzae* isolates.

Results: Between 1994-2008, ntHi accounted for 45% of the 2,111 invasive *H. influenzae* cases diagnosed in children aged < 15 years. The average annual incidence of invasive ntHi disease was 0.60 cases/100,000 children, but there was a small, gradual increase of 2.9% per year (95% CI, 1.0-4.9%; P=0.003) in disease incidence over the 15-year period. Almost a third of childhood ntHi infections (242/814, 30%) presented in the first month of life, where they were responsible for 94% (227/242) of all invasive *H. influenzae* infections and presented mainly with bacteraemia (197/227 [87%]. After this period, ntHi cases were evenly distributed among the different age groups and caused two-thirds of all *H. influenzae* bacteraemic pneumonia (53/83 cases, 64%).

Conclusions: The incidence of invasive ntHi disease in children remains low, but the year-on-year rise in incidence merits further study, particularly among neonates.

O150

ETIOLOGY OF MIDDLE EAR FLUID OF INFANTS WITH ACUTE OTITIS MEDIA (AOM) IN GERMANY, 2ND STUDY YEAR

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Background and aims: In December 2009, the pneumococcal conjugate vaccine PCV13 was introduced in Germany, where a general recommendation for pneumococcal conjugate vaccination was issued in 2006. In this poster, we analyzed the pathogens recovered from children suffering from severe AOM with efflux in the most recent study period from Oct. 2009 to Oct 2010.

Methods: Swabs were taken from the middle ear fluid of children with spontaneous draining AOM regardless of their immunization state. Serotyping of *Streptococcus pneumoniae* isolates was performed using the Neufeld-Quellung reaction. *Streptococcus pyogenes* isolates were *emm*-typed by sequencing of the *emm*-gene. *Haemophilus influenzae* was typed using type-specific antisera.

Results: From Oct. 2009 to Oct 2010, 310 children with severe AOM were documented, in comparison with the period Oct. 2008 - Oct 2009 considerably less patients (459). Following pathogens were identified from 120 of these patients: *S. pneumoniae* (35, 29.2%), *S. pyogenes* (35, 29.2%), *S. aureus* (32, 26.7%), *H. influenzae* (16, 13.3%) and *M. catarrhalis* (2, 1.7%). Unchanged to the previous study period, serotypes 3 (9, 25.7%), 19A (7, 20.0%) and 19F (4, 11.4%) were most prevalent. Coverage of the respective conjugate vaccines was as follows: PCV7: 11.4%, PCV10: 22.0%, PCV13: 68.6%. The vaccination rate increased from 71.9% (year 1) to 84.5% (year 2).

Conclusions: While the pathogens recovered were almost unchanged, considerably less children with severe AOM were documented in the second study year. A possible effect of the pneumococcal conjugate vaccination has to be carefully studied in the coming years.

O151

NASOPHARYNGEAL CARRIAGE ISOLATES (NCI) FROM INFANTS WITH ACUTE OTITIS MEDIA (AOM) IN GERMANY

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Background and aims: A general recommendation for pneumococcal conjugate vaccination was issued in Germany in 2006. In this presentation, we analyzed the NCI recovered from children suffering from severe AOM in the most recent study period from Oct. 2009 to Oct. 2010.

Methods: Nasopharyngeal swabs were taken from children with spontaneous draining AOM regardless of their immunization state. *Streptococcus pneumoniae* isolates were serotyped using the Neufeld-Quellung reaction. *Streptococcus pyogenes* isolates were *emm*-typed and *Haemophilus influenzae* isolates were typed using type-specific antisera.

Results: Nasopharyngeal swabs were obtained from 294 of 310 patients with AOM, with 243 swabs being positive for *S.pneumoniae*, *S. pyogenes*, *H. influenzae and/*or *M. catarrhalis*. The highest carriage rate was found for *S. pneumoniae* (57.8%), followed by *H. influenzae* (36.1%), *M. catarrhalis* (33.0%) and *S. pyogenes* (11.9%). All *S.pneumoniae* NCI revealed the same serotype as the corresponding isolate recovered from the middle-ear fluid (mef). Also both, the carriage and the mef *S. pyogenes* isolates showed the same *emm*-type. Almost all *H. influenzae* isolates were non-typable, not differing between NCI and mef-isolates. The most prevalent *S. pneumonia* serotypes were serotype 3 (20.0%), 19A (10.0%), 19F (6.5%), 11A (5.3%) and 35F (5.3%). Coverage of pneumococcal conjugate vaccines was as follows: PCV7, 10.6%; PCV10, 15.9%; PCV13, 48.2%.

Conclusions: Nasopharyngeal swabs were obtained from 94.8% of patients suffering from severe AOM, with *S. pneumoniae* being the most common pathogen recovered. Pneumococcal NCI had the same serotype as the mef-isolates. Most prevalent serotypes were serotypes 3 and 19A, both covered by PCV13.

O152

IMMUNOGENICITY AND SAFETY OF A HIB-MENC-TT BOOSTER VACCINE IN PRE-TERM AND FULL-TERM INFANTS IN THE SECOND YEAR OF LIFE

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Background and aims: Pre-term infants are at greater risk of morbidity from vaccine-preventable diseases with decreasing gestational age. The immunogenicity, reactogenicity and safety of combined *Haemophilus influenzae* type b-*Neisseria meningitidis* serogroup C (Hib-MenC-TT) booster vaccination was assessed in pre-term and full-term infants.
Methods: In this study (NCT00586612) 154 pre-term (n=50, < 31 weeks; n=104, 31-36 weeks) and 144 full-term Spanish infants (>36 weeks), previously vaccinated with Hib-MenC-TT (2, 4, 6 months) and DTPa-HBV-IPV and 7vCRM$_{197}$ vaccines, received a Hib-MenC-TT booster at age 16-18 months. Blood samples were collected pre- and 1 month post-booster. Serum bactericidal activity using rabbit complement (rSBA-MenC) and anti-PRP antibodies using ELISA were measured. Local/general solicited symptoms within 4 days and unsolicited AEs/SAEs within 31 days post-booster were recorded.
Results: One month post-booster, all subjects achieved anti-PRP ≥0.15µg/mL and ≥99.2% achieved rSBA-MenC titres ≥1:8 in all groups (Table). Hib-MenC-TT was generally well tolerated, with lower rates of drowsiness, injection-site reactions, and loss of appetite in pre-term infants (exploratory analysis). No vaccine-related SAEs were reported.

Table. Percentages of subjects with titres/concentrations greater than or equal to predefined cut-offs and GMTs/GMCs, for anti-PRP and rSBA-MenC (ATP cohort for immunogenicity)

Gestational age	Time-point	Anti-PRP			rSBA-MenC		
		N	% ≥0.15 µg/mL	GMC	N	% ≥1:8	GMT
<31 weeks	Pre-booster	38	89.5 [75.2–97.1]	0.75 [0.49–1.16]	38	71.1 [54.1-84.6]	84.2 [39.0–182.1]
	1 month post-booster	38	100 [90.7–100]	58.71 [40.55–84.98]	37	100 [90.5-100]	4570.8 [2784.1–7504.3]
31-36 weeks	Pre-booster	95	86.3 [77.7–92.5]	0.69 [0.53–0.89]	96	78.1 [68.5–85.9]	77.5 [53.0–113.2]
	1 month post-booster	94	100 [96.2–100]	47.31 [37.80–59.21]	96	99.0 [94.3–100]	5009.0 [3699.6–6781.9]
>36 weeks	Pre-booster	130	90.0 [83.5–94.6]	0.78 [0.62–0.97]	134	87.3 [80.5-92.4]	147.8 [110.9–197.1]
	1 month post-booster	134	100 [97.3–100]	54.63 [45.33–65.83]	137	99.3 [96.0-100]	5288.8 [4244.9–6589.4]

GMC/GMT = geometric mean antibody concentration/titre calculated on all subjects;
N= Number of subjects with available results; [ ] = lower and upper limits of 95% CI

Conclusion: Hib-MenC-TT booster vaccination in the second year of life was immunogenic and well tolerated in pre-term and full-term infants when co-administered with other recommended vaccines. Robust booster responses in pre-term and full-term infants, indicating similar immune memory priming, suggest no delay in vaccination with Hib-MenC-TT is needed in pre-term infants.

O153

HOST-PATHOGEN INTERACTION IN CHILDREN SUFFERING FROM OTITIS MEDIA

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Background: Since viral infections may result in Eustachian tube dysfunction, increased adherence of bacteria to epithelial cells and may modulate host immunity, we investigated the effect of bacteria and viruses on the inflammatory response in the middle ear of children suffering from OM.

Materials and methods: Children < 6 years of age, suffering from recurrent or chronic OM and scheduled for tympanostomy tube insertion, were enrolled in a prospective study. Middle ear fluids (*n*=116) were collected during surgery, and qPCR was performed to detect known bacterial and viral otopathogens (*Streptococcus pneumoniae*, *Haemophilus influenzae, Moraxella catarrhalis* and 15 respiratory viruses among which rhino-, adeno- entero- and (para)influenzavirus). To measure the inflammatory cytokine response, concentrations of IL-1β, IL-6, IL-8, IL-10, IL-17a, TNF-α and INF-γ were determined.

Results: Viruses (28%), bacteria (27%), bacteria and viruses (27%) or no otopathogens (19%) were detected in middle ear fluid, with *H. influenzae* and rhinovirus being predominant. Surprisingly, no cytokine differences were found between patients with viruses alone versus no otopathogens. In contrast, the detection of bacteria was associated with a significantly elevated inflammatory cytokine responses compared to when no bacteria were detected. This increase strongly correlated with the bacterial load. Finally, no synergy was observed for viral-bacterial co-infection compared to infection with bacteria alone.

Conclusion: In the middle ear of patients with recurrent or chronic OM, the presence of bacteria, but not viruses, is associated with an increased inflammatory response. This finding suggests that bacteria are an important factor determining the inflammatory process during OM.

O154

DISTRIBUTION BY CLINICAL PRESENTATION OF SEROTYPES ISOLATED FROM PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASES IN 2009-2010 IN MADRID, SPAIN

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Background and aims: Serotype may be an important determinant forserious infections. In 2006, Madrid (6 million inhabitants) included the heptavalent pneumococcal conjugate vaccine (PCV7) in the vaccination calendar. This study analyses per-clinical presentation distribution of serotypes causing invasive pneumococcal disease (IPD) in hospitalized children in Madrid in 2009-2010.

Methods: A prospective, laboratory-confirmed (culture and/or PCR) IPD surveillance was performed in May09-April10 in all hospitals with Pediatric department (28 centres). All isolates (for serotyping) and culture-negative pleural/cerebrospinal fluids were sent for PCR analysis.

Results: 169 IPDs were identified. Table shows distribution [n (%)] of serotypes by clinical presentation

Serotype	Bacteremic pneumonia (BP)	Parapneumonic pleural effusion (PPE)	Primary bacteremia (PB)	Meningitis (M)	Mastoiditis (MAST)	Other
1	21 (44.7)	28 (41.8)	1 (6.3)	2 (11.1)	0 (0.0)	2 (16.7)
3	2 (4.3)	7 (10.4)	1 (6.3)	0 (0.0)	0 (0.0)	1 (8.3)
5	2 (4.3)	1 (1.5)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)
6A	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
7F	8 (17.0)	0 (0.0)	1 (6.3)	1 (5.6)	0 (0.0)	1 (8.3)
19A	10 (21.3)	15 (22.4)	10 (62.5)	4 (22.2)	7 (77.8)	2 (16.7)
PCV7 serotypes	0 (0.0)	4 (6.0)	1 (6.3)	1 (5.6)	0 (0.0)	0 (0.0)
Other serotypes	4 (8.5)	12 (17.9)	2 (12.5)	9 (50.0)	2 (22.2)	5 (41.7)
TOTAL	**47 (100)**	**67 (100)**	**16 (100)**	**18 (100)**	**9 (100)**	**12 (100)**

[Per clinical presentation serotype distribution]

Calculated coverages by the new 13-valent pneumococcal conjugate vaccine (PCV13) were: 91.5% (BP), 82.1% (PPE), 87.5% (PB), 50% (M), and 77.8% (MAST).

Conclusions: Serotype 1 (followed by 19A) was the most prevalent in respiratory infections (BP and PPE) while serotype 19A was the most prevalent in non-respiratory infections, causing approx. 75% MAST.

O155

CROSS-SECTIONAL POPULATION-BASED STUDY TO EVALUATE THE SEROPREVALENCE OF 13 SEROTYPE SPECIFIC IGG ANTIBODIES AGAINST *STREPTOCOCCUS PNEUMONIAE*

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Background and aims: In 2006 the 7-valent pneumococcal vaccine was introduced in the Dutch National Immunization Program. We assessed the seroprevalence of IgG antibodies against 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) in the general population in the Netherlands before introduction of the vaccine, to establish baseline IgG concentrations against these serotypes.

Methods: A serum bank consisting of 7904 sera from individuals aged 0-79 years was used. The 13 serotype specific IgG concentrations were assessed simultaneously using a fluorescent bead-based multiplex immuno assay (MIA).

Results: Overall, the geometric mean IgG concentrations (GMCs) against the 13 serotypes increased with age up to 5 years and remained at a plateau thereafter. Individuals appeared to have antibodies against an increasing number of different serotypes with increasing age. The lowest GMCs were found for antibodies directed against serotype 4 and 5, and the highest against serotypes 14 and 19F. There was no uniform relationship between the occurrence of serotypes causing invasive pneumococcal disease (IPD) and the GMCs.

Conclusions: This study provides an overview of the seroprevalence of IgG against 13 pneumococcal serotypes in a cross-section of the Dutch population. The results of this study showed there was no uniform relationship between IPD incidence and GMCs. The GMCs are likely dependent on the immunogenicity of the polysaccharides and on the frequency and duration of pneumococcal exposure, which in turn depends on the frequency of circulation of the pneumococcal serotypes.

O156

FALL OR SPRING FOR PNEUMOCOCCUS? CHANGES IN INVASIVE PNEUMOCOCCAL DISEASE IN SPANISH CHILDREN

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Background: Epidemiology of invasive pneumococcal disease (IPD) has changed since routine introduction of 7-valent pneumococcal conjugate vaccine (PCV7) in childhood vaccination calendar. Data from Spain and other countries where PCV7 is not routinely included remain controversial.

Methods: A retrospective-prospective study was performed in a single tertiary care pediatric hospital in Barcelona (Spain), in which data from all children aged < 16 years with culture-proven IPD were compared in two different periods, before and after PCV7 introduction (prevaccine period, January 2000-December 2002; vaccine period, January 2007-December 2009).

Results: Twenty-seven and 84 cases of IPD were studied in the first and second period, respectively. The IPD rate increased from 19.65 to 50.84 episodes per 100,000 children-year between the two periods ($p < 0.05$). A dramatic decrease in PCV7 serotypes was observed (from 68.2% to 10.8%), and a consequent increase in non-PCV7 serotypes (from 31.8% to 89.2%) ($p < 0.05$). Penicillin susceptibility rose in the second period from 58.3% to 83.9% ($p < 0.05$). In the prevaccine period, bacteremia without focus and meningitis were the most common clinical forms of IPD (55.5%), whereas respiratory forms increased to 69% in the vaccine period ($p < 0.05$), with pneumococcal empyema being the most frequent clinical presentation (39.3%).

Conclusions: Our study found statistically significant variations in IPD presentation in our area between the prevaccine and vaccine eras, including a higher incidence and predominance of non-PCV7 serotypes in the vaccine period, increased susceptibility to penicillin, and more cases of respiratory disease. These changes are likely associated with the introduction of PCV7, among other factors.

O157

PNEUMOCOCCAL SEROTYPES IN COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN VACCINATED WITH PCV-7

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Aim: In countries with high vaccine coverage with PCV7, infections due to non-vaccine serotypes increase progressively, but little is known in community acquired pneumonia (CAP) in immunized children.

Methods and results: Among 76 children fully vaccinated with 7-valent conjugate vaccine and hospitalized from 2006 to 2009 for community-acquired pneumonia, ten (13.1%) had confirmed pneumococcal infections (4 pts with CAP and 6 patients with CAP & empyema). All *S. pneumoniae* isolated blood culture were non-vaccine serotypes : 19A (3 pts), 1 & 7F (2 pts each), 5 (1 pt) and 2 patients with positive Binax® test in pleural fluid. Other causes of CAP were *Mycoplasma pneumonia* (MP) in 10.5% and viruses in 26.3%. Two identical studies were performed in the same unit before introduction of PCV7 in France, in 1992-96 and 1996-99. During the first period, 8/71 (11.2%) children with CAP had positive blood culture for *S pneumoniae* and 10 /88 patients (11.4%) during the second period. The other causes of CAP in these two studies were respectively 11.3% and 21.1% for MP and 42% and 25.1% for viruses. Non-vaccine serotypes isolated in children CAP were non-vaccine were relatively rare : 13.1% for serotype 1 and 1% for each serotypes 7F, 5 and 19A as reported by national French survey in 1996, before vaccine introduction.

Conclusion: These data show that vaccine-type pneumococci are not rare in children immunized with PCV7. The new PCV13 vaccine will be usefull, but the bacteriological survey of CAP in children either immunized or not remains necessary.

O158

SEROTYPE DISTRIBUTION AND SENSIVITY TO PENICILLIN OF *STREPTOCOCCUS PNEUMONIAE* ISOLATES THAT CAUSE INVASIVE DISEASE AMONG BRAZIL CHILDREN

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In Brazil the 10-valent pneumococcal conjugate vaccine(PCV 10) was introduced in to de National Immunization Program in April 2010. We conducted a study to identify the most common pneumococcal serotypes in children with invasive disease, correlate isolated serotypes with those included in conjugate vaccines, and ascertain the sensivity to penicillin

Methods: From January 2003 to July 2010, a retrospective study of children with a diagnosis of invasive disease for *Streptococcus pneumoniae* was conducted at the University Hospital of São Paulo. Criteria for inclusion were: age greater than 29 day and less than 15 years, with isolation of pneumococcus from a normally sterile site.

Results: The study included 198 children. Of these, 142cases of pneumonia, 29 bacteremia , 20 meningitis, 3 cellulitis, 3 pyoarthritis and 1 pericarditis.The most common serotypes were: for pneumonia 14(42,3%), 5(13,8%), 1(13%), 6B(6,5%) and 19A(4,1%); for bacteremia were 14(34,5%), 6B(24,1%), 12F(6,9%), 19F(6,9%) and 18C(6,9%); for meningitis were 14(29,4%), 18C(11,8%), 10A(11,8%) and 19F(11,8%). The coverage rates of PCV10 and PCV13 in meningeal disease was 64,7% and 76,5% respectively. For non-meningeal disease was 84,4% and 93,8%. The sensitivity to penicillin in meningeal disease were: sensitive(MIC< 0,06µg/mL) in 13 cases (65%) and resistant(MIC≥0,12µg/mL) in 7 cases (35%). For non-meningeal disease were: sensitive(MIC< 0,06µg/mL) in 170 cases(95%), intermediate resistant(MIC=4µg/mL) in 9 cases(5%).

Conclusions: Our results confirm a significant potential impact of PCV 10 for non-meningeal disease but no for meningeal disease. The susceptibility testing results show that penicillin is still the treatment of choice for non-meningeal pneumococcal disease.

O159

EXPECTED IMPACT OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN INVASIVE BACTERIAL INFECTION RATE IN THE PEDIATRIC EMERGENCY DEPARTMENT

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Objective: To study the impact we can expect from the introduction of the 13-valent pneumococcal conjugate vaccine (PCV-13) in the spectrum of invasive bacterial infections (IBI) in the Pediatric Emergency Department (PED)

Methods: Retrospective study of children under 14 years diagnosed with an IBI (bacterial culture/protein chain reaction in blood or cerebrospinal fluid - CSF) in a PED of a tertiary hospital between January 2008 and December 2010.

Results: Among 180,202 episodes, an IBI was diagnosed in 88 patients (36, 40.9%, under 1 year).

The most frequent diagnoses were: sepsis with/without meningitis 28 (31.4%), bacteraemia 21 (23.6%), pneumonia 13 (14.6%), meningitis 9 (10.1%). The most commonly isolated bacteria were *S. pneumoniae* 33 (37.5%), *N. meningitidis* 21 (23.9%), *E. Coli* 9 (10.2%).

The bacterium was isolated from blood in 77 patients (27 pneumococcus, 18 meningococcus), from CSF in 3 (pneumococcus), and from both fluids in 8 (3 pneumococcus, 3 meningococcus, 2 Group B *Streptococcus*).

29 isolated pneumococcus were serotyped. The distribution of the serotypes related to the different PCV was: 5 were included in the PCV-7 (17.2% CI 95% 7.1-35.0), 15 in the PCV-10 (51.7%, 95% CI 34.4- 68.6) and 25 in the PCV-13 (86.2% CI 95% 68.8-95.1).

None of the patients died. Two patients with invasive pneumococcal infection had sequels.

Conclusions: In the era of 7-valent PCV, pneumococcus is the leading cause of IBI in PED. The introduction of 13-valent PCV may lead to a very significant decrease of IBI rate and meningococcus may become the leading cause of IBI.

O160

PROSPECTIVE, MULTINATIONAL ACTIVE HOSPITAL-BASED EPIDEMIOLOGIC SURVEILLANCE FOR IPD AND PNEUMONIA BURDEN AMONG CHILDREN IN BANGALORE SOUTH ZONE, BANGALORE, INDIA

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Background and aims: Pneumococcus is a leading cause of childhood morbidity and mortality. Invasive pneumococcal disease (IPD) data in India are scarce. This study estimated IPD in the targeted population.

Methods: Prospective, hospital-based surveillance conducted from 27/2/2009 -26/2/2010. Children 28d to ≤36m with temperature/temperature history ≥39.0°C (within 24h) or clinical suspicion of IPD or >36m to < 60m with suspected IPD, residing in surveillance area were eligible. Blood cultures were obtained from all enrolled children, cerebrospinal fluid (CSF) in suspected meningitis, and chest radiographs (CXRs) in suspected pneumonia. IPD was confirmed by pneumococcus-positive blood and/or CSF cultures.

Results: 5,249 children from estimated study population of 112,483 were enrolled.Mean age = 19.8m, (66.5% = 28d to < 24m).17 children with IPD were confirmed (12[70.6%] pneumonia, 3[17.6%] meningitis, 2[11.8%] bacteraemia). Overall, estimated IPD incidence was 15.11/100,000 (28d—60m). Highest IPD incidence occurred in 6m to < 12m age group: 46.01/100,000.Pneumococcal serotypes: 6A (n=5; 29.4%); 5 (n=3;17.6%); 1 (n=2;11.8%), 14 (n=2;11.8%), and 9V, 19F, 3, 18C and 19A each one. 7-, 10-, and 13-valent pneumococcal vaccine serotype coverage was 29.4%, 58.8%, and 100%, respectively.Four of 16(25.0%) isolates were resistant to trimethoprim/sulfamethoxazole, 3(18.8%) to erythromycin, and 1(5.9%) to ceftriaxone. 6A, 14, 1 and 19A showed antibiotic resistance. 6A isolates showed resistance to trimethoprim/sulfamethoxazole, ceftriaxone, and erythromycin.Clinical pneumonia incidence among children aged 28d to < 6m and 28d to < 24m: 2,107.87/100,000 and 3,452.04/100,000, respectively. Incidence of CXR-confirmed pneumonia: 983.26/100,000 (28d—60m).

Conclusions: IPD and pneumonia are important causes of morbidity in children of Bangalore South Zone.

O161

PEDIATRIC PARAPNEUMONIC EMPYEMA EPIDEMIOLOGY IN SOUTHERN SPAIN (2005-2009)

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Objetive: To describe pediatric parapneumonic empyema(PPE) epidemiology in the previous years to the introduction of the new generation of conjugate pneumococcal vaccines (10 and 13-valent).

Methods: All patients < 14 years old admitted to a tertiary pediatric hospital with a diagnosis of PPE were prospectively enrolled from January 2005 through December 2009.

Patients: Overall 219 patients had PPE. Incidence rates for PEE remained stable during the study period with a non statistically significant increase in 2009 (p=0.08 for comparison with 2005). There was a significant higher frequency of PPE cases in the last quarter of 2009 compared to historical data for the same term in previous four years (p=0.001),coincidental with increasing circulation of 2009 pandemic influenza A (H1N1) in our population. Median age and duration of symptoms prior to admission were 44 months (intercuartilic range 32-70 m) and 4 days (intercuartilic range 3-6 days), respectively. Nearly a third (30%) of patients were admitted to ICU. There were no fatalities. A microorganism was isolated from blood and/or pleural fluid cultures in 21% PPE cases. Pneumococci were detected in 72% of culture-positive and 79% culture-negative samples. Serotypes were determined for 104 PPE cases; serotype 1 was the most prevalent serotype identified (42%) followed by serotypes 7F (20%), 3 (16%), 19A (8%) y 5 (7%).

Conclusion: Pneumococcal serotype 1 remained the most common cause of PPE cases over the last 5 year period. Continued enhaced surveillance is essential to monitor impact of new generation of pneumococcal conjugate vaccines in PPE epidemiology.

O162

INFLUENZA A (H1N1) 2009: VIRAL LOAD CORRELATES WITH EPIDEMIOLOGYCAL CHARACTERISTICS AND COULD BE USED AS A RISK-MARKER OF SEVERITY[

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Aims: To describe the influenza A (H1N1) 2009 viral-load in admitted paediatric patients and its relation with epidemiological and clinical characteristics.

Methods: Patients admitted with (H1N1) 2009 infection (confirmed by positive RT Real-Time PCR for both matrix protein 2 (M2) and pandemic H1 genes in nasopharyngeal specimens) were prospectively included from July to November of 2009. Viral-load was determined through cycle-threshold (Ct) values of M2 gene corrected according to the Ct value of internal control (human-myostatine-gene). Poor quality samples (internal control Ct > 27), were excluded.

Results: Seventy patients were included. Viral-load was in relation with the time from onset of fever to the moment of collecting the nasal aspirate (Spearman rho=-0.4; p< 0.05) and with age (Spearman rho=0.4; p< 0.05). Children with encephalopathy and those with immunosuppressive-chemotherapy had higher viral loads. Having more than 35,000 copies/mL at any time of disease was associated with requiring for mechanical ventilation (invasive or non-invasive) with a relative risk (RR)=13.1 (95%CI:1.6-106). Patients who exceeded that viral-load after four days of symptoms had an increased risk of requiring mechanical ventilation (Fisher p< 0.02, RR=4.3 (95%CI:1.2-14.9) when comparing to those that exceeded that viral-load and were still within the first three days of symptoms.

Conclusions: (H1N1) 2009 viral-load was in relation with age, comorbidity, and the time from the onset of symptoms to the collection of the sample. Patients with high viral loads had an increased risk of needing for mechanical ventilation, especially if they had those viral-loads after four days of symptoms.

O163

CLINICAL CHARACTERISTICS OF SWINE FLU (H1N1) COMPARED TO OTHER RESPIRATORY VIRUSES IN THE UNITED KINGDOM

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Background and aims: During winter, paediatricians were concerned that clinical features would not differentiate between H1N1 and other viruses. We investigated whether Health Protection Agency (HPA) H1N1 criteria were accurate in discriminating between different viruses.

Methods: We reviewed the clinical characteristics of children presenting with viral illnesses to the Paediatric Assessment Unit, Heartlands Hospital, Birmingham, UK between 1st November and 1st December 2009. Data was analysed using StatsDirect.

Results: 217 patient notes were reviewed; 25 had positive viral throat swabs for respiratory syncytial virus (RSV), 23 H1N1, 22 human metapneumovirus, 17 rhinovirus, 11 parainfluenza, 6 adenovirus, and 13 multiple viruses. 100 had negative swabs.

Children positive for H1N1 had significantly higher recorded temperatures only when compared to RSV (p=0.02), rhinovirus (p=0.03) and negative swabs (p=0.02). Headache (p< 0.0001) and myalgia (p=0.041) occurred more frequently in H1N1 compared to all other viruses, but arose only in 34% and 17% of H1N1 cases respectively.

12 children required HDU/ITU admission (8 negative, 2 H1N1 (of which one died), 1 RSV, 1 parainfluenza).

Duration of admission did not significantly differ between viruses.

50 children (23%) had underlying disease; 5 of which had H1N1.

9% of all patients received oseltamivir and 32% received antibiotics with no significant difference between viruses.

The HPA criteria sensitivity and specificity for H1N1 were 73.9% and 54% respectively.

Conclusions: Children with viral infections during winter were clinically indistinguishable except for those positive for H1N1 with headache or myalgia. The HPA criteria did not identify or differentiate H1N1 from other viruses.

O164

DOSE-RANGING PAEDIATRIC STUDY: IDENTIFICATION OF A NOVEL MF59-ADJUVANTED 2A2B QUADRIVALENT INFLUENZA VACCINE

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Background and aims: Influenza B viruses from 2 antigenically dissimilar lineages often co-circulate, and there is no cross-protection between these lineages. Ideal paediatric vaccines are safe and offer long-term protection against all circulating influenza virus strains. This study aimed to assess the safety and immunogenicity of different combinations of MF59 adjuvant and/or a second B strain added to high or low doses of TIV.

Methods: 410 healthy children aged 6-35 months were randomly assigned to receive vaccines including combinations of 7.5µg or 15µg doses of the WHO recommended influenza strains, 0%, 12.5%, 25%, 50%, 100% of the MF59 adjuvant dose approved for elderly adults in FLUAD, and, for the quadrivalent vaccine, the addition of 7.5µg or 15µg of a second B strain. Antibody levels were measured by haemagglutination inhibition at Days 1, 29, and 50. Adverse reactions were recorded for 7 days after each vaccine dose, and adverse events were reported throughout the study period.

Results: The addition of a second B strain was immunogenic and did not affect immunogenicity of the other strains. MF59-adjuvanted formulations, even at low levels of MF59, induced superior antibody responses compared with non-adjuvanted influenza vaccines. A higher immune response was observed with increasing MF59 dose. There was no increase in adverse reactions with increasing MF59 dose, antigen dose, or the addition of a second B strain.

Conclusion: MF59-adjuvanted quadrivalent influenza vaccine appears a viable combination for use in young children. MF59 dose response supports the use of half the adult MF59 dose in children.

O165

M59®-ADJUVANTED H1N1 VACCINES IN CHILDREN 3-17 YEARS: SAFETY AND IMMUNOGENICITY FOLLOWING A 1-YEAR BOOSTER VACCINATION

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Background and aims: There is a need for effective and safe paediatric vaccines that offer broad, robust and long lasting protection. The aim of the present study was to assess the immunogenicity and safety after a 1-year booster dose of an egg-derived MF59-adjuvanted H1N1 vaccine (Focetria®). We also report 12 month follow-up safety data after the first 2 vaccine doses.

Methods: 410 children aged 3-17 years were randomly assigned to receive, at a 21 day interval, two doses of either 3.75µg antigen with 50% of the standard MF59 dose, 7.5µg antigen and the standard MF59 dose, or 15 µg antigen of H1N1 vaccine without adjuvant. A third vaccine dose was administered after approximately 1 year (data available for 25%-60% of the children across groups) using the MF59-adjuvanted seasonal influenza vaccine. Antibody levels were measured by hemagglutination inhibition, local and systemic adverse reactions were recorded for 7 days after the booster injection and adverse events were reported throughout the study period.

Results: Geometric mean titers ranged from 11-15 at study start, 122-252 after 1 year (pre-booster vaccination), and 2042-2260 at 3 weeks following the booster dose. Vaccinations were well tolerated with reactions mainly mild to moderate in severity. In the 6-12 month follow-up period, 8 SAEs and 6 cases of onset of chronic diseases were reported, none related to the study vaccine.

Conclusions: Results of the present study further support the use of MF59-adjuvanted H1N1 vaccine as a highly immunogenic and safe vaccine for active immunization against H1N1 influenza.

O166

ANTIBODY PERSISTENCE IN CHILDREN VACCINATED WITH ONE DOSE OF ASO3-ADJUVANTED A/H1N1/2009 VACCINE AND THE EFFECT OF SEASONAL 2010-2011 INFLUENZA VACCINE

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Background and aims: In Canada, two doses of ASO3-adjuvanted A/H1N1/2009 vaccine (Arepanrix®1.9µgHA) were recommended to children < 9 years. In the province of Quebec, one dose of vaccine was recommended. We assessed the persistence of antibody one year after a single dose of adjuvanted vaccine and the immunogenicity of seasonal 2010-2011 vaccine.

Methods: Children ≤9 year-old vaccinated in 2009 with ASO3-adjuvanted vaccine were eligible to participate. In 2010, participants naïve to seasonal vaccine received two and non-naïve, one dose of seasonal vaccine. Blood samples were collected before and 21-28 days post-each dose. HAI test was used.

Results: 155 children participated. Before seasonal vaccination, 80% of participants had a titer ≥1:10 and 46% a titer ≥1:40 to A/California/7/2009 (H1N1). Post-first dose of seasonal vaccine, 98.4% and post-dose two, 100% had a titer ≥1:40. A 16.5-fold GMT increase was observed post-first dose but none post-second dose. All 25 participants aged < 36 months with a titer < 1:40 to B/Brisbane/60/2008 (Victoria lineage) before vaccination remained under this threshold post-first dose. Twelve of these children received previously a seasonal vaccine containing B Yamagata lineage. Post-second dose, 87% of naive participants had a titer ≥1:40 to B/Brisbane/60/2008. The response to A/Perth/16/2009 (H3N2) was in the previously reported range (≥75% 1:40). No SAE were reported.

Conclusions: One dose of adjuvanted vaccine induced a long lasting immunity against A/California/7/2009 (H1N1) virus. One dose of seasonal vaccine was insufficient to induce an adequate immune response to B/Brisbane/60/2008 strain in children < 3 years naive to B Victoria lineage.

O167

SAFETY OF ADJUVANTED PANDEMIC INFLUENZA VACCINES: BACKGROUND RATE OF NARCOLEPSY IN EUROPE

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Aim: To calculate background rates of narcolepsy in Europe and assess rates before (< April 2009) and during (May-September) the pandemic and after the beginning of the vaccination campaign (October 2009).

Methods: Seven European countries united in the VAESCO consortium used population and health care databases to calculate background incidence rates (IRs). Countries used standardized Jerboa® software locally on common input data to produce uniform aggregated data, which could be transferred centrally for calculation of incidence rates (IR) and pooling.

Results: 193 million person years (PY) including 18 million PY in 2009 and 2010 from Finland, IPCI (NL) and GPRD (UK) were captured. Overall crude and non-validated narcolepsy rates varied between 1.00 and 2.04 per 100,000 PY per country. Age-specific incidence rates differed between countries. The pooled age standardized rate was 1.30 (95%CI: 1.10-1.52) per 100,000 PY. Overall rates remained within confidence limits of a 10-year secular trend after start of the vaccination campaign. In 2009 narcolepsy rates increased in 5-19 year olds in Finland and 20-59 year olds in IPCI while rates decreased in GPRD. Rates started increasing before the vaccination campaign.

Conclusion: Background rates show different age distributions between countries. The observed increase of narcolepsy rates in Finland and the Netherlands was significant but started prior to the immunization campaign and involved different age groups. In the Netherlands the affected age group did not correspond with the group targeted for vaccination, in Finland it did. A European case control study is underway.

O168

IMMUNOGENICITY AND SAFETY OF INTRADERMAL INFLUENZA VACCINES WITH DIFFERENT AMOUNT OF ANTIGENS IN OTHERWISE HEALTHY CHILDREN

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Background and aims: Use of influenza vaccine in healthy children is debated mainly because the conventional inactivated trivalent vaccine (TIV) is not always adequately immunogenic. The intradermal (ID) administration of TIV is used in adults in order to increase immunogenicity. This study was planned to evaluate the immunogenicity and safety of ID-TIV vaccine in pediatric age.

Methods: Primed healthy children aged 3-14 years were randomized to receive ID-TIV vaccine at the dose of 9 µg (n=38) or 15 µg (n=37) for each antigen using a pre-filled syringe with micro-injection system. As controls, 37 age-matched healthy children receiving the virosomal-adjuvanted influenza vaccine (VAIV) were enrolled. On blood samples drawn at enrollment and after 28 ± 3 days, antibody response was evaluated by hemagglutination inhibition assay. Safety in the month following vaccination was analysed.

Results: Seroconversion and seroprotection rates against H1 and H3 antigens were >90% in children receiving ID-TIV vaccine independently from the dose and 86.5% in those vaccinated with VAIV. Response to B antigen was significantly better in children receiving ID-TIV vaccines than VAIV (57.9% with ID-TIV 9 µg, 62.2% with ID-TIV 15 µg, 32.4% with VAIV; ID-TIV 9 µg or 15 µg vs VAIV, $p< 0.05$). All the vaccines were equally safe without differences between groups, although children receiving ID-TIVs had more local reactions.

Conclusions: ID-TIV administration can improve immunogenicity of influenza vaccination in pediatric age, particularly against B antigen. The antigens' dose of 9 µg seems adequate to obtain an optimal immune response with a favorable safety profile.

O169

SAFETY OF A THREE SUBUNIT INFLUENZA VACCINE IN HEALTH CARE WORKERS IN KURDISTAN: A CROSS SECTIONAL STUDY

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Background and aims: Influenza can cause severe morbidity and mortality. The most effective strategy for preventing influenza infections is annual vaccination. The safety and tolerability of several types of influenza vaccines have been investigated previously in different countries. In this study the safety of trivalent inactivated surface antigen (subunit) influenza vaccines Begrivac® (Novartis Company) was studied in health care workers.

Methods: This cross sectional study, started at August 2009 through July 2010 was conducted in the Sanandaj Center for Disease Control and Prevention and consisted of two parts: an early follow up for 2 weeks and late follow up 6 month after Vaccination. Nine hundreds persons were engaged in the study during one year of the study. In each case a questionnaire completed for the Person and all symptoms or abnormal physical findings were recorded.

Results: In part I of the study, post-vaccination complaints were as follows: Headache 5.3%, Fever 7.9%, Weakness 9.6%, Chills 10.1%, Sweating 10.5, Arthralgia 20.2%, Malaise 21.5%. All adverse events were mild. Swelling of injection site in 30.3% of cases and Pruritus of injection site in 32.9% of cases were observed. Redness and induration were also reported by 42.5% of subjects. Local reactions were mainly mild and lasted for 1-2 days. No systemic reactions were reported in part II. None of the subjects in part I or II experienced any inconvenience.

Conclusion: The trivalent inactivated split influenza vaccine Begrivac® was safe and well tolerated justifies the use of vaccine for the control of influenza.

O170

RISK FACTORS FOR PREVALENT TUBERCULOSIS INFECTION AMONG CHILDREN IN GREENLAND

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Objectives: It is unknown why tuberculosis infection remains a significant problem in Arctic communities. In the 1990ies the TB incidence in Greenland doubled and TB control efforts were re-enforced, however the effect is not yet visible. This study examines risk factors for Mycobacterium tuberculosis infection (MTI) among Greenlandic children in order to characterize the children most at risk of infection during the current epidemic.

Material and methods: Between 2005 and 2007, a survey was undertaken among 1,797 Greenlandic school children using questionnaire and registry data analysed by prevalence odds ratios (OR) and 95% confidence intervals. MTI was defined as a dual-positive interferon gamma release assay and tuberculin skin test.

Findings: The overall MTI prevalence was 8.4% (152/1797). Among children with known TB contact (10%), 26.6% were infected compared with 6.4% of children without TB contact. Overall MTI increased with Inuit ethnicity ($OR_{\text{inuit vs non-Inuit}} = 4.22(1.55\text{-}11.5)$) and narrow age gap to closest older sibling ($OR_{< 1yr \text{ vs } \geq 1 yr}=2.48(1.33\text{-}4.63)$. Self-reported TB contact modified the profile to include household crowding and mother's education. Notably, siblings of an older MTI-positive sibling were more than 14-fold more likely of being MTI-positive ($OR_{\text{infected older sibling vs non-infected}} = 14.2\ (5.75\text{-}35.0)$).

Conclusion: Ethnicity, sibship relations, domestic crowding, and maternal level of education are factors associated with TB infection among Greenlandic children. The strong clustering of MTI by household suggests family sources of exposure are important. The study findings could aid target operational TB-control efforts towards the most vulnerable groups of children in Greenland.

O171

EMERGENCE OF ESBL PRODUCING ORGANISMS IN PAEDIATRIC UTI

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Background and aims: Limited data are available regarding community-acquired infections due to extended spectrum beta-lactamase producing gram-negative pathogens (ESBL-GN), particularly in children. We studied the evolution of ESBL-GN recovered from children with UTI in a 170-beds tertiary care paediatric hospital in Brussels and analysed the potential impact on empirical antibiotic treatment.

Methods: ESBL-GN were recorded prospectively for the years 2003-2009. Patients with sampled urine growing an ESBL-GN in the first 24 hours were community acquired. UTI cases were defined as positive microscopic examination and culture obtained from catheterised sample, mid-stream or in very rare occasions bags in children with microscopic examination showing more than 500 leucocytes and a dipstick performed directly on the sample showing both positive leukocyte esterase and nitrites. Epidemiological and clinical data were completed retrospectively.

Results: During the study period, 20 demonstrated UTI caused by ESBL-GN were community-acquired, all occurring from 2006 onwards. Among these 20 children, 13 had risk factors for UTI (urinary tract abnormalities or recurrent UTI); 11 had pyelonephritis and were treated IV. Empirical therapy (amoxi-clavulanate, second generation cephalosporin) was inappropriate in 3 children, all with cystitis, all of them showed a favorable evolution. *E. coli* was isolated in all but one case due to a *K. pneumoniae*.

Conclusion: ESBL-GN, particularly *E. coli,* emerge as a cause of community-acquired UTI in children. Further studies are needed to determine how these common paediatric infections will be treated empirically in the future.

O172

OSTEO-ARTICULAR INFECTIONS CAUSED BY *STAPHYLOCOCCUS AUREUS* PRODUCING PANTON-VALENTINE LEUKOCIDIN IN CHILDREN

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Background: Panton-Valentine leukocidin (PVL) secreted by *Staphylococcus aureus* is known to cause severe osteo-articular infections (OAI) in children.

Aims: To analyze the complications of *S. aureus* IOA during adapted treatment (antibiotic and surgical drainage) and their occurrence in relation with PVL production.

Methods: We retrospectively analyzed cases of children hospitalized with SA OAI in Robert Debré Hospital (Paris, France) from April 2000 to May 2010.

Results: 73 children were identified (29arthritis, 32osteomyelitis, 12osteo-arthritis). The children mean age was 8,3years (range: 0.5-17.5). *S. aureus* was obtained from blood (n=37) or synovial fluid (n=28) or bone (n=8) were methicillin- susceptible in 88% of cases. 16/58 (28%) isolates were PLV+. 13/16 strains of *S. aureus* PVL+ were methicillin-susceptible.

44 children (49 %) presented complications. Complications were more frequent in group PVL+ versus PVL- (62% *vs* 38%, $p< 0,001$) with abscess (44 % *vs* 17 %), subperiosteal abscess (44 % vs 17 %), myositis (31 % *vs* 2 %), pneumonia (37 % *vs* 7 %), and thrombophlebitis (19 % vs 0 %). In group PVL+, 13/16 children (81%) presented complications occurred in the first 5 days of treatment versus 13/42 children (31%) in group PVL-. No complications occurred after 16 days of treatment in group LPV- whereas 2 children of the LPV+ group presented late suppurative complications, at 41 and 49 days of treatment.

Conclusions: The presence of PVL is associated with complications in 87% of cases, comforting its role in the severity of the disease.

O173

ASEPTIC MENINGITIS IN PEDIATRICS: A NEW INSIGHT INTO AN OLD DISEASE

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Background and aims: Aseptic Meningitis is a common infection of the central nervous system in children, for which the diagnosis is based on clinical criteria and conventional laboratory methods. Uncertainty in diagnosis results in prolonged hospitalization and unnecessary use of antibiotics.The aim of this study is to determine the epidemiological, clinical and laboratory characteristics of aseptic meningitis in a portuguese pediatric population.

Methods: Retrospective study of patients admitted to the Pediatric department of a tertiary care hospital who had as discharge diagnosis aseptic or viral meningitis from January 2005 through December 2010.

Results: A total 293 children, median age 4.9±3.7 years, were identified. Most cases occurred during summer. The dominant clinical signs were headache, vomiting and positive meningeal signs in children older than 2 years and fever, anorexia, irritability if younger than 2 years. The median of the cerebrospinal fluid (CSF) cell count was 75 /mm3. Enterovirus RNA was detected in CSF in 213 of 279 (76%) children tested. 101 cases (34.7%) received antimicrobial therapy, and 65.3% did not receive any.

Children with positive enterovirus PCR (polymerase chain reaction) had shorter hospitalization ($P < 0.001$) and shorter duration of antimicrobial therapy ($p < 0.001$) as compared to children who had negative PCR or were not tested. There were no serious complications or deaths.

Conclusions: Enteroviruses are the leading cause of aseptic meningitis in children. Enterovirus PCR reduces the time required for identification of the causative agent and may decrease the use of empiric therapy with antibiotics and shorten hospitalizations.

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OUTCOMES OF MENINGOCOCCAL SEROGROUP B DISEASE IN CHILDREN & ADOLESCENTS: FINDINGS FROM A LARGE NATIONAL CASE-CONTROL STUDY

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Background: Nations are facing imminent decisions about introduction of new vaccines against meningococcal serogroup B (MenB) disease. Contemporary robust data on sequelae of MenB disease are needed to inform these decisions.

Methods: We present final results from a nationally representative case-control study (UK) of 221 matched pairs aged 3-16 years. Cases were identified through a national database and controls via case GPs. Consenting subjects underwent a standardised assessment. Matched analyses were undertaken using Generalised Estimating Equations (GEE) and conditional logistic regression (CLR).

Results:

	Case	Control	Matched p	Effect size
Verbal IQ	100.7	107.4	<0.0001	-0.46
Performance IQ	98.2	105.0	<0.0001	-0.44
Bilateral Hearing loss <=40db	3.7%	1.0%	0.02	Odds ratio 2.9 (1.2, 7.0)
Cochlear implant	2.4%	0	0.006	-
Working memory	96.4	103.7	<0.0001	-0.44
Executive function	54.7	49.9	<0.0001	0.34
Psychiatric disorder	15%	3.5%	<0.0001	Odds ratio 3.0 (1.2, 7.5)
Amputation with disability	1.2%	0	0.04	-
Epilepsy	2.1%	0.3%	0.04	-

[Outcomes]

Cognitive findings were unchanged when repeated in those without significant HL.

Conclusions: MenB disease is associated with a marked series of deficits in survivors . This is the largest outcome study ever taken. Economic evaluation of these deficits will inform vaccine development and implementation decisions and improved aftercare for survivors.

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TICK-BORNE ENCEPHALITIS IN CHILDREN; CLINICAL COURSE AND OUTCOME

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Introduction: TBE is an important arthropod-borne infection in endemic areas. Sequelae are seen in 1/3 of adult patients. The aim was to study the clinical course and outcome after TBE in children.

Methods: All children with TBE in Stockholm during 2004-2008 were identified from records at the local CDC. Hospital records were studied retrospectively and questionnaires grading persisting symptoms and executive function were used at follow-up in 2010.

Results: 30/65 children had mild, 11 moderate and 24 had severe symptoms. Mean age was 10.8 years; children with mild symptoms tended to be younger. A biphasic course was seen in 47/65, 1 child had received vaccine in full dose. Fever, headache and nausea were seen in most children, stiffness of the neck, abdominal pain and focal neurological symptoms in 17-25. Six children had seizures during the acute phase. EEG changes were seen in 90% of children with moderate-severe symptoms. The white blood cell count, glucose, lactate and protein levels in the CSF did not differ with severity of the disease.

Three children were admitted to the ICU. Children with severe symptoms stayed longer at hospital (10.4 days) compared to children with milder symptoms (5.9).

36/60 children have, so far, returned the follow-up questionnaires showing persisting symptoms in 30; headache, cognitive problems, irritability and fatigue dominating. Problems with executive functions were seen in 39%.

Conclusions: TBE is a serious disease which seems to cause residual problems in a large proportion of infected children. Future studies are needed to elucidate this further.

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BRAIN SPECIFIC PROTEINS: NEURON SPECIFIC ENOLASE AND S 100B IN CHILDREN WITH ACUTE MENINGITIS

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Background: Despite the evident recent advances in diagnosis and treatment of meningitis, the disease continue to be a leading cause of mortality and sequelae. However, some biochemical markers have been studied with the aim of early diagnosis and management

Aim of work: Is to evaluate the levels of neuron specific enolase (NSE) and protein S100 в both in serum and CSF in cases with bacterial and non bacterial meningitis, as well as their relation to the outcome.

Patients and methods: The study included 48 patients with acute meningitis admitted to PICU at children university hospital .The age ranged from 2 month - 6 years. also 20 cases with matchable age and sex diagnosed as febrile convulsions were taken as controls. CSF examination blood culture, estimation of serum and CSF NSE and protein S100в were done.

Results: The levels of serum and CSF NSE were insignificantly different in cases with bacterial than non bacterial meningitis but significantly higher than controls. While the levels of protein S 100в in the serum and the CSF showed significantly higher levels in cases with bacterial than non bacterial meningitis The overall morbidity was 30.7% in bacterial versus 13.6 % in non bacterial meningitis.

In conclusion, CSF and serum NSE are reliable markers of brain damage in acute meningitis but cannot differentiate bacterial from nonbacterial meningitis. CSF and serum S 100в can be a helpful tool in differentiating bacterial from nonbacterial meningitis. CSF NSE may be used as a prognostic marker of outcome in bacterial meningitis

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SALMONELLA OSTEOARTICULAR INFECTION IN SICKLE CELL DISEASE CHILDREN IN PARIS AND ILE-DE-FRANCE, A 12 YEARS RETROSPECTIVE MULTICENTER STUDY

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Background and aims: *Salmonella* osteoarticular infection (OAI) is a severe condition in sickle cell disease (SCD) patients.

Methods: Retrospective analysis of SCD children hospitalized for *Salmonella* OAI between 1997 and 2009 in several hospital of Paris and the region of Ile de France. *Salmonella sp.* was isolated from the blood (n=16), pus (n=12) or articular aspirates (n=12).

Results: 24 cases were analyzed. The median age was 35 months (SD ±59.5, range 8 months to 15 years). Before admission, the most common symptoms were pain (92%), fever (67%) and gastro-intestinal symptoms (46%). At admission, 16 patients (67%) had a single site of OAI, 8 patients (33 %) had several concomitant sites of OAI. Arm was involved in 79% of children and the humerus was the most affected bone (50% of children). The initial median CRP was high (124 mg/L, SD ± 88.1, range: 0-275 mg/l). 38% of osteoarticular samples grew *Salmonella sp* despite initiation of antibiotic therapy (from 1 to 102 days). Intravenous antibiotics with a third generation cephalosporin and ciprofloxacin were given in all cases during a long period (mean: 9 days, SD±17, range 7 to 81 days). 79% of the patients needed surgical drainage. 50% of patients needed more than one surgical drainage for subsequent arthritis, osteomyelitis or sub periostal abscess.

Conclusions: *Salmonella* OAI remain a therapeutic challenge in children with SCD with frequent subsequent extension of the infection despite medical and surgical treatment.

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HIGH CONCENTRATIONS OF AMNIOTIC FLUID PRO-INFLAMMATORY CYTOKINES IN HEALTHY NEONATES ARE ASSOCIATED WITH LOW RISK OF RSV BRONCHIOLITIS

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Background and aims: The burden of respiratory syncytial virus (RSV) bronchiolitis in individual children and their families, the medical system, and society is considerable. Mechanisms underlying RSV bronchiolitis in healthy term infants are largely unknown. We aimed to determine whether high amniotic fluid interleukin-8 (IL-8) and tumor necrosis factor-α (TNF-α) protect against RSV bronchiolitis in healthy term infants.

Methods: Prospective birth cohort study of healthy term newborns, born after uncomplicated pregnancy of ≥37 weeks. Of 882 eligible newborns, 292 (33%) were enrolled. Amniotic fluid was collected during labour. In case of medical attention for respiratory symptoms during the first year of life, a nose-throat swab was taken to establish the presence of respiratory viruses by PCR.

Results: Physician-attended RSV infection was observed in 27 (9.3%) of 292 children at median age 6 months. Amniotic fluid concentrations of IL-8 were higher in children without physician-attended RSV infection than in children with physician-attended RSV infection (11.1 vs 5.5 ng/mL, *P*=.002). Similarly, in children without physician-attended RSV the proportion of detectable amniotic fluid TNF-α was higher (159/265 (60%) vs 8/27 (30%), *P*=.002). Among children with physician-attended RSV infection, amniotic fluid IL-8 was inversely correlated to the number of wheezing days during the first year of life (ρ=-0.38, *P*=.048).

Conclusions: High concentrations of amniotic fluid IL-8 and TNF-α are associated with low risk of RSV bronchiolitis in healthy infants. We hypothesize that direct exposure of fetal lungs to pro-inflammatory signals induces local protection against viral infection during infancy.

O179

LENGTH OF HOSPITAL STAY FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) IN PROPHYLAXED VERSUS NON-PROPHYLAXED PREMATURE INFANTS

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Background and objective: RSV is the most prevalent cause for lower respiratory tract infection (LRTI) hospitalizations in infants under 2 years of age. Palivizumab for RSV prophylaxis helps reduce the risk of severe RSV disease that requires hospitalization in high-risk infants. The objective was to determine the difference in hospital length of stay (LOS) among premature infants who received and did not receive RSV prophylaxis.

Methods: Premature infants (< 37 weeks of gestational age) hospitalized within the first year of life for a LRTI were extracted from the I3 Medical Claims database (2000-2008). Prophylaxed infants were defined as having at least 1 dose of palivizumab prior to hospitalization. Multivariate regression determined the difference in hospital LOS, while adjusting for confounders including birth gestational age, birth weight, age at admission and medical comorbidities.

Results: The database identified1728 premature infants that were hospitalized due to RSV-confirmed LRTI. 36 (2.1%) had received palivizumab. Univariate analysis showed palivizumab-prophylaxed infants had more comorbidities (p=0.038), and were born at an earlier gestational age (p=0.005). The multivariate model revealed that prophylaxed infants had, on average,1.4 fewer days LOS in hospital for severe RSV (p-value=0.032).

Conclusions: These data suggest that compared to premature infants not receiving at least 1 dose of palivizumab, there is an independent association between prophylaxed infants and a decreased LOS for a severe RSV hospitalization. Reasons for this finding, validation of these results in other country databases, as well as an assessment of the impact of full palivizumab adherence and LOS, warrant further research.

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EFFECT OF INHALED HYPERTONIC SALINE SOLUTION TO TREAT INFANTS HOSPITALIZED WITH VIRAL BRONCHIOLITIS

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Background and aims: At present there is only symptomatic treatment available for acute viral bronchiolitis. However none of these treatments are evidence-based. Recent trials show a reduction in hospital stay after inhalation of 3% hypertonic saline solution.This randomised double-blind, placebo-controlled, interventional multicenter trial, performed at 12 peripheral and academic Dutch hospitals, compares nebulization with hypertonic saline, either a 3% or 6%, with 0.9% isotonic saline.The primary end point is the time to discharge, aiming to achieve a 25% reduction in hospital stay.

Methods: Children younger than two years with clinical diagnosis of viral bronchiolitis, not responding to a single inhalation with Salbutamol 2.5 mg may be included after obtaining informed parental consent. Trial medication will be nebulized three times daily until discharge criteria are met.

Results: The analysis was performed on the data of 119 patients, all included in the season 2009-2010. Patient characteristics and the number of exclusions didn't differ significantly. The duration of hospital stay, need for tube feeding and supplemental oxygen shows no significant difference, but there is a trend that 3% seems to be more effective than the other two concentrations.

Conclusions: Preliminary analysis showed no significant reduction in hospital stay but a trend that 3% hypertonic saline is the most effective regarding reduction in duration of hospital stay, need for supplemental oxygen and tube feeding. The use of 6% hypertonic saline solution seems to be safe but has no additional benefit even compared with 0.9%. More research will be necessary to clear up this trend.

On behalf on the Trial Research Group: A.A.P.Vaessen-Verberne, J.Wesseling, A.L.M.Boehmer, R.vanGent, H.J.L.Brackel, C.C.J.M.Smeets, R.deMoor, P.P.Rosias, R.P.Droog, S.Potgieter, M.D.Ottink, J.J.E.Hendriks, D.Logtens-Stevens

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SURVEILLANCE OF VIRAL RESPIRATORY INFECTIONS IN THE EMERGENCY DEPARTMENT USING MICROARRAYS

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Introduction: Impact of viral coinfections and recently discovered viruses on epidemiology of respiratory infections (RI) is still unclear.

Aim: To study the viruses that are involved in the etiology of RI we used microarrays that allow simultaneous detection of many viruses.

Methods: Rhinopharyngeal washes were taken from children (1 month-14 years) who presented in the emergency department from 1/2009 - 12/2010 with RI and treated as outpatients. Laboratory investigation was done for 17 viruses using a microarray platform.

Results: Out of 200 children, upper (URI) and lower (LRI) respiratory infections were diagnosed in 104 and 96 respectively. Viral coinfections were found in 20% of children. The most frequent combinations in URI were the PIV3 -Rhinovirus(9%), PIV- RSV(3%) and in LRI RSV-INFL(8%) and RSVA-RSVB(5%). PIV in URI and RSV in LRI were the prevalent viruses found in coinfections. The most common causes of single infection in URI were PIV3(22.7%), HRSVB(9%), Rhinovirus(9%), Enterovirus(7.5%), Infl(3%), Bocavirus(3%), Adenovirus(3%), HMPV(1.5%) and in children with LRI were RSVB(14.5%), Rhinovirus(11.2%), PIV3(11.2%), PIV4(11.2%), Influenza(8%), HRSVA(5%) and HMPV(3.2%). Respiratory distress was associated with Rhinovirus infection (P = 0.006), while no statistically significant relationship with severity was observed regarding viral coinfections (P = 0.667).

Conclusions: Viral coinfections and recently discovered viruses are involved in significant percentage of outpatient RI. Nevertheless, they are not associated with more serious clinical presentation as happens with rhinovirus infection that is related with respiratory distress. Viral microarrays method can probably help to reduce unnecessary hospitalizations and use of antibiotics in outpatient settings.

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THE EFFICACY OF ZINC SUPPLEMENTATION IN YOUNG CHILDREN WITH RECURRENT ACUTE LOWER RESPIRATORY INFECTIONS: A RANDOMIZED DOUBLE-BLIND CONTROLLED TRIAL

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Aim: To assess the efficacy of zinc in reducing respiratory morbidity in children aged 6-59 months with recurrent acute lower respiratory Infection (ALRI).

Methods: This randomized double blind controlled trial selected children with recurrent ALRI referred to department of Pediatrics, Jawaharlal Nehru Medical College Hospital. Children were randomly assigned to receive either 10mg zinc gluconate or placebo for 60 days. Demographic and clinical data were collected at baseline and every two weeks during the six month study period.

Results: The final analysis included 96 children allocated equally to the two groups. The incidence of ALRI and severe ALRI were significantly lower in zinc group compared to placebo group (20.8% vs. 45.8% (p=0.009) and 21.7% vs. 58.3% (P< 0.001), respectively).The ALRI free days were higher in the zinc supplemented group (P< 0.001),whereas the duration of ALRI episode; fever and rapid breathing were significantly shorter in zinc group (P< 0.001). The medians of serum zinc concentration were comparable at baseline but increased significantly in the zinc group at two month (P= 0.000). The median recovery time of morbidity was significantly shorter in zinc group compared to placebo group (10 days vs.18days) (P< 0.001).Lower risk (20.8%) of two or more episodes of ALRI was observed in zinc group in comparison to placebo group 45.8% (p= 0.009), with absolute risk reduction (ARR) of 25%.

Conclusions: This trial proved a beneficial effect of the sole zinc supplement resulting in a significant reduction in respiratory morbidly among children less than 5 years with recurrent ALRI.

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BACTERIAL CELL WALL COMPONENT MURAMYL DIPEPTIDE SYNERGIZES WITH RESPIRATORY SYNCYTIAL VIRUS IN CYTOKINE PRODUCTION

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Hospitalizations due to respiratory syncytial virus (RSV) have been associated with respiratory bacterial co-infections. The mechanism behind this synergy is thus far unknown.

The bacterial cell-wall component muramyl dipeptide (MDP) is recognized by the intracellular pattern recognition receptor NOD2. NOD2 is a modulator of signals transmitted through TLRs. RSV can be recognized by TLR3, TLR4 and TLR7/8. Our hypothesis is that RSV induced TLR activation is enhanced by NOD2 stimulation.

Human PBMCs were stimulated for 24hrs with RSV-A2, purified TLR ligands and MDP. Subsequently cytokines were measured.

Stimulation with RSV-A2 or MDP resulted in low cytokine responses. However, a combination of both stimuli resulted in high cytokine responses. Ratio's were calculated; [RSV+MDP]/[RSV]+[MDP]. The combination of both stimuli resulted in a 2.0±0.28, 3.8±1.07, 2.2±0.30 fold increase in respectively IL-6, TNF and IL-1beta production.

Stimulation of PBMCs with specific ligands for TLR3 and TLR 7/8 in combination with MDP did not show synergy. Viral ssRNA and dsRNA are therefore not the viral ligands that cause the synergy. This excludes TLR3, TLR7 and TLR8 as potential receptors involved in the crosstalk with NOD2.

Blocking TLR4 internalization with dynasore induced a 3.5 fold increase of the synergy in cytokine production when MDP and RSV were combined. This suggests that the crosstalk between RSV and MDP is TLR4 dependent and TRIF independent.

We show a synergy between MDP and RSV for the induction of cytokines which is independent of intracellular TLR recognition and therefore most likely TLR4 dependent. Ongoing experiments have to confirm this conclusion.

O184

PERTUSSIS AFTER END OF A MASS VACCINATION PROJECT - END OF THE "VACCINATION HONEY- MOON"

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After 16 years of no vaccination against pertussis in Sweden, mass vaccination of infants and catch-up vaccination of children up to 10 years with a pertussis toxoid vaccine was performed in the Greater Gothenburg area 1995 - 1999. In 1999 56 % of all 10 year old children born in Greater Gothenburg had received 3 doses of the pertussis toxoid. No booster doses were given. This led to almost complete elimination of pertussis. The aim of the present study was to follow the incidence of pertussis after end of the mass vaccination project (1999 - 2009) as reflected by cultures and/or PCR. A reemergence was seen from the end of 1999 with a peak in 2004 followed by a decrease when booster doses to both 6 and 10 year old children were introduced in 2005 - 2006. From July 1, 1999 through December 31, 2009 a total of 1973 cases were diagnosed with culture or PCR. The disease was prevalent in all age groups. The highest documented incidence was seen in infants. 450 patients with verified pertussis had received 3 doses of pertussis toxoid in the mass vaccination project and some other trials (comprising a total of 69,423 children). The mean time from the last dose to the laboratory verification of pertussis was 5 years in these 450 cases. In conclusion, pertussis is still not eliminated from the area. Booster doses are needed but the numbers and optimal timing are not known.

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'DECLINE OF IGG-PERTUSSIS TOXIN MEASURED IN UMBILICAL CORD BLOOD AND NEONATAL SERUM'

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Background and aims: Maternal pertussis-specific antibodies are passively acquired by infants during pregnancy. IgG-pertussis toxin (IgG-PT) concentration of >20 U/ml (= >ln 3,0) is assumed to protect neonates against pertussis. To evaluate the amount at birth and course in the first two months of life of IgG-PT, we examined IgG-PT concentration in umbilical cord blood and at 3 times in the neonatal period.

Methods: IgG-PT was measured by validated IgG-specific enzyme-linked immunosorbent assays in umbilical cord blood and in dried blood spots on filter paper cards prepared from umbilical cord blood. These measurements were comparable. Children, born between April 2006-December 2008 with concentrations of IgG-PT >30 U/ml in umbilical cord blood were included. IgG-PT was again measured at the age of 5 days, 1 month and 2 months in dried blood spots. Mean concentrations of IgG-PT were calculated.

Results: The mean concentration of IgG-PT in umbilical cord blood was 60,1 U/ml (ln 4,1; 0,6 SD; N=103). At the age of 5 days, 1 month and 2 months, mean concentrations of IgG-PT were 40,6 U/ml (ln 3,7; 0,5 SD; N=103), 20,7 U/ml (ln 3,0; 0,7 SD; N=62) and 16,7 U/ml (ln 2,8; 0,9 SD; N=61) respectively.

	Umbilical cord blood IgG-PT	Umbilical cord blood IgG-PT Guthrie card	5 days IgG-PT Guthrie card	1 month IgG-PT Guthrie card	2 months IgG-PT Guthrie card
ln	4,1	4,0	3,7	3,0	2,8
SD	0,6	0,5	0,5	0,7	0,9
N	103	103	103	62	61
U/ml	60,1	56,4	40,6	20,7	16,7

[IgG-pertussis toxin concentration]

Conclusion: Only 4% of neonates had IgG-PT >30U/ml in umbilical cord blood, which declines to levels around the concentration needed for protection against pertussis (>20 U/ml) in the first two months of life. Hence, it is of great importance to further investigate safety of maternal immunization during pregnancy to prevent life-threatening pertussis in newborns.

O186

THE B-CELL RESPONSE TO PRIMARY AND BOOSTER DOSES OF MENACWY-CRM VACCINE ADMINISTERED AT 2, 4 AND 12 MONTHS OF AGE

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Background and aims: A new quadrivalent meningococcal vaccine conjugated to CRM (MenACWY-CRM) is immunogenic in young infants. In this study we assessed the memory B-cell and antibody responses after a primary course and a booster dose of MenACWY-CRM in infants.

Methods: 216 healthy infants were primed at 2 and 4 months of age and boosted at 12 months of age with MenACWY-CRM. Blood samples were obtained from all children at 5, 12 and 13 months of age. The memory B-cell response was measured by ELISPOT and serum antibodies measured using a serum bactericidal assay with human complement (hSBA).

Results: At 5 months of age, after primary immunisation, serogroup-specific memory B-cells were detectable in fewer than 25% of children, although protective hSBA antibody titres (≥1:8) were detectable in more than 94% of children against serogroup C and W-135, in 87% against serogroups Y, and in 58% against serogroup A. At 12 months of age, before booster immunisation the percentages with hSBA ≥1:8 were 2% for serogroup A, 40% for serogroup C, 59% for serogroup W-135 and 54% for serogroup Y. One month after the booster dose of MenACWY-CRM over 50% of children had detectable memory B-cells, more than 98% had protective antibody titres against serogroups C, W-135 and Y, and 91% against serogroup A.

Conclusions: These data indicate that few antigen-specific anticapsular memory B-cells can be detected after two doses priming with MenACWY-CRM, however, these cells rapidly proliferate after booster immunisation and induce a strong bactericidal antibody response.

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BOOSTER DOSE AT 12 MONTHS OF AN INVESTIGATIONAL MENINGOCOCCAL SEROGROUP B VACCINE (4CMENB) IN TODDLERS PREVIOUSLY PRIMED AT 2,4,6 MONTHS

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Background: Whole genome sequencing was used to identify three of four major protein components of an investigational multicomponent meningococcal vaccine (4CMenB).

Methods: In an observer-blind study in Santiago, Chile, 11-17-year-old adolescents were randomized to receive 1-3 doses of 4CMenB or placebo at baseline, one and/or two months later. Primary immunogenicity outcome was a titer ≥4 in a serum bactericidal assay using human complement (hSBA) against three test strains selected to evaluate the contribution of individual vaccine antigens. Tolerability was assessed by solicited local and systemic reactions within seven days of each study vaccination. Adverse events were monitored throughout the study.

Results: Overall, 1631 adolescents (56% female; mean age 13.8 ± 1.9 years) received 4CMenB and/or placebo. One month later 92-97% of recipients of one 4CMenB dose, 99-100% after 2 or 3 4CMenB doses and 29-50% of placebo recipients had hSBA titers ≥4 against the three test strains. Similar proportions of placebo and 4CMenB recipients reported solicited local (89-94%) and systemic (70-79%) reactions after the first study injection. At subsequent visits, reports of reactogenicity were less frequent in all groups, but placebo recipients were less likely to report reactogenicity outcomes than 4CMenB recipients.

Discussion: 4CMenB induced robust immune responses and had an acceptable tolerability profile following one, two, or three doses and all schedules administered. Three doses of 4CMenB imparted no additional benefits compared with two doses. No evidence of increased reactogenicity was observed with 2 or 3 doses compared with one dose of 4CMenB.

O188

MAINTENANCE OF IMMUNE RESPONSE THROUGHOUT CHILDHOOD FOLLOWING SEROGROUP C MENINGOCOCCAL CONJUGATE VACCINATION IN EARLY CHILDHOOD

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Background: Serogroup C meningococcal (MenC) conjugate vaccines were introduced into the UK routine infant immunisation schedule in 1999, along with a "catch-up" campaign for those aged 1-25 years. Previous cross-sectional studies demonstrated children immunised in early childhood have lower MenC bactericidal antibody 5 years after immunisation than children immunised in late childhood, however the kinetics of antibody decline have not been evaluated in a longitudinal study of a single cohort.

Method: Stored sera obtained at multiple time-points between 2001 and 2010 from children who had received a single dose of MenC vaccine at age 1-3.5 years, were analysed for MenC serum bactericidal antibody using rabbit complement (rSBA).

Results: The MenC rSBA geometric mean titre (GMT) at age 3.5 to 5 years, approximately one year after immunisation, was 8.0 (95% confidence interval [CI] 6.5 - 9.9, n = 292). Over the subsequent 9 years, rSBA GMT declined to 3.3 (CI 2.5 - 4.4, n = 98) at age 11.5-13.5 years. The percentage of children with rSBA titres ≥1:8 (threshold for protection) also declined from 38% (CI 35% - 41%) to 15% (CI 12% - 19%).

Conclusion: MenC rSBA titres wane rapidly following vaccination in early childhood, without evidence of natural boosting of antibody levels through cross-reactive antigens. In the UK, consideration should be given to a routine adolescent booster of MenC vaccine to protect this cohort of children who are entering the potentially high risk period of adolescence, and to prevent a resurgence in nasopharyngeal carriage and maintain herd immunity.

O189

PHASE I RANDOMISED CONTROLLED CLINICAL TRIAL OF SAFETY AND IMMUNOGENICITY OF A MENINGOCOCCAL B BIVALENT LP2086 VACCINE IN HEALTHY TODDLERS

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Background and aims: Neisseria meningitidis is a leading cause of meningitis and septicaemia globally, particularly in young children and adolescents. A bivalent factor H-binding protein (rLP2086) vaccine is being developed with an aim to provide broad protection against serogroup B meningococcal (MnB) infection. This study assessed the safety and immunogenicity of the bivalent rLP2086 vaccine in toddlers.

Methods: Ninety nine healthy toddlers aged 18 to 36 months were randomised (2:1) to receive rLP2086 vaccine (20, 60, or 200µg in ascending dose level cohorts) at 0, 1, and 6 months or control vaccine. Safety was assessed by parental reporting of local and systemic reactions using electronic diaries. Unsolicited AEs were also reported. rLP2086-specific immunoglobulin G binding and human serum bactericidal antibody (hSBA) titres against diverse strains expressing different LP2086 subfamily variants were assessed.

Results: The vaccine was generally safe and well-tolerated. Upper respiratory infection and cough were the most commonly reported adverse events in all groups. Tenderness was the commonest local reaction. Three toddlers (200µg group) developed severe erythema and 4 toddlers (60µg and 200µg groups) developed severe fever (>40.0°C). hSBA responder rates (titre ≥1:4) against strains with homologous and similar subfamily proteins were high after dose 3 (87.5%-93.3% at 60µg; 84.2%-89.5% at 200µg).

Conclusions: Results of this study suggest that the rLP2086 vaccine has an acceptable safety profile, is immunogenic in toddlers, and represents a candidate vaccine for broad protection against MnB disease in young children.

O190

INVASIVE MENINGOCOCCAL DISEASE IN QUEBEC 8 YEARS AFTER THE IMPLEMENTATION OF A PUBLIC SEROGROUP C MENINGOCCOCAL IMMUNIZATION PROGRAM

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Background/aims: In the province of Quebec, Canada, an increase in the incidence of serogroup C invasive meningococcal disease (IMD) occurred in 2001-2002. A mass-immunization campaign against serogroup C launched in 2001 was followed by a universal immunization program. In the perspective of changes in vaccination program, the dynamic of serogroup distribution was analyzed.

Methods: Review of 1997-2010 surveillance data on IMD isolates submitted to the Laboratoire de Santé Publique du Québec.

Results: Overall, 858 IMD were identified: 66%, 22%, 8%, and 3% were due to serogroups B, C, Y, and W135, respectively. 28% of cases were in children < 5 years of age and 18% in 15-19-year-olds. Serogroup B was consistently the most prevalent in < 5-year-olds. Over the last 3 years, serogroup B was responsible for 83% of all IMD: 97% in < 1-year-olds, 100% in 1-14-year-olds, and is decreasing from 95% in 15-19-year-olds to less than 60% in those ≥40-year-old. During 1997-2010, the incidence of serogroup B IMD (per 100 000) was stable in < 1-year-olds (12.4 to 12.3) and in 1-4-year-olds (1.2 to 2.1), and increased 6-fold (0.4 to 2.4) in 15-19-year-olds. *N.meningitidis* B:17:P1.19 (mostly corresponding to ST-269), first identified in 2003, is since accounting for 35% of all serogroup B IMD: 26% in < 5 year-olds, 38% in 10-14-year-olds, 51% in 15-24-year-olds and 38% in 25-39-year-olds.

Conclusion: Serogroup B is responsible for the vast majority of IMD in Quebec. An emerging clonal complex affecting mainly adolescents and young adults is spreading across the province.

O191

IMMUNOGENICITY AND TOLERABILITY OF AN INVESTIGATIONAL MULTICOMPONENT MENINGOCOCCAL SEROGROUP B (4CMENB) VACCINE IN HEALTHY ADOLESCENTS

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Background: Whole genome sequencing was used to identify three of four major protein components of an investigational multicomponent meningococcal vaccine (4CMenB).

Methods: In an observer-blind study in Santiago, Chile, 11-17-year-old adolescents were randomized to receive 1-3 doses of 4CMenB or placebo at baseline, one and/or two months later. Primary immunogenicity outcome was a titer ≥4 in a serum bactericidal assay using human complement (hSBA) against three test strains selected to evaluate the contribution of individual vaccine antigens. Tolerability was assessed by solicited local and systemic reactions within seven days of each study vaccination. Adverse events were monitored throughout the study.

Results: Overall, 1631 adolescents (56% female; mean age 13.8 ± 1.9 years) received 4CMenB and/or placebo. One month later 92-97% of recipients of one 4CMenB dose, 99-100% after 2 or 3 4CMenB doses and 29-50% of placebo recipients had hSBA titers ≥4 against the three test strains. Similar proportions of placebo and 4CMenB recipients reported solicited local (89-94%) and systemic (70-79%) reactions after the first study injection. At subsequent visits, reports of reactogenicity were less frequent in all groups, but placebo recipients were less likely to report reactogenicity outcomes than 4CMenB recipients.

Discussion: 4CMenB induced robust immune responses and had an acceptable tolerability profile following one, two, or three doses and all schedules administered. Three doses of 4CMenB imparted no additional benefits compared with two doses. No evidence of increased reactogenicity was observed with 2 or 3 doses compared with one dose of 4CMenB.

O192

PHASE II RANDOMISED CONTROLLED TRIAL OF SAFETY AND IMMUNOGENICITY OF A MENINGOCOCCAL B BIVALENT VACCINE (RLP2086) IN HEALTHY ADOLESCENTS

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Background and aims: *Neisseria meningitidis* serogroup B (MnB) is a major cause of invasive meningococcal disease, but a broadly protective vaccine is not commercially available. This study aimed to assess the immunogenicity, safety, and tolerability of a bivalent factor H binding protein vaccine (rLP2086) in adolescents, an age group at increased risk for MnB disease.

Methods: 539 healthy adolescents aged 11-18 years were randomized to receive placebo or rLP2086 (60µg, 120µg, or 200µg) at 0, 2, and 6-9 months. rLP2086-specific Immunoglobulin G (IgG) titres and human serum bactericidal assay (hSBA) against diverse strains expressing variants from the 2 different LP2086 subfamilies were assessed. Safety was assessed by solicited local and systemic reactions and unsolicited adverse events. .

Results: hSBA titres and geometric mean IgG titres increased after each rLP2086 vaccination. Among subjects receiving the 120ug and 200ug dose, hSBA titres ≥4 were achieved in 96%-100% (subfamily A) and 69%-92% (subfamily B) of participants. Mild-to-moderate injection site pain was the most common local reaction. Systemic events including fatigue and headache tended to increase with increasing rLP2086 dosage but were generally mild-to-moderate. Adverse events were similar among the control and vaccine arms. One related SAE was reported after dose 3 (200µg) that resolved without sequelae. No other serious adverse events were related to rLP2086 vaccination.

Conclusions: These results suggest that rLP2086 is immunogenic across diverse MnB strains and has an acceptable safety profile. Thus, rLP2086 represents a promising vaccine for broad protection against MnB disease in adolescents.

O193

IMMUNOGENICITY OF A QUADRIVALENT MENACWY-CRM CONJUGATE VACCINE ADMINISTERED IN VARIOUS SCHEDULES TO ARGENTINEAN INFANTS AND TODDLERS

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Introduction: Although young infants are at highest risk for developing meningococcal disease, a quadrivalent conjugate vaccine is not available for routine use in this population. We present immunogenicity results from a large Phase III study using the final MenACWY-CRM formulation.

Methods: In a subset of a large randomised, multinational open-label study, we measured immune responses after primary and booster doses of MenACWY-CRM, administered concomitantly with routine immunizations using two (2, 6 and 12 months) or three priming doses (2, 4, 6 and 16 months) in healthy Argentinean infants. Immunogenicity was measured one month after priming, pre- and post-booster by serum bactericidal assay using human complement (hSBA).

Results: At 7 months, seroprotection rates (% with hSBA titres ≥ 8) after priming with two (n~274) or three (n~268) doses were 74% and 89%, 94% and 97%, 99% and 98%, and 97% and 98% against serogroups A, C, W-135 and Y, respectively. GMTs for serogroup A were 31 and 43 after 2 and 3 doses, respectively, but were similar in both groups for serogroups C, W-135 and Y. MenACWY-CRM with MMR/V+HepA+PCV7 at 12 months after two primary doses (n~100) or with DTaP-Hib at 16 months after three primary doses (n~115) achieved hSBA titres ≥ 8 in 95-100% of subjects against all four serogroups, with similar GMTs in both groups.

Conclusion: When administered concomitantly with routine vaccinations, two or three doses of MenACWY-CRM elicited similar robust immune responses to all serogroups, and were boosted at 12 or 16 months, respectively.

O194

LONG-TERM RESPONSE TO HEPATITIS B VIRUS VACCINATION IN HIV-INFECTED CHILDREN; IMPLICATIONS OF HAART INTERRUPTION

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Background and aims: Response to vaccines is poorer in HIV-infected children. We describe the role HAART interruption plays in the long-term response to hepatitis B virus (HBV) vaccination.

Methods: Cross-sectional study within a cohort of HIV-infected children who received a complete HBV vaccination series. The following thresholds defined response to vaccination: optimal seroprotection, >100 IU/l; seroprotection, 10-100 IU/l; and no seroprotection, < 10 IU/l. Seroprotection levels were compared to different clinical, treatment and biological variables, including immune situation at the time of vaccination and at the time of assessment, and HAART interruptions.

Results: Seventy-six patients were included (60% females, 81% vertical transmission, 26% with AIDS); 60% of the children had received HAART as first antiretroviral treatment and 3 of them remained antiretroviral naive. Median number of HAART regimens was 3; 42% of patients had interrupted HAART at least once, for a median time of 36 months.At the time of assessment, all patients were symptom-free, none of them presented with severe immunosuppression and viral load was undetectable in 72%. Optimal seroprotection, seroprotection and no seroprotection were observed in 20%, 13% and 67% of the children, respectively. Having interrupted HAART was associated with a poorer seroprotection level against HBV (any seroprotection: 21% versus 42% of the patients; p=.06).

Conclusions: Despite vaccination, 67% of the patients in our cohort show no seroprotection against HBV. HAART interruption seems to associate a poorer seroprotection level against HBV.

Acknowledgements: Antoni Noguera-Julian is the recipient of an award from the European Society for Paediatric Infectious Diseases.

O195

IMPAIRED T-CELL DEPENDENT AND INDEPENDENT MEMORY B-CELL FORMATION IN HIV-INFECTED CHILDREN

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Background and aims: Patients infected with the human immunodeficiency virus (HIV) display multiple defects in their B-cell compartment, even under antiretroviral (ART) treatment. Since most studies were performed in adults, we studied the effects of vertically acquired HIV infection on the build-up of the B-cell compartment in children.

Methods: We studied 58 ART-treated HIV-infected children and 115 age-matched healthy controls. Patients were characterized by CD4+ T-cell numbers and serum HIV RNA levels (RNA copies/ml). Furthermore, the absolute numbers of 2 naive, 6 memory-B-cell subsets and CD21low B-cells were determined by 8-color flowcytometry in peripheral blood.

Results: All HIV-infected children had near normal CD4+ T-cell numbers. Most patients had undetectable or low serum HIV levels (< 1,000 RNA copies/ml), and only a few patients had a serum HIV level >15,000 RNA copies/ml. Most memory-B-cell subsets were reduced in young HIV-infected children (< 5yr), normal at 5-15yr and again reduced in 16-20yr as compared to healthy controls. Interestingly, T-cell independent CD27-IgA+ B-cell numbers were severely reduced in all age categories. In contrast, IgM-only memory-B-cell numbers were increased until 5-9yr of age and normal in older children. Patients with detectable serum HIV RNA showed increased CD21low B-cell numbers that lacked CD24 expression.

Discussion & conclusion: Our results demonstrate impaired build-up of both T-cell dependent and independent memory-B-cell subsets in HIV-infected children despite ART-treatment. Furthermore, our results suggest direct effects of HIV on the development of the aberrant CD21low B-cell population. We are currently further studying the nature of the CD21low B-cell population.

O196

CHARACTERISTICS OF CHILDREN BORN TO HIV-INFECTED MOTHERS IN EQUATORIAL GUINEA

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Introduction: Equatorial-Guinea had an estimated prevalence of HIV-infection in pregnant woman of 7,3% in 2008. Not much is known about the children born to HIV-infected mothers in the country. The aim was to describe the characteristics of HIV-exposed children in a country without virological-diagnosis.

Methods: We retrospectively analized the HIV serostatus of children born to HIV-infected mothers in Bata, Equatorial-Guinea from june 2008. Diagnosis was made through rapid tests based on WHO recommendations for countries without virological tests.

Results: 71 patients were included. 46% of the mothers received antiretroviral treatment (ART) during pregnancy, treatment most used in mothers was Zidovudine, Lamivude and Nevirapine; 36% of the newborns received antiretroviral-prophylaxis, the regimen most commonly used was single dose of nevirapine. 95% of the children were born vaginally; 4 children received mixed-feeding and all the others were exclusivelly formula fed. 31 patients abandoned follow up. Forty patients completed the follow-up, 12 children were infected (30%)(12/40), 6 children died before definitive diagnosis and 22 were antibody-free at 18 months. The transmission rate of children born to mothers that received ART was 15% (2/13) versus 37% (10/27) of the children born to mothers that did not receive ART. There were no infections in the fifteen children that received prophylaxis and that their mothers were on ART.

Conclusions: In our cohort, ART in HIV-infected pregnant woman decreased HIV-vertical transmission but the rate of mother to child transmission is still very high. Many children were lost to follow-up so methods to increase it are needed.

O197

HIV CHARACTERISTICS AND EDUCATIONAL ACHIEVEMENT OF A COHORT OF HIV INFECTED ADOLESCENTS DUE TO VERTICAL TRANSMISSION

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[1]Immunodeficiencies Department, Hospital 12 de Octubre, [2]Pediatrics Department, Hospital Carlos III, [3]Pediatrics Department, Hospital de Getafe, [4]Pediatrics Department, Hospital Gregorio Marañon, [5]Pediatrics Department, Hospital La Paz, [6]Psiquiatric Department, [7]Immunology Department, [8]Epidemiology Department, Hospital Gregorio Marañon, [9]Apoyo Positivo, [10]Pediatrics Department, Hospital Príncipe de Asturias, [11]Pediatrics Department, Hospital de Mostoles, [12]Pediatrics Department, Hospital Niño Jesus, [13]Pediatrics Department, Hospital Severo Ochoa, Leganés, Madrid, Spain

Objectives: To assess immunovirological situation, psychosocial profile and educational achievement in a cohort of HIV vertically infected adolescents followed in 5 hospitals in Madrid.

Methods: Cross-sectional descriptive study. Data related to HIV infection were obtained every 3 months in routine visits. Patients and their parent/tutors were interviewed using a semi-structured questionnaire designed to evaluate adherence and psychosocial profile. The Strengths and Difficulties Questionnaire (SDQ) was also administered.

Results: 95 adolescents (median age 16.5 years (12.4, 20.6), 97% Spanish, 10% hepatitis C). Fifty four % of their mothers acquired HIV infection by using injection drugs. Thirty four % were on C3 CDC category(18% had encephalopathy). CD4 nadir ≤ 15% (63%). Median age at HIV diagnosis (0.59 years (0, 12.2)), at the beginning of antiretroviral (3 years (0, 14.5)) and of HAART (5.7years (0.6, 18)); 42% had received ≥ 3 HAART based regimens.Nowadays, 97% of patients have CD4 ≥15% and 72% viral load ≤ 50copies/ml. Adherence ≥95% doses (48 %). Regarding educational achievement, 90% were at school or college, 19% had lost ≥ 2 years. Most common psychosocial problem concerning SDQ was hyperactivity (33%).There weren´t relationship between academic achievement and CDC stage, CD4 nadir, encephalopathy, adherence and HAART regimens; however it was related to the educational profile of their parents.

Conclusion: Although current immunovirological situation of our adolescents is good, they had a long history of failures and change of antiretroviral. An important percentage have academical difficulties but it hasn´t been related to HIV parameters; however, parent´s academic profile seems to be very important.

O198

IMPROVING ANTIRETROVIRAL THERAPY ADHERENCE IN HIV-INFECTED CHILDREN. PILOT STUDY

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Introduction: Poor adherence to antiretroviral treatment (ART) is the commonest cause of treatment failure in children and adults living with HIV, and this is especially important during adolescence. Therefore, any analysis of ART effectiveness in children should include an evaluation of adherence to ART. The aim of this study is to assess the usefulness of an ART adherence monitoring program in an HIV-infected pediatric population.

Patients and methods: A pilot study, observational and cross-sectional, was performed, within the framework of the "Health Education Program for Optimizing Adherence in Pediatric Patients with HIV", which is part of the "I am not alone" project. Adherence was assessed simultaneously by different methods: personal interview, therapeutic drug monitoring, pharmacy dispensing records and evolution of viral load and CD4+ lymphocyte count.

Results: Twenty patients were included (50% female, median age 14.5 years). Percentage of self-reported full adherence was 90% (95% CI: 70-97.2%); however, the median adherence percentage according to pharmacy dispensing records was significantly lower (83.3%, SD=32.88). The average of drugs and dosage forms per day were 3.5 (SD=0.83) and 5.5 (SD=2.72), respectively. There was an inverse relationship between the number of dosage forms per day and adherence scores ($F=13.8$; $p=0.002$). No single method was statistically related to adherence, although therapeutic drug monitoring showed a trend towards significance.

Conclusions: Global adherence to ART was high and was favored by simple regimens. Self-reported adherence overestimated real adherence to ART in our cohort. The simultaneous use of different methods to assess adherence is recommended in HIV-infected children.

O199

HIGH PREVALENCE OF LOW VITAMIN D IN HIV VERTICALLY INFECTED CHILDREN LIVING IN IRELAND

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Introduction: In addition to its key role in bone mineral metabolism, Vitamin D has important immunomodulatory and antiinfective properties. Development of clinical rickets in a 14 year old boy on HAART (FTC/TDF/EFV) prompted an audit of Vitamin D status in our HIV infected cohort.

Methods: Cross-sectional study of vertically HIV infected children attending the National Centre for Paediatric HIV in Ireland. 25 (OH) Vitamin D levels were defined as: deficient, ≤27.5nmol/L; low, >27.5-75nmol/L and normal, >75nmol/L. Parathyroid hormone (PTH) levels < 65ng/mL were considered normal.

Results: Data were available on 63 children (32 male). Ethnicity: African, 50; Caucasian, 10; and mixed African-Caucasian, 3. Forty-nine children were receiving HAART (TDF, 19; EFV, 19; and 8/19 both TDF and EFV). Median Vitamin D level was 43nmol/l (range, 7.8-101). Vitamin D levels were: deficient, 15 (24%); low, 42 (66.5%); and normal, 6 (9.5%). Median PTH level, 65ng/mL (range, 15.8 - 804). PTH levels were elevated in 9 (15%). Seven children (11%) were Vitamin D deficient with elevated PTH levels, 3 with associated hypocalcaemia and hypophosphatemia. Two received EFV; 1, TDF; and 3, TDF/EFV containing HAART. Urea, Creatinine, Urinary Calcium/Creatinine and Protein/Creatinine ratios were normal in 42 of 43 (98%) children. One child had pre-existing HIV nephropathy.

Conclusion: The majority (57/63, 90.5%) of our cohort of vertically HIV infected children have low Vitamin D. PTH levels were elevated in 15%. In the absence of demonstrable renal dysfunction, further study of additional mechanisms eg. inadequate intake, decreased absorption, drug-effect, insufficient sunlight, ethnicity is warranted.

O200

NORMAL BONE MINERAL CONTENT AMONG HIV-UNINFECTED CHILDREN PERINATALLY EXPOSED TO ANTIRETROVIRALS

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Background: A decrease < 2% in HIV mother-to-child transmission has occurred upon the implementation of prophylactic measures. Most HIV-uninfected infants are perinatally exposed to antiretrovirals, and potential long-term adverse effects of such exposure remains of concern. Low bone mineral content (BMC) is a recognized complication of HIV infection that has been noted more frequently in the era of highly active antiretroviral therapy (HAART), but very scarce data on this issue are available for children perinatally exposed to antiretrovirals.

Materials and methods: We performed a cross-sectional study in a cohort of HIV-uninfected prepubertal children born to HIV-infected mothers and perinatally exposed to antiretrovirals that are followed up in tertiary-care pediatric hospital in Barcelona (Spain). The following exclusion criteria were used: age at birth below 35 weeks, birth at weight >3SD or < 3SD, chronic conditions and long-term use of corticoids. BMC was measured by dual energy X-ray absorptiometry. Clinical, anthropometric data and dietary intake of calcium (mg/day) were obtained at the time of assessment.

Results: BMC was measured in 70 prepubertal children (51% females; mean age: 6.8 years, range: 4-9 years). Mean (range) daily calcium intake estimations were 820mg (600-1350mg). Mean (range) BMC Z-score values were -0.08 SD (-1.99 to +2.15) and were not different from a population norm Z-score. When exposure to antiretrovirals (type and time of exposure) and other perinatal variables (exposure to other drugs, ethnicity, weight at birth or prematurity) were taken into account, differences were neither observed.

Conclusions: HIV-uninfected prepubertal children perinatally exposed to antiretrovirals show normal BMC values.

O201

EFFECTS OF SIMPLIFICATION OF HAART IN HIV INFECTED CHILDREN

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Background and aims: HAART has improved survival in HIV-infected patients but may be associated with important adverse events. Simplification of HAART may improve adherence and metabolic alterations. The aim was to describe virologic, inmunologic, clinical and lipid profile outcomes in HIV-infected children after simplification.

Methods: Prospective, multicenter study of children from the 310 HIV-infected children and adolescents in the Madrid Cohort since 2003. Fifty-six simplifications were studied in 44 patients. The simplified regimens included protease inhibitor withdrawal (type 1), pill number decrease(type 2), change from BID to QD (type 3), change in nucleoside-analogs to decrease toxicity (type 4) and use of a “combo” with FTC+ABC+EFV(type 5).

Results: Median age at the time of simplification was 13.6(10.6-16.6) years; 18 (40.9%) were clinical category C and 11(25%) category B. In 13 patients (23.6%) simplification was type 1, 33(60%) type 2, 24(43.6%) type 3, 24(43.6%) type 4 and 18 (32.1%) type 5.

No patients experienced severe clinical events. Two patients developed an increase in viral load. The median baseline CD4% was 33.8%(SD 6.3), and increased at 6 (34.9%; p=0.021), 12(36.3%; p=0.005), 18(35.2%; p=0.050) and 24 months (34.8% p=0,074).

Median baseline lipids were: cholesterol 186(SD 44.6), triglycerides 157(SD 106), which decreased at 6(160 cholesterol; p< 0,01, 128 triglycerides; p=0.014), 12 (163 cholesterol; p=0.06, 108 triglycerides; p=0.04), 18(168 cholesterol; p=0,36, 116 triglycerides; p=0,3) and 24 months (163 cholesterol; p=0.021, 105 triglycerides 0.093).

Conclusions: In our cohort simplification was safe and well tolerated. Furthemore, the immunological function and lipid profile of these children improved.

O202

13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN CHILDREN PREVIOUSLY PARTIALLY IMMUNIZED WITH 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7): PHASE 3, OPEN-LABEL TRIAL

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Background and aims: As PCV13 is introduced, children who begin vaccination with PCV7 (serotypes 4, 6B, 9V, 14, 18C, 19F, 23F) may complete their vaccination with PCV13 (additional serotypes 1, 3, 5, 6A, 7F, and 19A). This open-label phase 3 study in Sweden evaluated immunogenicity and safety of PCV13 in children previously administered 1 or 2 doses of PCV7.

Methods: Healthy infants previously administered PCV7 at ages 3 months (group 1; n=118) or 3 and 5 months (group 2; n=116) received PCV13 at ages 5 (group 1 only) and 12 months (both groups). Serotype-specific IgG responses were assessed. Local reactions and systemic events were collected 7 days postvaccination. Adverse events were also collected.

Results: The Table shows serotype-specific IgG geometric mean concentrations before and after completion of the vaccine series. Local reactions and fever were mostly mild or moderate.

Conclusions: PCV13 was immunogenic and safe in infants and toddlers previously partially immunized with PCV7. One or two doses in infants or toddlers induced immune responses to the additional serotypes.

Serotype	Group 1 pre-12-month dose	Group 1 post-12-month dose	Group 2 pre-12-month dose	Group 2 post-12-month dose	**Serotype**	Group 1 pre-12-month dose	Group 1 post-12-month dose	Group 2 pre-12-month dose	Group 2 post-12-month dose
4	0.66	5.27	0.62	5.06	**1**	0.46	14.65	0.01	1.58
6B	0.83	9.63	0.65	8.75	**3**	0.40	1.85	0.05	1.34
9V	0.74	3.50	0.70	3.33	**5**	1.18	7.02	0.33	1.44
14	1.99	9.22	2.23	9.30	**6A**	0.71	6.14	0.24	2.48
18C	0.35	2.93	0.44	3.87	**7F**	1.08	5.86	0.02	3.55
19F	0.85	7.70	0.81	8.31	**19A**	1.06	7.25	1.55	13.16
23F	0.33	3.27	0.41	4.40					

[Pneumococcal serotype-specific IgG GMC (µg/mL)]

O203

HIGHER *STAPHYLOCOCCUS AUREUS* COLONIZATION IN 11-MONTH-OLD CHILDREN FOLLOWING PCV-7 VACCINATIONS IN INFANCY

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Background: Previously we observed in a randomized control trial (RCT) an increase in *S. aureus* carriage in PCV-7 vaccinated 11-month-old children (NCT00189020). A negative correlation between *S. aureus* and PCV-7-serotype carriage was suggested. We therefore investigated *S. aureus* colonization in a vaccinated population 3 and 4 years after PCV-7 implementation.

Methods: As a follow up of the RCT (2005), we performed in 2009 and 2010 two cross-sectional studies collecting nasopharyngeal swabs from PCV-7 vaccinated children 11 and 24 months of age, and from one of the parents of the latter group (n~330 per group). Swabs were cultured for *S. aureus* and *Streptococcus pneumoniae*: pneumococcal isolates were serotyped by Quellung method.

Results: *S. aureus* carriage rates increased from 5% in 2005, to 9% and 14% in 2009 and 2010, respectively, in 11-month-old children (2005 vs. 2009: $p=0.03$; 2005 vs. 2010: $p< 0.001$), but were stable over time in 24-month-old children (6-8%). *S. aureus* colonization in parents increased from 20% in 2005 to 32% and 34% in 2009 and 2010, respectively ($p< 0.01$). Pneumococcal carriage rates remained relatively stable between 2005 and 2010, although a strong shift from PCV-7 to non-PCV-7 serotypes was observed.

Conclusions: In line with the observations of the previous RCT, we observed increased *S. aureus* carriage rates after PCV-7 implementation in 11-month-old children and parents from 24-month-old children, but not in 24-month-old children. Clinical implications of our observations need to be further studied.

O204

LIMITED IMPACT OF THE 7-VALENT PNEUMOCOCCAL VACCINE ON PAEDIATRIC EMPYEMA IN THE NORTH OF ENGLAND

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Background: The incidence of paediatric empyema has increased substantially in the UK since 1995. Paediatric empyema in the UK is predominantly a pneumococcal disease and a 7-valent pneumococcal conjugate vaccine (PCV-7) was introduced into the UK routine immunisation schedule in September 2006. A recent report has suggested a significant reduction on the incidence of empyema following introduction of the vaccine[1]. The objective of this study was to investigate the impact of the pneumococcal conjugate vaccination programme on the incidence of paediatric empyema in our region.

Methods: An interrupted time-series analysis was performed using clinical data from empyema admissions for children aged up to 14 years in Northern England from May 1995 to April 2010. Seasonality was accounted for by including monthly temperature measurements within the regression models.

Results: A total of 298 patients were included in the study. The incidence of empyema increased from a mean monthly rate of 1.1 cases per million children in 1996 to 5.2 per million in 2009. No significant impact was observed on the number of cases following the introduction of the PCV-7 vaccine (regression co-efficient 0.096, 95 % CI -0.038 - 0.23, p = 0.16).

Conclusions: The PCV-7 vaccine had no impact on the incidence of paediatric empyema in Northern England. These findings do not confirm a recent report of a decline in the incidence of paediatric empyema following the introduction of this vaccine.

1. Koshy E, et al. Thorax. 2010; 65(9): 770-4.

O205

MEMORY B CELL RESPONSE TO A PCV-13 BOOSTER IN 3.5 YEAR OLD CHILDREN PRIMED WITH EITHER PCV-7 OR PCV-13

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Background/aims: Direct vaccine-induced host immunity to pneumococcal disease is determined by anti-polysaccharide antibodies and induction of immune memory. There is limited information about the role of memory B cells (MBC) in maintaining antibody levels following infant vaccination. We studied antigen-specific MBC in children 2.5 years after infant immunisation and after a booster dose of a 13-valent pneumococcal conjugate vaccine (PCV-13).

Methods: We recruited children who had participated in a previous multicentre RCT comparing PCV-7 and PCV-13 in infancy at the age of 3.5 years. Blood was taken before and 1 month post-booster. MBC were quantified using a stimulated ELISpot assay for serotypes 1,3,4,14,19A,23F.

Results: In total, 98 blood samples were available for analysis. Numbers of MBC specific for serotypes included in both the PCV-7 and PCV-13 (4,14,23F) were low at baseline and did not differ between the groups (except for serotype 14: higher in the PCV-13 group). MBC numbers post-booster were higher than baseline for these 3 serotypes with no differences between the groups. For serotypes only included in PCV-13 (1,3,19A), baseline MBC numbers were lower in the unprimed group for all 3 serotypes (6/0/9 versus 10/4/11 MBC/10^6 cells, significant only for serotype 3; $p< 0.01$). However, post-booster MC frequencies were similar for serotypes 1,3,19A in both groups (16-37 MBC/10^6 cells; $p>0.1$).

Conclusions: A PCV-13 pre-school booster results in similar post-booster MBC frequencies in individuals irrespective of prior priming with PCV-7 or PCV-13 for serotypes 1, 3 and 19A despite lower pre-booster MBC frequencies in the unprimed group.

O206

DEVELOPMENT OF A RAPID METHOD FOR IDENTIFICATION AND QUANTITATION OF PNEUMOCOCCAL CAPSULAR POLYSACCHARIDES

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Background and aims: During the development and release of a pneumococcal vaccines, it is essential to identify and estimate the concentration of capsular polysaccharides at various stages. The conventional methods employed for this purpose e.g. colorimetric assays, rate nephelometry, ELISAs etc., have limitations of lack of sensitivity/specificity and/or are time consuming. We developed a highly sensitive and rapid bead based assay for simultaneous identification and quantitation of pneumococcal polysaccharides(PnPS) at various stages of vaccine development viz., polysaccharide production, purification, conjugation and final vaccine formulation.

Methods: A competitive inhibition assay was performed using Luminex microspheres coupled to various target polysaccharides. The PnPS of various serotypes were coupled with polystyrene microspheres by standardized methods. The standard and unknown samples were incubated with defined specific antibody dilutions followed by incubation with PnPS-Beads and conjugated secondary antibody. The reaction was estimated using BioPlex 200 system. The assay was evaluated for various validation parameters as per ICH guidelines.

Results: The 3 hour assay was found to be highly specific and sensitive. Assay could detect upto 15 ng/ml of various PnPS with a spiking recovery of 80-120%. Assay was highly repeatable with an Inter- and Intra-assay percent CV within + 20%. The assay was applicable for multivalent sample analyses.

Conclusions: The x-MAP technology based assay can be highly useful tool with multiplexing possibilities for pneumococcal vaccine development and characterization. The assay is being explored for clinical diagnosis of pneumococcal infections also. The authors would thank PATH, USA and its consultants for providing all the technical inputs.

O207

COMPARISON THE EFFICACY OF ORAL DEXAMETHASONE WITH IM DEXAMETHASONE IN TREATMENT OF CROUP

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Backgrounds: Croup, or acute laryngotracheobronchitis, is the most common cause of upper airway obstruction in children. In this study, the efficacy of intramuscular dexamethasone and oral dexamethasone are compared for treatment of croup.

Methods: This is a double blind randomized trial involving 68 children with group that dived into two groups, the fist group received 0.6 mg/kg intramuscular dexamethasone and the second group received 0.6 mg/kg oral dexamethasone. The clinical score, respiratory rate, heart rate, O2 saturation and clinical response were assessed before and then hourly for four hours after treatment.

Results: The respiratory rate of the second group in the 4^{th} hours was significantly lower than first group. There was no statistical difference among clinical score, respiratory rate in the three first hour, heart rate, O2 saturation and clinical response.

Conclusion: Oral and intramuscular have the same effectiveness for treatment of croup and oral dexamethasone was proposed because this is a non invasive procedure.

O208

HOSPITALIZED CHILDHOOD COMMUNITY ACQUIRED PNEUMONIA (CAP) IN BELGIUM: PNEUMOCOCCAL ETIOLOGY AND SEROTYPE DISTRIBUTION BASED ON CULTURE AND SEROTYPE SPECIFIC SEROLOGY

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Aim: To evaluate pneumococcal etiology and serotype (ST) distribution in hospitalized children with community acquired pneumonia (CAP).

Methods: Children < 15y with X-ray confirmed CAP were included. Pneumococcal etiology was evaluated by culture with serotyping on blood (BC) and pleural fluid (PF) samples, and by IgA&IgG serotype specific serology (SSS) against the serotypes 1, 5, 6B, 7, 9N+V, 14, 19A, 19F, 23F. Seroconversion criteria: >3-fold rise in Ab-concentrations for IgG or ≥2-fold rise for IgA, with an Ab-concentration ≥600 pg in the convalescent sample. In case seroconversion criteria were met for ≥2 serotypes, the serotype with the highest Ab-concentration was retained.

Results: 561 eligible patients were included, median age: 3.6 years. 80% had lobar pneumonia, though 18% with pleural effusion. PF-culture was positive in 12/49 cases (24%), with S. pneumoniae isolated in 7.

From BC S. pneumoniae was isolated in 45 of 538 cases (8.4%). ST 1 was most prevalent and was identified in 53% of cases. ST 5, ST 3 and ST 19A were identified in 21%, 8%, and 8% respectively.

In 86 of 149 (58%) culture-negative cases, seroconversion was detected. IgA&IgG-SSS identified serotypes 1, 7, 19A and 5 as most prevalent.

None of the identified serotypes are included in the PCV7 currently used in Belgium.

Conclusions: The use of SSS may substantially increase the diagnostic yield in childhood-CAP. However, SSS results must be interpreted with caution as SSS-criteria need further validation

O209

THE EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE (ETS) ON PNEUMONIA RISK IN CHILDREN UNDER 7YEARS IN NORTHERN NIGERIA

E.O. Odiase, Children/Adolescents As SmokeFree Examples-CASE

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Background: The numerous effects of ETS on the non-smoking public have being evidenced through decades of research. This does not only affect adults but children. ETS effects on children have shown to be grave as it worsens asthma conditions, increases pneumonia cases and causes Sudden Infant Death Syndrome (SIDS). This study considers pneumonia risk on children under age 7 in Northern Nigeria exposed to ETS.

Methods: Most residents in all 44 Local Government Areas (LGAs) in Kano State of Northern Nigeria took part in a population-based large-scale cross-sectional survey in Kano state from 2007-2010. Demographic information coupled with socioeconomic status, smoking status and house environment of each household member, was collected from participants. General records were takent.

Results: Out of a total of 528, 800 people resident in 102,334 homes identified in the survey areas and visible/present, 52,888 (10%) were children aged 7 years and below. While the prevalence of ETS exposure on children was 81%, the prevalence of reported pneumonia cases was 3.5%. Multiple logistic regression analysis showed that exposure to ETS was independently associated with reports of pneumonia cases (adjusted odds ratio 1.55, 95% CI 1.25 to 1.92). The prevalence of tobacco smoking was higher among men than women (63.5% vs 44.1%). It is estimated that 32.7% of childhood pneumonia in the northern region of Nigeria is attributable to ETS.

Conclusions: Attention should be given to reduction to children's exposure to ETS not only in Nigeria but in all affected areas mostly all parts of the world.

O210

(PRE)SYNCOPE IN THREE MASS VACCINATION CAMPAIGNS IN THE NETHERLANDS; MENC IN 2002, HPV IN 2009, AND H1N1 IN 2009-2010

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Background and aims: In the Netherlands, three large vaccination campaigns were held, in 2002, 2009, and winter 2009/2010 against Meningococcal C (MenC), human papillomavirus (HPV) and pandemic influenza A(H1N1) infection, respectively.MenC (1 dose) targeted 1-18-year-olds, HPV (3 doses) girls 12-16-year-old and H1N1 (2 doses) children 0.5-4-years-old and parents/siblings of younger infants. Monitoring included immediate adverse events (imAE).
Methods: Questionnaires distributed to all vaccination sites addressed all imAE and numbers of vaccinees. Coverage- denominators (age, sex, and dose) were available from national vaccination registries.
Results: Reported imAE followed most frequently dose1. Presyncope/syncope were predominant (peak rates in pre-adolescents), sometimes with subsequent injury. Accompanying symptoms were nausea/vomiting, rash, or jerks.

	MenC	HPV	H1N1
Target group	1-18y	12-16y	0.5-4y + parents/siblings younger infants
Campaign Coverage	93%	51%	71%
Schedule	1 dose	3 doses	2 doses
Vaccinees monitored (%)	1,817,558 (63%)	143,278 (74%)	510,296 (70%)
Monitored doses	1,817,558	408,663	928,735
Any immediate AE/10,000 vaccinees (dose 1)	23.0	44.0	2.6
Any immediate AE/10,000 vaccinees (any dose)	23.0	77.0	3.4
Presyncope-syncope/10,000 vaccinees (dose 1)	21.4 (6-14y)	20.5 (12-16y)	26.5 (5-10y)
Presyncope-syncope/10,000 vaccinees (any dose)	21.4	48	33.4

[Comparison vaccination campaigns for imAE]

Conclusions: Most often reported imAE were presyncope and syncope. No serious imAE were reported. Careful follow-up of reports should avoid undue apprehension, false contra-indications, and the stigma of epileptic seizure in syncopal children with jerks. Attention should be paid to prevention of fainting and subsequent injury.

O211

SPECIAL IMMUNIZATION SERVICE (SIS) IN PADOVA: 8 YEARS OF EXPERIENCE

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Background and aims: Concerns on vaccines' safety are increasing, leading a lack of compliance in vaccination plans. Special Immunization Services (SIS) for children at risk of adverse reaction (AR) may improve immunization coverage. From 1999 a SIS has been activated at the Pediatric Emergency Unit of Padova. The aims of this study are to describe its experience, find out admission criteria and evaluate its role in improving vaccination coverage.

Methods: For each child evaluated for admission at SIS in the period 1 January 2002 - 31 July 2010, data on age, sex, type of vaccine required, previous AR to any vaccine were reported in a dedicated form. We performed a Univariate Analysis and a Multivariate Analysis to identify the most important admission to SIS's criteria.

Results: 489 vaccines (47.4 MMR or MMRV, 20.8% hexavalent) were administered to 352 children. All the children with a previous immediate AR to vaccination were admitted to SIS. The other admission to SIS's criteria resulted to be anaphylaxis and non-anaphylactic allergies (OR = 13.54 with CI (95%)= 1.78 to 103.23 and p value < 0.01 and OR= 2.01 with CI (95%) = 1.09 to 3.68 and p value < 0.02 respectively). We observed 6 (1.22%) mild but no severe AR. 99.9% of children admitted to the SIS completed their vaccination plan.

Conclusions: No serious AR after vaccination at SIS have been reported. The most important admission's criteria was previous AR to vaccination. SIS is an important means to complete the vaccination plan of high-risk children.

O212

VACCINE UPTAKE DETERMINANTS IN THE NETHERLANDS

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Background: Participation in nationwide vaccination programmes is not self-evident. Insight in determinants of vaccine uptake is important to guide future communication activities.

Methods: The study population consisted of children born in 2005 according to the national vaccination register Præventis. A hierarchical, or multilevel, logistic regression model was used to quantify associations between vaccination status (individual level) and proxy variables for ethnic background (country of birth parents, individual level), socioeconomic status ('status score' 2006, postcode level) and religious objection to vaccination (percentage voters for Reformed Political Party 2006, municipal level).

Results: Most children of whom parents were not both born in the Netherlands had a lower combined full uptake of all vaccines together. Although children of whom both parents were born in Turkey or Morocco did not have a lower full uptake for single vaccines, the combined full uptake was lower. The same counts for children of whom one parent was born in the Netherlands and one in another western country and children of whom one parent was born in a western and one in a non-western country. A possible explanation could be that foreigners are known to change their residence more often. Postcode areas with a higher socioeconomic status and municipalities with less religious objection to vaccination were associated with a higher full vaccine uptake.

Conclusions: Ethnic background, religious objection to vaccination and socioeconomic status to a lesser extent are important determinants of full vaccine uptake among children in the Netherlands. Future research should focus on reasons behind these differences.

O213

EPIDEMIOLOGY OF THE UNVACCINATED: A BEHAVIOUR CHANGE COMMUNICATIONS FRAMEWORK AND TOOLKIT FOR THE WHO EUROPEAN REGION

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Background and aims: The European Region has documented pockets of low immunization coverage for childhood vaccines, such as measles, mumps and rubella (MMR), oral polio vaccine (OPV) and pertussis which have led to growing susceptible populations being able to sustain disease transmission leading to outbreaks. In many countries, populations are excluded from services or refuse to be vaccinated.

To address the behavioural barriers to vaccination faced by such segments of the population, Member States need to better understand the epidemiology of the susceptible populations and appropriately create demand for vaccines, change risk perception and ensure equity to immunization services.

Method: The WHO Regional Office for Europe is developing a Toolkit that comprises of formative research questionnaires and moderator guides, a behaviour change communications framework, and a menu of best practices and lesson learned from social marketing and vaccine communications programmes around the world. The behavioural determinant framework is adapted from tried-and-tested social marketing approaches. The framework helps shape a response to the motivational, ability and opportunity determinants of vaccination behaviour of at-risk, susceptible or vulnerable populations.

Findings: Member States will be equipped with the Toolkit and trained to epidemiologically and socially profile and segment susceptible populations, and appropriately respond according to their circumstances, behavioural barriers and communication/media preferences. The Toolkit components will be piloted in Bulgaria in 2011.

Conclusions: The Toolkit will reframe the response to reaching the remaining susceptible populations in the WHO European Region and, in turn, assist the Region in meeting elimination and eradication goals.

O214

COST-EFFECTIVENESS OF A COCOONING STRATEGY IN NORWAY

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Background and aims: Norway has the highest reported incidence of pertussis in Europe.Immunity against pertussis wanes over time so adolescents and adults become susceptible and act as a reservoir for pertussis transmission.

Until completion of the primary vaccination course newborns remain vulnerable to pertussis which could be potentially fatal at this age.

Parents are the source of pertussis transmission to infants in 52% of the cases. Immunisation of newborns' parents (e.g. cocooning), would potentially reduce the risk in infants.This analysis assesses the cost-effectiveness of such immunisation strategy.

Methods: A decision-tree model was used, and data on pertussis morbidity and costs was collected for infants below 1y and adults (20-39-year). Infant's and parents' cohort sizes were 60,000 and 120,000 respectively. Pertussis in older age groups is highly under-reported, and for parents an under-reporting factor of 10 was assumed.

Health benefits and costs were estimated for both cohorts. Incremental cost-effectiveness ratios (ICER) were calculated from payer and societal perspectives. A univariate sensitivity analysis was performed.

Results: The cocooning strategy (55% coverage) was found to reduce by 24% the incidence of pertussis among infants and 49% among parents. The strategy was estimated to be cost-effective from payer's (NOK 338,158/QALY) and societal perspective (NOK 167,712/QALY). The sensitivity analysis shows the ICER to be most sensitive to the underreporting factor. Lower under-reporting factor (5), would still lead to an ICER below NOK 500,000/QALY (e.g. the Norwegian threshold).

Conclusion: This study estimated that pertussis cocooning strategy would likely be cost-effective in Norway.

O215

HPV-VACCINATION OF BOYS OR ADDITIONAL COHORTS OF GIRLS: WHERE IS THE GREATEST BENEFIT FOR CERVICAL CANCER PREVENTION IN ITALY?

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Background: Cervical cancer (CC) vaccination has been implemented in Italy primarily targeting girls aged 12. To further reduce the CC burden should a limited budget preferentially be used to extend vaccination to boys or improve coverage in young adult women?

Methods: A published cohort model adapted to Italy estimated the CC reduction from different vaccination strategies: vaccinating females at the age of 12, 15 or 25 or vaccinating boys at the age of 12. The maximum benefit from vaccinating boys is assumed to equal the CC reduction that would results from vaccinating all non-vaccinated of the same age girls. Each cohort size was 280,000. Vaccine efficacy (VE) was based on clinical trial results (including cross-protection of other non-vaccine HPV-types) and HPV-type distribution. VE was differentiated for pre- and post-sexual debut. Vaccine protection was assumed life-long. Sensitivity analysis was performed on vaccine coverage (VC), vaccinated boys and girls overlap, and all HPV cancer types inclusion.

Results: Under a fixed budget and 70% VC, vaccinating 12, 15, 25 years-old females or 12 years-old boys would prevent 937, 884, 647 or 401 CC respectively. Vaccination of boys will only add more health gain if 12 years-old girls VC is low with low overlap between vaccinated boys and girls and vaccinated boys have numerous partners, resulting in large indirect vaccine effect. The results are strengthened after accounting for other HPV-types.

Conclusion: For a fixed additional budget extending vaccination of female instead of boys will maximise the number of CC prevented.

O216

MUMPS OUTBREAK AMONG A HIGHLY VACCINATED STUDENTPOPULATION, THE NETHERLANDS, 2009-2011

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Background and aims: In December 2009, a mumps outbreak started among university students in the Netherlands. In March 2010, transmission during a student party caused a sudden increase in the incidence. Individuals aged 27 and below have been offered two doses of MMR in the Dutch immunisation programme. The coverage of this has consistently been over 90%.

Methods: We analysed mumps notification data between 1-12-2009 and 19-1-2011. A case of mumps was a person with at least one of the following: acute swelling of a salivary gland, orchitis or meningitis, with either laboratory confirmation of mumps or contact with a laboratory confirmed mumps case.

Results: In the study period, 590 notified mumps cases occurred. The median age was 22 years. Of cases, 57% was male and 61% was a university student. For 51 persons complicates were reported (9% of all cases), mainly orchitis (45 cases, 14% of male patients). Eleven persons (2%) were hospitalized, most frequently due to orchitis (7 cases). Information about vaccination status was available for 87% (513) of cases. Of these, 16% were unvaccinated, 10% were vaccinated once, and 74% were vaccinated at least twice. Genotype G5 is the circulating strain in this outbreak.

Conclusions: A mumps outbreak is ongoing mainly among university students who received two doses of MMR in the past. Orchitis is the most frequently reported complication. Subsequent sub-fertility is of concern. Further research into reasons for vaccine failure, mumps virus transmission in vaccinated populations, and chronic sequelae of mumps orchitis is required.

O217

GENOTYPE DISTRIBUTION AND ROTAVIRUS GASTROENTERITIS HOSPITALIZATIONS FOUR YEARS AFTER VACCINATION IN SAO PAULO, BRAZIL

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Background: Early effects, after implementation of rotavirus human vaccine in Brazil in 2006, were promising, showing a marked decline in rotavirus gastroenteritis (RVGE) hospitalizations among children aged < 5 years. A high predominance of G2P[4], probably reflecting natural annual fluctuation, was also observed. The aim of this study was to confirm the early impact of immunization on the incidence of severe RVGE and assess genotype distribution over time.

Methods: We performed a 7-year (2004 -2010) prospective surveillance, at two sentinel hospitals in Sao Paulo, monitoring the incidence of RVGE and acute gastroenteritis (AGE) hospitalizations among children younger than 5 years of age. Since 2006 genotypes of positive samples were determined by reverse transcription polymerase chain reaction.

Results: After vaccine introduction we observed a significant reduction in the proportion of rotavirus-positive results among children aged < 5 years hospitalized with RVGE of 42.2%*, 41.2%*, 72.2%* and 60.7%* (*p< 0.001), and a reduction in the number of all-cause hospitalizations for AGE of 29%, 28%, 39% and 40%, respectively from 2007 to 2010.

Genotype G2P[4] accounted for 8.8%, 58.8%, 73.7%, 75% and 66.7% of all cases identified, respectively, from 2006 to 2010.

Conclusions: Four years after vaccine implementation, a marked and sustained decline in RVGE hospitalizations was demonstrated among children aged < 5 years, confirming the early impact benefits of the vaccination. Although continued surveillance studies are still needed to correctly address this issue, it is unlikely to have persistent predominance of G2P[4], for four years, as an exclusive result of natural fluctuation.

O218

IMMUNOGLOBULIN DEFICIENCY IN CHILDREN WITH HIB VACCINE FAILURE

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Background: Immunoglobulin (Ig) deficiency in children with Hib vaccine failure is well-described, but its clinical significance is unknown.

Aims: To estimate the prevalence of Ig deficiency in children with Hib vaccine failure several years after infection and to determine their risk of recurrent infections.

Methods: Children who developed invasive Hib disease after immunization with Hib conjugate vaccine from 1992 to 2006 were identified through national surveillance. Participation involved completion of a questionnaire and a blood sample from the child.

Results: A completed questionnaire and blood sample was provided by 170 children at a median of 4 years after infection, equivalent to 1035 child-years of follow-up. Ig deficiency was present in 11.2% and was associated with age < 2 years at onset of Hib disease (63.2% vs. 39.7%, P=0.05) and receiving at least two antibiotic courses/year in early childhood (57.9% vs. 25.8%, P=0.004), but not with clinical presentation, severity of Hib infection or risk of other serious infections requiring hospitalization. In a logistic regression model, antibiotic use was independently associated with presence of an underlying medical condition (OR=7.3; 95% CI=2.3-22.7; P=0.001) and Ig deficiency (OR=5.4; 95%CI=1.8-16.0; P=0.003), while breastfeeding was protective (OR=0.30; 95%CI=0.14-0.65; P=0.002).

Conclusions: 4 years after infection, the prevalence of Ig deficiency in children with Hib vaccine failure is half that reported in the first few months after Hib infection. Young children with Hib vaccine failure may have quantitative as well as qualitative antibody defects, which predisposes them to recurrent minor and occasionally serious infections, but improves with age.

O219

PROPHYLACTIC PARACETAMOL IN INFANTS DECREASES FEVER FOLLOWING CONCOMITANT ADMINISTRATION OF AN INVESTIGATIONAL MENINGOCOCCAL SEROGROUP B VACCINE WITH ROUTINE IMMUNIZATIONS

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Background: Adding new vaccines to routine infant schedules necessitates concomitant administration, with consequences on reactogenicity profiles, notably temperature. As prophylactic paracetamol has been reported to interfere with immune responses (Prymula et al. Lancet 2009; 374: 1339-50), we present data showing effective temperature control by prophylactic paracetamol without compromising immunogenicity in a study of a novel, multicomponent, meningococcal serogroup B vaccine, 4CMenB.

Methods: Subsets of healthy infants (n = 183-184) from a large randomised, multicentre, partially observer-blind study received three doses of routine vaccines (DTaP-HPV-IPV/Hib and PCV7) at 2,3,4 months of age, administered concomitantly with 4CMenB or 4CMenB with prophylactic paracetamol at 0, 4-6 and 8-12 hours postvaccination. Immunogenicity at 5 months was measured by standard assays for routine vaccines, and serum bactericidal assay using human complement (hSBA) to three MenB strains selected for the vaccine antigens. Rectal temperature was monitored for 7 days after each dose.

Results: Postvaccination, temperatures ≥38.5ºC and ≥39.5ºC were observed after any dose in 69.0% and 8.2% with concomitant 4CMenB, and 39.3% and 3.3% with 4CMenB and prophylactic paracetamol. At 5 months, there were no significant differences in immune responses to routine vaccines between the groups. Three doses of 4CMenB elicited hSBA titers ≥5 in 75-100% of subjects against the three test strains, unaffected by paracetamol administration.

Conclusions: Prophylactic paracetamol decreased fever after 4CMenB with concomitant vaccines with minimal impact on immune responses to concomitant vaccines which probably have no clinical significance.

O220

DETECTION OF FUSOBACTERIAL INFECTION IN A CULTURE-NEGATIVE BRAIN ABSCESS WITH 16S RRNA GENE PCR

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Background and aims: We report a case of *Fusobacterium* mastoiditis complicating brain abscess, in a healthy child.

Methods: A 13 month-old girl presented with a 3-week history of right-ear discharge and pyrexia. She had already received 3 different courses of oral antibiotics following reviews in primary care. Examination revealed drowsiness and lethargy, left-sided gaze, hoarse voice, and increased muscle tone with opisthotonus. Mucopurulent pus was discharging from the right ear-canal. GCS was fluctuating between 12-14/15. An ear-swab obtained a week before, showed polymicrobic growth.An urgent CT revealed a rim-enhancing lesion within the right-cerebellar hemisphere, with skull disruption and bony destruction within the temporal and mastoid bone. There was mass effect with compression of the 4th ventricle and dilatation of the 3rd and lateral ventricles.

Results: Ceftriaxone and Metronidazole were commenced and she was treansferred for neurosurgical care. The abscess was drained and same antibiotic-regimen was continued with significant clinical improvement within 48-hours.Pus cultures were negative however bacterial 16-S-rRNA gene-PCR detected presence of *Fusobacterium species*. A 4-weeks course of the above antibiotics was administered. A repeat brain-MRI revealed residual collection an additional 2-weeks of IV antibiotics was continued, followed by 2-weeks of oral Linezolid.

Conclusions: Fusobacterial invasive infections are rare in children. Usually these patients have received 1-2 courses of oral antibiotics and the likelihood of pathogen isolation is very difficult.The use of 16SrRNA gene-PCR is of vital importance in these cases. Combined surgical and antimicrobial therapy is associated with recovery. However the appropriate duration of antimicrobial therapy remains unclear.

O221

TIMELINESS AND COMPLIANCE OF ROTAVIRUS VACCINATION IN AUSTRALIA

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Background and aims: Two licensed rotavirus (RV) vaccines are funded under the Australian National Immunisation Program for all children born since May 2007. A two-dose vaccine, RIX4414, (*Rotarix*™, GlaxoSmithKline Biologicals) is funded in New South Wales (NSW). A three-dose vaccine, RV5 (*RotaTeq*™, Merck and Co.) is funded in Queensland (QLD). We examined the compliance and timeliness of vaccination during 2007-2009.
Methods: Data from the Australian Childhood Immunisation Register (ACIR) was used to quantify the proportion of children completing the full vaccination series (CVS) regardless of age, mean age at each dose, and timeliness of receiving the two- dose or three-dose vaccine.
Results: Overall proportion of CVS was ~80%. Mean (median) age for the two-dose series was 1.5 (2) and 3.8 (4) months, and 1.7 (2), 3.8 (4) and 6 (6) months for the three dose series.

Table 1: Percentage of children vaccinated, by median age and those who successfully completed the vaccination series regardless of age

Year	Two dose vaccine in NSW+ (Rotarix™)				Three dose vaccine in QLD+ (Rotateq™)				
	Total Number of children	% of children receiving 1st dose by 2 months	% of children receiving 2nd dose by 4 mo	% of children complete vaccination at any age	Total number of children	% of children receiving 1st dose by 2 months	% of children receiving second dose by 4 mo	% of children receiving 3rd dose by 6 mo	% of children fully complete vaccination at any age
07/08	98,357	79.8%	74.3%*	81%	97,847	76.2%	76.2%	68.9%*	78.1%
08/09	63,384	82.2%	77.9%^	83.9%	62,388	84.6%	80.0%	74.0%^	82.0%

+States investigated have similar modes of vaccine delivery (HCP, councils, others) and % indigenous populations
*p value <0.001 between last scheduled dose at cut off of median age of vaccination,
^p value <0.001 between last scheduled dose at cut off of median age of vaccination

[Table 1 - completion of vaccine series]

Table 2: Timeliness of two-dose vaccine and three-dose vaccine in NSW and QLD

Rotavirus Vaccines	Children vaccinated	Dose 1	Dose 2	Dose 3
Two-dose vaccine in NSW (Rotarix™)	Children born 2007-08	98%*	92%*	N/A
	Children born 2008-09	97%^	93%^	N/A
Three-dose vaccine in QLD (Rotateq™)	Children born 2007-08	98%	92%**	88%**
	Children born 2008-09	98%	94%^^	90%^^

*p value <0.001; ** p value <.001, ^p value <0.001; ^^ p value <.001 N/A not applicable
Note: Timeliness was defined as the proportion of all children who received vaccine prior to median age at administration. 2 month, 4 month and 6 month for 1st, 2nd, and 3rd doses respectively.

[Table 2 - timeliness]

Conclusions: Overall completion of the full series of RV vaccination is high, although vaccination rates fall as a series progresses. A higher compliance with a two-dose schedule and decreased timeliness with increasing doses is suggested. Further investigation is warranted.

O222

IMPACT OF VACCINATION WITH RIX4414 ON ROTAVIRUS GASTROENTERITIS (RVGE) IN CHILDREN AGED < 5 YEARS IN AUSTRALIA

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Background and aims: Two licensed rotavirus vaccines are funded under the Australian National Immunisation Program (NIP) for all children born from 1 May 2007. We examined the impact of RIX4414 (*Rotarix*™, GlaxoSmithKline Biologicals) vaccination on rotavirus gastroenteritis (RVGE) hospitalizations in two states/territories: New South Wales (NSW), and the Australian Capital Territory (ACT).

Methods: A database analysis of state-based electronic hospital admissions was conducted to assess the trend of incidence rates of RVGE pre-introduction (1998-2006) with post-vaccination (2008-2009).

Results: RIX4414 coverage increased after initial introduction, rising to 83.4% in NSW and 91% in ACT within the first year of implementation[1]. In 2009, incidence of RVGE in children < 1 year decreased from a baseline of 35.85 to 2.69 per 10,000 child/year in NSW and 44.09 to 4.25 in ACT. The reduction of RVGE incidence was observed in all age groups (0-5 years). The overall reduction of RVGE in children < 5 years in 2009 compared with baseline was 90.1% in NSW and 92.1% in ACT.

Conclusions: This study demonstrates significant reduction of RVGE hospitalizations after introduction of mass vaccination with RIX4414 in two Australian states/territories. Reduction of RVGE hospitalizations was observed in all children < 5 years of age, even those were not eligible for vaccination according to their age, suggesting herd immunity.

Reference: 1. Hull B, Deeks S, Menzies R et al. Immunisation Coverage Annual Report, 2007. *Communicable Diseases Intelligence*.2009;33(2):170-87.

O223

EVALUATING THE EFFICACY OF 10-VALENT PNEUMOCOCCAL NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* PROTEIN-D CONJUGATE VACCINE (PHID-CV) AGAINST COMMUNITY-ACQUIRED PNEUMONIA IN LATIN AMERICA

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Background/aims: The **C**linical **O**titis **M**edia and **P**neumoni**A** **S**tudy (COMPAS) is the first pneumococcal conjugate vaccine (PCV) efficacy study conducted in Latin America. Measurement of a variety of pneumonia endpoints is important to assess the true public-health value of a PCV.

Methods: [1] 23,738 infants were randomised to receive either PHiD-CV and DTPa-HBV-IPV/Hib (PHiD-CV group) or HBV and DTPa-IPV/Hib (Control group) at 2-4-6 months of age, followed by PHiD-CV or HAV, respectively, at 15-18 months (both co-administered with DTPa-IPV/Hib).[1]

Results: Primary objective, based on first likely-bacterial-CAP episodes reported ≥2 weeks post-dose-3, was conclusive (22% VE [95%CI 8,34; p=0.002 with 1-sided alpha of 1.75%], according-to-protocol cohort).[2] The total vaccinated cohort results are tabulated below:

Occurrence of first episodes of CAP and vaccine efficacy anytime from the administration of dose 1						
	Number of first episodes				Difference in number of cases (Control – PHiD-CV)	Vaccine efficacy (95%CI)
	PHiD-CV (N=11,875)		Control (N=11,863)			
	n	%	n	%		
C-CAP	223	1.9%	289	2.4%	66	23% (9, 36)
B-CAP	341	2.9%	414	3.5%	73	18% (6, 29)
CXR-CAP	854	7.2%	947	8.0%	93	10% (2, 18)
S-CAP	2455	20.7%	2616	22.1%	161	7% (2, 12)

N = number of children in the total vaccinated cohort
n/% = number/percentage of children reporting at least one episode of CAP in a defined category
C-CAP = WHO-defined (consolidated) CAP
B-CAP = likely-bacterial-CAP (radiologically-confirmed CAP with alveolar consolidation/pleural effusion on chest X-ray, or with non-alveolar infiltrates and C-reactive protein ≥40 µg/mL)
CXR-CAP = any radiologically-confirmed CAP (child with abnormal pulmonary infiltrates on chest X-ray)
S-CAP = clinically-suspected CAP for which an X-ray was requested (regardless of final diagnosis)

[ITT results]

The observed efficacy against the specific C-CAP endpoint, proposed by the WHO to facilitate comparison of results across trials, suggests a PHiD-CV impact in the same range as seen with 7-, 9- and 11-valent PCVs in previous efficacy trials (in different settings). Despite lower efficacies, substantially higher numbers of cases were prevented with less-specific endpoints (such as S-CAP) than with more-specific endpoints (such as C-CAP). Endpoints such as S-CAP may potentially better reflect the overall public health impact of PHiD-CV vaccination.

Conclusion: The observed COMPAS results across various CAP endpoints demonstrate the clinical efficacy of PHiD-CV against pneumococcal infections; PHiD-CV could help address the pneumonia burden worldwide.

[1]Sáez-Llorens, ESPID 2011, Abstract 412; [2]Tregnaghi, SLIPE 2011

O224

PERSISTENCE OF ANTIBODY AGAINST H1N1 AND RESPONSE TO TRIVALENT INFLUENZA VACCINE 13 MONTHS AFTER 2 DOSES OF MONOVALENT PANDEMIC VACCINES

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Background and aims: We investigated antibody persistence in children 13 months after two doses of $AS03_B$-adjuvanted or non-adjuvanted monovalent pandemic H1N1 influenza vaccine and assessed the immunogenicity and reactogenicity of a further dose of a seasonal trivalent influenza vaccine (TIV).

Methods: After a blood sample assessing persistence of levels of antibody against the 2009 pandemic H1N1 influenza virus (n=323), 302 children received a single dose of a seasonal trivalent influenza vaccine. Immunogenicity was assessed at day 21.

Results: Although antibody levels had waned across all groups, at 13 months post-vaccination significantly more participants had microneutralisation (MN) titres ≥1:40 in the $AS03_B$-adjuvanted vaccine group compared to the non-adjuvanted vaccine group. For children aged < 3 years at first immunisation these percentages were 100% (95% CI 94.1-100%) for the $AS03_B$-adjuvanted vaccine versus 32.4% (21.5-44.8%) for the non-adjuvanted vaccine. For those aged 3 to 12 years at first immunisation these percentages were 96.9% (91.3-99.4%) versus 65.9% (55.3-75.5) ($p< 0.001$ for both comparisons). Following TIV all participants had MN titres ≥1:40. $AS03_B$-adjuvanted groups had higher absolute haemagglutination inhibition (HI) titre levels than non-adjuvanted groups. In under five year olds, redness >50mm and any severe local reaction were more frequent ($p< 0.05$) in previous recipients of $AS03_B$-adjuvanted versus non-adjuvanted vaccine (40.8% vs 24.2%, and 14.1% vs 1.5% respectively).

Conclusions: Almost all children who received two doses of the $AS03_B$-adjuvanted H1N1 pandemic influenza vaccine maintained adequate antibody levels one year after vaccination. TIV is safe and immunogenic in the season following pandemic vaccine administration.

P001

ANTIBIOTIC SUSCEPTIBILITIES OF BACTERIAL ISOLATES FROM PAEDIATRIC INTENSIVE CARE UNITS I NCLUDED IN MYSTIC PROGRAME

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Background: Meropenem Yearly Susceptibility test Information Collection (MYSTIC) Programme is a global, longitudinal resistance surveillance network that monitors the activity of meropenem and compares its activity with other broad-spectrum antimicrobials .

The aim of the study was to analyze antibiotic susceptibilities of Gram-negative and Gram-positive bacterial isolates from pediatric intensive care units included in Mystic programe.

Methods: The isolates were collected from various clinical specimens at pedriatic intensive care units of the Clinical Hospital Center Zagreb in Croatia. The minimum-inhibitory concentrations (MIC) were determined by broth microdilution method according to CLSI. Extended-spectrum β-lactamases (ESBL) were detected by double-disk synergy test.

Results: There was no resistance to either imipenem or meropenem observed for *E. coli*, *K. pneumoniae* and *P. mirabilis*. 37% of *E. coli* isolates showed resistance to gentamicin and 12% to ciprofloxacin. High rates of resistance of *K. pneumoniae* to ceftazidime and gentamicin (40%) are raising concern. Prevalence of ESBLs was 37% in *E. coli* and 50% in *K. pneumoniae*. All *A. baumannii* strains were resistant to gentamicin. 11% of *P. aeruginosa* strains were resistant to carbapenems and 22% to gentamicin, piperacillin/tazobactam and ciprofloxacin. Among Gram-positive pathogens staphylococci showed susceptibility to most tested antibiotics contrary to enterococci which showed 85% resistance to gentamicin.

Conclusions: These data provide evidence that despite the continued use of meropenem, carbapenem resistance is not increasing among those species tested except for P.*aeruginosa*, in pediatric ICU, and suggest that clinicians can still administer carbapenems as reliable choice in managing serious nosocomial infections in children.

P002

PHENOTYPICAL AND GENOTYPICAL CHARACTERIZATION OF MACROLIDE RESISTANCE IN PNEUMOCOCCAL NASOPHARYNX ISOLATES FROM CHILDREN IN VENEZUELA

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Background and aims: Streptococcus pneumoniae is part of the nasopharyngeal flora in children. Here we determined the prevalence and the mechanism of macrolide resistance in pneumococcal strains isolated from the nasopharynx in 3 different geographic regions of Venezuela.

Methods: A total of 319 strains of S. pneumoniae: 282 isolate from Amerindians (215 Delta Amacuro and 67 Bolivar State) and 37 from Caracas. Susceptibility was determined by the microdilution method, phenotypic characterization by the double disk diffusion method and detection of resistance genes erm (A), erm (B), erm (C) and mef (E) by PCR.

Results: A total 56 strains of S. pneumoniae were resistant to macrolide; the prevalence in the 3 groups was respectively 49% Caracas (18 strains), 14% Delta Amacuro (30 strains) and 12% (8 strains) Bolivar. The double disk test showed 3 different phenotypes: MLS_B inducible (2 isolates), MLS_B constitutive (38 isolates) and M phenotype (16 isolates). Of the 40 isolates of the MLS_B phenotype, 39 were confirmed as carrying the erm (B) gene. Of MLS_B constitutive phenotype, 16 strains had the genotype mef (E) and erm (B); 11 from Delta Amacuro (serotype 14, 6B, 15B and 19F), 1 from Bolivar (serotype 6C) and 4 from Caracas (serotype 14, 19A and 19F). All stains with the M phenotype had the mef (E) gene (8 different serotypes). The mef (A) gene was not detected.

Conclusion: This is the first report on macrolide resistance characterization of S. pneumoniae recovered from the nasopharynx of urban and Amerindian children in Venezuela.

P003

PHENOTYPICAL AND GENOTYPICAL CHARACTERIZATION OF MACROLIDE RESISTANCE IN PNEUMOCOCCAL NASOPHARYNX ISOLATES FROM CHILDREN IN VENEZUELA

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Background and aims: Streptococcus pneumoniae is part of the nasopharyngeal flora in children. Here we determined the prevalence and the mechanism of macrolide resistance in pneumococcal strains isolated from the nasopharynx in 3 different geographic regions of Venezuela.

Methods: A total of 319 strains of S. pneumoniae: 282 isolate from Amerindians (215 Delta Amacuro and 67 Bolivar State) and 37 from Caracas. Susceptibility was determined by the microdilution method, phenotypic characterization by the double disk diffusion method and detection of resistance genes erm (A), erm (B), erm (C) and mef (E) by PCR.

Results: A total 56 strains of S. pneumoniae were resistant to macrolide; the prevalence in the 3 groups was respectively 49% Caracas (18 strains), 14% Delta Amacuro (30 strains) and 12% (8 strains) Bolivar. The double disk test showed 3 different phenotypes: MLS_B inducible (2 isolates), MLS_B constitutive (38 isolates) and M phenotype (16 isolates). Of the 40 isolates of the MLS_B phenotype, 39 were confirmed as carrying the erm (B) gene. Of MLS_B constitutive phenotype, 16 strains had the genotype mef (E) and erm (B); 11 from Delta Amacuro (serotype 14, 6B, 15B and 19F), 1 from Bolivar (serotype 6C) and 4 from Caracas (serotype 14, 19A and 19F). All stains with the M phenotype had the mef (E) gene (8 different serotypes). The mef (A) gene was not detected.

Conclusion: This is the first report on macrolide resistance characterization of S. pneumoniae recovered from the nasopharynx of urban and Amerindian children in Venezuela.

P004

MULTIDRUG RESISTANCE STRAINS RESPONSIBLE FOR BACTERIAL INFECTIONS IN CHILDREN

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Background: Bacterial infections caused by multidrug resistant strains (MDRS) are a constant challenge for physicians throughout the world.

Aims of study: To phenotype MDRS and to determinate their incidence.

Material and methods: MDRS isolated from children (0-18 years) admitted to Children Hospital between April 2009 to September 2010 were phenotyped at Microbiology and Virology Department of UMF, Timisoara, Romania. Automated system Vitek®2 Compact 30 was used. Methicilino-Resistant Staphylococcus aureus (MRSA) and Methicilino-Resistant Coagulase-Negative (MRCoN), extended-spectrum beta-lactamase (ESBL)-producing E. coli and Klebsiella pneumoniae, carbapenems-resistance Pseudomonas aeruginosa and Acinetobacter baumanii were studied.

Results: Out of the 2816 bacterial strains isolated during the study period, 61 (2.16 %) were MDRS. The majority isolates were found in children admitted in ICUs (72%) and Newborn Departments (15%). These bacteria were isolated from bronchial aspirates (16.39%), wound secretions (13.11%), urine cultures (52.45%) and vascular catheters (4.91%) and others. The following phenotypes were identified: PBP mutations in *MRSA* (6.55%) and *MRCoN* (11.47%); ESBLs/acquired penicillinase + cephalosporinase, ESBLs or ESBLs (CTX-M) phenotypes in *E. coli* (37.7%); ESBLs, ESBLs + Cephamycine impermeability / ESBLs or carbapenems resistance / carbapenemase secretion (metal or KPC) in *Klebsiella pneumoniae* (22.9%) and high-level carbapenems resistance phenotype in *Pseudomonas aeruginosa* (13.11%) and *Acinetobacter baumanii* (8.19%). 13.11% of isolated strains were XDR.

Conclusion: The incidence of MDRS found was not so important, but it is necessary to continue the determination of resistance phenotypes, in order to a proper use of antibiotics and to prevent further emergences of MDRS.

P005

ANTIMICROBIAL RESISTANCE IN URINARY TRACT INFECTIONS IN A PAEDIATRIC POPULATION

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Background: Urinary Tract Infections (UTI) are common bacterial infections in children and responsible for a high use of antibiotics. The choice of empiric antibiotics should be guided by local resistance patterns. This institution uses cefuroxime as the 1st line antibiotic since 2001.

Aims: To study the type of bacterial pathogen causing UTI in children and their antimicrobial resistance patterns, since 2001. Determine the preferred antibiotic for empirical treatment of UTI in children.

Methods: Descriptive observational retrospective study of all urine cultures with growth of only one colony and respective antibiogram, from January to December of 2009, in children aged ≤ 13 years, with comparison of results with similar studies since 2001.

Results: A total of 459 urine cultures were identified, with a female preponderance (54,5%) and with 38,5% under 24m (n=177). *Escherichia coli* constitutes the most common pathogen isolated (70,8%), followed by *Proteus mirabilis* (14,5%), *Enterococcus species* (4%) and *Klebsiella species* (1,9%). Resistance in 2009 decreased, in comparison to 2008, for amoxicillin-clavulanic acid (16,3% vs 20%), second generation cephalosporins (4,6% vs 8%) and gentamicin (1,8% vs 5%), except for co-trimoxazole (30,4% vs 17%).

Conclusions: *E. coli* was the most frequent pathogen isolated. In the last years there has been a reduction in resistance patterns to amoxicillin-clavulanic acid, second generation cephalosporins and gentamicin, with an increase in resistance to co-trimoxazole. Cefuroxime remains the first choice in the treatment of UTI in children. Knowledge of the local antibiotic resistance is fundamental in guiding antibiotic choice.

P006

MOLECULAR TYPING OF SEROGROUP A *NEISSERIA MENINGITIDIS* ISOLATED FROM CEREBROSPINAL FLUID DURING 2008 TO 2010, DELHI (INDIA)

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Objectives: Ø Confirmation of *N. meningitidis* isolates using PCR.Ø PCR applied for identifying the serogroup of *N. meningitidis.*Ø Determination of the mechanism of ciprofloxacin resistance among *N. meningitidis* isolates by sequencing DNA *gyrase* A.Ø Examination the genetic relatedness of *N. meningitidis* by MLST.

Methods: Six isolates of *N.meningitidis* collected from January 2008 to May 2010 were characterized.

Molecular diagnosis: *N. meningitidis* was detected and confirmed by using species specific PCR for gene ctrA, and by PCR using 16s rDNA and specific gene for *N. meningitidis*.

Serogrouping: PCR was performed using oligonucleotide specific for orf-2 region of a gene cassette required for biosynthesis of the capsule of serogroup A .

Antimicrobial suscptibility: Strains were tested by Etest. Complete resistance was found to ciprofloxacin in all of the six strains of *N.meningitidis* resistance by Etest. Quniolone determining region of gyrase A gene was sequenced.

Multi locus sequence typing of *N.meningitidis*.

Housekeeping genes were sequenced to obtain distinct sequence type for six isolates.

Results: Six strains of *N. meningitidis* showed complete resistance to ciprofloxacin phenotypicaly and genotypicaly.• Mutation found in amino acid at 91 position from Threonine to isoleucine in all the resistant strains is in agreement with other reported studies of ciprofloxacin resistance among *N. meningitidis.*• MLST confirmed ST 4789 belonging to clonal complex ST-5/subgroup III for all the strains of *N. menigitidis.*This Clonal complex has been associated with recent outbreaks in Asian countries. **Conclusion:** Monitoring of antibiotic resistance is of paramount importance in areas where *N. meningitidis* is endemic.

P007

NITRIC OXIDE INDUCES DISPERSAL OF MULTISPECIES CYSTIC FIBROSIS BIOFILMS AND ENHANCES ANTIBIOTIC SENSITIVITY OF PSEUDOMONAS AERUGINOSA

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Background and aims: The presence of bacterial biofilms in the lower airways and their recalcitrance towards antimicrobials is important in the progression of patients with cystic fibrosis (CF). Recently, a key role for nitric oxide (NO) in the natural process of dispersal in biofilms has been described. As such, the application of NO to CF biofilms represents a potentially novel adjunctive therapy to conventional antibiotics.

Methods: *Ex vivo* multispecies biofilms were isolated from the sputum of CF patients undergoing an exacerbation. Clinical isolates of *P. aeruginosa* were obtained from patient sputum samples and biofilms cultured *in vitro*. Dispersal and antibiotic sensitivity was assessed by a combination of suspension optical density measurements, Syto 9/Propidium Iodide fluorescent staining combined with confocal laser scanning microscopy and viable cell counts.

Results: *Ex vivo* patient biofilms from a range of opportunistic CF pathogens were dispersed upon treatment with nano-molar concentrations of NO. With focus on *P. aeruginosa* as a pathogen of interest, the data demonstrates that the extent of biofilm dispersal is NO concentration dependent and accompanied by a removal of surface-bound biofilm into the planktonic suspension. Moreover, biofilm dispersal was accompanied by an increased susceptibility of *P. aeruginosa* to clinically relevant antibiotics such as Tobramycin and Ceftazadime, both *in vitro* and *ex vivo*.

Conclusion: NO-mediated dispersal subverts *P. aeruginosa* antibiotic resistance mechanisms associated with biofilm structure. An NIHR Respiratory Biomedical Unit funded proof-of-principle clinical trial is ongoing assessing the application of NO as adjunctive therapy in CF teenagers and young adults (EudraCT 2010-023529-39).

P008

SENSITIVITY PROFILE OF 76 *ENTEROBACTERIACEAE* ISOLATED FROM URINARY TRACT INFECTIONS IN THE PEDIATRIC SERVICE AT THE NINI HOSPITAL - LEBANON

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Background and aims: Internationally we are seeing an increase in the isolation of *Enterobacteriaceae*-producing extended spectrum beta lactamases (ESBLs). The aims of this study is to examine the sensitivity profile of 76 *Enterobacteriaceae* isolated from urinary tract infections in children .

Methods: The study took place between 01/06/2008 and 30/06/2010.After culture, enumeration and identification by API system, the antibiogram was carried out by disk method.

Results: *Escherichia coli* was predominant (68 isolates: 98.5%, of which 19: 28% were ESBL +) followed by *Klebsiella spp* (5 isolates: 6.6% of which 1 was ESBL +), *Enterobater cloacae* (2 isolates: 2.6%) and *Proteus mirabilis* (1 isolate: 1.3%).

The total susceptibility results of the 76 isolates showed that the sensitivity was: Ampicillin (21.1%) Amoxicillin + Clavulanic acid (57.9%), Ticarcillin and Piperacil (23.7%), Ticarcilin + clavulanic acid (53.9%), Piperacillin + tazobactam(90.7%), Cefalexin (57.9 %), Cefuroxime (69.7%), Cefotaxime (69.7%), Ceftazidime (69.7%), Cefixime (69.7%), Cefepime (71.1%), Aztreonam (69.7%), Cefoxitin (94.7%), Imipenem (100%) , Gentamicin (82.9%), Tobramycin (77.6%), Amikacin (100%), Netilmicin (92.1%), Colistin (98.7%), Cotrimoxazole (40.8%) Pipemidic acid (61.8%), Ofloxacin (84.2%) Ciprofloxacin (86.2%), Fosfomycin (97. 4%), Nitrofuran (92.1%) and Tigecyclin (96.1%).

Of the 76 isolates there were 20 ESBL-producing or 26.3%.

All are sensitive to: Imipenem,tigecyclin,colistin,amikacin and nitrofuran

Conclusion: The study shows an alarmingly high rate of ESBL isolates, hence the importance of making culture in each urinary infection, prohibit the issuance of antibiotics from pharmacies without a prescription and ultimately strengthen the rules of hygiene in hospitals.

P009

CLINICAL CHARACTERISTICS AND ANTIBIOTIC RESISTANCE OF SHIGELLA GASTROENTERITIS IN CENTRAL TURKEY: COMPARISON OF THE YEARS 1987-1994, 1995-2002 AND 2003-2009

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Background: Shigella epidemiology and antibiotic susceptibility changes over years. It´s necessary to trace the changes for good clinical management. In this study it's aimed to define epidemiologic, clinical and antibiotic susceptibility patterns of shigellosis cases between years 2003-2009 and compare it with the years 1987-2002.

Methods: The files of the children who admitted to Hacettepe University Children's Hospital Diarrheal Diseases Training and Treatment Unit between 2003 and 2009 (n=238) were reviewed. The clinical characteristics and antibiotic susceptibility results of Shigella species were recorded. The results were compared with the results of the two previous period (1987-1994 n=618; 1995-2002 n=218).

Results: The predominant species is S. Sonnei in all periods with increasing predominancy within periods (64.0%, 71.5% and 87.8%, respectively, p< 0.001). The prevalence of bloody diarrhea is not changing however the prevalence of dehydration shows an increasing trend (11.0%, 20.6% and 28.6% respectively, p< 0.001). During the 2003-2009 period 69.9 % of shigella cases were resistant to trimetoprim/sulfamethoxazole, 35.8% to ampicillin and 4.7% to nalidixic acid. No case resistant to ciprofloxacin was detected. This resistant pattern was comparable to the previous periods. Multidrug resistance was also found to be similar within the last two periods (24% vs. 28.1 % respectively, p=0.13).

Conclusion: In this setting there is both a microbiologic and clinic change of childhood shigellosis cases over the 12 years. Antibiotic resistance pattern seems to be stable for the last two periods. There is a need to resurge the criteria and clinical management guidelines for suspected shigellosis cases.

P010

VANCOMYCIN RESISTANT (VAN-A) *ENTEROCOCCUS FAECIUM* (VRE) OUTBREAK IN A NEONATAL UNIT (NU): RISK FACTORS FOR COLONIZATION

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Background and aims: Control of VRE colonization is important to prevent transmission between patients. The aim of this study was to determine potential factors associated with VRE colonization in neonates during a VRE outbreak in a NU.

Methods: A case control study was conducted in a 44-bed NU, containing 15 beds NICU, when active surveillance (using both microbiology and molecular testing) documented high levels of VRE colonization. Cases were neonates who had at least 1 surveillance culture positive for VRE, whereas controls were neonates with negative stool cultures for VRE. Case and control neonates were selected if they were admitted at any time after the first 10 days of active surveillance and for the next 3 months. Logistic regression was used for statistical analysis.

Results: During study period, 33 cases and equal number of controls were enrolled. VRE isolates harbored Van-A resistant gene and belonged to the same PFGE clone. In univariate analysis there was no difference regarding sex, gestational age, birth weight, mechanical ventilation, parenteral nutrition, presence of central catheters or nasogastric tube, and traveling off the department. Administration of at least one second line antimicrobial therapy was more frequent in cases ($p < 0.05$). Most of the cases were hospitalized during the first month of this outbreak. In multivariate analysis, admission of at least one second line antimicrobial therapy and length of hospitalization were risk factors for VRE colonization ($p < 0.01$).

Conclusions: Both high prevalence of VRE colonization and antimicrobial utilization promoted transmission of VRE during this outbreak.

P011

PENICILLIN RESISTANCE OF *NEISSERIA MENINGITIDIS* CLINICAL ISOLATES FROM CHILDREN IN MADRID (SPAIN), 2001-2010

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Background: Spain is one of the European countries with a higher rate of diminished penicillin susceptibility of *Neisseria meningitidis* (NM). Medium sensitivity was detected in over 50% of NM in 1990-1999. NM serogroups B and C are the leading cause of meningococcal disease. The serogroup C conjugate vaccine was implemented in Madrid in the immunization schedule in 2000. The aim of this study is assessment of actual penicillin susceptibility in NM clinical isolates.

Methods: A retrospective study of all children with microbiologically confirmed meningococcal disease admitted to our hospital between 2001 and 2010. NM cultures were obtained from blood or CSF. Bacterial identification and susceptibility were performed using the Wider and VITEK 2 automated systems. Antimicrobial susceptibilities were interpreted according to CLSI methodology (Penicillin MIC breakpoints: sensitive if MIC≤0.06 µg/ml; intermediate susceptibility MIC 0.12-0.25µg/ml and full resistance MIC ≥0.5 µg/ml).

Results: 39 NM isolates were evaluated. Median age was 3.1 years (range 0.1-16). Clinical diagnosis was sepsis in 23%, sepsis with meningeal involvement in 51% and isolated meningitis 26%. Overall, meningeal involvement was confirmed in 77% of patients. All the children received cefotaxime. NM serogroups were: B (34) and C (5). Intermediate penicillin susceptibility was present in 59% of NM isolates (23), resistance in 20.5%(8) and full susceptibility in 20.5%(8). Mortality was 7.7%

Conclusions: Diminished penicillin susceptibility was present in 79.5% of NM isolates. These rates are higher than those publicated in 1990-2000 in Spain. Cefotaxime and ceftriaxone are better choices for empirical treatment of NM sepsis and meningitis.

P012

CLINICAL IMPACT OF MULTI-RESISTANT ESBL AND AMP-C PRODUCING ORGANISMS IN CHILDREN

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Recently emergence of multi-resistant extended spectrum spectrum β-lactamases(ESBLs) & Amp-C producing gram-negative bacteria in children has been observed. There is limited published data on these infections. Hospital laboratory adopted a new method for surveillance in 2008.

Aims: We sought to evaluate clinical impact in teaching hospital from whom an ESBL & Amp-C producing organism had been isolated from 1st July 2009 to 31st December 2010.

Methods: Evaluation was undertaken over a period of from 1st July 2009 to 31st December 2010. Age of the patient, type of specimen, location where specimen was collected;, review of treatment for in-patients and those visiting children's emergency was recorded.

Results: 33 children were identified with ESBLs and 72 with Amp-C producers aged 2days to 16 years. 31(94%) ESBLs & 53(74%) Amp-C isolates were obtained from urine, while the others from a cough swab, pus, eye, ears and umbilicus (no bacteraemia). From available data, 2 patients with ESBL and Amp-C each were in-patients, 2/5 babies in NICU needed IV antibiotics, and 4 with Amp-C & 3 with ESBL presenting to children's emergency needed antibiotics. 57(79%) Amp-C isolates & 29(88%) ESBLs were obtained from the community specimens.

Conclusions: Thus Amp-C & ESBL-producing organisms are reported with increasing incidence in the children. From this study many of them were colonisers and no bacteraemia was seen; although they are potentially serious pathogens. However, given the mobile nature of the resistance element in case of ESBLs, colonised children may represent a reservoir from which multi-resistant pathogens can spread.

P013

MICROBIOLOGICAL INVESTIGATION OF *HAEMOPHILUS INFLUENZAE* STRAINS ISOLATED FROM CHILDREN WITH MENINGITIS, ACUTE OTITIS MEDIA AND RESPIRATORY DISEASES

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Background and aims: To investigate the serotype distribution and antimicrobial susceptibility of clinical strains *H. influenzae* from children.

Methods: A total of 178 *H. influenzae* strains were collected from children with meningitis, bacteremia, otitis media and respiratory tract infections, aged 0 to 14 years: 51 cerebrospinal fluid (CSF), 5 blood, 24 sputum, 33 middle ear fluid, and 65 upper respiratory tract (URT) samples. Serotyping was done by a coagglutination test and by PCR capsular genotyping. Beta-lactamase production was determined by the chromogenic cephalosporin test with nitrocephin. Antimicrobial susceptibility was performed by using the microbroth dilution method.

Results: Most of the isolated *H. influenzae* strains were from children under 5 years of age (89.3%). Overall, 57 strains belonged to serotype b (32%), 1 strain was type f, and 120 isolates (67.4%) were non-typeable. Among the infants and children with meningitis or other invasive infections, aged less than 6 years, all isolates, except one, were serotype b. In all children with respiratory tract infections (pneumonia, otitis media, sinusitis, cystic fibrosis) non-typeable strains were most common - 97.5%. The prevalence of beta-lactamase production was 18%, much higher for strains from CSF isolates - 39.2% and less frequent in respiratory tract isolates - 8.3% in sputum and 5.1% in URT samples.

Conclusions: The implementation of Hib vaccine in our country since 2010 will be accompanied by a reduction in invasive diseases caused by *H. influenzae* type b in children, but it is not useful in preventing infections caused by non-typeable *H. influenzae* strain.

P014

ANTIMICROBIAL RESISTANCE PATTERNS OF SHIGELLA ISOLATES IN CHILDREN WITH DYSENTERY IN IRAN

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Background and aims: Shigellosis is a major health problem in developing countries, causing more than 90 million episodes in Asia annually and sometimes results in death. Because of increasing trends towards drug resistance, this study was undertaken to evaluate the resistance pattern of shigella isolates from children with acute diarrhea to antimicrobial agents

Methods: This prospective cross sectional study has been conducted on 103 hospitalized children with final diagnosis of Shigellosis in Qods children Hospital, Qazvin, Iran in 2009-10. Stool specimens were received from study subjects and cultured. Isolates were confirmed by biochemical and serological tests. The isolates were tested for antimicrobial susceptibility by the disc diffusion method. Data was analyzed by using statistical methods.

Results: From a total of 103children with Shigellosis 51(49.5%) were male and 52(50.5%) females. Mean age was 54.5±2809 months. The most common Shigella isolates were: sonnei 80(77.7%), boydii 5(4.9%), dysenteriae 6 (5.8%) and flexneri 12 (207%).Resistance to antibiotics in isolates were: co-trimoxazole 85.1%, ampicillin 45.8%, nalidixic acid 63.8%, ceftriaxone20%, Cefixime2.9% and ciprofloxacin 0%. There was significant difference between shigella serotypes and resistance patterns($P< 0.05$).

Conclusions: High rate resistance of Shigella to antimicrobial agents particularly to nalidixic acid ceftriaxone is worried. Continuous monitoring of resistance patterns among Shigella isolates is recommended.

P015

ANTIMICROBIAL SUSCEPTIBILITIES OF CAMPYLOBACTER SPP ISOLATED FROM HOSPITALIZED CHILDREN AND ADULTS IN KAUNAS, LITHUANIA IN 2006-2010

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Aim: To identify susceptibility of *Campylobacter spp* strains to ciprofloxacin and erythromycin - most often used for antibacterial treatment.

Method: A total of 104 *Campylobacter spp* strains isolated from the stool of children 44 and adults 60 with clinical gastroenteritis were collected during a four-year period (2006-2010). They sensitivity to ciprofloxacin and erythromycin was analyzed according BSAC recommendations for a disc diffusion method (interpretation of sensitivity - zone diameter breakpoint for ciprofloxacin ≥ 18 mm, for erythromycin ≥ 20 mm).

Results: From analyzed 100 *Campylobacter spp* strains 65% (N=65) were sensitive to ciprofloxacin. The rest 35% (N=35) strains were resistant (30 strains with zone diameter 6mm and 5 strains - accordingly with zone diameter from 10 to 16mm.

From analyzed 80 *Campylobacter spp* strains 98,75 % were sensitive to erythromycin (only 1strain was resistant - zone diameter 6mm).

In the analyzed period there were no statisticaly confidential resistance changes.

Conclusions: Ciprofloxacin as a first drug of choice for the empiric treatment of the infection is questionable. The incidence of macrolide resistance remained low.

P016

ANTIMICROBIAL SUSCEPTIBILITIES OF CAMPYLOBACTER SPP ISOLATED FROM HOSPITALIZED CHILDREN AND ADULTS IN KAUNAS, LITHUANIA IN 2006-2010

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[1]*Lithuanian University of Health Sciences, Medical Academy, Clinic of Children Diseases,*
[2]*Lithuanian University of Health Sciences, Medical Academy, Clinic of Infectious Diseases, Kaunas, Lithuania*

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In the analyzed period there were no statisticaly confidential resistance changes.

Conclusions: Ciprofloxacin as a first drug of choice for the empiric treatment of the infection is questionable. The incidence of macrolide resistance remained low.

P017

EPIDEMIOLOGY AND ANTIBIOTIC SUSCEPTIBILITY SPECTRUM IN UPEC FROM URINE IN CHILDREN WITH UTI IN MOFID CHILDREN HOSPITAL

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Introduction: Urinary tract infection due to UPEC with antibiotic resistance is one of the most important problems in infants and children. Prevalence of UPEC isolated from children urine samples and their antimicrobial susceptibilities were considered in this study.

Material and methods: Urine samples of children were studied during one year. E.coli strains in urine samples were identified by conventional methods. The UPEC strains was confirmed by the gene including *by* decteting *papC*, *papGII* , *papGIII* , *sfa/foc*, *hlyC*, *c nf1* , *iucC*, *fyuA*, *iron N* genes by PCR method. Antibiotic susceptibility testing was done for *E. coli* by disk-diffusion method based on CLSI protecol. *E. coli* strain 25922 ATCC was used as the reference strain.

Results: 2572 urine samples of suspected children to have urinary infections were studied and then 378 E.coli strains were detected in which 149 of strains were UPEC (39/7%).All of Uropathogenic E.coli were resistant to penicillin,Oxacillin,Bacitracin,Cloxacillin and pipracillin.resistantto other antibiotics were: Sulfametoxazole 92%, Nalidixic acid 53%, Ampicillin 89%, Nitrofurantoin 9%, Cephotaxime55.3%, Cefixime67%, Gentamicin72% ,Cephalexin75.6%, Ciprofloxacin17.5%.the prevalence of *papC*12.37%, *papGII*15.06% , *papGIII*13.17% , *sfa/foc*17.23%, *hlyC*39.41%, *c nf1* 23.4% , *iucC* 7.35%, *fyuA*18.12%, *iron N*22.13% genes by PCR method.

Conclusion: Periodic review and formulation of antibiotic policy are needed for control of

Acquisition of drug resistance. Further studies on better understanding of interaction of different virulence factors at molecular level are necessary as most urovirulent strain express multiple virulence factors simultaneously.

Keywords: Uropathogenic E.coli, Antibiotic susceptibility pattern, UTI

P018

ETIOLOGICAL AGENTS AND THEIR ANTIBIORESISTANCE IN CHILDREN ACUTE DIARRHEAL SYNDROM IN BUCHAREST AREA

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Background/ aims: Acute diarrheal syndrome (ADS) is a major cause of morbidity and mortality in infants and children worldwide. Enteric pathogens frequently acquire resistance when they are exposed to resistant normal flora that colonize intestinal tracts of children, or may have acquired resistance in other environments before infecting human host.

Methods: Prospective study on children with ADS and fever, hospitalized in Dr "Victor Babes" Hospital of Infectious and Tropical Diseases Bucharest between 09.2009- 09.2010 for etiologic agents identification and antibioresistance. 1449 coprological samples were tested using classical isolation and enteric pathogens identification methods (exoenzimatic/ API, VITEK systems and antigenic markers). For antibioresistance patterns detection were used Kirby Bauer disc diffusion standard method and DDD, E-test methods (ESBL and MDR strains)/CLSI 2009-2010W.

Results: Bacterial etiological agents were identified in 86(5,9%) cases: E. coli/EPEC-28/85; VTEC-3/85; Salmonella/BO-18/85; Salmonella/CO-2/85; Salmonella/DO-16/85; Shigella flexneri-5/85 and S.sonnei-2/85; Klebsiella pneumoniae-10/85; Campylobacter-2/85. Salmonella strains were resistant to trimethoprim/ sulfamethoxazol(SXT) 4/36, nalidixic ac.(NA) 6/36, tetracycline(TE) 8/36, ampicilin (AMP) 12/36. Shigella strains were resistant to TE 3/7, AMP 4/7, SXT4/7. Most of E.coli were sensitive to cephalosporins/I, II, III generation (2/31 ESBL producing strains) and various resistance was found for TE 9/31, sulfonamide 9/31, SXT 6/31. Only 1 Klebsiella pneumoniae ESBL producing strain was MDR (beta-lactams, amino glycosides, sulphonamides, tetracycline, quinolons). No resistance to ciprofloxacin registered for enteric pathogen Gram negative bacteria.

Conclusions:

1.Antimicrobial agents for ADS should be prescribed with an appreciation of limitations including antimicrobial resistance.

2.Beta-lactams, quinolons and furans are a good choice of ADS treatment.

P019

AETIOLOGY AND RISK FACTORS FOR HOSPITAL-ACQUIRED BACTERAEMIA IN CHILDREN ADMITTED TO A LONDON TERTIARY REFERRAL HOSPITAL

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Background: Hospital-acquired infections are associated with significant morbidity and mortality because they are often caused by multi-resistant pathogens and usually affect children with serious underlying medical conditions. This study aimed to describe the aetiology and risk factors for hospital-acquired bacteraemia among children aged < 16 years admitted to a London tertiary hospital between 2001 and 2009.

Methods: A standard pro-forma is used by clinical microbiologists at St. George's Hospital, London, to document the management of all clinically significant bacteraemia. Bacteraemia was considered to be hospital-acquired if the blood culture was taken at least 72 hours after hospital admission in a child with clinical symptoms, signs and/or laboratory markers consistent with infection.

Results: There were 478 episodes of hospital-acquired bacteraemia over the 9-year period, with venous catheters being the main foci in 279 episodes (58%). Gram-positive cocci were responsible for 385 episodes (81%) and were mainly due to coagulase-negative staphylococci (63%). Overall, 45% of 33 *S. aureus* isolates were methicillin-resistant, but none exhibited reduced vancomycin susceptibility. Five (15%) of 34 enterococcal isolates tested for ampicillin were resistant and 2/29 (7%) isolates tested for vancomycin were resistant. Of the enteric Gram-negative rods, 20% (9/44 isolates) were resistant to cefotaxime (mainly *Enterobacter* spp.), 27% (12/44 isolates) to piperacillin/tazobactam and 13% (9/72 isolates) to gentamicin, but none produced extended-spectrum beta-lactamases.

Conclusions: Hospital-acquired bacteraemia in children are mainly due to venous catheter infections and caused by Gram-positive organisms. Antimicrobial resistance rates remain low compared to other countries and multi-resistant organisms are rare**.**

P020

ANALYSIS OF ANTIBIOTICS RESISTANCE IN CHILDREN WITH 1ST EPISODE OF UTI DUE TO ESCHERICHIA COLI. A RETROSPECTIVE STUDY

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Aim: To investigate the antibiotic resistance of e.coli in children with 1st episode of UTI.

Methods and materials: A retrospective study was carried out. Children between 1 month and 12 years old were recorded for a period of 24 months. All the children had their 1st episode of febrile UTI and were hospitalized. The diagnosis of UTI was based in positive urine culture. The samples were collected by supracubic aspiration in children less than 10 kgr, blabber catheterization or “clean catch” midstream specimen, in children more than 10 kgr. Any supracubic aspiration culture with any growth was accepted as positive. Also, any blabber catheterization with >1.000 cfu/ml and any “clean catch” specimen with >100.000 cfu/ were accepted as positive. The antibiotics tested for susceptibility were: ampicillin, gentamicin, cotrimoxazole, cefuroxime and ceftriaxone.

Results: 46 children were recorded (28 female, 18 male) with mean age 22.5± 20.9 months. 56, 5% of the isolated e.coli were susceptible in all the antibiotics used. 23.8% were resistant in ampicillin and 13% were resistant in cotrimoxazole. In addition, 2.2% of the isolated bacteria were resistant in both cotrimoxazole and gentamicin and 4.3% were resistant in both ampicillin and cotrimoxazole. All the isolated bacteria were susceptible in cefuroxime and ceftriaxone.

Conclusions: In our study the resistance of e.coli in ampicillin was high enough to raise concerns about its use in UTI. The use of cotrimoxazole as a first line antibiotic in UTI treatment is not challenged. Cephalosporins can be used as second line treatment.

P021

USE OF COLISTIN FOR ACINETOBACTER INFECTIONS IN PEDIATRIC PATIENTS

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Background: Increasing incidence of multi-drug resistant gram-negative bacteria necessitates reintroduction of colistin in clinical practice. Safety and effectiveness of colistin in children has yet to be proven. Here, we present a case series of children treated with intravenous colistin.

Methods and results: The records of 8 patients who received colistin in a tertiary care hospital intensive care unit between October and November 2010 were reviewed. Eight patients (mean age 45 months, range 3 months-114 months) received colistin for treatment of ventilatory associated pneumonia in all and accompanying bacteremia in 3 patients. Acinetobacter baumanii was isolated from tracheal aspirate of all patients and both tracheal aspirate and blood of 4 patients. Antibiotic susceptibility tests revealed only colistin and gentamicin susceptibility in 5 patients, colistin/gentamisin/ciprofloxacin susceptibility in 3 patients. Colistin was administered in a dosage of 5 mg/kg/day. Duration of administration ranged from 1 to 46 days. All patients received broad spectrum antibiotics prior to use of colistin. Other antimicrobials were co-administered in all courses of colistin: ciprofloksasin and gentamisin in 5 patients and only gentamisin in 3 patients. Clinical response (cure or improvement) of infection was observed in 7 of 8 patients. One patient, whose body specimens were cleared off A. baumanii has died due to non-infection related causes. Nephrotoxicity has not been observed during colistin therapy. No apnea or other evidence of neuromuscular blockade was noted in any of these patients.

Conclusion: Colistin appears to be safe and effective against severe infections caused by multi-drug resistant gram negative bacteria like Acinetobacter baumanii.

P022

ANTIMICROBIAL RESISTANCE OF *ESCHERICHIA COLI* CLINICAL ISOLATES CAUSING NEONATAL SEPSIS

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Background and aims: Neonatal meningitis and septicemia caused by Escherichia coli and Streptococcus agalactiae are still major health problems in industrialized countries. The objective of the present work was to evaluate the antimicrobial resistance of E. coli strains causing early and late neonatal sepsis and to compare them with E. coli strains isolated from healthy neonates.

Methods: Twenty-seven E. coli strains from early neonatal sepsis, 40 from late neonatal sepsis and 28 from healthy neonates were studied. Minimal inhibitory concentrations were determined using the NM37 Panel (Siemens). Detection and characterization of determinants of resistance, integrons, and gyrA and parC mutations were carried out by PCR and sequencing.

Results: No differences were found in the resistance to the antimicrobial agents used to treat late neonatal sepsis (amikacin, ceftazidime and imipenem). However, resistance to chloramphenicol and piperacillin was significantly more frequent among strains collected from septic than from healthy neonates (p=0.05 and 0.0004, respectively). Two strains from neonatal sepsis presented BLEAS (CTX-M14 and CTX-M15, respectively). Twenty strains (30%) presented class-1 integrons with different combination of gene cassettes. Finally, four strains presented mutations in the amino acid codons Ser83Leu and Asp87Asn from the gyrA gene, two only Ser83Leu and one Asp87Lys. Of these, five also presented the Ser80Ile mutation and one the Gly84Val mutation in the parC gene.

Conclusions: E. coli strains causing neonatal sepsis were more resistant to the antimicrobial agents studied than the strains collected from healthy neonates except in those related to ciprofloxacin and gentamycin resistance.

P023

HIGH-LEVEL GENTAMICIN RESISTANCE IN *STREPTOCOCCUS AGALACTIAE*

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Background: *Streptococcus agalactiae* causes life threatening invasive infections in newborn an adult patients. The recommended antibiotic treatment regime consists of a combination therapy of a penicillin plus aminoglycoside. We recently isolated a *S. agalactiae* strain demonstrating high-level-gentamicin-resistance (HLGR) with an MIC of ≥ 512 mg/l. The aim of this study was to characterize the resistance determinant of this strain and to investigate the frequency of HLGR in *S. agalactiae*.

Methods: Molecular characterization of the HLGR in our strain was carried out by PCR and DNA sequencing. Transfer of the resistance determinant was investigated by transformation of *Enterococcus faecalis*. The frequency of HLGR in *S. agalactiae* was determined by culturing strains on a HLGR screening agar supplemented with 256mg/l of gentamicin.

Results: PCR of the HLGR *S. agalactiae* strain detected the *aacA-aphD* gene, but not the flanking transposon structure, which is typically associated with this gene. Plasmid purification and subsequent DNA sequencing resulted in the isolation of a novel extrachromosomal element. Transfer of this element into *E. faecalis* caused a HLGR in this strain. To evaluate, the frequency of HLGR in *S. agalactiae* more than 500 colonizing and invasive *S. agalactiae* strains were cultured on a HLGR screening agar. In none of these strains HLGR was found.

Conclusions: We identified a novel HLGR resistance determinant in *S. agalactiae* that has previously not been described. The potential spread within the *S. agalactiae* population represents a serious clinical threat, since gentamicin is part of the recommended treatment regimen of *S. agalactiae*.

P024

MACROLIDE RESISTANCE DETERMINATION AND MOLECULAR TYPING OF *MYCOPLASMA PNEUMONIAE* BY PYROSEQUENCING

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Background and aims: The first choice antibiotics for treatment of *Mycoplasma pneumoniae (Mpn)* infections in children are macrolides. However, the prevalence of macrolide (ML)-resistance, determined by mutations in the bacterial 23S rRNA, is increasing among *Mpn* isolates. Consequently, it is imperative that ML-resistance in *Mpn* can be rapidly detected to allow appropriate treatment of patients. We set out to determine the utility of pyrosequencing as technique to determine ML-resistance genotypes and molecular subtype of *Mpn* isolates.

Methods: A total of four separate assays were designed such as to determine a short genomic sequence from four different sites, i.e. two locations within the 23S rRNA gene, one within the MPN141 gene and one within the MPN528a gene. These assays were performed on a collection of 108 *Mpn* isolates, including 4 ML-resistant isolates, and 116 clinical samples positive for *Mpn* by standard PCR.

Results: The ML-resistant isolates within the collection were readily identified by pyrosequencing. Moreover, each strain was correctly typed as a subtype 1 or subtype 2 strain. From the collection of clinical samples, 88 samples could be confirmed as *Mpn*-positive by real-time PCR. In 75 of these samples, a genotype could be determined. ML-resistant genotypes were not found in this collection.

Conclusion: Pyrosequencing is a convenient technique for ML-resistance determination as well as molecular typing of both *Mpn* isolates and *Mpn*-positive clinical samples. Since culturing of *Mpn* is insensitive the direct determination of ML-resistance on clinical samples could have a significant impact on the antibiotic therapy of *Mpn*-infected patients.

P025

PREVALENCE OF COMMUNITY-ACQUIRED METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS AMONG CHILDREN WITH SKIN AND SOFT TISSUE INFECTIONS IN BROOKLYN, NEW YORK

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Background: The prevalence of community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) infections among the pediatric population has been gradually increasing over the years leading to a large burden to the health system.

Objectives: To determine the prevalence and sensitivity pattern in accordance with D-Test of CA-MRSA among skin and soft tissue infections in our community. We also describe and analysis the most common diagnosis, days of hospitalization and chosen antibiotics with CA-MRSA.

Methods: We retrospectively reviewed medical records of patients under 18 years of age with the diagnosis of skin or soft tissue infections from January 2008 to august 2010. Only those cultures positive for MRSA meeting criteria of community acquired infection were included and analyzed.

Results: 603 were reviewed. Culture was obtained in181 patients. 126 of them were positive for Staphylococcus aureus, of which 76(60.3%) were CA-MRSA. 97.3% of the isolates were sensitive to co-trimoxazole, 88.1% to clindamycin and only 7.8% to erythromycin. Inducible resistance was detected in only 2% of strains. The main diagnosis associated with CA-MRSA was gluteal abscess (34.2%), leg cellulitis and knee abscess (11.8%). 57.8% of the CA-MRSA required hospitalization (mean 3.3±2.5 days). Clindamycin was the preferred drug in hospitalized patients (65.1%). Cephalexin (40.2%) followed by clindamycin (28.5%) were the favorites initial drugs prescribed for outpatient cases.

Conclusions: The prevalence of CA-MRSA is high (41.9%) in our children community. The sensitivity of CA-MRSA to co-trimoxazole and clindamycin is still favorably high, and the presence of clindamycin inducible resistance among the strains is very low in our community.

P026

PULMONARY ASPERGILLOSIS CAUSED BY A PAN-AZOLE-RESISTANT *ASPERGILLUS FUMIGATUS* IN A CHILD AFTER HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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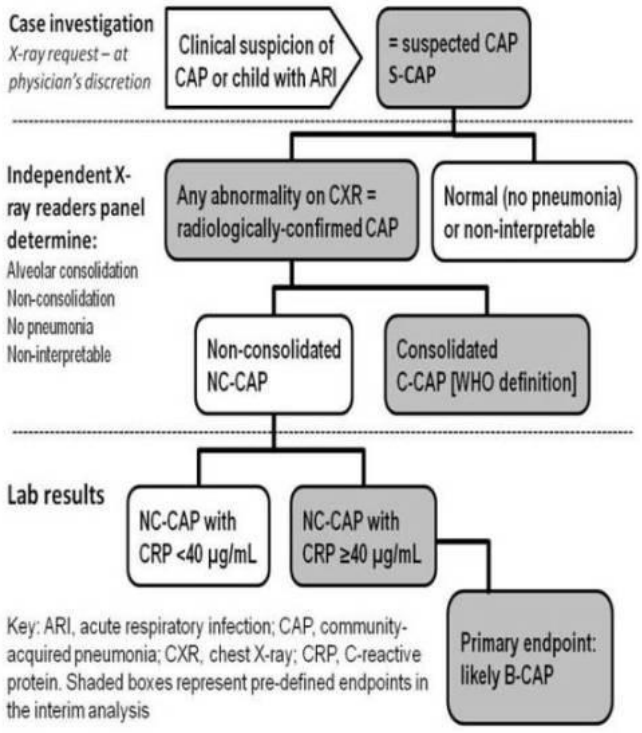
Background: Invasive aspergillosis is one of the most threatening fungal infections in children undergoing treatment for hematologic malignancies and after hematopoietic stem-cell transplantations. In recent years the incidence of invasive fungal infections has increased, probably due to longer periods of immunosuppression. The mortality of invasive aspergillosis is high, ranging from 70-93% 1 year after diagnosis, although the survival has been improving in recent years. The diagnostic criteria of an invasive fungal infection is often based on detection of galactomannan (GM) in serum or bronchoalveolar lavage fluid combined with high-resolution computed tomography (CT) scan. These diagnostic tools do not provide specification of the causative Aspergillus isolate nor its susceptibility to antifungal agents. Normally A. fumigatus is susceptible to the clinically licensed triazoles itraconazole, voriconazole, and posaconazole. However, recent reports from the Netherlands and other European countries indicate that acquired resistance of A.fumigatus to azoles is emerging.
Case report: A 10-year old male with high-risk acute lymphoblastic leukemia treated with hematopoietic stem-cell transplantation developed pulmonary aspergillosis under prophylactic voriconazole. Before the transplantation there was suspicion of a fungal infection but was never proven. A transpleuric aspiration culture revealed a pan-azole-resistant *Aspergillus fumigatus*. Treatment with liposomal amphotericin B resulted in complete recovery.



[Chronological events]

Conclusions: Our case report emphasizes that azole resistance should be considered in patients who are failing azole therapy. As the frequency of azole resistance in *A. fumigatus* increases, invasive procedures to isolate fungi for species identification and susceptibilty testing becomes even more important.

P027

CIPROFLOXACIN RESISTANCE AMONG GRAM NEGATIVE ISOLATES OBTAINED FROM SURFACE SWABS AND BLOOD CULTURE IN A UK NEONATAL UNIT

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Background: Ciprofloxacin is on the WHO Essential Medicines List for Children but data is lacking about resistance patterns when it is used in routine practice for neonatal sepsis. We have used ciprofloxacin as "second line" treatment for more than 10 years and here report the incidence of resistance among Gram Negative (GN) isolates during this time.

Methods: The microbiology database for a tertiary neonatal unit was searched between 1997 and 2010 for GN isolates from surface swabs (SS) and blood cultures (BC).

Results: 24,552 SS yielded at least one GN isolate, from 5548 individuals. 243 individuals (4.4%) had at least one SS GN isolate that was resistant to ciprofloxacin. 242 GN isolates from BC were found in 169 individuals (3.0%). 14 individuals had BC GN isolates reported as resistant to ciprofloxacin (8.3% of individuals with BC GN isolates; 0.25% of neonates contributing to the database). These were isolated within 7 days of birth in 4 individuals (29% of individuals with GN isolates from BC); late onset GN BC resistant to ciprofloxacin occured in 0.2% of babies contributing to the database. None of the individuals with GN isolates from BC resistant to ciprofloxacin had SS GN isolates resistant to Ciprofloxacin.

Discussion: The extent of ciprofloxacin resistance in our unit is relatively low. Some resistance reflects vertical transmission from mothers. Ciprofloxacin resistance in GN from SS may not predict resistance among BC isolates. Ciprofloxacin continues to be a useful agent when it is important to avoid cephalosporins on neonatal units.

P028

CIPROFLOXACIN RESISTANCE AMONG GRAM NEGATIVE ISOLATES OBTAINED FROM SURFACE SWABS AND BLOOD CULTURE IN A UK NEONATAL UNIT

M. Turner[1], H. Hill[1], E. Jacqz-Aigrain[2], T. Neal[3], TINN, Treat Infections in Neo Nates

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Discussion: The extent of ciprofloxacin resistance in our unit is relatively low. Some resistance reflects vertical transmission from mothers. Ciprofloxacin resistance in GN from SS may not predict resistance among BC isolates. Ciprofloxacin continues to be a useful agent when it is important to avoid cephalosporins on neonatal units.

P029

CLINICAL EVOLUTION OF CHILDREN HOSPITALIZED WITH CELLULITIS TREATED WITH OXACILLIN OR CEPHALOTHIN

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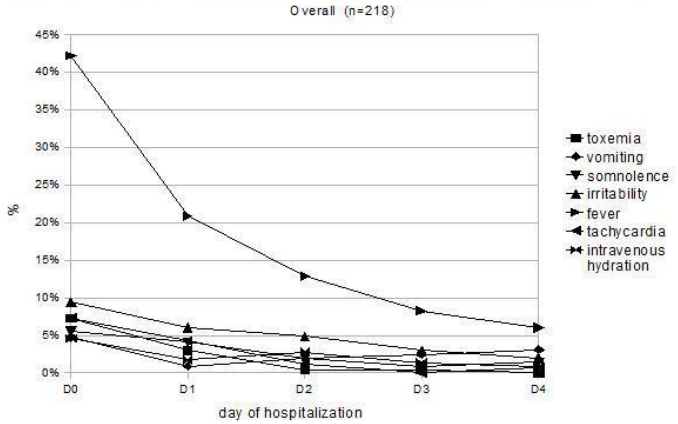
Backgroud and aims: Cellulitis is an important cause of hospitalization in pediatrics and therapeutics must consider changing on resistance profile of *Staphylococcus aureus*, because it is the main pathogen of cellulitis. We aimed to evaluate the evolution and outcome of children hospitalized because of cellulitis treated with oxacillin or cephalothin.

Methods: This retrospective cohort study enrolled 218 children hospitalized, from 2001 to 2008 in Salvador, Northeast Brazil, with cellulitis and treated with oxacillin or cephalothin ($\geq$ 100 mg/Kg/day).

Results: The median age was 2 years and 56.7% were males. Frequencies of signs and symptoms used in the clinical diagnosis were**:** swelling 91.3%, redness 81.7%, warmth 47.2% and tenderness 31.7%**.** All patients were discharged due to clinical recovery and the mean length of hospitalization was 7 ± 4 days; none of the patients died, needed intensive care or had sequels**.** By comparing the daily frequencies of clinical findings during hospitalization, significant decrease were found in frequencies of fever (admission day [42.2%], first day [20.8%], second day [12.9%], third day [8.3%], fourth day [6.1%]), toxemia, irritability, somnolence, vomiting, tachycardia and intravenous hydration (Graph 1).

Conclusion: Oxacillin or cephalothin remain the drugs of choice to treat uncomplicated cellulitis in regions were CA-MRSA is infrequent (< 10%).

Graph 1. Daily frequency of significant clinical findings during hospitalization of all patients with cellulitis.



[Graph1]

P030

EMERGENCE OF A MACROLIDE-RESISTANT SEROTYPE 19A PNEUMOCOCCAL STRAIN IN TWO CROATIAN REGIONS

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Background and aims: Antibiotic resistance within *Streptococcus pneumoniae* represents a major health problem in many countries. Increase in pneumococcal resistance to macrolides is particularly high in Croatia in the last years and macrolide resistance raised significantly from 25% in 2005 to 40% in 2008. The aim of this study was to compare the distribution of serotypes among resistant strains collected in four Croatian regions.

Methods: A total of 165 macrolide-resistant isolates were obtained from children under 16 years of age in different regions of Croatia (Zagreb, Rijeka, Osijek and Varazdin regions), with a mean age of three years. The macrolide-resistant isolates were collected in two month period (November 2009 till January 2010) from nasopharyngeal swabs, and serotyping of the strains was carried out by latex agglutination and Neufeld quellung test.

Results: The most common serotypes were 19A (23.6%) and 19F (23.6%). Other serotypes (1, 2, 3, 4, 5, 8, 6A, 6B, 6C, 7, 8, 9, 10, 11, 14, 15, 17, 18C, 19C and 23F) were detected with a low frequency. The macrolide-resistance in strains collected in Osijek and Varazdin regions was associated with serotype 19A, and the resistance in strains collected in Zagreb and Rijeka regions was associated with serotype 19F ($p < 0.01$).

Conclusions: Serotype coverage for the 7-valent conjugate vaccine in Osijek and Varazdin regions is low (< 20%) and emergence of a macrolide-resistant serotype 19A pneumococcal strain not included in 7-valent conjugate vaccine is detected.

P031

DETECTION OF ANTIBIOTICS RESISTANCE PATTERNS OF ISOLATES IN CHILDREN UNDER 14 WITH BACTERIAL INFECTIONS IN HAMADAN, WEST OF IRAN

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Background and aims: Bacterial infections are one of the main problems for pediatric diseases 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, West of Iran.

Methods: This study was performed on 6391 children under 14 years of age who admitted at pediatric wards in Ekbatan hospital in Hamadan city. All children which were diagnosed with pneumonia, meningitis, septicemia, 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 bacteria. 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, 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.

P032

ANTIBIOTIC PRESCRIBING FOR CHILDREN IN EMERGENCY DEPARTMENT IN A BUSY TERTIARY HOSPITAL IN LONDON

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Background and aims: Increasingly more children in the UK are seen in hospital emergency department (ED). There is limited published data on antibiotic prescribing in this setting. In contrast, detailed data is available on antibiotic prescribing by general practitioners. We carried out an audit to determine antibiotic use in the ED in a hospital in London.

Methods: We conducted a retrospective audit of antibiotic use in children aged under 16 years attending the ED between 1st - 5th November 2010. A standardised questionnaire was designed to collect data from medical notes and pharmacy records including doctor´s training-grade, patient demographics, diagnosis, and antibiotic therapy.

Results: Of 362 children (median age of 3 years, IQR 1.25, 9) who attended ED over a 5 day period, 61 (17%) received antibiotics. 10 (6%) of 166 children with surgical problems and 51 (26%) of 196 with medical diagnosis received antibiotics. The four main medical diagnosis were upper respiratory tract infection 41 (21%), viral gastroenteritis 21 (11%), lower respiratory tract infection 15 (8%) and tonsillitis 11 (7%) with 5%, 0%, 87% and 100% receiving antibiotics respectively. The commonest antibiotics prescribed were co-amoxiclav 16 (26%), amoxicillin 12 (19%), and phenoxymethylpenicillin 12 (19%). Antibiotic prescribing was not affected by doctor's training-grade in this preliminary dataset.

Conclusion: A high proportion of children seen in ED for a medical diagnosis were prescribed antibiotics in our cohort with all children diagnosed with tonsillitis receiving antibiotics without delayed prescribing. This is against current UK NICE-guidelines. This highlights the need for antibiotic stewardship.

P033

SERUM LEVEL MONITORING OF DAPTOMYCIN IN PAEDIATRIC PATIENTS

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Background and aims: Little is known about daptomycin pharmacokinetics in the paediatric population, particularly in neonates and infants. We determined serum levels of daptomycin in paediatric patients treated with this agent.

Methods: Blood sampling was performed from hospitalized paediatric patients of all age groups who had normal renal function and received daptomycin from May 2009 - December 2010. Sampling was performed before and 30 min after the end of the infusion, provided that ≥3 doses of daptomycin had been already administered. Serum levels were determined using Ultra-Performance Liquid Chromatography-UV detection.

Results: A total of 4 daptomycin dosages in 4 patients were studied. Patient characteristics, dosages and serum concentrations of daptomycin (mean of 2 measurements) are presented in Table 1. No adverse effects were associated with daptomycin treatment.

Patient	Gestational age at birth	Age / weight at sampling	Dosage of daptomycin	Daptomycin concentration (mg/l) before infusion	Daptomycin concentration (mg/l) after infusion
1	34 w	89 d / 4.4 kg	6 mg/kg/12h	7.1	10.9
2	38 w	26 d / 3.6 kg	6 mg/kg/12h	8.4	17.7
3	29 w	56 d / 2.0 kg	6 mg/kg/12h	<4	12.5
3	29 w	61 d / 2.1 kg	11 mg/kg/12h	6.3	15.1
3	29 w	65 d / 2.2 kg	15 mg/kg/12h	11.7	35.5
4	-	7 y / 25 kg	12 mg/kg/d	4.2	103.4

[Table 1]

Conclusions: Using a dosage of 6 mg/kg/12 hourly of daptomycin, serum concentrations after infusion in neonates and small infants are lower than those observed in adults receiving 4 mg/kg/day. It is likely that doses > 6 mg/kg/12 hourly are needed for these age groups to achieve similar drug exposure with adults.

P034

THE ACETYLATION PHENOTYPE AND DRUG INDUCED HEPATOTOXICITY IN THE TREATMENT OF TUBERCULOSIS IN CHILDREN

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Background: The incidence tuberculosis in children in Indonesia increases, some patients may be at risk for antituberculosis drug induced hepatotoxicity (DIH). However, as the acetylator type´s patients influence serum level of drug, therefore, acetylator status may predict DIH among TB-treated patients.

Objective: This study aimed to know association between acetylation phenotype status and antituberculosis DIH in children.

Methods: Prospective cohort of 61 children with pulmonary tuberculosis (boys/girls= 25/36, age 3.75±2.44 yr) who admitted to four hospitals in Yogyakarta area were enrolled in this study. Laboratory data had been followed before and 1-month after starting antituberculosis chemotherapy. Phenotype status (rapid, intermediate and slow acetylator) was based on the concentration ratio of urine acetylisoniazid and isoniazid that were determined by HPLC analyses. DIH was defined by elevation of serum aspartate or alanine aminotransferase (AST or ALT) at 1-month after starting anti-tuberculosis chemotherapy ≥1.5 times from the initial serum level.

Results: Among the 61 patients; 37 (61%), 8 (13%), 16 (26%) patients were rapid, intermediate and slow type acetylation, respectively. The mean of serum AST and ALT level after 1-month of treatment are increase significantly in slow acetylator compared to intermediate/rapid acetylator, 20.83 vs. 0.15 and 27.00 vs. 0.16, respectively. The total incidence of DIH was 6/61 (10%). The proportion of DIH in slow acetylator is significantly higher compared to intermediate and rapid acetylator with RR (adjusted with nutritional status and age) was 16.01 (95%CI 1.70-120.72)

Conclusions: There is significantly association between acetylation phenotype and antituberculosis drug-induced hepatotoxicity in children

P035

PAEDIATRIC ANTIMICROBIAL STEWARDSHIP PROGRAMS - HAVE WE STARTED YET IN EUROPE?

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Background and aims: An Antimicrobial Stewardship Program (ASP) comprises a series of measures adopted to optimize appropriate use of antimicrobials, thus improving efficacy, minimizing adverse effects, limiting the spread of antimicrobial resistance while promoting cost-effectiveness. The aim of this study was to determine the spread of ASP in paediatric medicine in Europe.

Methods: Systematic review of published literature on ASP, up to January 2011, in Medline, Embase and Web of Science, using the terms “antimicrobial stewardship; program(s); pediatric(s); Europe” in various combinations and a systematic hand search of the websites of major Children's Hospitals across Europe.

Results: Overall we found 174 published papers on ASP, from 26 countries, 49 (28%) papers from Europe. Regarding paediatric ASP, there are 13 published papers, none of which were from European countries. We could find no evidence of ASPs on any of the websites we searched (although not all hospitals could be identified).

Conclusions: In 2007, IDSA guidelines highlighted the paediatric population as a priority research group for effectiveness of ASPs. It is estimated that about a third of paediatric institutions now have formal ASPs in the USA. A systematic review of ASPs in paediatric settings found 28 studies that fulfilled the inclusion criteria, 75% of which had positive outcomes, although only 16 were held in a hospital. We could find no evidence as yet of the widespread uptake of ASP in the community or Children's Hospitals in Europe.

P036

REVIEW OF USEFULNESS OF GENTAMICIN PEAK LEVEL AND CRP IN PRESUMED EARLY SEPSIS IN OUR NEONATAL INTENSIVE CARE UNIT

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Background: Gentamicin is commonly used antibiotic for presumed early sepsis in NICU but associated with potential side effects.Most of the neonatal unit routinely monitor antibiotic levels (peak & trough). Monitoring CRP is also a common practice to aid in the diagnosis and/or monitor sepsis in newborn.

Aim: To review the usefulness and reliability of monitoring peak gentamicin level and day 1 CRP in suspected early neonatal sepsis.

Study design: A retrosepctive analysis of cases with suspected early sepsis in Neonatal Unit, Crosshouse Hospital, Scotland, UK over 6 months period (April-2010 to October-2010). Information gathered on gentamicin levels(peak, trough), CRP trends(day1 and subsequent levels on day2/3), other blood inflammatory markers(Blood counts, blood culture, other culture(CSF, Urine) and renal function during the first few days of life.

Result: Total 65 eligible cases were reviewed for gentamicin peak level of which 10 cases(15%)were found to have level more than 10(Normal peak level was considered between 5 and 10) although none of the doses were adjusted. Among the 63 eligible cases for trough, 7 cases(10%) were documented as more than 2(acceptable level with once daily gentamicin dose was between 1 and 2).

Majotiry of the day 1 CRP was normal, most of them showed delayed response and only one case had borderline high CRP which became normal by day 2/3.Neither White cell or Platelet count was strongly associated with sepsis.

Conclusion: Exclusion of routine monitoring of gentamicin peak level and day 1CRP might save extra cost and infection risk in neonatal unit.

P037

ANTIBIOTIC TREATMENT FOR NEONATAL COAGULASE-NEGATIVE STAPHYLOCOCCAL SEPSIS: 3 DAYS IS ENOUGH!

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Background and aims: The incidence of coagulase-negative staphylococcal (CONS) sepsis is high in neonatal intensive care units (NICUs) and treatment significantly adds to the antibiotic pressure, increasing the threat of resistance. Because infants recover within 24-48 hours, blood cultures are negative within 48 hours and CRP normalizes within 72 hours, we reduced anti-CONS treatment from 7 to 3 days in infants with uncomplicated CONS sepsis. Aim of the study was to evaluate the safety and efficiency of short (3 days) treatment duration for CONS sepsis.

Methods: All infants with CONS sepsis during January 2006- June 2010 were evaluated. Before 2008 the duration of anti-CONS treatment was 7 days, in 2008 it was reduced to 3 days, provided that infants recovered within 48 hours, CRP value decreased, thrombocytes were normal and there was no indwelling catheter. Clinical results of infants with 3-days treatment duration were compared with infants with 7-days treatment duration.

Results: In 142 infants CONS sepsis was confirmed, of which 62 (44%) were treated during 7 days and 80 (56%) during 3 days. Clinical characteristics were not different between the groups. All infants recovered within 48 hours and CONS sepsis did not relapse.

Conclusions: Antibiotic treatment for CONS sepsis can be shortened to 3 days when clinical improvement is rapid and central lines are not present. Prospective randomized studies are needed to confirm the results of this single-center study. Future studies may reveal the effects on the development of antimicrobial resistance.

P038

EVIDENCE BASED EMPIRIC ANTIBIOTIC CHOICES FOR PAEDIATRIC BACTERAEMIA: NATIONAL SUSCEPTIBILITY PROFILES OF GRAM-POSITIVE AND GRAM-NEGATIVE BACTERAEMIA IN ENGLAND AND WALES

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Background and aims: To compare the activity of combinations of antibiotics recommended for empirical treatment of paediatric sepsis by the British National Formulary guidelines for Children (BNF-C). The guidelines recommend: gentamicin+amoxicillin, or cefotaxime/ceftriaxone alone or aminoglycoside+anti-pseudomonal beta-lactam if pseudomonas suspected, or flucloxacillin or vancomycin if Gram-positive infection suspected.

Methods: The Health Protection Agency's national surveillance database was interrogated to determine the 10 commonest pathogens causing bacteraemia in children (1 month - 18yrs) and their antimicrobial susceptibility. Data were aggregated to capture resistance rates for the time period July 2008-June 2010 in England and Wales.

Results: The 10 commonest pathogen groups (accounting for ~80% of reported paediatric bacteraemias) comprised coagulase-negative staphylococci (CoNS) (28%), *Staphylococcus aureus* (10%), non-pyogenic streptococci (9%), *Streptococcus pneumoniae* (7%), *Enterococcus* spp. (7%), *Escherichia coli* (5%), *Neisseria meningitidis* (5%), *Klebsiella* spp. (4%), *Enterobacter* spp. (3%) and *Pseudomonas aeruginosa* (2%). For Gram-positives, resistance to gentamicin+amoxicillin was ≤1% apart from CoNS (28%); the corresponding figures for Gram-negatives were 3-9%. Resistance to cefotaxime/ceftriaxone varied with species (0-12%) but was not commonly reported for staphylococci. Staphylococci remained fully-susceptible to gentamicin+vancomycin. *Pseudomonas* spp. remained susceptible (>96%) to anti-pseudomonal combinations.

Conclusions: The susceptibility results show that for each organism, at least one of the recommended antibiotic therapies was appropriate. However, this study does highlight the need for regular and timely surveillance of antimicrobial susceptibility of bacteria causing invasive disease in children to allow objective assessment of the continued appropriateness of national treatment guidelines.

P039

ANTIMICROBIAL RESISTANCE PATTERNS IN A UK LEVEL 3 NEONATAL INTENSIVE CARE UNIT, A 5 YEAR EXPERIENCE

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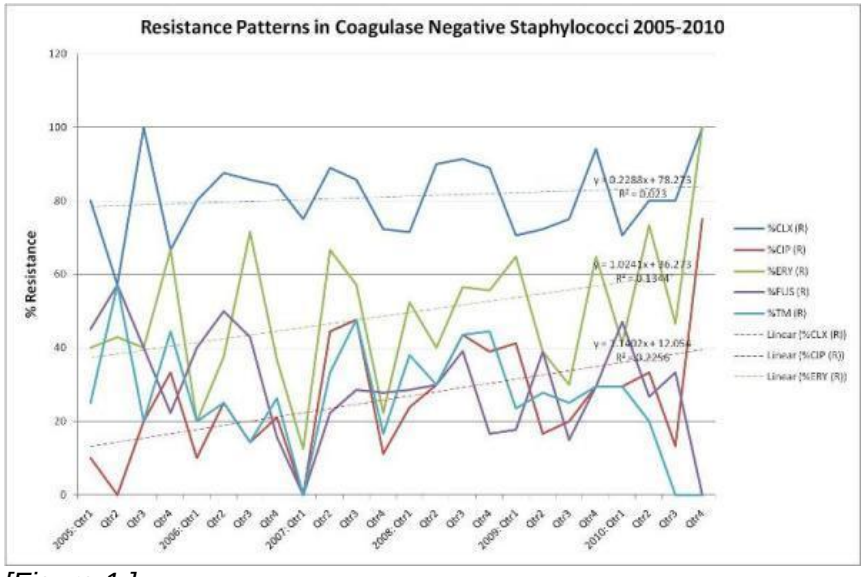
Background and aims: Empirical antimicrobial guidelines are constantly evolving in response to laboratory susceptibility data. Broad spectrum agents exert selection pressure gradually increasing antimicrobial resistance over time, particularly in those patients with lengthy inpatient admissions. In the neonatal intensive care unit (NICU), the majority of blood culture isolates are coagulase negative staphylococcocci (CoNS), which require appropriate empirical therapy. We present 5 years of antimicrobial susceptibility data from significant bacteraemia isolates of our NICU patients.

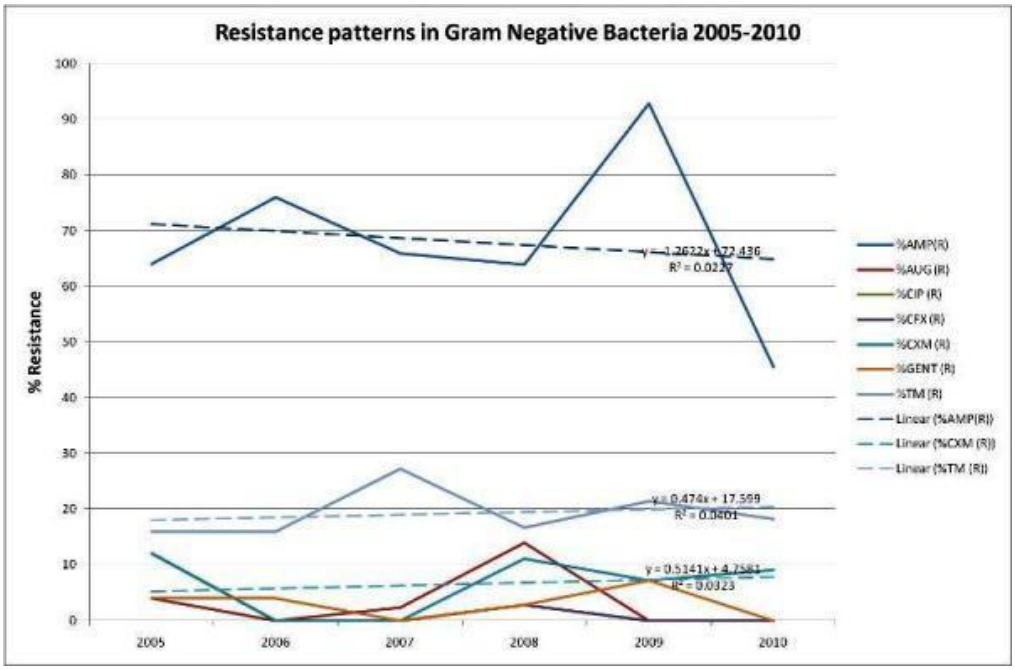
Methods: A retrospective analysis was performed of all positive blood cultures from January 2005 to October 2010. Speciation and susceptibilities were downloaded from the pathology system, analysed in Microsoft^{Ò}Excel 2010, and best fit analyses performed.

Results: There were 794 positive blood cultures during the study period, with 639 isolates (80.5%) identified as CoNS. The remaining 155 included 34 other Gram positives (4.3%) (Fig 1.)



[Figure 1.]

and 121 Gram Negatives (16.5%) (Fig 2)



[Figure 2.]

. There is an increase in CoNS resistance over 5 years to cloxacillin with no resistance to vancomycin identified. Gram negative resistances appear more stable, with a decreasing resistance to amoxicillin reflecting changes in prescribing policies.

Conclusion: Changing local trends in antimicrobial susceptibility should be considered when formulating empiric antimicrobial policies.

P040

OUR EXPERIENCE IN THE MANAGEMENT OF RHEUMATIC FEVER RECURRENCES

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Rheumatic fever (RF) recurrences, as the most important RF features, reflect the success of secondary prophylaxis.

Objective: To present RF recurrences during a long term period and to stress our experience in the secondary prophylaxis of RF.

Material and methods: Retrospective study of precompleted case protocols of children with RF recurrences, hospitalized at University Children´s Hospital, Prishtina, between 1974/1998. The diagnosis of RF has been made following the revised Jones criteria. This retrospective study was conducted to include a period of 25 years, which is characterised (especially period to 90s) with a high number of patients with RF and RF recurrences.

Results: Of 1050 patients with RF, 889 (85%) manifested only one RF attack, while the remaining 161 (15%) had one, two or more recurrences. So, 94 patients (58.4%) had only one recurrence, others 67 (41.6%) had two or more recurrences.The majority of recurrences occured in the first year of initial attack of RF; there was a strong correlation between RF recurrences and irregular prophylaxis ($p< 0.01$). There were also some recurrences occuring after interruption of regular five year prophylaxis, but in some instances RF appeared many, even ten years after the end of prophylaxis.

Twenty recurrences have been reported even during continuous regular, monthly prophylaxis with Benzathine Penicillin G. After 90s, when the new, every three weeks regimen of BPG prophylaxis, is in use, no recurrences occured in children in regular prophylaxis.

Conclusion: Every three weeks schedule was sufficient for RF secondary prophylaxis in our patients.

P041

USE OF THE BETA-LACTAM (BL) AMOXICILLIN (A), AMOXICILLIN/CLAVULANATE (A/C) AND CEFACLOR (C) IN THE ITALIAN PEDIATRIC POPULATION

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Background and aims: Antibiotics (AB) are the most prescribed drugs by italian Family Pediatricians (FP). The most used are BL, especially A, A/C and C. AB are often prescribed even without a confirmed bacterial infection, so the risk of adverse events, bacterial AB-resistance and infection related costs rise up. Aim of this study is to describe the use of these BL (indications, duration and switching) by age and sex.

Methods: All the children ≤ 12 years of the Pedianet (an Italian FP research network) database receiving at least one prescription of A, A/C or C in the period 1/1/2003-30/6/2007 were considered. Prevalence of use, diagnosis at prescription and characteristic of switching were assessed.

Results: A total of 785,326 drugs were prescribed to 110,747 children. 335,352 (42.7%) were AB. Among them 168,458 (50.2%) were BL. A was prescribed in 87,305 cases (51,8%), A/C in 55,791(33.1%) and C 25,362 cases (15.1%). The overall prevalence of BL use was 21.5%. Diagnosis at the time of prescription was viral-URTI (25.1%), bacterial-URTI (21.1%), otitis (14.5%), bronchitis (5.2%), bronchitis with bronchospasm (2.3%), pneumonia (0,8%) and urinary tract infection (0.1%). A is the most prescribed AB in all age groups ($p < 0.0001$). The mean dose was in the expected range.

Conclusions: A is the first choice in the main childhood diseases as recommended by the guidelines. Despite probable viral etiology, antibiotic prescribing for URTI is still high. These data suggest that a programme to promote a more appropriate use of antibiotics has to be improved.

P042

COMPARING THE EFFECT OF SECNIDAZOLE AND METRONIDAZOLE FOR THE TREATMENT OF GIARDIASIS IN CHILDREN

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Giardiasis is one of the most common intestinal parasitic infection among children . It is a world wide and an important disease in Iran.

Abdominal pain, bloat, chronic or intermitant diarrhea and steaturrhea which cause malabsorption are the main clinical signs.

The etilogic agent is Giardia lamblia which is found in the form of trophozite

(pathogenic form) and cyst (infective form).

The infective form is Transmitted by water, direct contact, vegetables and flies In order to evaluate the efficacy of secnidazole (a new drug) and comparing with the effect of metronidazole, a study was undertaken over a 15 month period on 83 patients suffering from giardiasis in Imam Reza Hospital.

After a questionair was complited for each patient , the patients were treated with secnidazole (30 mg/kg single dose) and metronidazole (15 mg/kg tid for 7 days) randomly.Two weeks after the end of treatment , direct and formol- ether fecal examination was performed on 3 consecutive days for each child.

Examinations showed that secnidazole is effective in 94.4% and metronidazole is effective in 80% of infected children ($P< 0.05$).

Since secnidazole had milder side effects and was more effective in relation to metronidazole and it can be used in single dose it can be concluded as a better drug than metronidazole for treatment of giardiasis in childrens .

P043

STUDY OF PROTEIN LOAD INFLUENCE AND DIFFERENT PH STATUS OF NUTRIENT MEDIUIM ON ANTIMICROBIAL ACTIVITIES OF DECAMETOXINE AND FIXATIVE COMPOSITIONS

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[1]Vinnitsa National Medical University named after N. Pyrogof, Vinnitsa, [2]Khmelnytskyi National Uiversity, Khmelnytskyi, Ukraine

Background and aims: There are a lot of unsolved problems in chronic wound treatment [1] and one of the right ways up recovery is the investigation of wound dressings with antseptic decametoxine with fixative composition carboxymethylamylum (CMA).

Methods: Antimicrobial properties of decametoxine while combining it with CMA that can be used for making fixative composition of antiseptics' impregnated fabrics have been studied in this research work.We studied antimicrobial activity both decametoxine and composition of decametoxine with CMA in conditions of protein load, pH changes of nutrient mediuim. We studied the sensitivity of different groups of microorganisms to decametoxine compositions.

Conclusions: Results of our study have shown high antimicrobial abilities of 0,1 % decametoxine solution in the composition with carboxymethylamylum as to S. aureus strains (minimal bactericidal concentrations (MBcC) - 0,78 - 6,25 mkg/ml) so as to Gram-negative bacteria (M±m=55±20,54 mkg/ml) regardless of mediuim's pH changes. In conditions of protein load the McC, in S. aureus group, ranged 0,48 - 12,5 mkg/ml and in the Gram-negative bacteria the meanings of decametoxine composition with carboxymethylamylum were no more than 125 mkg/ml. We proved that composition of decametoxine and carboxymethylamylum has strong and stable antibacterial effect and can be used for future investigation of modern antiseptic wound dressings.

P044

SENSITIVITY OF S. AUREUS STRAINS TO WOUND DRESSINGS IMPREGNATED WITH SURFACE-ACTIVE ANTISEPTICS

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Background and aims: Local treatment by means of antimicrobic dressings has very important role. There are majority of attempts concentrated on developing additional antimicrobial properties by the way of adding antiseptics in textile fibre, chlorhexidine and decametoxine are one of them.

The aim of our research work was to identify inhibitory and bactericidal concentrations of chlorhexidine and decametoxine, which can be used for wound dressings' impregnation.

Methods: In this study inhibitory and bactericidal concentrations of chlorhexidine and decametoxine being used for the impregnation were the bodies of interest.

Static and bactericidal concentrations were determined according to the museum and clinical strains of S. aureus (31, 24, 72, 2289, 25316) by the method of serial delutions.

Results: As a result of the experiment, we have got the next data:

1) chlorhexidine static concentration was 0,49 mkg/ml for strains N 31, 24, 72, 25316 and 0,24 mkg/ml for 2289; in the case of decametoxine inhibitory concentrations were - 3,9; 0,12; 0,24; 0,98; 0,24 mkg/ml for the same srains;

2) chlorhexidine bactericidal concentrations was 0,98 mkg/ml for strains N 24, 72, 25316; 1,9 mkg/ml for N 31 and 3,9 mkg/ml for N 2289; speaking about decametoxine the meanings were 7,8; 0,24; 0,48; 1,9; 0,48 mkg/ml for these strains of S. aureus.

Conclusions: The results testify that decametoxine have demonstrated better inhibitory and higher bactericidal activity in comparison with chlorhexidine. We prognosticate that wound dressings impregnated with decametoxine will posses higher antiseptic activity than chlorhexidine.

P045

PERSPECTIVE USING OF DECAMETOXINE FOR FRAMING WOUND DRESSINGS WITH STEADY POTENT ANTIMICROBIAL ACTIVITIES

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Background and aims: Nowadays when new technologies present us a wide variety of pus and septic wounds' treatment, topical antiseptics have prominent role in this process. Framing of new wound dressings, impregnated with antiseptics especially decametoxine is very perspective and of great importance. We aimed to study antimicrobial activities of decametoxine composition with modified polysaccharide, which can be used for textile impregnation.

Methods: We studied minimal bacteriostatic and bacteriocydic concentrations of decametoxine and its complex with modified polysaccharide (carboxymethylamylum) by the method of serial dilutions**.**

Microbial spectrum included 10 clinical strains of S. aureus and museum's strains of P. aureginosa, P. mirabilis, K. pneumoniae, E. coli 0111, E. coli M 17. Fungistatic and fyngicydic activities were studied accordind to the strains of C.albicans.

Results: As a result of the experiment we have found very high antimicrobial activities of decametoxine according all studied strains of S. aureus. The meaning of MBSC in this group was 0,06 - 1,9 mkg/ml and MBCC - 0,48 - 31,2 mkg/ml (M±m= 4,52 ± 4,1). Some more resistant were Gram-negative microorganisms. P. mirabilis, K. pneumoniae, E. coli in this group were the most sensitive to decametoxine, having MBCC - 125, 125, 62,5 mkg/ml accordingly. Carboxymethylamylum, added to the composition of decametoxine, maintained high fungicydic activity. Decametoxine along and in the combination with modified polysaccharide had minimal fungicydic activity - 1,9 mkg/ml.

Conclusions: Everything that was mentioned gives us the possibility to use carboxymethylamylum as the component of fixative composition in medical textile impregnation with antiseptics.

P046

STUDY OF PROTEIN LOAD INFLUENCE AND DIFFERENT PH STATUS OF NUTRIENT MEDIUIM ON ANTIMICROBIAL ACTIVITIES OF DECAMETOXINE AND FIXATIVE COMPOSITIONS

G.K. Paliy[1], **O.A. Nazarchuk**[1], O.I. Kulakov[2]

[1]Vinnitsa National Medical University named after N. Pyrogof, Vinnitsa, [2]Khmelnytskyi National Uiversity, Khmelnytskyi, Ukraine

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Methods: Antimicrobial properties of decametoxine while combining it with CMA that can be used for making fixative composition of antiseptics' impregnated fabrics have been studied in this research work.We studied antimicrobial activity both decametoxine and composition of decametoxine with CMA in conditions of protein load, pH changes of nutrient mediuim. We studied the sensitivity of different groups of microorganisms to decametoxine compositions.

Conclusions: Results of our study have shown high antimicrobial abilities of 0,1 % decametoxine solution in the composition with carboxymethylamylum as to S. aureus strains (minimal bactericidal concentrations (MBcC) - 0,78 - 6,25 mkg/ml) so as to Gram-negative bacteria (M±m=55±20,54 mkg/ml) regardless of mediuim's pH changes. In conditions of protein load the McC, in S. aureus group, ranged 0,48 - 12,5 mkg/ml and in the Gram-negative bacteria the meanings of decametoxine composition with carboxymethylamylum were no more than 125 mkg/ml. We proved that composition of decametoxine and carboxymethylamylum has strong and stable antibacterial effect and can be used for future investigation of modern antiseptic wound dressings.

P047

SENSITIVITY OF S. AUREUS STRAINS TO WOUND DRESSINGS IMPREGNATED WITH SURFACE-ACTIVE ANTISEPTICS

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Background and aims: Local treatment by means of antimicrobic dressings has very important role. There are majority of attempts concentrated on developing additional antimicrobial properties by the way of adding antiseptics in textile fibre, chlorhexidine and decametoxine are one of them.

The aim of our research work was to identify inhibitory and bactericidal concentrations of chlorhexidine and decametoxine, which can be used for wound dressings' impregnation.

Methods: In this study inhibitory and bactericidal concentrations of chlorhexidine and decametoxine being used for the impregnation were the bodies of interest.

Static and bactericidal concentrations were determined according to the museum and clinical strains of S. aureus (31, 24, 72, 2289, 25316) by the method of serial delutions.

Results: As a result of the experiment, we have got the next data:

1) chlorhexidine static concentration was 0,49 mkg/ml for strains N 31, 24, 72, 25316 and 0,24 mkg/ml for 2289; in the case of decametoxine inhibitory concentrations were - 3,9; 0,12; 0,24; 0,98; 0,24 mkg/ml for the same srains;

2) chlorhexidine bactericidal concentrations was 0,98 mkg/ml for strains N 24, 72, 25316; 1,9 mkg/ml for N 31 and 3,9 mkg/ml for N 2289; speaking about decametoxine the meanings were 7,8; 0,24; 0,48; 1,9; 0,48 mkg/ml for these strains of S. aureus.

Conclusions: The results testify that decametoxine have demonstrated better inhibitory and higher bactericidal activity in comparison with chlorhexidine. We prognosticate that wound dressings impregnated with decametoxine will posses higher antiseptic activity than chlorhexidine.

P048

PERSPECTIVE USING OF DECAMETOXINE FOR FRAMING WOUND DRESSINGS WITH STEADY POTENT ANTIMICROBIAL ACTIVITIES

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Background and aims: Nowadays when new technologies present us a wide variety of pus and septic wounds' treatment, topical antiseptics have prominent role in this process. Framing of new wound dressings, impregnated with antiseptics especially decametoxine is very perspective and of great importance. We aimed to study antimicrobial activities of decametoxine composition with modified polysaccharide, which can be used for textile impregnation.

Methods: We studied minimal bacteriostatic and bacteriocydic concentrations of decametoxine and its complex with modified polysaccharide (carboxymethylamylum) by the method of serial dilutions**.**

Microbial spectrum included 10 clinical strains of S. aureus and museum's strains of P. aureginosa, P. mirabilis, K. pneumoniae, E. coli 0111, E. coli M 17. Fungistatic and fyngicydic activities were studied accordind to the strains of C.albicans.

Results: As a result of the experiment we have found very high antimicrobial activities of decametoxine according all studied strains of S. aureus. The meaning of MBSC in this group was 0,06 - 1,9 mkg/ml and MBCC - 0,48 - 31,2 mkg/ml (M±m= 4,52 ± 4,1). Some more resistant were Gram-negative microorganisms. P. mirabilis, K. pneumoniae, E. coli in this group were the most sensitive to decametoxine, having MBCC - 125, 125, 62,5 mkg/ml accordingly. Carboxymethylamylum, added to the composition of decametoxine, maintained high fungicydic activity. Decametoxine along and in the combination with modified polysaccharide had minimal fungicydic activity - 1,9 mkg/ml.

Conclusions: Everything that was mentioned gives us the possibility to use carboxymethylamylum as the component of fixative composition in medical textile impregnation with antiseptics.

P049

THE NEW ATTEMPT TO INVESTIGATE ANTISEPTIC-FIXATIVE COMPOSITION, RESISTANT TO CONDITIONS OF DIFFERENT MICROBIAL LOAD

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Background and aims: Accordingly to National Nosocomial Infections Surveillance (NNIS) data surgical square has 14-16% of different nozocomial infections, wound microflora is represented by bacteria association [1]. For excellent wound's treatment using dressings with antiseptic abilities is of great importance. Dressing's efficacy is dependent on fixative composition of antiseptic because of its compatibility to antiseptic molecular structure and micro-environmental influence in the wound on them.

Methods: We aimed to study antimicrobial properties of decametoxine while combining it with carboxymethylamylum (CMA) - the modified polysaccharide complex that can be used as fixative composition while developing antiseptics' impregnated fabrics. Antimicrobial activity both of decametoxine and decametoxine with carboxymethylamylum in conditions of different microbial load (from 10^3 to 10^9 colony generating unital per ml) were studied. We, also, studied the sensitivity of different groups of microorganisms to carboxymethylamylum without its combining with antiseptics.

Conclusions: Results of our research have demonstrated high antimicrobial abilities of 0,1 % decametoxine solution in the complex with modified polysaccharide, which improved decametoxine activity and provided its antiseptic's stability despite microbial rate. Minimal bactericidal concentrations (MBcC) to S. aureus strains ranged M ± m=2,68±1,16 mkg/ml. Among Gram-negative bacteria, K. pneumoniae NCTC 5055, E. coli have been shown were the most sensitive (maximum MBcC were 50 mkg/ml for both).

P050

ACUTE RHEUMATIC FEVER; REALITIES BEHIND PENICILLIN PROPHYLAXIS AND FUTURE

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Background: Acute rheumatic fever (ARF) is a systemic immunologic response to group A streptococci (GAS). Traditional descriptions of classic features of ARF were established in pre-modern rheumatology era when the armamentarium of laboratory test was poor and wide classification of diverse rheumatologic conditions was not taken in to consideration. Anti-inflammatory and anti-degenerative actions of penicillin (PCN) derivatives are discovered several years after establishing monthly PCN as antibiotic prophylaxis for ARF.

Objectives: To clarify the realities behind routine diagnosis and PCN prophylaxis in ARF

Methods: Searching ARF and ARF-mimickers among 25,000 records of a general rheumatology clinic during 2003-2010 in Yazd, central Iran

Results: Around 80 patients were diagnosed for ARF by non -rheumatologist physicians but only 4 patients fulfilled the Jone´s criteria for acute rheumatic fever. Almost all patients who were receiving monthly penicillin showed some clinical improvement in their arthritis regardless of diagnoses. About 10% of patients who were diagnosed initially for ARF found to have classic picture of some specific rheumatic disorders. Main features against the diagnosis of ARF in remaining 90%, were chronic joint involvement, persistent elevated acute phase reactants, anemia of chronic disease and other findings suggestive of specific rheumatic disorder

Conclusions: Almost all cases with diagnosis of ARF by non-rheumatologist doctors were misdiagnosed. Considering anti-inflammatory effect of PCN, clinical efficacy of PCN could not be simply attributed to its antibiotic effects. Further studies might prove that ARF also would be simply managed as other chronic rheumatic diseases after per-case eradication of GAS infections

P051

PROTECTIVE EFFECTS OF PYRIDOXINE AGAINST OXIDATIVE STRESS AND HEMATOLOGIC SIDE EFFECTS OF LINEZOLID

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Background and aims: Increase in gram-positive infections caused marked consumption of vancomycin and, in turn, global dissemination of its resistance. Linezolid is produced for serious gram-positive infections. However, its possible side-effects on bone marrow may limit its use. There is no data in the children concerning the protection against linezolid side-effects by pyridoxine. We wanted to evaluate the protective effect of pyridoxine against oxidative stress and hematologic side-effects of linezolid.

Methods: We used 40 male pediatric (8-weeks old) Spraque Dawley rats and divided them into four groups. We administered 1 mL of saline solution to the control group (C, n:10), 125 mg/kg/day of linezolid to the the linezolid group (L, n:10), 100 mg/kg/day of pyridoxine to the the pyridoxine group (P, n:10) and 125 mg/kg/day of linezolid and 100 mg/kg/day pyridoxine to the last group (LP, n:10) for 14 days by gavage. Blood samples were collected before and after the drug administration period to measure complete blood count, serum urea, creatinine, ALT, AST, total and direct bilirubin values. Glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), catalase (CAT) activities, and malondialdehyde (MDA) levels were measured in the erythrocytes.

Results: When we compared the results of linezolid group to the LP group; serum MDA & ALT levels and SOD, GSH-Px, CAT activities increased significantly ($p < 0.05$).

Conclusion: It was documented that pyridoxine prevented anemia but has no protective effects on linezolid-induced leukopenia and increased ALT level. These results suggest that pyridoxine may protect against linezolid-induced oxidative stress by decreasing MDA levels.

P052

POPULATION PHARMACOKINETICS OF MEROPENEM IN VERY LOW BIRTH WEIGHT NEONATES

H. Padari[1], E. Germovsek[2], M.-L. Ilmoja[3], K. Kipper[4], K. Herodes[4], J. Standing[2], L.-T. Heidmets[1], T. Metsvaht[1], I. Lutsar[5]

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Background and aims: Meropenem, a broad-spectrum antibiotic, is well tolerated by neonates and effective as monotherapy with good penetration into body fluids and tissues. We aimed to describe the pharmacokinetic profile of meropenem in very low birth weight (VLBW) infants.

Methods: Prospective open-label two-centre study included septic neonates with BW < 1500g. Meropenem diluted in 0.9% sodium chloride to a concentration of 10mg/ml was given over 30 min at a dose of 20mg/kg q12h. Blood samples were collected at steady state before; 0.5; 1.5; 4; 8 and 12h of drug administration. Meropenem concentration was measured by UHPLC. Data were modelled with non-linear mixed effects software NONMEM, non-compartmental analysis performed with R.

Results: Nine neonates with mean (SD) BW of 896 (239) g and GA of 26.9 (1.4) wk, were studied at 17.7 (11.0) day of life, 5 had culture positive sepsis. One-compartment model with linear clearance (CL) scaled with weight and maturation based on empirical model of renal CL from Rhodin et al 2008 was used. Volume distributon (VD) was scaled by linear body weight. The final parameter estimates were: CL = 7.01 L/h/70kg (RSE = 8.90 %) and VD = 18.0 L/70kg (RSE = 12.89 %). Mean (SD) $AUC_{(0\text{-}t)}$ was 377.4 (31.4) mg.h/L. Model predictions of AUC were unbiased: median relative prediction error was -2.6%.

Conclusions: A dose of 20 mg/kg given over 30 min is appropriate for the treatment of serious infections in neonates although estimate of CL is lower than previously reported.

P053

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P054

PREREQUISITES OF PHAGE THERAPY OF BACTERIAL INFECTIONS IN NEWBORNS

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Background: The emergence of antibiotic-resistant bacteria is a world-wide problem of modern medicine, incl. pediatrics and neonatology. Antibiotic-resistant bacterial infections worsen the clinical course of diseases and raise the cost of treatment. A number of new generation antibiotics have restrictions for their usage in newborns. Bacteriophages (phages) are considered to be alternatives to conventional drugs. Nevertheless, references indicating the reasonability of phage therapy in newborns are scarce.

Aim: To reveal possible prerequisites of phage therapy for bacterial infections in newborns.

Methods: The systemic analysis of literature 1990-2010 concerning the clinical aspects of phage therapy in pediatrics was performed.

Results: The majority of papers came from Poland, Russia and Georgia. Phages were administered orally, topically or systemically. Double blind clinical trials were not found. It was shown that

a) Phages could be active against Proteus, Klebsiella, Escherichia, Shigella, Pseudomonas, Salmonella, Streptococcus, Staphylococcus;

b) Phage therapy has no significant adverse reactions;

c) Orally given phages are capable of disseminating into blood, stool, and urine;

d) There are some data about the effectiveness of phage therapy in infants.

Conclusions: Received results give promise in terms of employing the phage therapy in the treatment of bacterial infections in newborns. It is necessary to carry out controlled, double-blind clinical trials designed according to modern requirements in order to establish the appropriateness of this therapeutic approach.

This work was supported by STCU4316/GNSF127.

P055

MONITORING ANTIBIOTIC USE IN HOSPITALISED CHILDREN. IS IT FEASIBLE?

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Background and aims: The aim of the present study was to assess antibiotic use in paediatric wards by comparing defined daily doses (DDD) per 100 bed-days methodology to a simple method for monitoring weight adjusted antibiotic use.

Methods: A retrospective study (2002-2006) was carried out in 3 paediatric wards at Oslo University Hospital, Rikshospitalet. Antibiotic consumption data (ATC-group J01) was extracted from the hospital pharmacy database. Conversion to DDD per 100 bed-days was done in accordance with WHO recommendations. Individual length of stay, sex and age in months were retrieved. Weight adjusted consumption corrected for bed-days (kg-doses/100 kg-days) was calculated based on median weight for gender and age for Norwegian children and recommended daily doses (RDD) in mg/kg*day^-1 based on national guidelines for hospital antibiotic use. We developed a mathematical model in order to analyse trends over time and compare the two methods.

Results: There was significant increase in consumption of ´other beta-lactam antibacterials´ (J01D) for both methods (p=0.002), mainly due to increased consumption of carbapenems. Carbapenem use increased from 6.5 to 14.0% (DDD/100 bed-days) and 4.0 to 10.0% (kg-doses/100 kg-days) of total antibiotic use. Penicillins with extended spectrum (J01CA) were most frequently used, regardless of method. Carbapenems (J01DH) ranked second for DDD/100 bed-days, but fifth for kg-doses/100 kg-days.

Conclusion: When monitoring major trends over time, the two methods yielded comparable results. However, when adjusting for weight, the rank between the antibiotics changed substantially. In our opinion, this method provides a more accurate description of the consumption patterns.

P056

SIDE EFFECTS OF OSELTAMIVIR AMONG CHILDREN AND ADOLESCENTS IN SINGAPORE - A CROSS SECTIONAL SURVEY

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Background: Before the Influenza A (H1N1) 2009 pandemic, neuro-psychiatric adverse events in patients receiving oseltamivir for seasonal influenza have been reported in Japan.

Aims: To examine oseltamivir compliance rates, side effects and incidence of these side effects among children and adolescents in Singapore during the Influenza A (H1N1) 2009 pandemic.

Methods: A cross-sectional study using a structured telephone interview administered to all patients under 18 years old residing in Singapore, who were prescribed oseltamivir (for treatment or prophylaxis) by KK Women´s and Children´s Hospital from 1 June 2009 to 15 Aug 2009.

Results: The positive response rate in our survey was 79.4% (n=3654).The oseltamivir compliance rate was 82.1%. Among those surveyed, 16.6% had at least 1 side effect of oseltamivir. The main side effects were gastrointestinal (9.7%), followed by neuropsychiatric eg behaving strangely, feeling confused, hallucinations, mood swings or seizures (3.7%).

Risk factors for neuropsychiatric side effects were presence of underlying psychological disorder or epilepsy (OR 4.8, 95% CI 2.0-11.7, p= < 0.0001; adjusted OR 4.8, 95% CI 2.0-11.7, p= 0.001) and older children aged 10 to 18 years [OR 1.5, 95% Confidence interval 1.0-2.3, p= 0.057 (approaching significance)].

Conclusions: The burden of side effects must be considered when deciding on oseltamivir prophylaxis or treatment of Influenza A (H1N1) 2009 infection in children considering the disease is generally mild. Children with underlying psychological disorder or epilepsy and children aged 10 to 18 years are at higher risk of having neuropsychiatric side effects of oseltamivir.

P057

ANTIMICROBIAL UTILIZATION PATTERN IN INDIAN PEDIATRIC OUTPATIENT SETTING

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Objective: To study the drug utilization pattern, with reference to use of antimicrobials, in pediatric outpatient setting.

Methodology: The prescriptions of children up to 18 years visiting the clinic were studied during the study period of October 07-March 09. The WHO recommended prescribing indicators were used as a tool for evaluating the drug prescribing patterns. The total cost of drugs prescribed was estimated by utilizing the WHO recommended complementary indicators for cost. The cost determination was done for the entire duration of therapy prescribed.

Results: A total of 4059 consecutive prescriptions were studied. The study population comprised 2509 male and 1550 female patients. The average number of drugs per encounter was 2.86±0.20. Though infections contributed to approx. 60% of the total cases, only 18% of the patients were prescribed with AMDs. Further, none of the prescriptions had more than one AMD prescribed in it. As many as fourteen AMDs were prescribed to the over 700 patients for a total of 2339 days. The average duration of AMDs for each encounter was 3.2±0.6 days. Azithromycin was the most frequently prescribed AMD (164 patients). The average cost of drugs per prescription was found to be INR135.5±0.5. Only 8.5% and less than 1% of the total cost of drugs was spent on the AMDs and injections respectively.

Conclusion: The results of this study have provided evidence for very judicious use of antimicrobial drugs and injections in children, which has led to a reduction in the cost of prescriptions.

P058

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P059

POTENTIALLY TOXIC EXCIPIENTS ARE FOUND IN ORAL ANTIMICROBIAL AGENTS USED IN UK NEONATAL UNITS

M. Turner[1], W. Clarke[2], T. Nunn[1], U. Shah[3], H. Mulla[2], H. Pandya[2], European Study on Neonatal Excipient Exposure (ESNEE)

[1]Women's and Chidren's Health, University of Liverpool, Liverpool, [2]University of Leicester, Leicester, [3]Alder Hey Children's NHS Foundation Trust, Liverpool, UK

Background: Excipients are used to facilitate the manufacture of dosage forms and maintain the stability of medications in the face of chemical and microbial challenges. Some excipients have been associated with mortality and significant morbidity in neonates but the extent of exposure to excipients related to antimicrobials used in neonates has not been reported.

Methods: A survey of UK neonatal units was conducted using the NIHR MCRN Neonatal Network. Units were asked to report the number of babies who received medicines in a two week period of their choice. The excipient content of each medicine was determined from material in the public domain and by contacting manufacturers.

Results: 31 units responded to the survey reporting a total of 642 prescriptions for enteral medications. Excipient content could be identified in 64 unique products 16 of which (25%) were antimicrobials. 30 taste enhancers or colourants were included in antimicrobial formulations and 10 agents to modify chemical or physical properties of the formulation. 9 excipients known to be harmful in neonates, or potentially harmful (since they are metabolised by pathways known to be immature in neonates) were found in a total of 12 antimicrobials.

Discussion: Three quarters of enteral antimicrobial preparations used in UK neonatal units contain additives that are potentially toxic. Further study of the extent of excipient use among neonates is required, including clinical work to define the extent of excipient exposure and identify whether reformulation is required.

P060

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Discussion: Three quarters of enteral antimicrobial preparations used in UK neonatal units contain additives that are potentially toxic. Further study of the extent of excipient use among neonates is required, including clinical work to define the extent of excipient exposure and identify whether reformulation is required.

P061

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Discussion: Three quarters of enteral antimicrobial preparations used in UK neonatal units contain additives that are potentially toxic. Further study of the extent of excipient use among neonates is required, including clinical work to define the extent of excipient exposure and identify whether reformulation is required.

P062

MANIPULATIONS OF ANTIMICROBIAL DOSAGE FORMS IN PAEDIATRIC AND NEONATAL PRACTICE

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Background: Antimicrobials are often marketed in presentations that do not allow an accurate dose to be administered reliably to children and babies. Health care professionals and parents are frequently forced to manipulate dosage forms but guidelines are not available. Here we aim to inform guideline development by describing the nature of manipulations in use and the extant data about the consequences of manipulations.

Methods: To identify manipulations for dosage accuracy used in UK paediatric and neonatal practice a questionnaire was sent to nurses and pharmacists, this was supplemented by direct observation in 3 units (tertiary paediatric, tertiary neonatal and a district general hospital). To identify extant data a scoping systematic review was conducted covering PubMed, EMBASE, CINAHL and International Pharmaceutical Abstracts.

Results: The questionnaire and observations identified manipulations for 10 antimicrobial drugs including 3 tablets, 3 capsules, 5 intravenous and 1 oral liquid. The systematic review identified data about bioavailabiliy after manipulations for 4 antimicrobial tablets (ketoconazole, moxifloxacin, telithromycin, voericonazole). There was no overlap between drugs manipulated in UK paediatric practice and those covered by the published literature about the consequences of manipulations.

Discussion: Manipulations for dosage accuracy are currently unsupported. Manipulations for dosage accuracy of tablets and capsules may be hampered by inconsistent concentration of active drug within the dosage form; manipulations of intravenous agents may lead to errors with dilution. At present, the risks inherent in dosage form manipulations can only be managed by clinical judgment and expert opinion. A broadened evidence-base relevant to paediatric practice is required.

P063

THE ECDC *PILOT* POINT PREVALENCE SURVEY OF HEALTHCARE ASSOCIATED INFECTIONS AND ANTIMICROBIAL USE: PAEDIATRIC DATA

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Background and aims: Previous prevalence surveys did not have standardized identical protocols or objectives. The aims of the 'pilot ECDC point-prevalence survey (PPS) on antimicrobial use and Healthcare-associated-infections (HAI)' (ECDC-PPS) were to: provide a standardized methodology for European Union (EU) Member States; estimate the prevalence of HAI and antimicrobial use in EU acute-care hospitals and; describe patients, invasive procedures, infections and antimicrobials prescribed.

Methods: The pilot ECDC-PPS used two data collection protocols, a patient-based protocol where denominator data including demographics and risk factors were collected for each patient and a unit-based protocol aggregating denominator data at ward level. Thus, for this analysis only children (≤15 years) from hospitals using the patient-based protocol could be included.

Results: From a total of 14,329 patients 1,406 (9.8%) were ≤15 years old. 465 (33.1%) had antimicrobials whilst 89 (6.3%) HAI. Differences in use and infection rate for various risk factors are shown in table.

Conclusions: The full-scale representative European PPS, planned for 2011-2012, will provide reliable, standardised European, national and local hospital data on HAI and antimicrobial use. The patient-based protocol (more detailed information) is preferred to the unit-based protocol allowing better data analysis (e.g., prevalence amongst paediatric patients).

Risk Factor	(%) of patients with Prescription (without:with) risk factor	p value	(%) of patients with Healthcare associated infection (without:with) risk factor	p value	Statistical Test
Surgery since admission	28.69%:49.47%	<0.0001	4.83%:12.46%	<0.0001	Z test
Central vascular catheter	27.97%:73.08%	<0.0001	3.96%:24.36%	<0.0001	Z test
Mechanical ventilation	30.78%:75.34%	<0.0001	4.36%:42.47%	<0.0001	Z test
McCabe Score	Non-Fatal 29.38%:Ultimately-Fatal 59.20%:Rapidly-Fatal 69.23%	<0.0001	Non-Fatal 4.16%: Ultimately-Fatal 20.80%: Rapidly-Fatal 8.46%	<0.0001	Chi-Squared

[Effect of risk factors on HAI & Presciptions]

P064

MANAGEMENT OF GROUP A STREPTOCOCCAL PHARYNGITIS: A UK HOSPITAL EXPERIENCE

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Background: Local data suggested that invasive Group A streptococcal (GAS) infections were increasing. We considered that this may be associated with H1N1 or inadequate treatment of GAS pharyngitis. We reviewed all laboratory reported cases locally prior to the first H1N1 cases in the UK in an attempt to assess adequacy of treatment

Aims: To investigate the management of suspected GAS pharyngitis in children seen at the Alexandra Hospital. To identify any correlation between positive microbiology diagnosis of GAS pharyngitis and age, time of presentation and history of exposure to GAS.

Method: All GAS-positive throat swabs in children taken between June 2006 to May 2009 were manually extracted from our laboratory files (n=29). Case notes were reviewed for history on presentation and management.

Results: Most patients were appropriately investigated with throat swabs. All of the GAS grown was sensitive to penicillin and erythromycin. Generally swab cultures took 72 hours or more to be reported. A third of patients were treated with a 10 day course of antibiotics however most were treated for 5-7 days. Of the 7 recurrent presentations, all were treated with appropriate antibiotics - majority had repeat throat swabs. Age, season of presentation and history of exposure did not correlate with positive swabs.

Conclusions: Patients with GAS-positive pharyngitis presented with identifiable symptoms. Most received antibiotics but of varying duration. There was no correlation with age, presentation season or contact history in our sample.

P065

THE EFFICIENCY COMPARISON OF CULTURE AND PCR METHODS IN DETECTION OF *MYCOPLASMA HUMINIS* IN PREGNANT WOMENWITH GENITOURINARY TRACT INFECTION

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Background and aims: *Mycoplasma huminis* is cause of serious problems (infertility, genitourinary tract and infant infections) in the individuals who have sexual activities.. Our aim in this survey is reveal that the PCR method (using specific primers) is more useful method in compare by culture assays.

Methods: We have collected 113 genitourinary tract samples from pregnant women who have symptoms. We have picked up 2 swabs of each place for PCR assay and the transferred to PPLO medium immediately. Then we have transferred the culture on the PPLO to H broth which contain Arg (amino acid) and incubated at 37°C and 5% CO2 for one week and has checked frequently. After a week the bacteria have transferred to H Agar to investigate the colonies forms. We have used specific primers to performed PCR assays. These primers are used to amplify a 334bp sequence of 16srRNA region (RNA H_1 : F : 5´ CAATGGCTAATGCCGGATACGC 3´- RNA H_2 : R : 5´ GGTACCGTCAGTCTGCAAT 3´).

Results: 24 samples among the 113 samples were positive for *Mycoplasma huminis*. One of these samples was positive just in culture, 12 cases were positive just by PCR method and 15 cases were positive both by PCR and cultures methods.

Conclusions: Main problem in *Mycoplasma* diagnosis is time-consuming and need a professional labor worker to detect it. Considering to time and costs in one hand and the decisive diagnosis and treatment in other hand, we suggest the PCR method is favorable method to diagnosis of *Mycoplasma.*

P066

SELECTION FOR THE HAPTOGLOBIN 2 ALLELE MAY BE MEDIATED BY RESISTANCE TO INVASIVE BACTERIAL DISEASE

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Background: Bacteraemia and *Plasmodium falciparum* malaria account for a major proportion of childhood deaths in Sub-Saharan Africa. Haptoglobin (Hp), a haemoglobin-binding protein, exists in three phenotypes, Hp1-1, Hp2-1 and Hp2-2, with differing immune function. *In vitro*, the Hp2 type agglutinates streptococci and inhibits bacterial growth. It is not know what selective pressure has accounted for the global spread of the common HP^{2} allele.

Methods: We typed the *HP* gene in 1345 Kenyan children, 672 with severe malaria, 235 with invasive bacterial disease and 438 community controls. We estimated odds ratios for disease using multivariable logistic regression models.

Results: We did not find an association between *HP* genotype and severe malaria. In a pilot study the $HP^{2/2}$ genotype was associated with a reduced risk of bacteraemia (OR 0.52; 95% CI 0.34-0.80; P=0.003) and meningitis (n=35/235; OR 0.20; 0.06-0.71; P=0.01). To determine whether protection was due to a specific effect of the Hp2-2 protein we typed the *HP* promoter A-61C SNP, which causes a 10-fold reduction in Hp2 transcription. The protection against bacteraemia afforded by the $HP^{2/2}$ type was lost in the presence of the A-61C SNP suggesting that the protective effect of $HP^{2/2}$ was not seen when the protein was not synthesised.

Conclusions: Risk of invasive bacterial infection was approximately half in children carrying the $HP^{2/2}$ genotype suggesting that *in vitro* functional differences might result in a reduced risk of clinical infection. High mortality rates from invasive bacterial disease may explain the global spread of this common human polymorphism.

P067

EFFECT OF BREWED BLACK TEA AS ADJUST TREATMENT IN SEVERITY OF INFANTS´ CONJUNCTIVITIS

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Material & methods: This was a randomized clinical trial study in the Pediatric Clinic of Amir Kabir Hospital in Arak. A total of 110 infants were randomized into 2 treatment groups who received either brewed black tea add ophthalmic erythromycin ointment 1% with sulfastamid ophthalmic solution 10% (group A)TDS or just antibiotics (group B) for 7 days. In group A, before used of antibiotics sticky eyelids were wiped with a sterile cotten of brewed black tea and in control group just antibiotics were applied. Severity of conjunctivitis at first, 3th and 7th days during treatment and duration of disease were determined.

Results: At first day of prescribing strategies, group A severity of infants´ conjunctivitis were mild in12/7 %(7), moderate 32/7 %(18) and sever 54/5%(30). In just antibiotics were 18/2 %(10), 30/9%, 50/9 %(28) respectively. Difference wasn´t significant. At 3rd in group A 74/5 %(41) of infants were cured, in 25/5 %(14) of them severity were mild. Mild severity were 9/1 %(5), moderate 47/2 %(26) and sever 21/8 %(12) in group B.

Differences was significant (P=0/001). At 7th days, in group A 100 %(55), in just antibiotics 34/5 %(19) of infants were cured. Mild severity of conjunctivitis were 45/5 %(25) and moderate severity were 20 %(11) in group B.

Conclusion: Brewed black tea adds antibiotics reduced severity of infants´ conjunctivitis and duration of treatment.This is safe; effectiveness, accessible and cost benefit for adjust treatment of this disease.

P068

INFECTIVE ENDOCARDITIS, DIAGNOSIS, TREATMENT AND OUTCOMES A SINGLE CENTRE EXPERIENCE

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Introduction: Infective endocarditis (IE) presented inflammation of the endocardial structures caused by many infective agents. It is a significant cause of morbidity and mortality in children, despite of advances in the management and prophylaxis of the disease with antimicrobial agents. Two factors are important in the pathogenesis of IE: the presence of structural abnormalities bacteremia.

Objective: The purpose of this study is to present our results in diagnosis, treatment and outcomes of patient with IE treated in Pediatric Clinic in Prishtina.

Methods: Medical records and echocardiograms of 19 patients, aged from 3 years 8 month to 16 years, with equal participation (10 male (52%) and 9 female 48%) treated from IE. in our Division during the period 2000 - 2010. were analyzed retrospectively.

Results: During this period 3247 patients were diagnosed with one forms of CHD. Despite of regular giving information and advices for IE prevention in 19 children IE was manifested. All of them has a history of CHD. 8 out of 19 (42%) had ventricular septal defect, 7 (36.8%) had bicuspid aortic valve where, 3 before the IE have been asymptomatic. Two patients had mild pulmonary stenosis, 2 had TOF and 1 patent has a ducts. 5 children (three with VSD and 2 with AS) manifested signs of HF. Both children with IE localized at the aortic valve level, died with signs of CHF, during the medical therapy, in preclusion for surgical intervention. In two children beginner of IE was circumcision whereas in other 17 cause was teeth caries.

P069

ASSESSMENT OF FEVER WITHOUT A SOURCE: SIGNS AND SYMPTOMS OF BACTERIAL INFECTION

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Background: Fever, probably the commonest reason for a child/caretakers to seek medical attention and the second most common reason for hospital admission, might be a diagnostic challenge for healthcare professionals. Especially in young children, most cases of fever without source have an infectious origin, requiring urgent evaluation and empirical treatment. Despite advances in healthcare, infections remain the leading cause of death in children under 5 years of age.

Objectives: To recognize signs, symptoms and laboratory tests useful in identifying bacterial infection.

Materials and methods: The retrospective study is based on data collected from the medical files of all children diagnosed with „Fever without a source" on their first visit in a primary health care clinic in Bucharest.

Results: 154 children (46% males, 54% females) were diagnosed with „Fever without a source"over a 1 year period (October 2009 - October 2010). The median age in the study group was 2,17 years. Of all the evaluated children 10,4% were identified as bacterial diseases: 3,97% Upper Respiratory Bacterial Infections, 5,83% Acute Pyelonephritis and 0,6% Pneumonia. Fever value over 39^0 C had a 81,80% sensibility and a 39,33% specificity, while clinical signs had a 20% sensibility and a 93,4% specificity in predicting bacterial illness. Leucocytosis showed a 80% sensibility and 87% specificity while elevated CRP showed 80% sensibility but only 58% specificity in detecting bacterial infection.

Conclusions: In assessing a child with fever one should combine history, clinical and biological data in order to identify bacterial infection.

P070

ETIOLOGY OF INTRA-ABDOMINAL INFECTION IN CHILDREN

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Background: Management of intra-abdominal infections remains difficult and requires a multifaceted approach. The primary treatment is surgery, but choosing the proper antimicrobial therapy is essential for patient's outcome.

Material and methods: This study is an analysis into the etiological agents of intra-abdominal infections in children and their sensitivity to several antimicrobial agents. We report a retrospective review of 30 patient with intra-abdominal infections from January to December 2010, identifying clinical features and risk factors, analyzing epidemiology and patient survival.

Results: Perforated appendicitis was the most frequent cause for intra-abdominal infection (98%). E.coli was the most frequent single pathogens, comprising 76% of organisms and revealing the highest sensitivity rates at antibiogram to Colistin (87%), Piperacilin/ tazobactam (82%), Imipenem (82%) and Meropenem (82%). In 2 patients pseudomonas aeruginosa (7%) was identified. Other pathogens isolated from peritoneal cultures were Enterobacter, Seratia, Klebsiela, and Staphylococcus aureus. In non - E. coli pathogens the highest sensitivity was at Imipenem (85%), Meropenem (57%) and Ciprofloxacin (57%).

Conclusion: Most intra-abdominal infections develop from a source in the gastrointestinal tract. Management generally involves an invasive procedure to control the source of the infection and antimicrobial therapy directed against the causative microorganisms.

P071

SERIOUS BACTERIAL INFECTIONS IN CHILDREN ADMITTED TO A TERTIARY REFERRAL HOSPITAL IN ENGLAND: THE CHILDHOOD ACUTE BACTERIAL INFECTIONS NETWORK (CABIN)

M. Buettcher[1], A. Ali[1], C. Eiffe[1], A. Irwin[1], C. Hawcroft[1], P. Riley[2], M. Sharland[1], S. Ladhani[1]

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Background: Although serious bacterial infections (SBI) have declined dramatically following the introduction of routine vaccination, they still contribute to ~20% of childhood deaths in England and Wales. There are currently limited clinical data on children who develop invasive bacterial infections.

Methods: A standardised questionnaire was used to collect clinical, laboratory, microbiological and outcome data from the case notes of all children aged 1 month to 15 years with positive blood or CSF cultures who were admitted to a 96 bed tertiary hospital in south London between July 2008-June 2009.

Results: Over the 12 months, 268 children (56% male/44% female) had 381 episodes of SBI (87% blood, 13% CSF). The age distribution was 40% among 1-11 month-olds, 30% among 1-4 year-olds and 30% among 5-15 year-olds. Positive culture rate was 9.7% and 9.2% for BC and CSF, respectively. The main pathogens isolated were coagulase-negative staphylococci (49%), Enterococci (6%), Staphylococcus aureus (4%) and Escherichia coli (4%). Analysis of case records of the first 64 cases revealed that 33% had hospital-acquired infection, 60% had an underlying medical condition (45% malignancy, 11% surgical, 44% other) and 33% had an indwelling venous catheter. The median duration of hospital stay was 8 (IQR 3-23) days. Six children (9.4%) died, including 4 with central line-related sepsis caused by Gram negative pathogens.

Conclusions: Children with underlying medical conditions accounted for 60% of childhood SBI and almost all the deaths. Further studies are warranted to determine whether such children might benefit from more aggressive empiric antimicrobial therapy.

P072

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M. Buettcher[1], A. Ali[1], C. Eiffe[1], A. Irwin[1], C. Hawcroft[1], P. Riley[2], M. Sharland[1], S. Ladhani[1]

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Conclusions: Children with underlying medical conditions accounted for 60% of childhood SBI and almost all the deaths. Further studies are warranted to determine whether such children might benefit from more aggressive empiric antimicrobial therapy.

P073

POSITIVE BLOOD CULTURES FROM A CHILDREN INFECTIOUS DISEASES CLINIC

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Objective: To analyze positive blood culture (BC) from a Children Infectious Diseases Clinic of Constanta.

Methods: Retrospective review of medical records from children with positive BC observed in Children Infectious Diseases Clinic over a period of 3 years (2008 - 2010).

Results: It was isolated a pathogen in 34 cases, of which 17 had ≤3 years of age, 18 were girls and 24 children were from urban area. The year with more isolation was 2008 with 17 cases. The most frequently isolated pathogens were Actinomyces spp. in 10 cases, Staphylococcus spp. in 6 cases and gram negative bacteria in 4 cases (Pseudomonas aeruginosa, Salmonella group B, Escherichia coli, Bacteroides ovatus). Actinomyces spp was isolated in 4 cases of children with pneumonia, in 4 cases with digestive infections and in 2 cases with mouth infections. Bacteraemia with Actinomyces was considered in 6 cases. Staphylococcal infections occur in children with ORL infections in 4 cases, and cutaneous infections in 2 cases. Sepsis with E. coli was found in a child with urinary tract infections and sepsis with Salmonella group B in a child with enterocolitis. All Staphylococci were methicillin sensitive except one case which was methicillin resistant. All isolates of Actinomyces were sensible to Eritromycin, Clindamycin, Penicillin and Ceftriaxon. All anaerobic germs (Clostridium spp, Eubacterium limosum, and Bifidobacterium spp.) responded well at treatment with Metronidazol.

Conclusions: The most common pathogens isolated in BC were Actinomyces spp. and Staphylococcus spp. There were a few cases of resistance to antibiotics.

P074

BACTERIOLOGIC EXAMS IN INFANTS LESS THAN THREE MONTHS

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Infectious diseases are a frequent cause of hospitalization of infants under 3 months of age. Frequently, even suspecting of a viral aetiology, multiple tests are required, including microbiologic exams, and an empirical antibacterial therapy is established. The authors aimed to characterize the most frequently performed bacteriological exams in this age group and their relationship to diagnosis and antibacterial treatment.

We included 157 previously healthy infants with less than 3 months of age, to whom cultural examinations were ordered. The age distribution was: < 28 days (30.6%), 29-59 days (36.9%) and 60-89 days (32.5%). Organic products most commonly subjected to cultural examination were: blood (131), urine (109) and liquor (47), with isolation of bacterial agent in 13%, 36.7% and 8.5% respectively. Antibiotic therapy was instituted in 52.9% of patients, lasting an average of 8 days: 32.5% in monotherapy (mostly cefotaxime) and 67.5% with combined antibiotic therapy (ampicillin with cefotaxime or gentamicin). We identified three cases of antibiotic resistance. 38.2% of the patients had a final diagnosis of bacterial infection: pyelonephritis (51.2%), sepsis (13.3%), otitis (10%), meningitis (6.7%), pneumonia (5%) and other (13 8%).The value of C-reactive protein (32.6 mg/L versus 9.6 mg/L) and leukocyte count (14480/µL versus 11152/µL) were higher in patients with final diagnosis of bacterial infection ($p < 0.001$).

In this age group, many bacteriological exams and antibiotics were performed without evidence of bacterial infection (62.8%). Therefore, to avoid excessive intervention, it is necessary to create more objective markers of bacterial infection for the future.

P075

MENINGOCOCCAL C DISEASE OUTBREAK IN AN OIL REFINERY: WHAT IS THE BEST STRATEGY TO AVOID THE SPREDING OF THIS DISEASE?

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Background and objectives: In 2010, an outbreak of meningococcal disease (MD) was registered among workers of an oil refinery. This study describes the outbreak investigation, disease control measures and the outbreak's social impact.

Methods: In Brazil, MD requires compulsory notification. The São Paulo State Epidemiologic Surveillance Center, Respiratory Diseases Branch investigated the registered cases.

Results: From 24 March/2010 until 10 Apr/2010, 9 cases (age range, 8 m-43 y), and 3 deaths caused by *N. meningitidis* C:23:P1.14-6 were registered in oil refinery workers and their contacts. Rifampicin was recommended for close contact cases, and polysaccharide A/C vaccine was offered to 17,500 refinery employers from 17 Apr until 24 Jun/2010 (coverage rate = 90%). Nine additional cases (1 death) were registered after immunization; 2 in workers (< 14 days post-immunization) and 7 in their family contacts (all < 7 years) who lived in Cosmopolis city. The MD incidence rate in children 2m-19y living in Cosmopolis was 18.5/100,000, and a campaign of immunization was undertaken from 06/30 until 07/03/2010 for this age group (coverage = 90.5%).

Conclusions: MD caused morbidity and lethality among the oil refinery workers and their family members. Measures to control the outbreak were effective at the oil refinery, but did not prevent the spreading of MC to the community and to children at higher risk. Asymptomatic carriage probably caused the chain of MC transmission.

P076

S. PYOGENES INVASIVE DISEASE IN CHILDREN IN A PEDIATRIC DEPARTMENT OF A LEVEL II HOSPITAL

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Background and aims: *S. pyogenes* is among the most common bacteria in Pediatrics, and is associated with a wide variety of infections and large range of severity. The aim was to evaluate trends of Group A Streptococcal invasive disease in a Paediatric Department of a level II Hospital.

Methods: Retrospective analyses of the medical records of all children with group A streptococcal invasive disease (positive culture obtained from sterile sites), from January 2004 to December 2009 (6 years).

Results: There were 8 cases, with a maximum of two cases/year. Seventy five percent were boys and the median age was twenty eight month (28M). The most frequent clinical manifestations were fever (100%), rash (38%) and arthalgia/limbs' pain (25%). The diagnoses were Pneumonia with empiema (four), bacteraemia with toxic shock syndrome (two), meningitis (one) and mastoiditis (one).

Median neutrophyl count was 19.687x105/L and median C reactive protein was 261mg/L. Bacteria were isolated mainly from pleural effusion (50%). The outcome was good for most cases but there was one death due to toxic shock syndrome. M typing and the presence of virulence factors genes were not assessed.

Conclusion: The number of invasive disease was small. Fatal outcome was associated with toxic shock syndromes. Microbiological investigation is essential to understand which M types or virulence factors genes are involved.

P077

PNEUMOCOCCAL PLEURAL EMPYEMA AND OTOMASTOIDITIS: EMERGENCE OF SEROTYPES 19A, 7F AND 3 IN NORTHERN MEXICO

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Background: Pleural empyema (PE) and otomastoiditis (OM) are caused mostly by *Streptococcus pneumoniae* (*Sn*). Serotype distribution is unknown in Northern Mexico. Tijuana, Mexico, borders with San Diego, CA, and is considered the most transited frontier in the world. Mexico is the first country in Latinamerica which implemented heptavalent conjugated pneumococcal vaccine (PCV-7) as part of the routine immunization schedule.

Methods: Between October - 2005 and January - 2011, all patients < 16 years old with confirmed PE and OM were prospectively admitted at Tijuana General Hospital. Following culture (from pleural fluid, blood and/or mastoid-pus) serotype identification was performed with the Quellung reaction using serotype-specific pneumococcal antisera.

Results: A total of 24 PE and 9 OM were admitted. Culture-confirmation was obtained in 15 of PE (62.5%) and 6 of OM (66.6%). Isolation of *Sn* was of 14 of all PE (93.3%) and of all OM. Before implementation of PCV-7 (August-2007) serotypes 19A, 7F and 3 were isolated in 2 (25%) cases of PE, while following implementation of PCV-7 these same serotypes were found in 4 (66%) ($p < 0.01$). All 6 cases of *Sn*-confirmed (before and after PCV-7 implementation) OM were caused by serotypes 19A, 3 and 7F.

Conclusions: *Sn* is the main cause of PE and OM. Following PCV-7 vaccination in northern Mexico, pneumococcal serotypes 19A, 7F and 3 emerge as the most common causes of PE and OM. These data leads to further evaluation of immunization strategies, and prompt identification of pneumococcal serotype substitution following PCV-7 vaccination in Mexico.

P078

NOSOCOMIAL INFECTIONS DUE TO *ACINETOBACTER BAUMANNII* IN APEDIATRIC INTENSIVE CARE UNIT IN TURKEY

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

Methods: We reviewed the medical and laboratory records of 15 critically ill children who were infected by A*. baumannii* infections between January 2008 and December 2008 at the Department of PICU in Ankara University Medical School, Turkey.

Results: The age ranged from 1 month to 16 years with a mean age of 55.5 months and male-to-female ratio was 1:1.5. Ventilator-associated pneumonia (10 patients) was the leading diagnosis followed by, catheter related blood stream infection (4 patients), bacteremia and ventilator-associated pneumonia associated with meningitis (1 patient) due to *A. baumannii*. There were frequently mechanical ventilation (93.3%), central venous catheter (73.3%), urinary catheter (93.3%) and broad spectrum antibiotic usage (80%) as the risk factors. Neuromuscular (40%) and malignant (26.7%) disorders were the most common underlying diseases.

Conclusions: Nosocomial acquired *A. baumannii* are commonly multi-drug resistant and it causes to prolong the lenghts of stay in PICU and increases the mortality rates in pediatric critical care.

P079

CLINICAL AND LABORATORY CHARACTERISTICS OF CHILDREN AND ADOLESCENTS HOSPITALIZED WITH *STAPHYLOCOCCUS AUREUS*INFECTION IN TEACHING HOSPITAL IN NORTHEAST BRAZIL

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Background and aims: *Staphylococcus aureus* infections have great range of clinical presentation and severity. They vary since mild cutaneous infections to severe ones, such as pneumonia and septicemia. Methicillin-resistant *S. aureus* acquired in hospitals (HA-MRSA) and in community (CA-MRSA) have encouraged researches because of their impact in antibiotics prescription and screening of asymptomatic carriers. Our aim was to describe the clinical characteristics of *S. aureus* infection and to determine the isolates resistance to antibiotics in children in Northeast Brazil.

Methods: Children younger than 14 years old hospitalized in a tertiary hospital between october 2008 and march 2010 with a positive culture to *S. aureus* had their medical records analyzed. The microbiology laboratory techniques were performed according to standards of the Brazilian Ministry of Health and sensitivity to antibiotics was determined by the disc diffusion test (Kirby-Bauer).

Results: 112 patients were enrolled. The median age was two months and the majority was male (56%). 24 children and adolescents (21%) had previous diagnosis of chronic diseases. Among 31 (28%) patients with primary bacteremia, four were associated to central venous catheter. Fourteen patients died (13%), mortality was higher in younger than one month (50%) old. Mortality rates for MRSA and MSSA were 17% and 12% respectively (p=0,64).

Conclusions: *S. aureus* isolates in children hospitalized in a teaching hospital in Northeast Brazil predominated in younger than one year old. Those were more affected by primary bacteremia and had higher lethality. One in ten *S. aureus* isolated was MRSA.

P080

INCREASED INCIDENCE OF PERITONSILLAR ABSCESS IN CHILDREN IN SOUTHERN SPAIN

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Introduction: Peritonsillar abscess is the most common deep neck infection.

Objective: To describe clinical presentation, diagnosis and management of children with peritonsillar abscess admitted to the University Hospital Virgen del Rocio, Sevilla.

Methods: Retrospective study of patients diagnosed with peritonsillar abscess from 2000 to 2009 in our tertiary-care center. Parameters included clinical, epidemiological, microbiological, therapeutic data as well as overall outcome.

Results: Fifty-eight patients were identified. An increase from 4,4 cases per year during 2000-2004 to 7,2 cases per year during 2005-2009. The mean age at diagnosis was 8,1±3,5 years. Thirty-six per cent of patients had a history of prior tonsillar infections and 52% received oral antibiotics pre-admission , mainly beta-lactamics.Clinical findings at presentation were: odynophagia (91%), tonsillitis (90%), fever (78%), neck mass(76%), uvula deviation (72%), dysphagia (57%) and trismus (51%). Mean WBC count and CRP were 15854±4188 cells/mm^3 and 79,9±72,6 mg/L respectively. CT scan was performed in 17% of patients. A microbiological culture of the abscess was requested in 59% of patients and a microorganism was isolated in 21% *S.pyogenes* was the most frequent. All patients received parenteral antibiotics; median duration of treatment was 4 days (range 2-12) and 59% underwent surgical procedures; needle aspiration 27% and incision-drainage in 32%. Clinical recurrence occurred in 12% of the cases.

Conclusions: Children with peritonsillar abscess presented generally with characteristical clinical findings.Over 40% of the cases resolved without surgical intervention and the overall recurrence rate was low. An increasing trend in the number of peritonsillar abscess cases was observed over the last years.

P081

PREVALENCE OF *CAMPYLOBACTER* IN CHILDHOOD DIARRHEA IN NORTH LEBANON

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Background and aims: *Campylobacter* species are a major cause of human diarrheal disease worldwide. In Lebanon, The true incidence of *Campylobacter* infections and the species distribution in childhood diarrhea diseases are not known because the search for *Campylobacter* is not part of the routine stool culture. The aim of this study was to investigate the prevalence of *Campylobacter* species and its possible etiologic role in childhood diarrhea in north Lebanon using polymerase chain reaction technique (PCR).

Methods: 90 stool samples from children presenting diarrhea aged between 1 month and 10 years were collected from five hospitals. This study was undertaken between April and June 2010. The DNA extraction from stool sample was performed using the QIAamp DNA Stool Mini Kit. A screening PCR reaction was performed for each sample using primers for the amplification of all *Campylobacter* species followed by 5 PCR reactions for the amplification of *C. jejuni*, *C. hyointestinalis*, *C. coli*, *C. fetus* and *C. upsaliensis*. To control the PCR reaction 7 reference strains were used.

Results: 10 stool samples were positive for *Campylobacter* species (11.1%). One sample was positive for *C .coli*, one for *C. jejuni* and two samples for both *C. jejuni* and *C. coli*. 6 positive samples could not be identified to the species level with the available primers.

Conclusions: We conclude that *Campylobacter* species can frequently associated with childhood diarrhea. In North Lebanon, the *Campylobacter* infection may be significantly underdiagnosed. We emphasize the need to screen routinely for *Campylobacter* during stool culture.

P082

IMPACT OF HIV ON THE AETIOLOGY AND OUTCOME OF NEONATAL SEPSIS IN MALAWI

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Background: Most neonatal deaths arise in developing countries. Infections account for almost 30% of neonatal deaths in Malawi. In the developing world gram negative organisms are a prominent cause of neonatal sepsis and meningitis. The objective of the study is to describe the impact of HIV on the aetiology and outcome of neonatal sepsis in Malawi.

Methods: This is a prospective cohort observational study on babies admitted with a diagnosis of neonatal sepsis or meningitis at Queen Elizabeth Central Hospital in Blantyre, Malawi from March 2009 to March 2012. Descriptive statistics were used to analyse the results.

Results: We have enrolled 105 cases so far with 31% of the babies being HIV exposed. 19 cases (18%) had bacterial meningitis with 6 (32%) caused by streptococcus pneumonia and 6 (32%) Group B Streptococcus [GBS]. 5 of the GBS meningitis cases were HIV exposed. On the other hand only 1 of the streptococcus pneumonia cases was HIV exposed. 4 meningitis cases developed hydrocephalus. Streptococcus pneumonia contributed 29% and GBS 21% of the 14 cases with a positive blood culture. 10% of the study participants were readmitted within 1 month with equal proportions between the HIV exposed and unexposed. The overall mortality rate was 15% with half of the deaths occurring in HIV exposed babies.

Conclusions: Streptococcus pneumonia and GBS are a significant cause of neonatal sepsis and meningitis in Malawi. Acknowledgements All the study participants, staff and supervisors. Malawi- Liverpool Wellcome Trust for funding the study.

P083

SEVERE STREPTOCOCCAL GROUP A DISEASE IN CHILDREN WITH OR WITHOUT RISK FACTORS OF INVASIVE INFECTION: CLINICAL FEATURES AND *EMM*-TYPES DISTRIBUTION

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Background and aims: The molecular characterization of Group A streptococcus (GAS) leading to invasive infection in children is poorly described. We aimed to assess the clinical, microbiological and molecular characteristics of invasive GAS infections in 65 children hospitalized between 2000 and 2009 in 7 French Pediatric tertiary care centers.

Methods: Emm-typing and determination of the main virulence factors: SpeA, SpeB, SpeC, SmeZ-1, Ssa, SIC et Sil was performed to characterized molecularly the GAS isolates.

Results: The median age of the children was 2,8 years. Osteoarticular infection and pulmonary infection were the main clinical manifestations (38.5% and 37% respectfully). 31/65 children had at least one of the following risk factors of invasive GAS infection: use of non steroidal anti-inflammatory drugs or corticosteroids, varicella, surgical intervention, underlying chronic disease or immunodepression. Emm 1, emm 3, emm 4 and emm 12 accounted for 70% of the isolates and SpeA and SmeZ-1 were present in more than half of the isolates. No significant correlation was found between emm type and clinical manifestations. However, patients without risk factor (n=34) were younger than those presenting risk factors (1.7 *versus* 3.6 years, p=0.03) and a larger variability of emm-type was found in these patients without risk factors compare to patients with risk factors (18 *versus* 9 different emm-types).

Conclusion: In patients without risk factors of invasive GAS infection, young age and large variability of emm-types might suggest a role of host immunity in the pathogenesis of severe infection.

P084

INFLUENCE OF SEX ON GRAM NEGATIVE SEPTICAEMIA IN GHANAIAN CHILDREN PRESENTING WITH SEVERE MALARIA

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Background: Malaria and septicaemia co-infection has been observed by experienced clinicians in Ghanaian children. This study was to characterize the co-infection through a well thought design.

Method: Children admitted with malaria (documented parasitaemia) were also screened for septicaemia by blood culture as part of the routine case diagnosis and management procedure between August 2006 and December 2008.Blood culture results were followed-up for bacterial growth.

Results: A total of 1030 cases were recruited. 16.3 % (n=168) had organisms isolated from blood cultures (56 % were males). Gram positive organisms were identified in 69% of the cultures. There was no difference between sexes in the frequency of gram positive organisms. Salmonella sp. (53.5%) and coliforms (35.7%) were the main gram negative organisms isolated from males and females respectively. Gram negative organisms affected younger age (in months) group (26.5 v 36, p=0.017) and also resulted in lower hemoglobin levels (5.7 v 6.9, p=0.006).

Conclusion: Malaria and septicaemia co-infection is prevalent in Ghanaian children.Sex seems to influence the distribution of gram negative organism in children with malaria. Further studies are needed in both the children and bacterial to explain this trend.

P085

CERVICAL LYMPH NODE ABSCESS FOLLOWING MOTHER-TO-INFANT TRANSMISSION OF COMMUNITY-ACQUIRED METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (CA-MRSA)

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Background and aims: MRSA colonization or infection may be spread within households and to other contacts in the community. We describe the clinical course and management of a cervical lymph node abscess caused by CA-MRSA in an infant following mother-to-infant transmission.

Methods and results: An 8-weeks old, 5300 grams female infant was admitted with fever and a rapidly growing neck mass that was noticed 2 days before admission. The infant was febrile (38.5^0C) and painful, mobile and reddish left laterocervical mass was diagnosed. Physical examination was otherwise unremarkable. Laboratory examination revealed a WBC count of 16,390/mm^3 with 80% neutrophils, hemoglobin 10.9 g/dl and platelets 338,000/mm^3. Sedimentation rate was 90 mm/h and CRP 4.45 mg/dl. Ultrasound and computerized tomography examinations revealed a left hypoechogenic 4/3/4 cm poorly defined laterocervical mass, in close proximity to the parotid gland and great neck vessels. Oropharyngeal and nasopharyngeal cultures returned positive for MRSA susceptible to clindamycin, erythromycin and vancomycin. A maternal nasopharyngeal culture grew MRSA with the same antibiotic susceptibility pattern. Treatment was started with intravenous ceftriaxone and netilmicin for 5 days followed by teicoplanin for 13 additional days with a modest decrease in abscess dimensions. On day 18 redness and fluctuation were noted and the lymph node was surgically removed and cultured, with recovery of the same MRSA. Teicoplanin was continued for 5 additional days and the patient was discharged in good general condition.

Conclusions: The possibility of intrafamilial transmission should be considered in children without identifiable risk factors for MRSA infection.

P086

PREVALENCE OF THE *STREPTOCOCCI GROUP B* IN NEONATES WHO SUSPECTED TO SEPSIS IN IRAN

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Background & aims: Group B *Streptococcus* (GBS) is the most common cause of neonatal sepsis. Isolation of bacteria by culture technique especially in neonates who are receiving antibiotics prior, have low sensitivity. Recently, molecular methods had proved to be a useful diagnostic tool to increase sensitivity and specificity detection of broad- range bacterial agents associated to neonatal sepsis.

The aim of this study was identification of the GBS in neonates who suspected to sepsis by Nested-PCR

Methods: Amount of 0.5 ml blood in micro tube containing EDTA to prevent cloth, was taking from neonates who suspected septicemia. DNA was extracted from blood by DNA extraction kit (Fermentas CO), and it used for perform Nested-PCR protocols. The first and second round was done by external and internal primers that identified by amplify 259bp and 153bp bands in gel electrophoresis respectively.

Results: Evaluate from a total of 400 blood samples was collected from neonates who suspected to septicemia by using Nested-PCR (with the 99/6 % specificity and 99/2 sensitivity), were indicated that 2 % of neonates (8 positive samples) have had GBS in blood specimens.

Conclusions: It concluded that, the GBS is a considerable pathogenic agent in sepsis in Iran as well as in other countries. So physicians should be pay more attention regarding this bacterial agent in neonatal sepsis.

P087

INVASIVE GROUP A STREPTOCOCCAL INFECTIONS IN THE VARICELLA VACCINE ERA

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Background: Varicella is an important risk factor for Invasive Group A Streptococcal Infection (IGASI). We aimed to describe IGASI before and after inclusion, in January 2006, of varicella vaccine (VV) in Quebec's routine immunization schedule.

Methods: We retrospectively reviewed medical charts of all patients (0-18 years) admitted at a tertiary care center in Quebec, for whom Group A *Streptococcus* strains were isolated from normally sterile biologic sites between January 1998 and December 2010.

Results: IGASI was diagnosed in 126 children. Median age was 50.5 months (range, 1-207). Eighty-five IGASI were identified prior to inclusion of VV in the immunization schedule and 41 cases after. The mean number of IGASI cases hospitalized per year was 10.6 (SD 8.0) prior to VV inclusion, and 8.2 (SD 5.0) post inclusion (p=0.5, mean difference 2.4;, 95%CI: -5.5-10.4). Post VV inclusion, patients with IGASI were significantly less likely to have had recent chickenpox (OR 0.2;, 95%CI: 0.03-0.7).

The mean number of skin and soft tissue infections (SSTI), including necrotizing fasciitis and bacteriemic cellulitis, decreased significantly from 5.2 cases per year (SD 3.9) to 1.0 (SD 1.7) following VV inclusion (p=0.02, mean difference 4.2, 95%CI: 0.7-7.8). Pneumonia and osteo-articular infections represented 18.8% and 16.5% of IGASI before VV inclusion, and 24.2% and 24.2% afterwards, respectively.

Conclusion: At a single center, IGASI were not significantly decreased after VV inclusion in a routine immunization schedule, but SSTIs were. The direct impact of VV on individual risk of IGASI has to be explored.

P088

FERRITIN AS A MARKER OF SEVERE SEPSIS AND SEPTIC SHOCK

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Objective: To evaluate serum ferritin level in children with systemic inflammatory response syndrome (SIRS), sepsis, and septic shock.

Methods: A cross-sectional study enrolling children (one month to 18 years old) admitted to the department of paediatrics at Hospital Sao Lucas, PUCRS University (Brazil), from June 2008 to June 2010. A priori, three groups ordered according to hierarchy in severity were studied:

1) children with SIRS after elective paediatric surgery where there was no evidence of infection (SIRS group);

2) children with fluid responsive sepsis; and

3) children with septic shock.

We measured serum ferritin and C-reactive protein (CRP) levels in all children on the first day of admission. The serum ferritin level and ferritin index (serum ferritin divided by maximum normal value of serum ferritin according to age and gender) were compared between groups.

Results: 147 patients (41 SIRS, 39 sepsis, and 67 septic shock) were studied. Ferritin level was associated with worsening clinical severity: SIRS (29 ng/mL), sepsis (101 ng/mL), and septic shock (287 ng/mL). Ferritin level higher than 760 ng/mL was associated with high likelihood of septic shock. The relative risk of death was 3.41 for patients with serum ferritin above 500 ng/mL and 5.06 with ferritin index above 1.7. There was no association between CRP and mortality.

Conclusions: Ferritin level is associated with clinical severity in children with sepsis. Ferritin index and high ferritin levels were independently associated with death in children with sepsis.

P089

MENINGOCOCCAL DISEASE: WHAT RISK FACTORS?

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Background and aims: Infection by *Neisseria meningitidis* is associated with high mortality and morbidity in the pediatric age. We tried to assess the association of patient and strain characteristics with the outcome of meningococcal disease.

Methods: Descriptive study of children admitted with meningococcal disease between January 2000 and December 2009. Sepsis was defined according to the criteria of the *International Consensus Conference on Pediatric Sepsis*. The agent was isolated in blood agar or identified by PCR from blood or CSF and then genotyped.

Results: 101 children were identified: 2000-2005 (75%) and 2006-2009 (25%), the median age was 2 years (44% younger than 24 months). Serotyping (34 cases): serogroup B (26), with most frequent phenotypes: NT:P1.22 (8), B:P1.18 (4), B:NT:21 (4) and B:P1:19 (4); serogroups A (2); W135 (1); Y (1) and serogroup C (3). Most of the children (67.6%) had sequelae: severe developmental delay (9), language delay (4), deafness (3), cutaneous scarring (4) hydrocephaly (1). The case-fatality rate was 5.8%. A poor outcome was associated to sepsis without meningitis (p 0.027), previously viral infection (p 0.028) and in children under 24 months with parental smoking (p 0.04). The phenotypes B:NT:P1.22 and B:P1.18 seem related to greater incidence of sequelae (p 0.05).

Conclusions: Even though the small sample size, host factors and clinical presentation were more determinant of a poor outcome than specific serotypes of meningococos. The phenotypes B:NT:P1.22 and B:P1.18 interestingly seemed to be related to poor prognosis in children. Further studies are needed to confirm this new finding.

P090

ARE 15 DAYS OF AGE AN APPROPIATE CUT-OFF POINT FOR HIGH RISK SERIOUS BACTERIAL INFECTION WHEN EVALUATING YOUNG FEBRILE INFANTS?

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Introduction: In recent years the management of febrile infants under 3 months has undergone several modifications. Some protocols recommend distinguishing febrile infants under 15 days as the highest risk group for serious bacterial infection (SBI). In this way, they recommend admitting to the ward all those febrile infants and to consider outpatient management for selected patients over one month of age and, more cautiously, between 14 and 28 days old.

Objective: To determine whether 15 days of age is an adequate cut-off point for detecting infants in increased risk of SBI.

Patients and methods: Retrospective study based on a prospective registry of infants under 3 months of age with fever without a source (FWS) admitted between September 2003 and August 2010 in the Paediatric Emergency Department of a tertiary teaching hospital. We include in the registry all infants under 3 months with FWS (temperature of at least 38 º C).

Results: 1575 infants were included, of whom 310 (19.7%, 95% CI 17.8-21.7) were diagnosed with a SBI. SBI rate in patients aged 15-21 days was 33.3% (95% CI 24.5 to 43.4%), similar to that in infants from 7-14 days (31.9%, 95% 22.2-43.4%) and higher than that in infants older than 21 days (18.1%, 95% CI 16.2-20.3%).

Conclusions: The febrile infants 15-21 days of age have a SBI rate similar to the younger infants but higher than those older than 21 days old. Establishing a cut-off point for SBI related to the age of 15 days seems to be inappropiate.

P091

PREVALENCE OF SEPSIS IN CHILDREN IN THE EMERGENCY DEPARTMENT OF A TERTIARY LEVEL CHILDREN'S HOSPITAL IN LATVIA

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Background and aims: Sepsis is one of the most common causes of death in children. Studies have shown that the most important action in reducing mortality from sepsis is its early diagnosis and treatment. The aim of this study was to evaluate the prevalence of sepsis in the Emergency department of a tertiary level hospital.

Methods: In a descriptive prospective study we analyzed data about 471 children examined and hospitalised in February to December, 2008. We evaluated SIRS criteria, and analyzed data about diagnosis and laboratory tests after patients were discharged.

Results: SIRS was detected in 28.4% of all patients, and 37% (134) patients with fever. In 12,9% (61) SIRS was detected without fever, the main criteria being changes in the leukocyte count. There were statistically significant diferences in groups with and without fever in C reactive protein levels ($p< 0,01$) and hospital stay ($p< 0,05$). Retrospectively sepsis was diagnosed in 5% of all patients, and 33,5% (45) patients with SIRS ($p< 0,01$). 5.0% (6) of patients without fever and 7,0% (25) of patients with fever had microbiologically proven presence of a pathogen.

Conclusion: SIRS incidence in patients was 28,4%. SIRS prevalence was 27.5% (CI 22.8%; 32.2%). Sepsis prevalence was 25.1% (CI 17.7%; 32.6%). SIRS or sepsis had never been marked in patients' case histories.

This study was conducted as a part of the State research program “Scientific research with help of multidiscipline consortium of main pathologies endangering survival and quality of life of inhabitants of Latvia”.

P092

EPIDEMIOLOGY AND MANAGEMENT OF ACUTE MASTOIDITIS, ACUTE ETHMOIDITIS, ACUTE PERITONSILLAR ABSCESS, RETRO OR PARAPHARYNGEAL ABSCESS IN CHILDREN IN SOUTH FRANCE

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Objective: To analyze epidemiology and management of acute mastoiditis (AM), acute ethmoiditis (AE), acute peritonsillar abscess (APA), retro or parapharyngeal abscess (RPA/PPA) in children.

Patients and methods: Retrospective study in 2 pediatric hospitals from 01/01/2005 to 31/12/2009, including children < 18 years of age with AM, AE, APA, ARP or APP.

Results: 159 children included. AM is the most frequent infection (n = 72)(mean age = 3.8 years), Pneumococcus is predominant (n = 13/57)(30% peniR but amoxS) followed by Pseudomonas aeruginosa (n = 8/57) and group A streptococcus (n = 5/57). In AE (n=61)(mean age = 5.2 years), pneumococcus is also predominant (n = 8/22, 100% PenicillinS), but only one MRSA isolated. The most prescribed antibiotics in these 2 diseases are association C3G/Vancomycin/Metronidazole (42%).APA (n = 17)(mean age = 13.3 years) and RPA/PPA (n = 9)(mean age = 3.5 years) are rare but seem to rise, cured in most cases by amoxicillin-clavulanate. Group A Streptococcus is predominant (n = 7/14 with a strain cotrimoxazoleR and a strain EryR), no anaerobic bacteria isolated.

Discussion: Data are in agreement with those of the literature. Emergence of Pseudomonas aeruginosa in AM remains to be confirmed., MRSA in AE are very rare in contrast to what is found in USA. The decrease in pneumococcal resistance is probably related to “best prescription of antibiotics” campaigns and pneumococcal vaccine introduction in 2005.

Conclusion: AM, AE, APA, RPA, PPA, remain a concern because of their potential severity and secondly a probabilistic antibiotic little consensus and often inappropriate.

P093

WEIGHTINESS OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (C- MRSA) IN COMMUNITY SUPPURATIVE SKIN INFECTIONS IN CHILDREN IN A PEDIATRIC EMERGENCY DEPARTMENT

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Background and aims: C-MRSA in suppurative skin infections (SSI) is a public health problem in USA (> 57%) and in some European countries. In France, the incidence is estimated at 6% but studies concern mainly adults but not children. The main objective is to study the prevalence of community SSI with S. aureus and the resistance profile in children. Secondary aim: type of suppurative skin infections and clinical course.

Material and methods: Prospective study in a Pediatric Emergency Department in NICE (France) between January 1 and July 31, 2010. Inclusion criteria were: age < 18 years, clinical diagnosis of community SSI, availability of results of bacteriological sampling of the skin lesion.

Results: The prevalence of SSI with S. aureus was 75% (n = 21/28) over the period studied. The mean age was 6.7 years (ext: 15j - 17 years). Impetigo represented 39.3% of cases (n = 11/28), then the abscess 25% (n = 7/28), whitlow or ingrown nails 21.5% (n = 6/28), boils 2% (n = 2/28). The prevalence of C-MRSA strains (MIC> 2 mg / l) was 14.3% (n = 3/21). Among these strains, 2 were Ery R but all were cotrimoxazole S and pristinamycin S. No ST80 clone was isolated (The main resistance profile in France).

Conclusion: The prevalence of C-MRSA in community suppurative skin infections in our Pediatric Emergency Department is low (< 15%) but but we must remain vigilant and make as many as possible samples for bacteriological monitoring.

P094

TRENDS IN *STAPHYLOCOCCUS AUREUS* BACTERAEMIAS AT A SCOTTISH CHILDREN'S HOSPITAL

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Background and aims: The most common causative organisms in paediatric bacteraemias are reported as *Staphylococcus aureus* and enterococci. The literature from England has shown an increasing incidence of meticillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia, from 0.9% in 1990 to 13.1% in 2000. Furthermore, in 2010 reports from Germany indicated rising hospital acquired infections in paediatric hospitals. This study examined trends in bacteraemia in a Scottish children's hospital from 1999 to 2009. It also investigated the possible effect of social deprivation, maternal smoking and infant feeding.

Methods: A retrospective review of all *Staphyloccocus aureus* bacteraemias at the Royal Hospital for Sick Children, Edinburgh from 1999 to 2009 was undertaken. Patient case notes were reviewed for epidemiological factors, and whether hospital acquired. Deprivation scores were given using the Scottish Index of Multiple Deprivation 2006.

Results: *Staphylococcus aureus* (14.1%) was the most common cause of significant bacteraemia. The average rate of *Staphylococcus aureus* bacteraemia was 2.2 per 1000 total admissions, with 6% due to MRSA. Thirty-nine percent were hospital acquired infections. The mortality rate was 3.5%. No relation existed with deprivation, maternal smoking or infant feeding.

Conclusions: To the author's knowledge this is the first published data of *Staphylococcus aureus* bacteraemia from the Scottish paediatric population, which has shown no increase in incidence over the last 10 years. MRSA accounts for a small proportion. Mortality rates remain low compared with adults, but a prospective and more rigorous audit would be needed to effectively analyse trends and establish epidemiological factors.

P095

SAFETY OF CIPROFLOXACIN IN NEONATES WITH SEPSIS

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Background: Newborn sepsis is a major cause of child mortality across the world and considerable experience exists with different antibiotics. Ciprofloxacin is used as a second-line treatment, but its use is increasing in life-threatening neonatal infections. Evidence on its use is not of high quality, however, and joint toxicity was described in animals after high doses. A systematic review of published studies of ciprofloxacin use in newborns was therefore undertaken to assess the adequacy of safety evaluations.

Methods: A bibliographic search in the MEDLINE and EMBASE databases, and in the Cochrane Central Register of Controlled Trials, was performed.

Results: 109 papers from Medline, 76 from Embase, and none from the Cochrane Register were found. After exclusion of irrelevant articles, 5 studies remained: 4 prospective and 1 retrospective. In all, 225 newborns were monitored for adverse events. Doses administered varied from 10-20 mg/kg/die, and treatment duration from 3 to >14 days.No effect on linear growth or acute or subclinical joint toxicity was detected. No significant differences in haematological indices or biochemical markers of hepatic and renal function were found with ciprofloxacin use.

Conclusions: The results of all 5 studies considered support the idea that ciprofloxacin in newborns does not cause serious adverse effects. The major side effects described in animals have not been found in humans. The studies´ methods differed widely, however. A large multicentre study of adequate duration, addressing safety and efficacy of standard dosages, is warranted.

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P096

UNUSUAL PRESENTATION OF MELIOIDOSIS IN ADOLESCENT

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Melioidosis is regarded endemic in southeast asia and northern Australia. Strauss et al had isolated this organism from soil and waters in all states in western Malaysia.

We report here a case of severe form of melioidosis presenting with bacteraemia and hepatosplenic and iliopsoas abscessess complicated by deep vein thrombosis.

A 16 year old adolescent with Insulin dependent diabetic mellitus (IDDM) presented with Pyrexia of Unknown Origin (PUO).The fever was associated with loss of appetite ,weight and with no pronged cough or any skin lesion except for leg ulcer, 5 months earlier. He is a student in vocational school and had no exposure to paddy fields or plantations.

Examination revealed underweight adolescent with high grade fever with chills and rigors and normal blood pressure.No jaundice but pallor noted. No lymphadenopathy with old healing ulcer at Lt foot.All other systems examination were normal except for an enlarged,non tender liver with splenomegaly. He exhibited pain at Lt hip but range of movement was good.

Blood culture: *Burkhoderia pseudomallei* with ultrasound showed hepatosplenic abscesses with thrombosis at Rt femoral vein and Lt. iliopsoas collection.

He was first treated with meropenem however when cultures were known, switch to co-trimoxazole and ceftazidime.He completed 8 weeks of intravenous therapy with resolution of both hepatosplenic abscess and thrombus. Iliopsoas abscess were drained surgically.

This case illustrate that even severe melliodosis with disseminated abscesses can present without full blown septicaemia and DVT and adequate antibiotic treatment alone with limited surgical intervention resolved all symptoms.

P097

STAPHYLOCOCCUS AUREUS BACTEREMIA AMONG CHILDREN IN NORTHERN ISRAEL

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Background and aims: The epidemiology of pediatric staphylococcal bacteremia (PSAB), particularly community-acquired (CA), has not been extensively studied. The epidemiology of PSAB in our region has not been described. This study was designed to evaluate the incidence and characteristics of PSAB in northern Israel.

Methods: A retrospective review, (January 2002- December 2005), in 7 medical centers serving the entire population of hospitalized children of northern Israel.

Results: The annual incidence of PSAB during the study period was 4.7 and 2.1/100,000, overall, and for CA- PSAB, respectively. 47/106 (44.3%) episodes were CA- PSAB (mean age 73 months); all CA isolates were methicillin-susceptible. 71% were male. 59 (55.7%) were hospital-acquired (HA), median age 15 months, mean 49 months, 8 (14%) had MRSA. Predispositions for HA-PSAB included intravascular catheter 31 (52.5%); neonates, 16 (27%); immune suppression 12 (11.3 %). Primary diagnoses among those with CA-PSAB included osteoarticular infection (26, 55.5%), skin infection (4, 8.5%), primary bacteremia (5, 10.6%), pneumonia (4, 8.5%), endocarditis (2, 4.3%), and isolated cases of pyelonephritis, necrotizing fasciitis, lymphadenitis, otitis, paronychia, intra-abdominal abscess. In 5 (4.6%) there was a history of staphylococcal infection in a family member. Average duration of total antibiotic treatment was 24.6 days. There were no deaths directly related to staphylococcal bacteremia in the study group.

Conclusions: CA-PSAB occurs rarely and is associated with bone, joint and skin disease. CA-MRSA was not isolated during the study period. Groups at risk for HA-PSAB included mainly neonates especially post complicated delivery, immune suppressed patients, and those with intravascular lines.

P098

ACTIVE SURVEILLANCE IS NEEDED FOR AMP-C B-LACTAMASEAND ESBL-PRODUCING ORGANISMS IN CHILDREN

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Background and aims: The emergence of multi-resistant Amp-C & ESBL-producing gram-negative bacteria in the community is one of the most significant recent epidemiologic changes in infectious diseases. In the years 2007-8 laboratory had vitek1 machine which could identify extended-spectrum β-lactamases (ESBLs) from isolates which were cefpodoxime (used as a marker) resistant. In an audit done from January 2007 to June 2008, 17 ESBLs were isolated from children. A method which can identify Amp-C β-lactamase and ESBL producing bacteria was adopted and evaluated for active surveillance.

Methods: Laboratory in the hospital adopted the five disc diffusion method on a single plate in the last quarter of 2008. Evaluation was done over a period of from 1st July 2009 to 31st December 2010.Type of specimen, location where specimen was collected; age of the patient was recorded.

Results: 72 children were identified with Amp C producers and 33 with ESBLs aged 2days to 16 years. 53(74%) Amp-C isolates & 31(94%) ESBLs were obtained from urine, while the others from a cough swab, pus, eye, ears and umbilicus (no bacteraemia). 57(79%) Amp-C isolates & 29(88%) ESBLs were obtained from the community specimens.

Conclusions: Thus Amp-C & ESBL-producing organisms are reported with increasing incidence in the children and the number increased manifold with active surveillance which was sought as they are potentially serious pathogens. It is important to look for these multi-resistant infections so as maintain high standard of quality of children care and best management of children's illness episodes in the hospitals & community.

P099

EPIDEMIOLOGY AND RISK FACTORS FOR COMMUNITY ASSOCIATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (CA-MRSA) INFECTIONS IN A TERTIARY HOSPITAL

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Introduction: Community-associated methicillin resistant S.aureus (CA-MRSA) can cause serious invasive infections with high mortality in otherwise healthy children.

Aim: To assess epidemiological and clinical characteristics, antibiotic resistance profile and identify risk factors associated with CA-MRSA infections in the paediatric population of Athens.

Methods: 179 children (1 month-14 years) who were treated as outpatients or hospitalized because of staphylococcal infection from 2/2010-3/2011 were included in the study.

Results: CA-MRSA was isolated in 68/179 children (38%), while it was more common in hospitalized (44.4%) than in outpatient (25.8%) children (P=0.015). The most common clinical manifestations for outpatients were impetigo (33.9%), soft tissue abscesses (12.9%) and infected atopic dermatitis (12.9%) and for hospitalized children, soft tissue abscesses (31.6%), furuncles (13.7%) and lymph node abscesses (10.3%). Among the hospitalized children, 20.5% had invasive infections. The most common CA-MRSA invasive infections were osteomyelitis (30%), septic arthritis (30%) and pneumonia (20%). CA-MRSA infections were associated with history of atopic dermatitis (P=0.055), recurrent skin infections (P=0.012), need for hospitalization (P=0.015) and surgical drainage (P=0.002). Resistance rates of CA-MRSA strains were for fucidic acid 66.2%, for erythromycin 22.1%, for clindamycin 13.2%, and for rifampicin, gentamycin, ciprofloxacin and cotrimoxazole 0%.

Conclusions: The prevalence of CA-MRSA in the paediatric population in our area is high, while the risk for hospitalization and complications is increased. History of atopic dermatitis and recurrent skin infections increase the possibility for CA-MRSA infection.

P100

AETIOLOGY AND RESISTANCE OF CHILDHOOD BACTERIAL ENTEROPATHOGENS IN CRETE

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Aim: To investigate the long-term trends in prevalence and antimicrobial resistance of bacterial enteropathogens among children in a well-defined geographical area.

Methods: All children younger than 14 years treated as inpatients or outpatients for enteritis at the University General Hospital at Heraklion, Crete, Greece during the 18-year period January 1993 to December 2010 were included. Stool specimens were examined by the standards methods for enteropathogenic *Escherichia coli* (EPEC), *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*, and *Aeromonas* species.

Results: Of a total of 33,032 stool samples processed, 1,315 yielded a bacterial pathogen in adults and 1,597 in children. Among childhood pathogens, *S. enterica* was the most common (42.3%), followed by *Campylobacter* spp. (33.6%), EPEC (17.4%), *Y. enterocolitica* (5.82%), *A. hydrophila* (0.44%), and *Shigella* spp. (0.38%). A summer peak was principally attributed to *Salmonella* infections. *Salmonella* was the leading cause of bacterial enteritis all during the study with increasing prevalence ($p< 0.0001$). *Campylobacter* prevalence increased through the study period ($p=0.0008$ by chi-square for trend), but EPEC prevalence decreased ($p< 0.0001$ by chi-square for trend). The last *S. typhi* was observed in 1996. The overall rates of resistance to amoxicillin, imipenem, gentamicin, tetracycline, cotrimoxazole and cirpofloxacin were 40.4, 0.06, 1.17, 30.2, 32.9 and 17.0%, respectively.

Conclusions: In the study area bacterial enteritis continues to be principally caused by nontyphoidal Salmonellae. Considerable changes in the long-term morbidity of specific pathogens call for ongoing surveillance and tailored management.

P101

STAPHYLOCOCCUS AUREUS CARRIAGE AND MRSA PREVALENCE IN INFANTS IN CRETE

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Background: *Staphylococcus aureus* carriage and resistance rates in infants in the community setting are not adequately known. In this study, we investigated the prevalence and resistance to methicillin of *S. aureus* in infants in Crete, Greece.

Study design: In this prospective study conducted from December 2004 to May 2007, healthy infants were randomly recruited from the community setting at the age of 6 months and again at the age of 12 months. Nasal swabs were obtained, and a questionnaire regarding potentially predisposing factors was administered.

Results: Among 162 enrolled 6-month old infants 38 (23.5%) were found to be colonized by *S. aureus*, of whom 16 (42.1%) by MRSA. From the 162 infants, 121 were available for follow-up at the age of 12 months, when *S. aureus* was isolated in 21 (17.4%), 14/21 (66.7%) of the isolates being MRSA. Among the 121 infants swabbed both at the ages of 6 and 12 months, 11 (9.09%) were found to be persistent carriers, 7 of whom (63.6%) were carrying MRSA at both occasions. None of the children colonized by *S. aureus* proceeded to clinical infection.

Conclusions: Our findings suggest that *S. aureus* colonization rates in infants in our community are comparable to these reported elsewhere, however the widespread MRSA colonization should be taken into consideration when choosing empirical treatment for presumed *S. aureus* infections.

P102

COMMUNITY UROPATHOGENS IN CRETE: PREVALENCE AND RESISTANCE TO ANTIBIOTICS

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Background and aims: Surveillance of the epidemiology and resistance of pathogens facilitates optional treatment of urinary tract infection (UTI). In this study we investigated the long-term trends of uropathogens isolated from children in Crete.

Methods: All positive urine samples from children hospitalized for UTI in a tertiary setting for the 12-year period 1997-2008 were included and analyzed for 3 consecutive 4-year periods, 1997-2000, 2001-2004 and 2005-2008.

Results: Among a total of 638 isolates from 569 children, the leading pathogen was *E. coli* (69.0%), followed by *Klebsiella* spp (9.70%), *P. aeruginosa* (6.70%), *Enterococcus* spp (5.60%), *Proteus* spp (4.40%) and *Enterobacter/Citrobacter* spp (3.90%), their prevalence remaining similar throughout the study periods. 55.9% of isolates were resistant to amoxicillin, 32.9% to amoxicillin-clavulanate, 37.3% to trimethoprim-sulfamethoxazole, 21.0% to cefuroxime, 15.9% to nitrofurantoin, and 7.10% to ciprofloxacin and 14.7% were resistant to ceftriaxone, 8.90% to ceftazidime, 8.21% to gentamicin and 2.70% to imipenem. Resistance decreased through the study period for cefuroxime and gentamicin (chi-square for trend p=0.016 and p=0.014, respectively) but increased for nitrofurantoin and ceftriaxone (chi-square for trend p=0.0002 and p=0.0034, respectively). In particular for *E. coli*, resistance rates were reduced throughout the study period for cefuroxime and amoxicillin-clavulanate (chi-square for trend p=0.0003 and p=0.0084, respectively) but increased for nitrofurantoin, ceftriaxone and ceftazidime (chi-square for trend p=0.015, p=0.011 and p=0.0018, respectively).

Conclusions: Our findings confirm high resistance rates of uropathogens to common oral and parenteral agents, with alarmingly rising trends for broad spectrum antibiotics.

P103

THE CHANGE OF DRUG-RESISTANCE AND GENOTYPE OF EXTENDED-SPECTRUM BETA-LACTAMASES PRODUCING ESEHERICHIA COIL IN CHILDREN WITH LOWER RESPIRATORY TRACT INFECTION

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Objective: Analysis of drug resisitance of Producing Extended-spectrum beta-Lactamases in Eseherichia coli.

Methods: Phenotypic confirmatory and the resistance of ESBLs was detected in 117strains of E.coli isolated from patients with lower respiratory tract infection.The positive rates were compared between the year 2009~2010 and 2006~2007.

Results: The 52.1% strains were considered ESBLs-producing in our research. The resistance rates to common antibiotics were up to 90%, including to aztreonam, cefepime and ceftazidime.The higher resistance rates were found in ampicillin,ceftriaxone and cephazolin which were 100%. Further more, the resistance was multiple resistant to cephalosporins, penicillins and chemitrim. The resistance rates of imipenem, ertapenem, piperacillin/tazobact, amikacin sulphate, tobramycin, ciprofloxacin, levofloxacin, cefotetan, furadantin to ESBLs-producing strains were the lower and imipenem was the most sensitive. The comparison had no significance between 2009~2010 and 2006~2007.

Conclusions: The prevalence of ESBLs was high in Escherichia coli and the resistance rates are high to lots of common antibiotics, especially to penicillin and cephalosporin except for sensitive to Carbapenems. The imipenem or beta -lactamase inhibitor of the complex were main antibiotics to bacteria-producing ESBLs.

P104

THE PREVALENCE OF SEVERE PNEUMOCCOCAL INFECTIONS IN CHILDREN FROM TIMIS AREA BETWEEN 2009-2010

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Material and method: From 01.01.2010 to 31.12.2010 we study the prevalence of pneumococcal infections in children admitted in our Hospital. We have tree groups of patients: group A - less then 2 years, group B age between 2 -9 years, group C more than 10 years. The study protocol involves: anamnesis, clinical examinations, routine analyses, culture from biologic products, inflammatory factors, and in selected cases other investigations adapted to the clinical pictures / evolution of the disease.

Results and discussions: From 16723 to admitted in our hospital during 1 year, 679 (5.9%) have symptomatic pneumococcal infections. In group A, 324 children had mostly invasive infections 252 (77.77%) cases with (pneumonia 83.02%, meningitis 8.9%, osteomielitis 7.7%), in group B, 207 children we have 178 (85.99%) children with invasive infections and 29 with non invasive infection; in group C ,148 children we had invasive infections (pneumonia 93.91%, meningitis 4.75 osteomielitis 1.34%). The non - invasive infections was otitis, rhinitis and pharingitis. The therapeutic protocol involve the initial treatment with penicillin G in height doses, like first choice and then when the sensibility of the germs were tested with III th generations cephalosporin's. The severe forms of pneumoccocal infections was in group A and in the children with anemia and / immune deficiencies in group B and C.

Conclusions:

1.The pneunococcal infections in south - west of Romania is still height.

2.The severity of infections depends of age and immune status of child.

3.The pneumoccocal vaccine must be performed by a national programmer.

P105

BACILLUS CEREUS SEPSIS IN TWO PRETERM NEONATES

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Introduction: Bacillus cereus, a Gram-positive, aerobic or facultative anaerobic spore-forming motile rod, is an environmental organism commonly found in soil, vegetation, dairy products, and infrequently causes disease such as gastroenteritis by preformed toxins upon ingestion. It is frequently associated with contamination.

Patients and results: Patient F.H. (male, 929g) was born at 27+2 weeks gestation suffering from asphyxia as well as amnioninfection syndrome. After good recovery he developed a recent sepsis on day 13 after live birth with rising infection parameters and corresponding clinical symptoms. Blood culture was positive for Bacillus cereus. According to his antibiogram he was treated with meropeneme, vancomycine and rifoldine for 3 weeks. One week after finishing this therapy F.H. developed septic symptoms again. Blood culture was positive for Bacillus cereus once more. Therefore he received clindamycine and rifoldine intravenously for 3 weeks followed by oral administration of therapy for further 3 weeks.

Patient D.E. (male, 1577g) was born at 28+6 weeks gestation. On admission, he was suffering from respiratory distress syndrome. On the second day of life he developed clinical symptoms according to early-onset sepsis and rising infection parameters. In blood culture we detected Bacillus cereus. He received meropeneme and vancomycine for 21 days and recovered promptly.

Conclusions: Bacillus cereus is to be considered as a potential pathogen in neonates and can cause serial invasive infections. Usually it is resistant to penicillin, ampicillin and cephalosporins, which are primarily used in early-onset sepsis. Special attention is to be payed towards the necessity of prolonged treatment periods.

P106

PATHOGENS CAUSING SEPSIS IN PEDIATRIC CANCER PATIENTS PRESENTING WITH FEBRILE NEUTROPENIA: SPECTRUM AND SUSCEPTIBILITY PATTERNS

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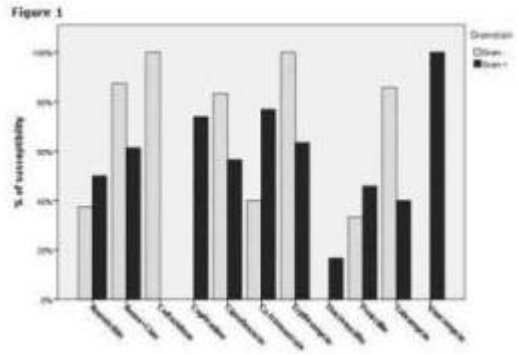
Background and aims: The introduction of empirical and prophylactic antibiotics in pediatric cancer patients has reduced the occurrence of infectious complications considerably. On the other hand, this is also the most important determinant in causing a shift in the etiology of bacteremias from gram-negative to gram-positive organisms, and their susceptibility patterns. The aim of this study was to map out the microbiological spectrum and susceptibility patterns of pathogens causing sepsis in the pas five years.

Methods: We analyzed the blood cultures of pediatric cancer patients presenting with febrile neutropenia (FN) between 2005 and 2010. Information on isolated strains including etiology and susceptibility to antibiotics was obtained using standard microbiological procedures.

Results: A total of 224 FN episodes occurred in 204 pediatric cancer patients. Overall, 68 organisms were isolated in 53 of FN episodes (23.7%): Gram-positive bacteria 52/68 (76.5%), Gram-negative bacteria 15/68 (22%), fungal infection 1/71 (1.5%). Figure 1 shows the resistance patterns of empirical and prophylactic antibiotic regimens.

Complications (including admission at the ICU) occurred in 15.4% of Gram-positive bacteremias, and in 20.0% of Gram-negative bacteremias.

Conclusions: Our results show that the shift to Gram-positive organisms causing bacteremia in pediatric cancer patients with FN has proceeded to more than 75%. In our population, ceftazidime is a good choice for covering Gram-negative bacteria; vancomycin is a good choice for Gram-positive bacteria. Therapeutic strategies for febrile neutropenia should be modified based on the local antibiotic resistance pattern.



[Figure 1]

P107

BACTEREMIA IN YOUNG CHILDREN WITH FEVER WITHOUT SOURCE PRESENTING TO THE PEDIATRIC EMERGENCY DEPARTMENT IN THE ERA OF PCV-7

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Background and aims: In the Veneto region, in north-eastern Italy, a universal immunization with a 2+1-dose schedule (given at 3, 5, and 11-12 months) of PCV-7 was implemented in 2006, gaining a 92% coverage for children born since 2007. The aim of the present study was to evaluate the incidence of bacteremia, and the isolated pathogens, in children with fever without source(FWS) in the era of PCV-7.

Methods: Retrospective study that included children 1-36 months old who presented with FWS and had a blood culture(BC) performed as part of their evaluation at the Pediatric Emergency Department of Padova, from 1/6/2006 to 31/1/2009.

Results: Of the 409 patients included 54% had fever < 24 hours; 70% had received at least one dose of PCV-7, and 65.5% at least 2 doses. A BC was positive in 7 patients (1.7%) and none grew Streptococcus pneumoniae(SP) *(Table 1)*. No difference was found in children aged 1-3 months compared to the older ones, with a bacteremia rate of 2% and 1.6% respectively. The contaminant rate was 3.6%.

Conclusions: SP is a rare cause of bacteremia in children with FWS in the PCV-7 era in our region. Other different pathogens have to be considered as a cause of bacteremia, isolated or associated to a subsequently manifested site of infection. Previous strategies aimed at screening for SP bacteremia, the most common cause of bacteremia prior to PCV-7 introduction, need to be reviewed.

Pathogen isolated in the BC (Final Diagnosis)
2 Streptococcus pyogenes (1 Osteomyelitis, 1 Cellulitis); 1 Salmonella enteritidis (Enteritis); 1 Klebsiella ornithinolytica (Urinary tract infection); 1 Streptococcus agalactiae (Occult Bacteremia); 1 Escherichia coli (Occult Bacteremia); 1 Enterococcus faecium (Occult Bacteremia)

[Table 1]

P108

PARAPHARYNGEAL ABSCESS WITH MEDIASTINAL EXTENSION AS COMPLICATION OF URTI IN AN 11-MONTH OLD BABY: A CASE REPORT

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Parapharyngeal abscess is a severe complication of URTI. Initial symptoms may be underestimated with the risk of extension to mediastinum, a rare occurrence related to high mortality.

We report the case of an 11-month old baby who was hospitalised because of submandibular cellulitis, right basal pneumonia and initial septic state. She has had 4 days of fever, rhinitis, cough and 3 days of deteriorating swelling of the neck with feeding difficulties. At admission her general conditions were compromised: respiratory rate 36/min, SatO2 97%, reduction of air entry at the right lung base with crackles, painful swelling of the mandible's angle region, hyperaemic pharynx and laterocervical bilateral lymph nodes.

Laboratory: WBC 21.000/mmc (N 18.000/mmc), CRP >250 mg/l, PCT 37,5ug/l. Chest radiography: right pneumonia with pleural effusion. Neck echography: cellulitis extended to muscular planes. Despite treatment with ceftriaxone and metronidazole, she rapidly worsened requiring oxygen. Neck-chest-CT scan showed a retropharyngeal fluid collection with extension to the contiguous cellular tissue and mediastinum. She underwent surgical toilet and then treatment with oxacillin, gentamicin, metronidazole, with clinical, laboratory and radiological improvement. A Streptococcus group A grew from blood and soft tissues cultures. The child was discharged after 40 days of hospitalisation.

URTI in infants should not be underestimated because the immaturity of the immune system as well as the aspecificity of early clinical findings, and consequent diagnostic delay, makes high the risk of evolution into a deep neck abscess with extension into the mediastinum. CT scan is the best diagnostic test for diagnosis and follow-up.

P109

A CASE OF SUBCUTANEOUS NODULES AND FEVER FOLLOWING STREPTOCOCCAL INFECTION-CHALLENGES IN DIAGNOSIS

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Background: Streptococcus has been associated with erythema nodosum and polyarteritis nodosa in childhood.

Although different entities, both EN and PAN demonstrate clinical features of subcutaneous nodules with fever.

Histologic findings include septal panniculitis in case of EN and necrotizing vasculitis for PAN.

The therapeutical approach and courses are different.

Methods: 12-year old boy has been admitted with a 6-day history of fever, arthralgias, subcutaneous nodules and rash. An upper respiratory tract infection preceded the current symptoms.

The clinical examination revealed tender erythematous nodules, patchy rash on the anterior and dorsal surface of the lower limbs and instep of the foot, swelling of the knees and ankles. Laboratory investigations showed acute phase response with leucocytosis and raised inflammatory markers, negative autoimmune panel except ANA, proteinuria and microscopic hematuria.

Evidence of previous streptococcal infection has been documented with raised ASTO and anti-DNaseB titer, and other causes of EN have been excluded.

The evidence of severe ongoing inflammation, renal involvement, atypical for EN distribution of the skin findings prompted the suspicion of PAN and a biopsy of subcutaneous nodule was performed.

Results: The histological examination revealed findings consistent with EN.

The use of NSAIDs and antibiotic therapy resulted in clinical improvement , with cessation of fever, resolution of arthritis and renal involvement findings by day 14 of illness. The subcutaneous nodules relapsed over 4 weeks.

Conclusions: We highlight the severe course of Streptococcus-associated EN in this patient, with systemic involvement, and the need for deep skin incisional biopsy for diagnostically difficult cases.

P110

SURVEILLANCE OF INVASIVE COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS INFECTIONS IN IRISH CHILDREN

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Background and aims: Community-acquired *Staphylococcus aureus* (CA-SA) infection can cause devastating disease in previously healthy children. The aim of this study was to calculate the rate of invasive CA-SA infections in Irish children < 14 years old and describe the clinical picture.

Methods: Via the Irish Paediatric Surveillance Unit, over a 12-month period, paediatricians throughout the island of Ireland prospectively reported cases of invasive CA-SA infections meeting study criteria. Cases were defined as having SA isolated from blood or other sterile body fluid except urine. Excuding patients in neonatal intensive care setting and those hospitalised > 48 hours. Each reporting physician was contacted and specific data gathered and analysed.

Results: To date 14 cases have been reported (complete data from 10). Patients have all been Caucasian, male, previously healthy, a mean of age of 57.7 months (range, 2 weeks to 14 years). Three (30%) patients had SA soft tissue infection prior to presentation. Osteoarticular infections were most frequently reported (6/10); 1/6 required surgery (repeated hip wash out and drainage). Three patients (30%) developed sepsis, with one death. Based on most current census figures, we estimate an incidence rate of 1.5 cases per 100,000 children with a mortality rate of 0.11 per 100,000. All blood isolates were methicillin susceptible.

Conclusion: From our study, invasive CA-SA appears more common in male children. Acknowledging the small numbers, there is a high associated morbidity and mortality rate. Reported patients have typically been healthy. So far, there have been no reports of methicillin resistant isolates.

P111

STUDY OF THE BACTERIAL AGENTS IN NOSOCOMIAL AND ACQUIRED INFECTIONS BASED ON THE BLOOD CULTURE IN NEONATAL INTENSIVE CARE UNIT

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Objective: To study the distribution of bacterial agents in bloodstream infections among hospitalized patients in the neonatal intensive care unit (NICU).

Methods: Blood samples were taken from hospitalized infants in NICU. In this study, 6 ml of blood was extracted from the patients having septicemia, which was then added to the bottle containing the blood culture broth. The bottles were labeled and incubated at 35 degrees C for maximum of 7 days.

Results: The result shows that out of the 173 patients with positive blood cultures 99 had gram positive organisms while 74 had gram negative organisms. In those with gram-positive bacteria, 70 cases were acquired infection and 29 cases were nosocomial infection. These results for gram negative bacteria showed that 48 cases were due to acquired infection and 26 cases due to nosocomial infection. In determining the relation between the rate of death and the type of infection, we found that out of 173 patients 51 (29%) died. Of these cases 36 (70%) were due to acquired infection and 15 (30%) were due to nosocomial infection.

Conclusion: We conclude that nosocomial bloodstream infection is an important target for the most aggressive strategies for prevention and control.

P112

INVASIVE BACTERIAL INFECTIONS AMONG CHILDREN ADMITTED TO A LOCAL GENERAL HOSPITAL IN ENGLAND: THE CHILDHOOD ACUTE BACTERIAL INFECTIONS NETWORK (CABIN)

A.-L. Nichols[1], H. Payne[1], J. Handforth[1], M. Sharland[2], S. Ladhani[2]

[1]General Paediatrics, Croydon University Hospital, [2]Paediatric Infectious Diseases Unit, St George's Healthcare NHS Trust, London, UK

Background: Little is known about children who develop invasive bacterial infections in the era of routine immunisation. CABIN was developed to collect clinico-epidemiological data on children with invasive bacterial infections in south London. This pilot study reports on cases admitted to a local general hospital in 2009-2010.

Methods: A standardised questionnaire was used to collect clinical, laboratory, microbiological and outcome data from the case notes of all children aged 1 month to 15 years with positive blood or cerebrospinal fluid (CSF) cultures.

Results: Over the two-year period, 210 episodes were identified with 223 positive blood (n=218) or CSF (n=5) cultures. Of these, 142 episodes (68%) were documented as contaminants. Of the remaining 68 episodes, 20 (29%) occurred in children aged 1-11 months, 23 (34%) among 1-4 year-olds and 25 (37%) among 5-15 year-olds. Underlying medical conditions were documented for 10%, 70% and 88% in these age groups, respectively. The most common pathogens were coagulase-negative staphylococci (n=6), Group B streptococci (n=5) and *Escherichia coli* (n=3) in 1-11 month-olds, coagulase-negative staphylococci (n=10) and *Staphylococcus aureus* (n=4) in 1-4 year-olds and *Acinetobacter* sp.(n=6), coagulase-negative staphylococci (n=4)*, Enterobacter cloacae* (n=3) and *Micrococcus* sp. (n=3) in 5-15 year-olds. Only one child in the 1-4 year-old age group died of pneumococcal septicaemia.

Conclusions: Invasive bacterial infections remain a major cause of morbidity in children, particularly among those with underlying medical conditions. The CABIN programme will help determine the leading pathogens, identify risk factors and guide empiric antimicrobial therapy for children with suspected invasive bacterial infections.

P113

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Conclusions: Invasive bacterial infections remain a major cause of morbidity in children, particularly among those with underlying medical conditions. The CABIN programme will help determine the leading pathogens, identify risk factors and guide empiric antimicrobial therapy for children with suspected invasive bacterial infections.

P114

TYPHOID FORM OF TULAREMIA IN INFANT (CASE REPORT)

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Background: Clinical manifestations of F. tularensis infection depend on the portal of entry, the extent of systemic involvement, the virulence of the pathogen, and the immune status of the host.

The typhoidal form of tularemia occurs in 5-10% of cases and results after any path of transmission.

Case report: We present the case of a nine months child hospitalized to 2nd Clinic of Infectious Diseases during 15.04.2010 - 10.05.2010 with the diagnosis of tularemia.

The child was admitted with fever, diarrhea, vomiting, cough, bad general condition, drowsiness and apathy which were not justified by the number of bowel movements, by the mild syndrome of acute dehydration or biological changes (WBC = 11.340/mmc, ESR = 20/55 mm 1h/2h, fibrinogen = 5.6 g%).

After a slight improvement of diarrhea, in 19.04.2010 the child presented blood in the stools and the rotavirus antigen was revealed.

The bad general condition, anorexia, vomiting, cough persisted and the child was sleepy, sad, "foggy" (typhous state). Secondary pulmonary involvement was present as pulmonary infiltrates. Francisella tularensis was isolated in 26.04.2010 in blood culture.

The evolution was favorable after the treatment with gentamicin and ciprofloxacin (26.04 to 05.05.2010)

Conclusion:

1- The diagnosis was delayed by rotavirus concomitant nosocomial infection and the late results of blood culture.

2- The contribution of modern diagnosis methods was essential in isolating and testing the antimicrobial susceptibility of Francisella tularensis.

3- The child evolution was favorable only after appropriate therapy, consistent with the results of susceptibility tests to antimicrobial agents.

P115

STREPTOCOCCUS PYOGENES SEROTYPE M4/T4 CAUSING ACUTE ENDOCARDITIS IN NATIVE VALVE WITH MULTIPLE SEVERE COMPLICATIONS

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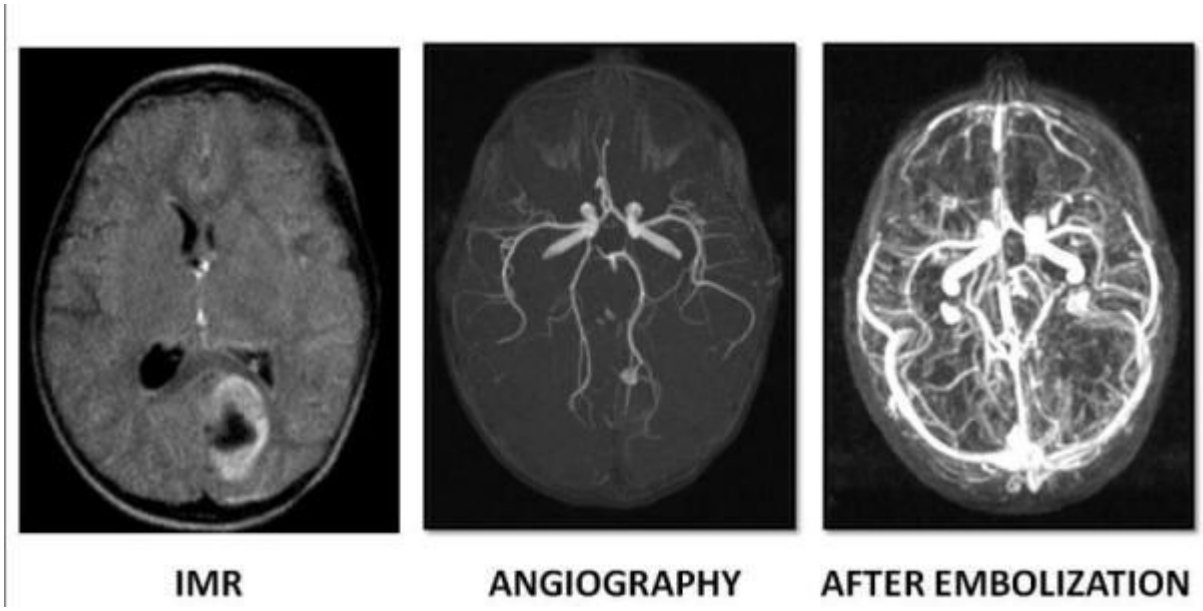
BACKGROUND AND Aims: Acute infective endocarditis of native valve without cardiopathy is rare in children, even more if it's caused by Streptococcus pyogenes (SP). We present a case involved a native aortic valve with multiple severe complications produced by an infrequent serotype of SP.

RESULTS: A 3 year-old female is admitted with 5 days of fever, vomiting, abdominal pain and myalgia. Twelve hours before, a macular rash with few disseminated purpuric-petechiae lesions flared. Examination: jaundice, pharyngeal hyperaemia, palatal petechiae, strawberry tongue, abdominal distension. Investigations: marked elevation of acute phase reactants, elevation of transaminases, pleocytosis, leucocituria and hydrops vesicular. Cefotaxime is initiated. Twenty-four hours later ankle swelling appears, so Kawasaki's disease is suspected and gammaglobulin+aspirin are associated. Afterwards, there is clinical worsening with heart failure. Echocardiography: aortic valve vegetation. Blood culture: SP serotype M4/T4 (toxins B/ C/ F/ Z). She is admitted in intensive care where diuretics, vasodilators and penicillin+gentamycin are started. The 12th day, she suffers 2 generalized seizures. IMR: left occipital haemorrhage. Angiography: mycotic aneurysm in left posterior cerebral artery, which is embolized.



[Mycotic aneurysm]

Other complication was subvalvular abscess that required Ross' surgery (32th day). Favourable outcome after 8 weeks of antibiotics, without cardiological or neurological symptoms.

Conclusions: The diagnosis of SP invasive disease may be delayed because of its similarity with Kawasaki's disease, probably due to the action of superantigens in both diseases. Torpid outcome despite of empiric antibiotic treatment and multiple complications show the aggressiveness of the serotype M4/T4.

P116

NEONATAL LISTERIOSIS IN ENGLAND (2004-2009)

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Background: *Listeria monocytogenes* (LM) is a rare but important cause of sepsis and meningitis in neonates. Despite increasing cases in England there are limited data on clinical presentation and risk factors.

Methods: Positive blood cultures for LM were identified prospectively from neonatal units participating in the neonatal infection surveillance network (neonIN). Demographic, risk factors and outcome data were collected.

Results: During a five year period (2004-2009), ten babies (7 female, 3 male) with LM infection were identified. The incidence is ~5/100,000 live births (46/100,000 neonatal admissions) and represents about 7% of all early onset (EO) pathogens among neonIN participating neonatal units over this period. Most mothers (8/10, 80%) reported signs of infection before delivery, 6/10 (60%) had meconium at delivery, 8/10 (80%) babies were premature and 8/10 (80%) babies required resuscitation at birth. Median gestational age and birth weight (range) were 32.5 (27-39 weeks) and 1820 (1070-3210grams) respectively.

All babies presented within 48 hours of delivery (EO) with non-specific features of sepsis, and one baby had a clinical diagnosis of meningitis. All received a combination of a penicillin based antibiotic and gentamicin. 4/10 (40%) babies died (median age at death 89.5, range 6-144 hours), of the 6 surviving infants, one (16.7%) has severe neurological sequelae (global developmental delay, seizures and faltering growth).

Conclusions: LM is an uncommon cause of EO neonatal infection but has a high mortality and morbidity. As opportunities for better treatment appear limited, better identification of risk factors and implementation of prevention strategies should be prioritised

P117

ANTIBODY LEVELS AGAINST *B. PERTUSSIS* IN NEONATES MEASURED IN GUTHRIE CARDS

C.V. Ommen[1], L.H. Elvers[2], D.W. Notermans[2], J.C.M. van Huisseling[3], P.F.M. Teunis[4], F.G.A. Versteegh[1]

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Aim: We designed this study to investigate if IgG-PT against B. pertussis in umbilical cord blood can reliably be determined in dried blood spots on filter paper (Guthrie) cards.

Patients and methods: We prospectively included 129 mothers and their newborns born in a general hospital in the Netherlands. The relation between IgG-PT against B. pertussis from the umbilical cord measured in dried blood spots (Guthrie card) and in serum samples was studied by means of a Bland-Altman graph, using regression analysis to evaluate the equivalence of both measurement methods.

Results: IgG-PT in Guthrie cards were well correlated with IgG-PT in serum samples from the umbilical cord when calibrated against blood spot calibrators ($p < 0.05$).

Conclusion: Maternal IgG-PT against B. pertussis measured in cord blood applied to Guthrie cards and calibrated against bloodspot calibrators are equivalent with measurement of IgG-PT in cord serum. This offers new perspectives for future studies concerning B. pertussis antibodies in newborns.

P118

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P119

ACUTE OTITIS MEDIA IN PEDIATRIC FIRST AID: DIAGNOSIS AND TREATMENT

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Background and aims: Acute otitis media (AOM) is one of the most common childhood infections. Recent Italian guidelines for the treatment of AOM represent a major step forward to the approach to the management of this disease. We aimed to evaluate the epidemiological trends of disease and different treatment with a retrospective study at Department of Pediatrics of Modena from 1 January 2007 to 31 December 2010.

Methods: 2917 children admitted at the “Pediatric first aid “ for the presence of symptoms and otoscopic signs of acute otitis media were selected. We evaluated medical history and therapy of each one, matched with italian guidelines.

Results: The incidence of acute otitis media was higher in children younger than 2 years. We observed a slow prevalence of male rate. The strategy of “wait and see” has been used only in 4% of cases, while antibiotic treatment included in 46% amoxicillin and amoxicillin-clavulanate in 48% of the cases. At least 65% of the children have been visited also by the ENT specialist .

Only 30 children needed hospitalization for respiratory distress or persistent fever. Acute mastoiditis was diagnosed in 3 cases and treated with intravenous antibiotic therapy.

Conclusion: Amoxicillin, alone or in association ,as first-line treatment, is efficient therapy and it's not showing the development of antibiotic resistance. The incidence of acute mastoiditis do not seem to be on increase. Clinical practice guidelines are being renewed constantly, emphasizing the ongoing research on this still unrevealing disease.

P120

BACTERIAL INFECTION OF SEVERE WOUND BURNS IN CHILDREN

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Background: Wound infection is probably the most important and potentially serious complications that affect the outcomes of burns. Understanding of the epidemiology of burn wound infections is essential for their correct treatment and for the prevention of systemic complications. The major sources of infection in burns are: colonization by the patient's own flora and by nosocomial transmission of microorganism.

Material and methods: This study analyze the epidemiology of infections in children with severe (> 20%), full thickness burns. We reviewed the medical charts of all the patients, admitted in 2010, to the Emergency Children's Hospital “Louis Turcanu”, Pediatric Surgery Department, Timisoara, Romania with severe (> 20%), full thickness burns.

Results: A number of six patients, between 1 and 5 years old, with severe full thickness burns were admitted to our hospital. Infection was detected by wound cultures in 4 patients. The most isolated micro-organism was meticilin-resistant Staphylococcus aureus (3 cases) with a tested sensitivity at Vancomycin, Linezolid and Teicoplanin. In one case Pseudomonas aeruginosa was detected sensitive at antibiogram to Amoxicilin/Clavulanic acid, Ampicilin/ Sulbactam, Ciprofloxacin, Meronem, Piperacilin/ Tazobactam, Teicoplanin, Cefuroxime and Vancomicin.

Conclusion: The pathogens mainly implicated in infection of severe burns were meticiln-resistant Staphylococcus aureus and Pseudomonas aeruginosa. No deaths were encountered, but the mean hospitalization stay was 32 days.

P121

COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS INFECTIONS ACROSS EUROPE

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Background: Community-acquired, methicillin-resistant S. aureus (CA-MRSA) infections in children are increasing in the USA and in some other parts of the world. Data from Europe is unclear.

Objectives: To describe the clinical and microbiological characteristics of children presenting to Pediatric Emergency Departments across Europe with a Staphylococcus aureus infection.

Methods: We prospectively enrolled children under 16 years of age with community-acquired S. aureus infections during the month of June 2010 in different European hospitals.

Results: During the study period, 155 cases were collected from 16 centres in 10 different countries (Spain, England, Lithuania, Germany, Israel, Romania, Cyprus, Estonia, Italy and Georgia). The prevalence of CA-MRSA was 12 % in this study. The Panton-Valentine leukocidin (PVL) genes were detected in 30 % (35/117) of the isolates tested. The children had a median age of 31,5 months and 59% were male. Diagnoses included: superficial infections 56%, cellulitis or abscess 31% and deep infections 13%. 12% of the patients had one or more established risk factors for health care-associated infection. 61% of the patients were admitted to the hospital and 44% required drainage. There were no significant differences between CA-MRSA and CA-MSSA infections related to hospitalization, need for drainage or type of infection.

Conclusions: There is an emergence of CA-MRSA infections across Europe, but less than in the USA. In this study there were no significant clinical differences between CA-MRSA and CA-MSSA infections. A significant proportion of infections were caused by PVL-positive isolates.

P122

LEMIERRE'S SYNDROME ASSOCIATED WITH SEPTIC PULMONARY EMBOLISM: A CASE REPORT

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Background and aims: Lemierre's syndrome is a severe complication of an acute oropharyngeal infection that can lead to internal jugular vein thrombophlebitis (IJVT) with secondary dissemination of septic emboli. It commonly affects adolescents and young adults and is caused by *Fusobacterium species* in approximately 80% of cases. Although it remains a rare disease, recent papers suggested a rising incidence of this condition.

Methods: We present a case of Lemierre's syndrome complicated by septic pulmonary embolism in a 15-year-old girl.

Results: A previously healthy girl was transferred to our hospital with a 5 day history of fever and sore throat followed by tender swelling and intense pain in the right laterocervical region, complicated by sepsis, acute renal failure and dyspnoea. The patient was previously treated with ceftriaxone. Neck ultrasounds demonstrated the presence of right IJVT and chest computerized tomography showed septic emboli in both lungs. Antibiotic therapy with meropenem and metronidazole in association with anticoagulants were promptly started due to the clinical and instrumental findings highly suggestive of Lemierre's syndrome. Blood cultures were negative and hypercoagulable state was detected. Clinical conditions rapidly improved and the patient was discharged after 55 days of hospitalization.

Conclusion: Lemierre's syndrome is a rare but severe life-threatening condition and appropriate diagnosis is often difficult because of poor awareness of this syndrome. Imaging diagnosis of neck region can facilitate the correct and prompt management of this illness. Anticoagulant therapy is effective and should be administered promptly especially in the case of severe thrombotic complications and thrombophilic conditions.

P123

SERUM BRAIN NATRIURETIC PEPTIDE IN CHILDREN WITH SEPTIC SHOCK

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Background and aims: Brain natriuretic peptide (BNP) is a marker of myocardial dysfunction that is elevated in children with heart failure from congenital heart defects and has recently shown that elevated in septic shock patients due to myocardial dysfunction. Our aims to compare serum BNP levels in children with sepsis with/without cardiac dysfunction and the role of BNP as a marker of severity and mortality in those children.

Methods: A prospective observational study was performed in a six-bed pediatric intensive care unit between June 2009 and August 2010. Serial blood samples were collected at admission(0.hour), 24.hours, 48.hours, 72.hours, 96.hours. At the same hour, clinical and laboratory data were recorded.

Results: 20 children with septic shock, 14 children with sepsis and 26 healthy controls were recruited. The mean BNP levels at admission(BNP(0)) significantly higher in children with sepsis syndrome than those of the healthy controls (242.13±929.6pg/ml vs. 2.61±1.26pg/ml; $p< 0.001$). Mean BNP(0) level was significantly higher in septic shock group than sepsis group (384.88±1191.3pg/ml vs. 28±38.94pg/ml; $p< 0.001$). In septic shock group; BNP(0) levels were significantly higher in non-survivors than those of survivors ($p< 0.01$). The BNP levels at 24^{th} and 48^{th} hours were significantly higher than at admission ($p< 0.001$). BNP(0) values also related with number of organ dysfunction in particular cardiac and neurologic dysfunction, PRISM score, PELOD score, platelet count, coagulation status and serum calcium levels.

Conclusion: Serum BNP levels at admission, 24^{th} and 48^{th} hours as clinically relevant to assess severity and mortality risk of sepsis.

P124

PERTUSSIS CASES HOSPITALISED DURING THE WINTER-FALL-SUMMER PERIOD OF 2010

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Background and aims: The aim of this study was to present the epidemiological data of Pertussis cases who were admitted to the Pediatric Infectious Diseases Ward between February and July 2010.

Methods: Nasopharyngeal specimens were taken from all 26 patients who were admitted with pertussis like syndrome between February and July 2010. These specimens were examined for B. Pertussis by using RT PCR assay in the laboratory of Microbiology and Clinical Microbiology Department.

Results: Pertussis PCR was found positive in 12 (46%) patients. The median age of patients was 7 months, (ranging 40 days-28 months). Most of the patients were admitted on May and June.

The mean leucocyte and lymphocyte counts were 17200±11700 /mm3 (7200-43000) and 11310± 9500 /mm3 (3200-36000), respectively. Two patients had CRP values >5 mg/dL. All the remaining patients had normal levels of CRP. Father of 3 patients, mother of 4 patients, both parents of 2 patients and siblings of the 3 patients had a history of cough. An 18-month old patient required mechanical ventilation support for deep apnea. Three patients were not vaccinated with DaPT yet because they were under 2 months old. A single dose of DaPT vaccine was performed in 5 patients, 2 doses in 3 patients and 4 doses in 2 patients.

Conclusions: Although Pertussis vaccination exists in the routine vaccination protocol, still remains as an important health problem. In order to prevent infants against Pertussis, parents, siblings and other primary care givers must have complete immunity against Pertussis.

P125

THE INVESTIGATION OF IGG SUBCLASSES IN CHILDREN WITH CHRONIC BRUCELLOSIS

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Background: Brucellosis is a multi-system disease that show by broad spectrum of clinical manifestations and that requires laboratory testing for diagnosis. Some studies have shown that antibody response in patients with brucellosis consists of IgG3 for LPS and IgG1 and IgG2 for protein antigens .Several investigators were reported that different type´s subclasses of IgG (IgG3orIgG4) were secreted in chronic stage of disease. It was several controversies in the subject. Thus, we were studied the IgG subclasses in brucellosis patients in chronic stage.

Method: 45 children (5-16) in chronic stage of brucellosis were selected from individuals who referred to clinics in 2008-2009. Blood sampling was done for Wright and 2ME test. Titers of total IgG and IgG subclasses were measured by ELISA.

Results: The subjects consisted of 19(42.2%) males and 26(57.8%) females with an average age of 11 years. One hundred percent and 92% of the patients had positive Wright and 2ME test, respectively.IgG3 was the highest titer (35%) and IgG2 was the lowest titer (14.5%) among chronic brucellosis. The subclasses showed statistically significant association with clinical presentation, and response to antibiotic therapy.

Conclusion: Compared to the other IgG subclasses, the IgG3 titer is the highest in patients with chronic brucellosis and it might be deduced that IgG3 titer is a suitable tool to diagnostic chronic.

P126

ASSOCIATION BETWEEN NECROTISING ENTEROCOLITIS (NEC) AND INTESTINAL COLONISATION WITH EXTENDED SPECTRUM BETA LACTAMASE- (ESBL-) PRODUCING ENTEROBACTERIACEAE

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Background and aims: Intestinal bacterial overgrowth is known to be a risk factor for developing necrotising enterocolitis (NEC) in neonates. ESBL-producing *enterobacteriaceae* (ESBL-E.) pose a growing problem in neonatal intensive care units (NICU). Aim of the study was to identify a possible association between colonisation with ESBL-E. and development of NEC.

Methods: As a consequence of first detection of ESBL-E. colonisation at the NICU of the Medical University Graz in 2004, stool cultures of all hospitalised patients were routinely taken twice a week. We retrospectively analysed all NICU patients from 2005 through 2009 for a possible association between intestinal colonisation with ESBL-E. and development of NEC. We used RepPCR (Diversilab Instrument, BioMerieux) to assess strain-clonality.

Results: 103 out of 2986 neonates (3,5%) had stool cultures positive for ESBL-E. (74 *Klebsiella pneumonia* [*Kp*], 13 *Klebsiella oxytoca*, 8 *Escherichia coli*, 8 *Citrobacter freundii,* 6 *Serratia marcescens* - 5 neonates were colonised with 2 or more ESBL-E). 15 neonates (0,5%) were diagnosed as having NEC, 6 of them (40%) were intestinally colonised with ESBL-*Kp.* Among these, we identified 2 different clones, 2 isolates were not available for molecular typing. Further results see table 1.

	NEC (n=15)	no NEC (n=2971)	p-value	odds ratio	95% CI
GA	27-39 (35)	21-43 (36)	<0.001*	25,9	8,2-81,8
BW	500-3550 (2300)	360-5300 (2505)	<0.001*	11,8	4,0-34,7
ESBL-E.	6 (40%)	97 (3%)	<0.001**	19,8	6,9-56,6

Table 1: Risk factors for patients with necrotising enterocolitis (NEC) and without NEC (no NEC); „GA" gestational age in weeks, „BW" birth weight in g, „ESBL-E." colonised with extended spectrum beta lactamase producing enterobacteriaceae; „CI" confidence interval
* t-test of SPSS for Windows
** Chi square test of SPSS for Windows

[Table 1]

Conclusions: In addition to known risk factors (low gestational age, low birth weight), intestinal colonisation with ESBL-E. might be a possible risk factor for the development of NEC.

P127

CAT SCRATCH DISEASE IN PEDIATRIC AGE. DIFFERENT CLINICAL PRESENTATIONS

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The typical manifestation of B. henselae infection is cat scratch disease (CSD), a subacute lymphadenopathy, hepatosplenic granulomatosus lesions and unusual ocular manifestations. We report on three cases.

The first case, 4-year-old female with a five daylong fever and a one-month history of inguinal lymphadenopathy. Laboratory showed anti Bartonella antibodies (IgG 1/1024, IgM 1/40), negative abdominal ultrasound. Lymphadenopathy evolved in abscess drained surgically. 3 month follow-up showed anti Bartonella IgG and lymph node calcifications on echography.

The second case, 16-year-old male with a 10 days history of fever and abdominal pain, enlarged and painful liver on physical examination. Laboratory studies presented anti B. henselae antibodies (IgG 1/512, IgM 1/160), hepatosplenic multiple lesions on ultrasound and CT scan. Treatment regimen was amikacin and azithromycin, then rifamycin for 1 month. Fever disappeared in 15 days. 6-month follow-up was negative for IgM anti Bartonella with normal abdominal ultrasound. The third case, 10-year-old female with right armpit suppurative lymphadenopathy and a 2-week fever history, lesion on right upper arm and spleen enlargement on physical examination. B.Henselae antibodies (IgG 1/256, IgM 1/80) were found, with hepatosplenic multiple lesions on echography. Treatment with gentamycin and rifamycin was performed for 18 days during which erythema nodosum appeared and vanished. However the limphadenopathy was surgically drained. At 6 months, patient was negative for IgM anti Bartonella with hepatosplenic calcifications. Bartonella infection is generally asymptomatic, however may evolve in CSD, with hepatosplenic and self-limiting lymphatic lesions. Antibiotic treatment is not recommended, but surgical drainage may be necessary.

P128

ECHTYMA GANGRENOSUM-LIKE ERUPTION ASSOCIATED WITH *ACHROMOBACTER XYLOSOXIDANS* BACTEREMIA

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Ecthyma gangrenosum (EG) is considered to be pathognomonic sign of *Pseudomonas aeruginosa* but numerous other organisms have been reported to cause clinically identical lesions. We describe a premature newborn treated in neonatal intensive care unit (NICU) who developed EG-like skin lesions associated with *A. xylosoxidans* bacteremia.

A male infant born at 25 weeks gestation with birth weight 660 g. transferred to NICU and received surfactant replacement therapy for respiratory distress syndrome. On the 8 th day his admission vancomycin and meropenem initiated with suspicion of necrotising enterocolitis. On the 30 th day, access site on his left foot became erythematous. His clinical condition deteriorated rapidly and he developed apnea. Physical examination revealed cyanosis and erythematous, hemorrhagic vesicles over fingers, both arms and lower limbs which evolved into necrotic ulcers with escar and surrounding erythema, consistent with echtyma gangrenosum. Laboratory evaluation revealed anemia, thrombocytopenia, neutropenia and increased CRP. Ciprofloxasin was added pending culture results. *Achromobacter xylosoxidans* growth was detected in two sets of blood cultures and meropenem was continued according to antibiotic susceptibility results. During follow up he was extubated, blood cultures remained sterile and skin lesions were completely healed at the 15th of therapy.

Achromobacter xylosoxidans is an opportunistic pathogen causing infection in immunocompromised patients and premature babies. It has been isolated from several aqueous environmental sources some of which have been associated with nosocomial outbreaks of infection.

P129

MORBIDITY AND MORTALITY PREDICTORS IN SEPSIS, IN A PEDIATRIC INTENSIVE CARE UNIT (PICU) FROM A REFERENCE HOSPITAL

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Background and aims: Sepsis and septic shock account high morbidity and mortality.

Objectives: Determine the factors related to morbidity and sequelae of sepsis in a PICU.

Methods: Prospective descriptive study of patients with sepsis (between 7 days and 18 years old) admitted to the PICU of the Hospital Sant Joan de Deu de Barcelona during 2010.

Results: Sixty three patients with sepsis were included. Forty were males (63´5%). Median age 18 months (P25-75 6 months-5 years). The main etiology in comunitary sepsis was *N. meningitidis* in 14 (22'2%) and *S. pneumoniae* in 10 (15'8%). Fourteen cases were nosocomial infections. Cefotaxime was used in 42 cases, and in 30 of them associated with vancomycin. Statistically significant factors associated with mortality were the PRISM score, the lactate and lower platelet count at admission. The presence of underlying disease, a nosocomial infection and septic shock were also statistically significant predictors of mortality, a length stay more than 7 days in the PICU and the presence of sequelae.

Multivariate analysis showed that nosocomial infection and multiple organ failure were variables that were independently associated to exitus. The PRISM score, C-reactive protein (CRP) on admission, need of mechanical ventilation and lactate on admission were associated with poor outcome with more length stay and more sequelae.

Conclusions: Patients with sepsis and multiorgan failure, especially nosocomial and higher values of PRISM, CRP and lactate, are at greater risk of poor outcome and should therefore be carefully monitored and treated.

P130

GENES ESSENTIAL FOR *MORAXELLA CATARRHALIS* SURVIVAL UNDER IRON-LIMITING CONDITIONS

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Background and aims: *Moraxella catarrhalis* is an emerging human-restricted respiratory tract pathogen that is a common cause of childhood otitis media. Successful colonization of the human respiratory tract mucosa is an important step towards infection and depends on its ability to acquire essential iron. To evaluate the role and importance of iron metabolism in *M. catarrhalis*, we used genomic array footprinting (GAF), a genome-wide negative selection screen, to identify genes essential for survival under iron-limiting conditions.

Methods: *M. catarrhalis* RH4 transposon mutant libraries of ~28,000 mutants were either grown under standard or under iron-limiting conditions. Mutants that failed to survive under iron-limiting conditions were subsequently identified by differential hybridization of mutant-specific DNA probes to microarrays. For validation, growth of directed gene deletion mutants was tested individually under iron-limiting conditions.

Results: In total, 5 genes were identified as being essential for survival under iron-limiting conditions, including genes predicted to be involved in haem biosynthesis and in RNA maturation and degradation. Known *M. catarrhalis* iron-acquisition factors were not among the identified genes, which is most likely due to the high redundancy in iron-transport mechanisms. Finally, growth of 4 directed mutants selected for validation was attenuated under iron-limiting conditions, confirming observed GAF phenotypes.

Conclusions: We have successfully applied GAF to identify genes that are essential for *M. catarrhalis* survival under in vitro iron-limiting conditions, in this way mimicking host-like stress conditions. Currently, the specific roles of the identified genes in *M. catarrhalis* iron metabolism in vitro and at mucosal surfaces are under investigation.

P131

COMPARISON OF VIRULENCE TRAITS BETWEEN *ESCHERICHIA COLI* CLINICAL ISOLATES CAUSING EARLY NEONATAL SEPSIS AND THOSE COLLECTED FROM HEALTHY NEONATES

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Background and aims: Neonatal risk factors for invasive bacterial disease and its diagnosis and therapy remain an important problem for obstetricians and pediatricians being Escherichia coli and Streptococcus agalactiae the cause of major health problems in industrialized countries. The objective of the present work was to evaluate the virulence of E. coli strains causing early and late neonatal sepsis and to compare them with E. coli strains isolated from healthy neonates.

Methods: Twenty-seven E. coli strains from early neonatal sepsis and 28 from healthy neonates were studied. Detection of virulence genes was carried out by PCR. Phylogenetic group analysis was carried out by multiplex-PCR. Type 1 fimbriae expression was performed by agglutination with Saccharomyces cerevisiae. Fisher´s exact test was used for statistical analysis.

Results: Among the genes studied hly (hemolysin), cnf1 (cytotoxic necrotizing factor 1) and pap genes, all contained in a pathogenicity island, were significantly more frequent among strains causing early neonatal sepsis (p= 0.05, 0.02 and 0.04, respectively). In addition to these genes, the ibeA gene, involved in the translocation of membrane, was also significantly more frequent among strains causing early neonatal sepsis. On the other hand, type 1 expression and the papGIII allele encoding for the tip of the P-fimbria were more frequently presented in strains from healthy neonates.

Conclusions: E. coli strains causing neonatal sepsis were more virulent than the strains collected from healthy neonates and more frequently presented virulence genes contained in pathogenicity islands.

P132

NASOPHARYNGEAL COLONISATION WITH RESPIRATORY PATHOGENS IN HEALTHY CHILDREN, FOCUSING ON THE EFFECTS OF COLONISATION WITH *MORAXELLA CATARRHALIS*

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Background and aims: Nasopharyngeal colonisation with respiratory pathogens is common and often stated to be asymptomatic. This study aimed to investigate the rate and density of colonisation with *Moraxella catarrhalis* (Mcat), *Haemophilus influenzae* (Hflu), *Streptococcus pneumoniae* (Pnc) and *Staphylococcus aureus* (Sa) and associations with nasal discharge.

Methods: 586 nasal swabs, stored in STGG broth, from healthy children, aged 6 months to 6 years, were cultured using standard methods & semi-quantitative density scores recorded. Nasal symptom scores obtained at sampling (n=566) were analysed with density scores.

Results: Mcat, Hflu Pnc and Sa carriage rates were 68.8%, 51.7%, 46.6% and 15.5% respectively. 66% of children carrying Mcat had the organism detected at high density. Rates were significantly higher in younger than older children ($p < 0.05$), as for Pnc, whereas Sa rates rose progressively with age. Logistic regression analysis of co-colonisation controlling for age and other organisms revealed strong negative association between Mcat & Sa and positive association between Hflu and Pnc (both $p < 0.0005$).

Conclusions: This study provides evidence of a previously undescribed inhibitory or competitive relationship between Mcat and Sa. Our data do not support observations made previously in children & animals suggesting inhibitory or competitive relationships between Pnc & both Sa & Hflu. They suggest that Mcat, a relatively non-pathogenic & hitherto largely ignored species, may play a critical role in the ecology of the nasopharynx in young children. They also suggest that changes in nasopharyngeal carriage induced by conjugate vaccines might also have indirect effects on other species.

P133

MOLECULAR EPIDEMIOLOGY OF *SHIGELLA*: COMPARISON OF THE CLINICAL ISOLATES FROM CASES AND APPARENTLY HEALTHY SUBJECTS

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Shigella infection causes invasion of colonic mucosa. Infection can be asymptomatic and may persist following resolution of symptoms. Invasiveness of Shigella may be linked to the virulence plasmid. Molecular characteristics of Shigella isolated from patients and asymptomatic patients conducted to elucidate molecular basis of invasiveness. Isolates of Shigella obtained from surveillance among population with limited sanitation and hygiene within Dhaka. Specimens were collected from age-matched cases and controls. Shigella was isolated from 596 (13.3%) of 4492 patients and from 42 (6.9%) of 608 controls. Either cases or controls, S. flexneri predominated (55-65%) with majority of subtype 3a (26.9% cases and 35.7% controls). Serotype, sub-serotype and time-matched 14 strains, 7 from each cases and controls were randomly selected for molecular characterization. The invasive plasmid (140 MDa) was present in 6 (85.7%) of 7 clinical isolates except in one S. flexneri 1c), while 5 (71.4%) of 7 of controls. Isolates of cases and controls possessing 140 MDa plasmid were Sereny test positive, attesting their invasiveness, when ipaH genes were present 100% cases and controls. The PFGE pattern was similar in 2 (40%) of 5 pairs of S. flexneri; remaining 3 (60%) pairs showed dissimilarity. S. dysenteriae 14 pair had similar PFGE pattern, and S. boydii 18 showed dissimilarity. Similarities and differences observed at molecular level between cases and controls. Pathophysiology in inducing symptoms or asymptomatic carrier state in individuals could be related to genetic variation in strains and host immunity. Broader molecular study on cases and controls is required for confirmation.

P134

VARIATION IN A SURFACE-EXPOSED REGION OF THE *MYCOPLASMA PNEUMONIAE* P40 PROTEIN AS A CONSEQUENCE OF DNA RECOMBINATION BETWEEN REPMP5 ELEMENTS

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Background and aims: *Mycoplasma pneumoniae (Mpn)* is a human pathogen that causes respiratory tract infections. The first step in infection is adherence of the bacteria to the respiratory epithelium, which is mediated by a specialized organelle containing several adherence proteins (cytadhesins). Two of these proteins are encoded by the MPN142 gene. This gene contains a repetitive DNA element, RepMP5, of which homologs are found at seven other loci within the *Mpn* genome. It has been hypothesized that these elements may provide a source of sequence variation for MPN142 by homologous DNA recombination. As this variation may give rise to amino acids changes within P40 and P90, the recombination between RepMP5 elements may constitute the basis of antigenic variation and immune evasion by *Mpn*.

Methods: To investigate the sequence variation of MPN142 in relation to inter-RepMP5 recombination, we determined the sequences of all RepMP5 elements in a collection of 25 strains isolated between 1962 and 1995. Sequences were analyzed and aligned using the application SeqManTM II (DNASTAR) and the sequence alignment program ClustalW.

Results: In two strains, the RepMP5 element within the MPN142 gene contained an aberrant sequence indicative of an inter-RepMP5 recombination event and resulting in amino acid changes in a surface-exposed part of the P40 protein.

Conclusion: This is the first time that variation in the MPN142 gene has been established. Since the proteins encoded by MPN142 are surface-exposed and highly immunogenic, homologous DNA recombination of RepMP5 could play an important role in immune evasive strategies of *Mpn*.

P135

MICROBIAL ANALYSIS DOES NOT FACILITATE THE DIFFERENTIATION OF CHILDHOOD RECURRENT ACUTE OTITIS MEDIA FROM CHRONIC OTITIS MEDIA WITH EFFUSION

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Background: Otitis media (OM) is one of the most frequent diseases in childhood. Although often self-limiting, in some cases recurrent acute otitis media (rAOM) or chronic otitis media with effusion (COME) occurs. Presence of bacteria and viruses is primarily associated with (r)AOM, whereas COME is considered to be mostly a sterile condition. We investigated whether the microbiological conditions could be used to differentiate rAOM and COME.

Materials and methods: Children < 6 years of age, suffering from rAOM (*n*=46) or COME (*n*=131) and scheduled for tympanostomy tube insertion were enrolled in a prospective study between April 2008 - June 2009. Middle ear fluids (*n*=127) and nasopharyngeal samples (*n*=177) were collected during surgery for bacterial culture and PCR analysis for *S. pneumoniae*, *H. influenzae* and *M. catarrhalis*, as well as multiplex PCR to detect 15 respiratory viruses. Serotyping and genotyping analyses were performed to further characterize the bacterial pathogens isolated.

Results: The pattern of bacterial and viral pathogens in middle ear fluids did not significantly differ between patients suffering from rAOM or COME, with a single bacterial pathogen being primarily cultured. Seventy seven percent (*H. influenzae*) to 100% (*S. pneumoniae* and *M. catarrhalis*) of the cultured bacteria were genetically identical between middle ear fluid and nasopharynx. In both patient groups, *H. influenzae* and rhinovirus were the predominant pathogens in the middle ear and nasopharynx.

Conclusion: From our results, the common perception that rAOM is associated with recurrent episodes of microbiologically-mediated AOM, whereas COME is generally a sterile inflammation, should be reconsidered.

P136

MOST FREQUENT SOURCE OF BACTERIAL INFECTION OF THE RESPERATORY CHANELS WITH CHILDREN TREATED IN OUR INSTITUTION

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Respiratory infections have been a reason for a pediatric examination with 80% of the infected children, out of which 20% belong to the infections of the lower part of the respiratory system.Goal: early microbiological confirmation of the reasons, an early etiological treatment which leads to reduced number of complications and small number of hospitalized children.

Materials and methods: Data from the health records of the children treated in our institution. In addition the microbiological results about a two year period from the Institute for Preventive Medicine (Military Hospital), Skopje have been used. Data processing has been done by analytical and descriptive method.

Results: Out of 45878 examined children in the period of 2009 to 2010 samples from the nose and the throat have been taken from 4800 children. Positive results have been confirmed by 1600 samples (33,33%). The following results have been received: Streptococcus pneumoniae with 420 (26,25%),Branchamella catarrhalis-Moraxella with 285 (17,8%), Haemophillus influenzae with 315(19,6%) and Streptococcus pyogenes with 215(13,43%) from the samples. The other 365 (21,9%) have been caused by other sources. The children have been treated according to the antibiogram mostly with semi synthetic penicillin and cephalosporin. Control samples have been taken from all the children and 136 (8,5%)confirmed positive again. Only 6,5% of the treated children have been sent for a sub specialist consultation.

Conclusion: Microbiological examinations contribute to a successful etiological treatment of the children in infirmaries. It reduces the expenses for treating children and bacteriological spread of the infections in the medical centers.

P137

A RARE CASE OF RECURRENT OSTEOMYELITIS…

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Introduction: Multifocal osteomyelitis is a clinical entity within self-inflammatory syndromes implying negative cultures. *Cellulosimicrobium cellulans* rarely causes human infection. Infections have been reported to immunocompromised hosts and/or in patients with foreign bodies.

Case report: A 16-year-old boy, without past medical history, presented recurrent episodes of osteomyelitis in the proximal metaphysis of right tibia, proximal third of left humerus and distal extremity of left femur, since January 2006. The condition began with continuous pain in the right knee predominantly at night with no other inflammatory signs. Treatment with cefuroxime resolved the pain.

Two months later he had pain again in the right knee concomitantly with inflammatory signs. Radiologic study and scintigraphy suggested inflammatory/infectious process requiring repeated antibiotic treatment. Second recurrence in July 2007 involving right tibia and left humerus. Patient condition improved with oral flucloxacillin treatment.

In July 2009 he presented inflammatory signs of contralateral knee. Radiologic studies showed lesions suggestive of osteomyelitis sequelae in right tibia and osteomyelitis of distal left femur. Clinical improvement with oral flucloxacillin repeated treatment. New clinical recurrence in July 2010, with inflammatory parameters elevation and persistence of radiologic changes. A biopsy was done; in the microbiological culture was isolated a *methicillin-sensitive Staphylococcus aureus and in* 16S rRNA gene Polymerase Chain Reaction was identified *Cellulosimicrobium cellulans*.

Discussion: *Cellulosimicrobium cellulans* has been associated with indolent and relatively avirulent course; its microbiological identification can be difficult. *In vitro* studies have shown that this organism is intrinsically resistant to a range of antibiotics, which may explain the different recurrence.

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A RARE CASE OF RECURRENT OSTEOMYELITIS…

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SALMONELLA OSTEOARTICULAR INFECTION IN SICKLE CELL DISEASE CHILDREN IN PARIS AND ILE-DE-FRANCE, A 12 YEARS RETROSPECTIVE MULTICENTER STUDY

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Background and aims: *Salmonella* osteoarticular infection (OAI) is a severe condition in sickle cell disease (SCD) patients.

Methods: Retrospective analysis of SCD children hospitalized for *Salmonella* OAI between 1997 and 2009 in several hospital of Paris and the region of Ile de France. *Salmonella sp.* was isolated from the blood (n=16), pus (n=12) or articular aspirates (n=12).

Results: 24 cases were analyzed. The median age was 35 months (SD ±59.5, range 8 months to 15 years). Before admission, the most common symptoms were pain (92%), fever (67%) and gastro-intestinal symptoms (46%). At admission, 16 patients (67%) had a single site of OAI, 8 patients (33 %) had several concomitant sites of OAI. Arm was involved in 79% of children and the humerus was the most affected bone (50% of children). The initial median CRP was high (124 mg/L, SD ± 88.1, range: 0-275 mg/l). 38% of osteoarticular samples grew *Salmonella sp* despite initiation of antibiotic therapy (from 1 to 102 days). Intravenous antibiotics with a third generation cephalosporin and ciprofloxacin were given in all cases during a long period (mean: 9 days, SD±17, range 7 to 81 days). 79% of the patients needed surgical drainage. 50% of patients needed more than one surgical drainage for subsequent arthritis, osteomyelitis or sub periostal abscess.

Conclusions: *Salmonella* OAI remain a therapeutic challenge in children with SCD with frequent subsequent extension of the infection despite medical and surgical treatment.

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PASTEURELLA CANIS OSTEOMYELITIS: EXPERIENCE AT A TERTIARY PAEDIATRIC HOSPITAL WITH PASTEURELLA BONE AND JOINT INFECTIONS AND REVIEW OF THE LITERATURE

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Background and aims: *Pasteurella* species are important bacterial pathogens in both animals and humans. Most reported *Pasteurella* infections in humans involve skin and soft tissues, often after an animal bite, scratch, or a lick to an open wound. Infections involving bone and joints are well recognised, and these have occasionally been reported in patients without a history of penetrating injury or recognised animal exposure.

Methods: We report a case of *Pasteurella canis* osteomyelitis in a 14-month old girl without any preceding penetrating injury. Review of all *Pasteurella* osteomyelitis and septic arthritis cases at our tertiary paediatric hospital over the past 10 years was performed by reviewing the patient records of all children with positive bacterial cultures from any site for *Pasteurella* spp. as identified through our microbiology laboratory database. A MEDLINE and EMBASE database search was then performed to identify all published cases in the literature since 1950.

Results: In addition to the case of *P. canis* osteomyelitis outlined, we identified eight children with positive cultures for *Pasteurella* spp. from the hospital's microbiology database over the past ten years. Two of these children had deep tissue contamination involving bone and/or joints secondary to animal bites. Ten further published cases were identified from the literature since 1950.

Conclusions: Established *Pasteurella* osteomyelitis and septic arthritis secondary to animal bites can be largely prevented through appropriate debridement and wound management at the time of injury. However, the potential for deep tissue infection with this organism without prior penetrating injury should be recognised.

P141

OSTEO-ARTICULAR INFECTIONS CAUSED BY *STAPHYLOCOCCUS AUREUS* PRODUCING PANTON-VALENTINE LEUKOCIDIN IN CHILDREN

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Background: Panton-Valentine leukocidin (PVL) secreted by *Staphylococcus aureus* is known to cause severe osteo-articular infections (OAI) in children.

Aims: To analyze the complications of *S. aureus* IOA during adapted treatment (antibiotic and surgical drainage) and their occurrence in relation with PVL production.

Methods: We retrospectively analyzed cases of children hospitalized with SA OAI in Robert Debré Hospital (Paris, France) from April 2000 to May 2010.

Results: 73 children were identified (29arthritis, 32osteomyelitis, 12osteo-arthritis). The children mean age was 8,3years (range: 0.5-17.5). *S. aureus* was obtained from blood (n=37) or synovial fluid (n=28) or bone (n=8) were methicillin- susceptible in 88% of cases. 16/58 (28%) isolates were PLV+. 13/16 strains of *S. aureus* PVL+ were methicillin-susceptible.

44 children (49 %) presented complications. Complications were more frequent in group PVL+ versus PVL- (62% *vs* 38%, $p< 0,001$) with abscess (44 % *vs* 17 %), subperiosteal abscess (44 % vs 17 %), myositis (31 % *vs* 2 %), pneumonia (37 % *vs* 7 %), and thrombophlebitis (19 % vs 0 %). In group PVL+, 13/16 children (81%) presented complications occurred in the first 5 days of treatment versus 13/42 children (31%) in group PVL-. No complications occurred after 16 days of treatment in group LPV- whereas 2 children of the LPV+ group presented late suppurative complications, at 41 and 49 days of treatment.

Conclusions: The presence of PVL is associated with complications in 87% of cases, comforting its role in the severity of the disease.

P142

PYOGENIC VERTEBRAL OSTEOMYELITIS - CASE REPORT

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Background and aims: Pyogenic vertebral osteomyelitis is uncommon in children and the correct diagnosis is often missed or delayed due to unspecific and insidious clinical symptoms.

Methods: The authors present a case of a pyogenic vertebral osteomyelitis in an adolescent.

Results: A previously healthy 11 year-old girl, with no past history of trauma, was admitted to our hospital with a 5 days history of progressive back pain, refusal to walk and low grade fever. Three weeks before, she referred similar symptoms with partial response to non-steroid anti-inflammatory drugs. At admission, she presented inability to flex the lower back, loss of lumbar lordosis and local tenderness. The remaining physical examination was normal. Radiographs did not demonstrate any bone alteration, but laboratory studies showed a raise of erythrocyte sedimentation rate. Bone Scintigraphy showed increased uptake in the 5th lumbar and first sacral vertebra and Magnetic Resonance imaging revealed typical signs of spondylodiscitis, with a destructive vertebral body process, collapse of the intervening disc space and a contiguous anterior epidural abscess. Bed rest, opioid analgesics and empiric therapy with parenteral Ceftriaxone and Flucloxacilina were started. During the hospital stay, she got afebrile, without any focal neurological symptoms. Oxacillin-sensitive Staphylococcus aureus was isolated. Flucloxacylin was continued for 4 weeks, with full recover.

Conclusions: Antimicrobial therapy (in rare cases, surgery) leads to a good outcome in most patients with vertebral osteomyelitis. Early diagnosis and careful follow-up evaluating ongoing symptoms and serially measuring the CRP and/or ESR, rather than repeating imaging studies, are crucial.

P143

SPONDYLODISCITIS IN CHILDREN - ABOUT 4 CASES AND A DECISION ALGORITHM

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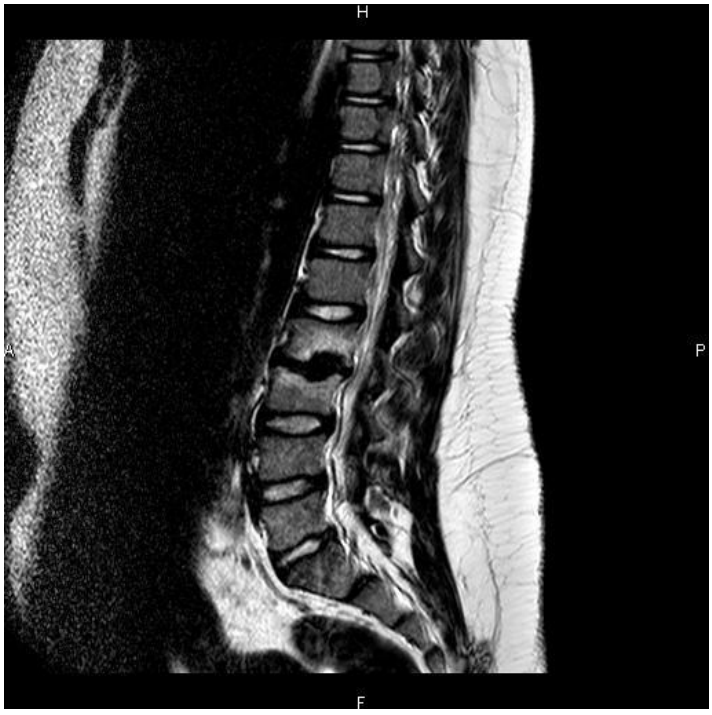
Background and aims: Spondylodiscitis accounts for about 2-4% of all bone infections. A late diagnostic associated with an incorrect therapeutic plan may be followed by important complications and disabilities. The aim of the presentation is to highlight a few clinical situations and propose a decision algorithm which may help a faster diagnostic and treatment.

Method: The 4 patients aged 20 months to 12 years presented different clinical panels.

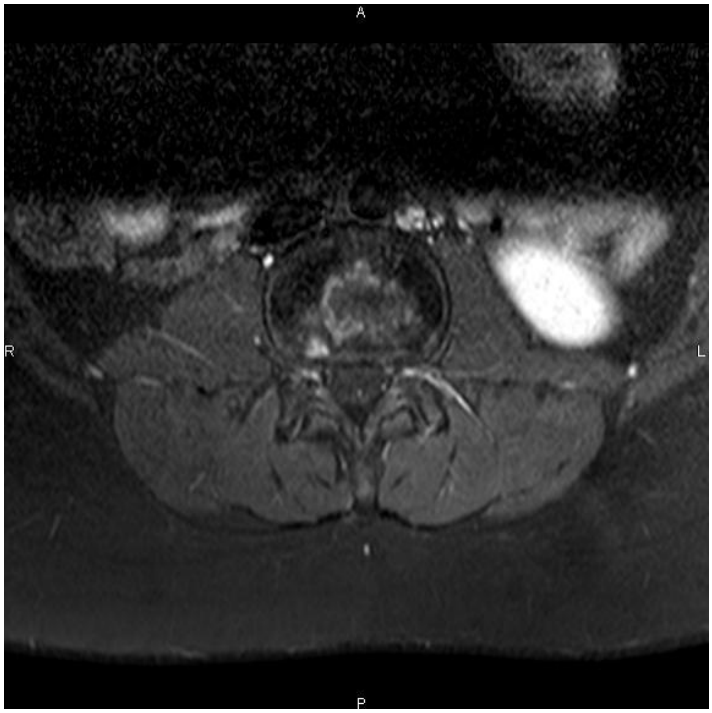
Refusal of sitting and crying while being changed, abdominal pain confused with an mesenteric adenitis, back pain that coincided with a respiratory infection were evoked. I will detail the last case: back pain without inflammatory markers followed by septic metastasis and scoliotic deviation of the spine, important increase of the inflammatory markers, impressive destruction on the MRI and positive cultures for staphylococcus aureus.

All of the patients received an anti-staphylococcic antibiotic and an orthopedic follow-up.

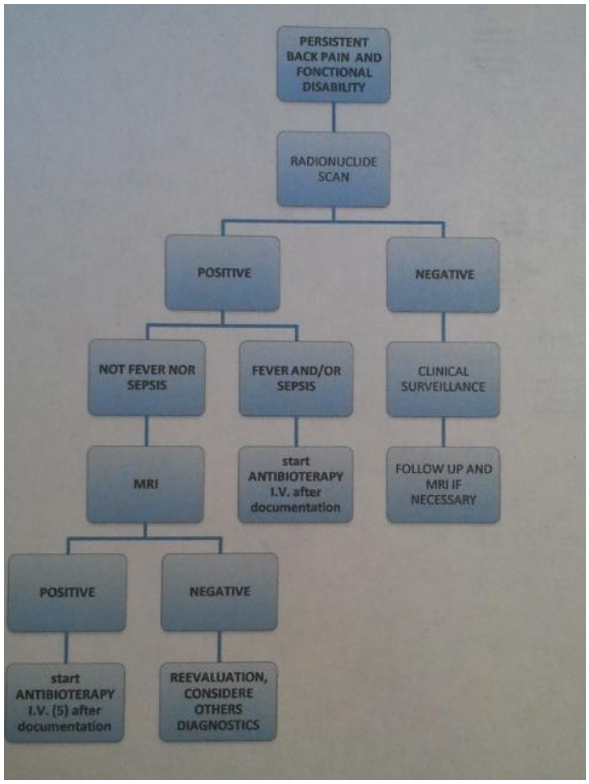
Results: The cardinal symptom, back pain, was translated through different clinical panels. The blood sample is not a helpful diagnostic tool, nor the X-ray or the ultrasound. The MRI is the best exam to prove the destruction of the spine (100% specificity and sensitivity). The radionuclide scan is useful in the workup of fever of unknown origin.



[Spine distruction T1 signal]



[Spine distruction T2 signal]



[Diagnostic algorithm]

Conclusion: That's why a simple algorithm might help to pose the diagnostic in an acceptable time frame. In most of the cases the evolution is auspicious, but when complications are present, the orthopedic disabilities might be important.

P144

SECONDARY PSOAS ABSCESS DUE TO RENAL PATHOLOGY

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An eleven year old boy presented with a history of fever, pain and swelling in the right loin for two weeks. The swelling progressively got worse. He also had dysuria and frequency and had already been on oral amoxicillin for a urinary tract infection.

On examination, he had loss of the lumbar curvature and was limping on walking. There was a tender mass with diffuse margins over his right loin reaching up to the lumbosacral region. The overlying skin was erythematous.

His inflammatory markers were high and the urine culture revealed sterile pyuria. A Renal ultrasound showed multiple calculi in the right kidney calyces with pyelonephritis. A CT urogram showed a dilated right renal pelvis with a calculus in it causing pyeloureteric junction obstruction. There was lower pole focal pyelonephritis with adjacent abscesses invading the psoas and posterior abdominal wall. A Mercaptuacetyltriglycine scan revealed 12% function on the right side and hence a right sided nephrectomy was performed.

Secondary psoas abscesses have been reported in adults due to osteomyelitis of the spine or colitis. It is uncommon in children and is usually due to primary infection of the retroperitoneal lymph nodes by Staphylococcus aureus. Clinically children with psoas abscess can present with the triad of limp, fever and pain.

An association with a renal pathology is described only infrequently. A literature review of psoas abscesses of renal aetiology included only one child, and among 104 cases of non-tuberculous psoas abscesses in children, none had any underlying renal pathology.

P145

DIAGNOSTIC VALUE FOR STREM-1 LEVEL IN SYNOVIAL FLUID OF CHILDREN WITH ARTHRITIS; TEHRAN, IRAN

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Objective: To evaluate the usefulness of STREM-1 level in synovial fluid (SF) to differentiate septic from aseptic arthritis.

Methods: A cross sectional study performed in in the Department of Pediatrics, Rasul Hospital,Tehran, IRAN between 2008 and 2009.

Cases included 62 children with arthritis (;mean = 25.6± 29 months) . Quantification of STREM-1 in Synovial fluid done by EIAThe STREM-1 levels compared between bacterial and non bacterial (aseptic) arthritis.

Results: Septic arthritis proved in 46% of cases .Cut off level 825 pg/mlfor SF-STREM-1 yielded 50% sensitivity, 70% specificity, 64%PPV; 64%, NPV.Poor agreement seen between SF -STREM-1levels and positive SFculture.(P value: 0.037;Kappa=0.28). The area under the ROC curve for discriminating was 0.603 (95% CI; 0.757-0.448, *P* = 0.1)

Conclusion: SF-STREM-1 level had intermediate (50%) sensitivity. 70% specificity are excellent and sufficient for definite diagnosis but could not differentiate bacterial arthritis from other inflammatory process in SF in near 30% of cases .The presence of STREM-1 in SFA can potentially assist clinicians in the diagnosis of half but not all cases with bacterial arthritis. Combination of of new biologic markers (PCT and sTREM-1) in SFA could be more helpful in high suspicious cases who are already on antibiotic treatment (negative culture). A larger group of patients needed to be studied to confirm our findings.

P146

PYOGENIC SACROILIITIS IN CHILDREN AND ADOLESCENTS: REPORT OF THREE CASES

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Background and aims: Pyogenic sacroiliitis is an uncommon entity accounted for less than 2 % of joint infections in children. Diagnosis is often delayed in many cases because of nonspecific clinical presentation, the physician´s low suspicion and the absence of systematic examination of the sacroiliac joint.

Methods: This report summarizes the main clinical and diagnostic features of three cases of pyogenic sacroiliitis in children.

Results: The three male patients were 4, 8 and 19 years old, respectively. All of them had a sudden onset of high fever, worsening hip pain and limp. On admission, they appeared acutely ill and laboratory inflammatory markers were elevated. Although septic arthritis of the hip was initially suspected, hip joint ultrasound was interpreted as normal in all three, which led to the examination of the sacroiliac joints and to perform a magnetic resonance imaging (MRI) that eventually confirmed the diagnosis. Blood cultures were positive in all of them, yielded *Staphyolococcus aureus*, *Streptococcus pyogenes* and *Streptococcus pneumoniae*, respectively. They were successfully treated with 4-6 weeks of antibiotics. Although one of them required surgical drainage of a periarticular abscess, no orthopaedic disabilities were observed at the end of the follow-up.

Conclusios: Pyogenic sacroiliitis is a rare condition in children in which timely recognition remains a challenge. The diagnosis mostly relies on imaging techniques, especially MRI, though bone scan can be initially more helpful in children with poorly localized complaints. With prompt diagnosis, patients can be successfully treated following the therapeutic principles used in other osteoarticular infections.

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P148

DISCITIS IN INFANTS AND TODDLERS: REPORT OF THREE CASES

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Background and aims: Discitis is a rare condition in the paediatric population mostly seen in children under 6. The diagnosis is often difficult in infants and toddlers due to a variety of poorly localized manifestations than can mimic a number of other processes, leading to a diagnostic delay in many cases.

Methods: Three cases of discitis in children diagnosed in Majorca's Fundación Hospital Manacor are presented here.

Results: The first case was a 9-month-old infant with cervical discitis who presented with neck pain, torticollis and irritability. The other were two toddlers of 17 and 18 months of age with lumbar involvement who were admitted because of worsening limp that finally evolved to inability to walk. None of the children has history of previous trauma, viral infection or fever and they appeared to be in good general condition on admission. Laboratory inflammatory markers were normal or minimally altered, whereas blood cultures were negative. Magnetic resonance (MRI) was the key diagnostic tool. It showed disk space narrowing, bone marrow oedema, and adjacent soft tissue inflammatory changes. All cases were fully recovered after 3-6 weeks of antibiotic treatment.

Conclusions: Discitis should be considered in the differential diagnosis of young children with unexplained torticollis or sudden onset of refusing to walk and bear weight. MRI is the technique of choice for diagnosing and evaluating potential complications. Although its aetiology is still matter of controversy, the fact that our patients promptly improved with antimicrobial therapy suggests that bacterial infection may have played a critical role.

P149

DISCITIS IN INFANTS AND TODDLERS: REPORT OF THREE CASES

A. Mora[1], I. Marimon[1], **A. Pérez**[2], J. Mesquida[3], M.L. Orta[2], M.E. Alemany[2]

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P150

ST. AUREUS PUBIC SYMPHYSIS ARTHRITIS AND ENDOCARDITIS IN A YOUNG ATHLETE

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Septic arthritis of the pubic symphysis is rare. Risk factors include genitourinary surgery, sports, pelvic malignancy and intravenous drug use. Complications include abscess formation, septicemia, and hematogenous spread. Osteitis pubis in athletes, by contrast, is a frequent noninfectious periostitis.

A previously healthy 17-year old soccer player presented with a 5-day history of fever, dysuria, pubic and thigh pain with waddling gait.

He was ill-appearing, had pubic/suprapubic tenderness, pain with internal right hip rotation, and a heel laceration.

Laboratory workup showed marked leucocytosis and increased CRP/ESR. Urinalysis was normal, with negative urine culture.

He was admitted and started on IV flucloxacillin and cefotaxime for suspected osteomyelitis/septic arthritis.

MRI showed septic arthritis of pubic symphysis with a large prevesical and right internal obturator abscesses.

A *de novo* heart murmur lead to the finding of tricuspid valve endocarditis, confirmed by transesophagic echocardiogram.

Serial blood cultures were positive for meticillin-sensitive *Staphylococcus aureus*.

Evaluation for immune function was normal, HIV negative.

Due to a rapid good clinical response, conservative management with IV antibiotics was chosen and will be continued for 6 weeks.

Repeat MRI at 4 weeks showed signs of bone-marrow edema, without abscesses.

Athletic patients may be susceptible to staphylococcal infection of their cartilaginous non-synovial joints.

This unusual cause of febrile illness should not be overlooked, since serious complications, such as endocarditis, can arise.

A high-index of suspicion is crucial particularly as localizing signs may not be evident at presentation.

The early treatment was fundamental for a good vital and functional outcome.

P151

COMMUNITY-ACQUIRED SKIN AND SOFT TISSUE STAPHYLOCOCCUS AUREUS INFECTIONS IN CHILDREN ACROSS EUROPE, INFLUENCE OF PANTON-VALENTINE LEUKOCIDIN

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Background: Panton-Valentine Leukocidin (PVL) and methicillin resistance have been related to virulence in Community-acquired S. aureus (CA-SA) infections.

Objectives: To analyze the influence of methicillin resistance and PVL presence in the clinical characteristics of CA-SA skin and soft tissue infections (SSTIs).

Patients and methods: We prospectively enrolled children with community-acquired SSTIs caused by S. aureus during June 2010.

Results: 105 cases were collected from 13 centers in 8 different countries (Spain, England, Lithuania, Germany, Israel, Romania, Cyprus and Italy). Methicillin-resistant S. aureus (MRSA) was detected in 15 cases (14%) and PVL genes in 34 (9 MRSA and 25 MSSA) (32%). Children had a median age of 32 months. 9% of the patients had one or more established risk factors for health care-associated infection. 60% of the patients were admitted to the hospital and 47% required surgical intervention.There were no significant differences in the clinical characteristics between CA-MRSA and CA-MSSA isolates, however, PVL-positive infections more commonly required incision and drainage (73% vs. 34%, $p < 0,001$) and occurred in older children (91 ± 61 months vs. 44 ± 55 months, $p < 0,001$) than PVL-negative infections. There were no significant differences related to the rate or duration of hospitalization. Molecular characterization showed a predominant clone among PVL-positive-MSSA: ST-121-agr4 was found in 14/19 isolates and in 5 different countries.

Conclusions: This multicenter European study highlights that a significant proportion of infections were caused by PVL-positive isolates and that children with PVL-positive S. aureus SSTIs needed more surgical intervention than PVL-negative cases.

P152

KINGELLA AS A CAUSE OF SEPTIC ARTHRITIS IN CHILDREN: THE BENEFIT OF MOLECULAR TECHNIQUES FOR MICROBIOLOGICAL DIAGNOSIS

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[1]Pediatrics, [2]Microbiology, [3]Pediatric Orthopedics, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Background: Septic arthritis (SA) is a potentially severe disease in children. *Kingella* is a common cause of SA in young children, but often underdiagnosed by classical microbiological procedures. The aim of this study was to evaluate the effect of molecular techniques on the diagnosis of this infection.

Methods: We compared the clinical and diagnostic characteristics of children with SA before (retrospectively) and after (prospectively) the implementation of bacterial PCR in synovial fluid.

Results: Forty-nine children diagnosed with SA were evaluated between 2002-2010. Thirty-two were diagnosed before the PCR analysis was implemented in our hospital (2009) and 17 after that. Microbiological diagnosis was achieved in 31% during the first period vs 59% in the second period (p=0.12). *Kingella* was isolated in 7 of 10 cases in the second period but in none in the first period. Children with *Kingella* were younger (13 vs 27 months; p=0.059), had fever more often (100% vs 43%; p= 0.01), and higher ESR at admission (74 vs 50; p=0.031), but the duration of hospitalization (7 vs 11 days; p=0.06) and IV antibiotics (6 vs 10 days; p=0.01) was shorter. However, total duration of antibiotics was similar (31 vs 36 days). There were no sequelae in children with *Kingella* SA vs 20% in children with other types of SA (p=0.58).

Conclusions: *Kingella* is an important cause of SA in children that may be underdiagnosed with classical microbiological procedures. Although *Kingella* SA may be severe at presentation, it seems to respond optimally to therapy without sequelae.

P153

SOFT TISSUE ABSCESS AND OSTEOMYELITIS IN A NEW BORN AFTER IMMUNIZATION WITH HEPATITIS B VACCINE: A CASE REPORT

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Background: Immunization is one of the most beneficial and cost-effective disease prevention measures. Bone and soft-tissue complications following immunization are rare. In this case report, we aimed to present a newborn that developed an abscess in the soft tissue of femoral region and osteomyelitis in femur after the first dose of hepatitis B vaccine.

Case: One-month-old girl was admitted with a history of swelling and hyperemia at the lateral side of right thigh a week after the injection of first dose of Hepatitis B vaccine. She was initially diagnosed to have a local reaction at injection site. On clinical follow up fever and significant limitation in the range of motion developed while swelling and hyperemia gradually increased. Subsequently observed fluctuation indicated an abscess formation. Routine laboratory tests revealed leukocytosis, elevation of ESR and CRP levels. An AP radiograph showed an evident periost reaction compatible with osteomyelitis. An ultrasound imaging yielded abscess formation. Orthopedic surgery was performed and abscess was drained from soft tissue and diaphysis of femur. Microscopic examination showed polymorphonuclear leucocytes and gram positive cocci. Antibiotherapy with teicoplanin and cefotaxime was initiated. Blood and abscess culture specimens were positive for methicillin-resistant *Staphylococcus aureus.* The clinical and laboratory parameters improved after early debridement and six weeks of antimicrobial therapy.

Conclusion: In case of a local reaction after immunization, a careful review of the history and physical examination is mandatory in order to rule out an infection which may progress to even osteomyelitis as in the case above.

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LISTERIA MONOCYTOGENES MENINGOENCEPHALITIS IN AN ADOLESCENT PATIENT

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Listeria monocytogenes is a gram positive bacillus that infects mainly newborns, elderly patients, pregnant women and immunosuppressed patients with impaired cellular immunity. The central nervous system (CNS) is especially vulnerable to *Listeria monocytogenes,* causing severe disease.

Case report: 13 year-old-female, diagnosed 6 weeks earlier with Crohn´s disease and recent-onset steroid therapy, suffering from fever, headache and diplopia. In the physical examination menigeal stiffness and VI cranial pair paralysis was observed. In additional examinations she presented leukocytosis and neutrophilia, CRP of 88 mg / L and a CT without pathological findings. The cerebrospinal fluid (CSF) examination presented glucose of 9 mg/dl, protein 186 mg/dl, lactate 9´1 mmol/l, 165 leukocytes (PMN 35%, Monocytes 65%). Empirical treatment was started, with a coverage for bacteria (including Listeria), virus and tuberculosis. Twenty-four hours afterwards *Listeria monocytogenes* was identified in the CSF culture, thereby the antibiotic treatment was optimized. However, the evolution of the patient within 72 hours was not favorable. Her consciousness level was progressively deteriorating, consequent of a non-obstructive hydrocephalus, which required ventricular drainage. Afterwards the patient´s clinical state improved.

Comments: The immunosuppressed patients are at risk of atypical infections. *Listeria monocytogenes* and other opportunistic pathogens should be present in our differential diagnosis. Suspecting this etiology may be decisive for the patient´s prognosis. In this case, the clinical and analytical data did not orient towards this etiology. Patients underlying these infections require close monitoring; in spite of the rapid introduction of the appropriate treatment, the progress of this infection can be fatal.

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GENOTYPING OF THE PATHOGENS ISOLATED FROM CHILDREN WITH BACTERIAL MENINGITIS

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Background: Monitoring of S.pneumoniae, N.meningitidis and H.influenzae genotypes allows to implement epidemiological control for circulation of vaccine strains.

Objectives: Isolates of S.pneumoniae, N.meningitidis and H.influenzae, isolated from patients.

Methods: Multiplex real-time PCR was used to verify the species S.pneumoniae, N.meningitidis and H.influenzae. Genotyping by PCR of H.influenzae and N.meningitidis strains, isolated from cerebrospinal fluid (CSF), S.pneumoniae, isolated from nasopharynx and from CSF of children aged under 5 years.

Results: The study of clinical material in real-time PCR revealed presence of pathogens in 84,3% of cases, of which H.influenzae-20,3%, N.meningitidis-33,9%, S.pneumoniae-45,8%. The genotyping determined belonging of isolates to curtain types - H.influenzae type b, N.meningitidis-types C-75% and A-25%. Isolates of S.pneumoniae from children with meningitis belonged to genotypes 6A/B/C-7 (43.7%), 23F-1 (6.2%), 14-2 (12.5%), 9V/A-1 (6.2%), 3-4 (25%), 15B/C-1 (6.2%); from patients with nasopharynx pathology - 6A/B/C-3 (27.3%), 23F-1 (9%), 14-1 (9%), 15B/C-1 (9%), 19F-3 (27.3%), 3-1 (9%), 17F-1(9%). Hence in patients with nasopharynx pathology, the most part of isolated S.pneumoniae belonged to genotypes 6A/B/C and 19F, in patients with meningitis to 6A/B/C and 3. S.pneumoniae genotypes, obtained from children with meningitis, were also isolated from patients with pathology of nasopharynx.

Conclusions: Verification of pathogens, not only in CSF, but also in material from nasopharynx is reasonable for monitoring of vaccine strains circulation.

P156

A RARE CASE OF SALMONELLA MENINGITIS

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A 12 day old, term baby presented with a one day history of poor feeding, constipation and lethargy. She had lost 14% of her birth weight. There were no maternal risk factors for sepsis. She was afebrile and lethargic with a bulging fontanelle but no focal neurological signs or rash. Intermittent tachypnoea was observed.

Initial investigations showed a C-reactive protein of 215 mg/L, CSF microscopy: WCC 189 mm^3 (70% lymphocytes, 30% polymorphs), RCC 2200 mm^3, Gram stain: Gram negative rods, protein 2.57 mg/dL, glucose CSF/blood % < 8.3%. IV cefotaxime and amoxicillin were commenced empirically with the addition of IV gentamicin on day 2. She spiked a temperature of 38.5°C on day 1 but remained afebrile thereafter.

Blood and CSF cultures grew *Salmonella ajiobo* I 13, 23:z4, z23:- sensitive to cefotaxime and gentamicin but resistant to ciprofloxacin. Cranial ultrasound on day 4 detected no abnormalities. She completed six weeks of ceftriaxone and made an uncomplicated recovery. Despite extensive investigation, no source was identified.

Neonatal salmonella meningitis is associated with high mortality and neurological morbidity. Concomitant use of a third generation cephalosporin with ciprofloxacin has been recommended but there is little consensus for alternative regimes in resistant cases and no European guidelines on duration of treatment. A UK outbreak of *Salmonella ajiobo* in 2006 caused 119 cases of severe gastroenteritis, but ours is the first reported case of this serotype causing neonatal meningitis in the UK. Early presentation and initiation of appropriate treatment may have contributed to the patient's positive outcome.

P157

SEROGROUP DETERMINATION OF *NEISSERIA MENINGIDITIS* IN BACTERIAL MENINGITIS: TURKISH NATIONAL BACTERIAL MENINGITIS SURVEILLANCE: 2006-2009

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Neisseria meningiditis is one of the most common cause of bacterial meningitis. Herein we invastigated serogroup determination of *N. meningitis* causing bacterial meningitis by real time and conventional multiplex PCR metot in Turkey between 2006 to 2009. A total of 1510 cerebrospinal fluid (CSF) samples obtained from 35 different medical center arroud the country. Among them 47 patients revealed *N. meningiditis.* Serogroup distrubution of N. meningiditis were as following:

***N. meningiditis* group B:** in 29 patients,

***N. meningiditis* group C:** in 2 patients,

***N. meningiditis* group A:** in 1 patients,

***N. meningiditis* grup X:** in 1 patients,

***N. meningiditis* group W135:** in 1 patients, and in 13 örnekte *N. meningiditis* were non-typeable.

N. meningiditis was second most common cause of bacterial meningitis and serogroup B was the most common serogroup determined in our country.

P158

TURKISH NATIONAL BACTERIAL MENINGITIS SURVEILLANCE: 2006-2009

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Bacterial meningitis is one of the leading cause of mortality and morbidity in children. Herein we invastigated bacterial meningitis etiology by real time and conventional multiplex PCR metot in Turkey between 2006 to 2009. A total of 1510 cerebrospinal fluid (CSF) samples obtained from 35 different medical center arroud the country. Among them 849 CSF sample had a purulent CSF characteristics. Of the 849 CSF samples 605 revealed that no bacterial DNA. In 131 patients *S. pneumoniae*, in 38 patients *Heamophilus influenzae* type b (Hib), in 47 patients *N. meningitis*, in 5 patients non-typeable *H. influenzae* were detected. Amond 23 patients C_t for *S. pneumoniae* lyt A were ≥35. *Streptococcus pneumoniae* is the most common cause of bacterial meningitis in our country. After intoduction of routine Hib vaccination dramatic reduction of Hib was noticed.

P159

MENINGITIS: A CASUISTIC OF 10 YEARS

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Introduction and objectives: Meningitis is a potentially serious disease, which is extremely important to be included in the differential diagnosis of febrile children. It is intended to characterize the cases of meningitis as the etiology, treatment and outcome.

Methods: A descriptive, retrospective study of cases of children admitted with the diagnosis of meningitis, from 1 January 2001 to December 31, 2010

Results: Included 186 meningitis: 29 viral meningitis and 23 bacterial meningitis (being the remaining aseptic or decapitaded). The clinic attended with fever (90.3%), headache (71.5%) and vomiting (69.7%) at admission and only 66.0% had positive meningeal signs and 18.3% petechial rash. We detected statistically significant differences ($p < 0.05$) between groups (bacterial versus viral meningitis) in relation to age (< 5 and ≥ 5 years), laboratory parameters (white blood cell count, C-reactive protein, leukocytes in the cerebrospinal fluid) and season (Spring-Summer and Autumn-Winter). The etiologic agent was identified in 51 cases, the most prevalent, the enteroviruses (49.0%) and meningococcus (29.4%). The empirical antibiotic therapy (72.0%) always included a 3rd generation cephalosporin, ceftriaxone being the most widely used. The average length of hospital stay was 7 ± 4 days, showing an inverse correlation with age ($p = 0.004$).

Conclusions: The results are in agreement with the literature, reinforces the differences between viral and bacterial meningitis with regard to epidemiological, clinical and laboratory.

P160

CLINICAL FEATURES OF TICK - BORNE ENCEPHALITIS (TBE) IN CHILDREN TREATED AT VILNIUS UNIVERSITY CHILDREN'S HOSPITAL

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Background and aims: Lithuania is an endemic area of TBE and morbidity has increased during the last decade. There is a lack of studies concerning TBE in paediatric population. Our aim was to analyse clinical features of TBE in children.

Methods: A retrospective study was conducted at Vilnius University Children's Hospital. Case records of children with clinically and laboratory confirmed TBE hospitalized between January 2006 and December 2010 were reviewed.

Results: During the five-year period 46 children (19 girls, 27 boys) aged from 1.5 to 17 (the mean age 11.7±4.3) were hospitalized because of TBE and 54% of them were treated at intensive care unit (ICU). A tick bite was reported in 25 (54%) cases. In 7 (15%) cases drinking of unpasteurized milk was suspected as a way of transmission of TBE virus and 2 of them were family cases. The disease had a biphasic course in 54% of cases. TBE manifested as meningitis (47.8%) and meningoencephalitis (52.2%). Headache (95.7%), vomiting (91.3%) and fever (97.8%) were dominating symptoms. Photophobia (30.4%), coordination disorder (30.4%), tremor (28.3%), ataxia (15.2%), speech disorder (19.6%) and generalized seizures (2.2%) were less frequent. In 3 patients TBE was extremely severe: 1 had sopor, 2 were in coma.

Conclusions: Clinically manifesting TBE is present in children. Severe course of the disease requiring treatment at ICU was frequent in hospitalized patients.

P161

ACUTE BACTERIAL MENINGITIS IN CHILDREN

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Background and aims: To evaluate the clinical and laboratory findings and etiological spectrum of the patients with acute bacterial meningitis in last 9 years.

Methods: A retrospective chart review was conducted of 44 patients with acute bacterial meningitis.

Results: The median age of the patients was 11 months (1 month-13 years) and the male/female ratio was 2.38. The most common symptoms were fever (90.9%), vomiting (61.4%), lethargy (40.9%), headache (38.6%) and convulsion (25%). The agents were detected in 25 patients (56.8%). The most frequently detected agents were *Streptococcus pneumoniae* (27.3%), *Haemophilus influenzae* type b (11.4%) and *Neisseria. meningitidis* (11.4%), and in 19 patients (43.2%) we could not determine any agents. In 11 patients (25%) complications developed and those complications were subdural effusion (3 patients), subdural empyema (3 patients), hydrocephalus (2 patients), hearing loss (2 patients), and hydrocephalus-epilepsy (1 patient). None of the patients died.

Conclusions: *Streptococcus pneumoniae* is the most common agent. Despite advances in vaccine development, chemoprophylaxis and treatment, acute bacterial meningitis remains a significant cause of substantial morbidity in children.

P162

ENCEPHALITIS IN CHILDREN: PRESENTATION OF 27 CASES

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Background and aims: To determine the etiology, clinical presentation and prognosis of the patients with encephalitis in the last nine years.

Methods: Data from patients with encephalitis, who were treated between 2000 and 2008 were examined retrospectively.

Results: Twenty seven patients were diagnosed as encephalitis. The median age of the patients was 90 months (5 months-15 years) and male/female ratio was 2/1. The most common symptoms on admission were fever (85%), alterations in consciousness (77%), convulsion (59%), headache (59%), and vomiting (52%). In 17 (63%) patients, the etiological agents were determined, which were mumps virus (4 patients), rubella virus (4 patients), Epstein-Barr virus (3 patients), herpes simplex virus type 1 (2 patients), cytomegalovirus (1 patient), measles virus (1 patient), varicella-zoster virus (1 patient) and enterovirus (1 patient). In 10 patients, the etiological agents could not be found. In five patients, permanent sequelae developed. One patient died.

Conclusions: The spectrum of the etiological agents of encephalitis is vast. Those agents can change with time according to epidemiological features and vaccination programs. The agents could not be detected in the majority of the cases. In our country, the morbidity and the mortality will decrease as the possibilities of detection of etiological agents and administration of appropriate treatment and the proportion of the patients vaccinated with measles-mumps-rubella and chickenpox vaccines increases.

P163

MENINGITIS IN PEDIATRIC PATIENTS: CHARACTERIZATION OF A POPULATION IN PORTUGAL

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Meningitis is a severe acute infectious disease. The recent introduction of vaccines against its most frequent bacterial agents is expected to reduce the burden of disease.

Our aim was to characterize the epidemiology of children admitted with meningitis, and compare patients with bacterial and aseptic meningitis.

Retrospective review of patients admitted to the pediatrics department of a tertiary care hospital in Portugal, between 2005 and 2010, with a diagnosis of meningitis.

We included 331 patients, mean age 4.6±3.7 years; for those with known immunization status, 66% were vaccinated against *Neisseria meningitidis* type C and 38% against *Streptococcus pneumoniae*. 11.5% had bacterial meningitis and 88.5% aseptic meningitis, the most frequent agents being enterovirus (64%), *Neisseria meningitidis* (3.9%) and *Streptococcus pneumoniae* (3.3%). The most frequent signs in children younger than two years were fever, anorexia, irritability and decreased level of consciousness; and in children two years or older, headache, positive meningeal signs, vomiting and fever. Irritability (p0.004), seizures (p0.013), decreased level of consciousness (p0.001) and petechial rash (p0.029) were more frequent in patients with bacterial meningitis; headache and vomiting ($p< 0.001$) in aseptic meningitis. A higher blood leukocyte count (p0.002), CRP above 50 mg/L ($p< 0.001$), CSF cell count above 500/mm^3 ($p< 0.001$) and higher CSF protein level ($p< 0.001$) were associated with bacterial aetiology.

Despite available immunization against *Neisseria meningitidis* type C and *Streptococcus pneumonia*, *Neisseria meningitidis* and *Streptococcus pneumoniae* remain the two most frequent bacterial agents of meningitis. In young children, a higher level of suspicion is required for diagnosis.

P164

BRAIN SPECIFIC PROTEINS: NEURON SPECIFIC ENOLASE AND S 100B IN CHILDREN WITH ACUTE MENINGITIS

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Background: Despite the evident recent advances in diagnosis and treatment of meningitis, the disease continue to be a leading cause of mortality and sequelae. However, some biochemical markers have been studied with the aim of early diagnosis and management

Aim of work: Is to evaluate the levels of neuron specific enolase (NSE) and protein S100 в both in serum and CSF in cases with bacterial and non bacterial meningitis, as well as their relation to the outcome.

Patients and methods: The study included 48 patients with acute meningitis admitted to PICU at children university hospital .The age ranged from 2 month - 6 years. also 20 cases with matchable age and sex diagnosed as febrile convulsions were taken as controls. CSF examination blood culture, estimation of serum and CSF NSE and protein S100в were done.

Results: The levels of serum and CSF NSE were insignificantly different in cases with bacterial than non bacterial meningitis but significantly higher than controls. While the levels of protein S 100в in the serum and the CSF showed significantly higher levels in cases with bacterial than non bacterial meningitis The overall morbidity was 30.7% in bacterial versus 13.6 % in non bacterial meningitis.

In conclusion, CSF and serum NSE are reliable markers of brain damage in acute meningitis but cannot differentiate bacterial from nonbacterial meningitis. CSF and serum S 100в can be a helpful tool in differentiating bacterial from nonbacterial meningitis. CSF NSE may be used as a prognostic marker of outcome in bacterial meningitis

P165

CEREBROSPINAL LIQUID SHUNT INFECTION DUE TO S. PNEUMONIAE AND H. INFLUENZA SPP

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Background: Common nasopharyngeal colonizing microorganisms such as Streptococcus pneumoniae and Haemophilus Influenzae spp are uncommon in CSF (cerebrospinal fluid) shunt infections. Normally CSF shunt-infections of the above pathogens occur many months after shunt insertion due to haematogenous spreading rather than wound colonization post surgery.

Methods: Retrospective analysis of patients with ventriculoperitoneal (VPS) or external shunt (ES) infection due to S.pneumoniae and H. influenzae spp. between 2004-2011.

Results: A total of 6 patients (pts) were identified: S.pneumoniae n=4, and H.influenzae spp n=2. Underlying pathology was as follows: Astrocytoma, intraventricular haemorrhage (n=2), CSF leak, Dandy-Walker syndrome and myelomeningocele. 5 children carried a VPS and 1 pt an ES. Mean age at diagnosis of infection was 55 months (range 11-72), mean post-operative time since last surgical intervention was 5.3 months (range 0.25-10).
All 6 pts presented with fever, in addition 4 pts with vomiting and 3 pts with headaches. Treatment was according to resistance profile with penicillin or vancomycin or cefotaxime (+/-rifampicin) for S.pneumoniae and cefotaxime for H.influenza spp. 1pt each with S.pneumonia shunt infection suffered from concomitant pneumonia and pneumococcal sepsis respectively. Both of these patients died subsequently. The remaining 4pts responded well to antibiotic therapy +/- shunt replacement.

Patients Nº	Infectious agent	Patient age at time of infection (months)	Initial status	Presenting symptoms	Time since last CNS operation (months)	Antibiotics	OP
1	S. pneumoniae	64	Pylocitic astrocytoma (EVD)	Fever+headache+vomit	1.5	Vancomycin+Cefotaxime+Rifampicine	No
2	S. pneumoniae	51	Intraventricular hemorrhage	Fever+vomit	0,25	Vancomycin+Cefotaxime	No
3	S. pneumoniae	72	Intraventricular hemorrhage	Fever+vomit	57	Vancomycin+Meropenem/Cefotaxime+Clindamycin	No (EVD)
4	S. pneumoniae	64	Cerebroespinal liquid (CSL) leak	Fever+headache	5	Vancomycin/Cefotaxime/Penicilin	No
5	H. influenzae spp.	11	Dandy-Walker syndrome	Fever+diarrhea	10	Vancomycin+Cefotaxime	Yes
6	H. influenzae spp.	67	Myelomeningocele	Fever+headache+vomit	7	Vancomycin+Cefotaxime	Yes

[Epidemiology and manegament of shunt infections]

Conclusion: Clinical presentation of children suffering from S.pneumoniae or H.influenzae spp shunt infections were similar to those suffering from common pathogens such as Staphylococcus spp and Gram-negative bacteria. Pts with CSF shunts are at risk for S.pneumoniae or H.influenzae spp. and the administration of pneumococcal vaccine should be mandatory in this patient group.

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TICK-BORNE ENCEPHALITIS IN CHILDREN; CLINICAL COURSE AND OUTCOME

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Introduction: TBE is an important arthropod-borne infection in endemic areas. Sequelae are seen in 1/3 of adult patients. The aim was to study the clinical course and outcome after TBE in children.

Methods: All children with TBE in Stockholm during 2004-2008 were identified from records at the local CDC. Hospital records were studied retrospectively and questionnaires grading persisting symptoms and executive function were used at follow-up in 2010.

Results: 30/65 children had mild, 11 moderate and 24 had severe symptoms. Mean age was 10.8 years; children with mild symptoms tended to be younger. A biphasic course was seen in 47/65, 1 child had received vaccine in full dose. Fever, headache and nausea were seen in most children, stiffness of the neck, abdominal pain and focal neurological symptoms in 17-25. Six children had seizures during the acute phase. EEG changes were seen in 90% of children with moderate-severe symptoms. The white blood cell count, glucose, lactate and protein levels in the CSF did not differ with severity of the disease.

Three children were admitted to the ICU. Children with severe symptoms stayed longer at hospital (10.4 days) compared to children with milder symptoms (5.9).

36/60 children have, so far, returned the follow-up questionnaires showing persisting symptoms in 30; headache, cognitive problems, irritability and fatigue dominating. Problems with executive functions were seen in 39%.

Conclusions: TBE is a serious disease which seems to cause residual problems in a large proportion of infected children. Future studies are needed to elucidate this further.

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ETIOLOGICAL STRUCTURE AND DIAGNOSTIC MARKERS OF MENINGITIS IN CHILDREN

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Background: The problem of neuroinfections in children is still urgent. In our country every year from 70 to 90 patients are hospitalized with meningitis. Outcome of the disease depends on many factors, including general health, properties of the pathogen and sufficiency of the therapy.

Aims: To study etiological structure and to determine diagnostic markers of meningitis in children at the modern stage.

Methods: Under our supervision were 50 children with acute meningitis who were hospitalized into Children's Hospital of the Infectious Diseases in Minsk.

Results: High level of meningitis with unknown causative agent was found - 40 %. Identified etiological structure was the following: 50% enterovirus infection (EVI), 17% herpes simplex virus (HSV), 13% meningococcal infection, 7% Haemophilus influensae type b, 3 % Streptococcus pneumoniae and 10% meningitis of mixed etiology. The first symptom in 64% of cases was fever, which was stopped poorly using standard doses of antipyretic drugs, in 28% - a constant headache and in 8% - vomiting, not bringing relief and not associated with food intake. Lethargy, skin hypersensitivity, meningeal symptoms took place too. Outcome of bacterial and viral meningitis was full recovery. But in the case of bacterial meningitis it took longer (($p< 0,05$) and needed several years of rehabilitation.

Conclusions: The main clinical manifestations of meningitis are the following: fever, headache, vomiting, lethargy, skin hypersensitivity, meningeal symptoms. Improvement of the etiological verification of meningitis is necessary. It will make better the treatment policy and outcomes.

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EPIDEMIC MENINGITIS IN HOSPITALIZED CHILDREN IN GOMBE, NORTH EAST NIGERIA

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Background and aims: An epidemic of meningococcal meningitis occurred in Nigeria in 2009. The aim was to describe the features in hospitalized children during the outbreak.

Methods: Consecutive cases of children presenting with meningitis in March 2009 were evaluated.

Results: 19% (11/58) were less 2years. 57% (33/58) were males, 43% (25/58) females. 45% (26/58) of the mothers at least had primary education. 40% (20/49) of households had more than 9 children, 43% (25/39) were from polygamous homes. 44% of households were poorly ventilated. Mean number of children sleeping per room was 4. 35% (19/54) of cases had meningitis in the household, 31% (16/51) had reported receiving vaccine.

Fever, headache and neck pain (25%), fever and convulsions (16%) while fever, vomiting, irrational behaviour, headache (14%). Convulsions occurred in 26% of the children. 7% (4/58) had ear purulent ear discharge. 45% (26/58) had GCS of 6 - 10. 90% (52/58) had neck stiffness and Kernigs. 4% (2/57) had petechiae.

CSF was turbid in 63% (32/51). CSF protein was elevated in 73% (37/51). CSF/blood glucose ratio was less 75% in 90% (46/51). Gram negative diplococci were reported in 31/51 (61%), wbc was >5 with PMN leukocytosis in 62% (32/51).

All received Dexamethasone. 34%(18/58) benzyl penicillin and chloramphenicol, 43%(25/58) chloramphenicol, 17% (10/58) ceftriaxone and 9%(5/58) received ampicillin and chloramphenicol.

Two contacts received ceftriaxone prophylaxis.

7% (4/58) died, 100% below 2 years. 7% (4/58) had eight cranial deficit. 1/58(2%) had cortical blindness.

Conclusion: Meningococcal meningitis has high mortality in children less than 2 years.

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A CASE OF ACUTE HEMORRAGIC ENCEPHALITIS (AHEM) DUE TO INFECTION WITH HUMAN HERPESVIRUS TYPE 6 IN A PREVIOUSLY HEALTHY CHILD

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Background & methods: Human Herpesvirus type 6 (HHV-6) causes exanthema subitum, a common exanthematous infectious disease of childhood. Usually these infections are regarded as harmless but HHV-6 infection can have serious consequences, as shown in this case report.

Results: A 2-year-old boy was seen at our tertiary emergency department with complaints of vomiting and altered consiousness. Encephalitis was suspected and a MRI scan was performed, showing hemorragic changes, consistent with acute hemorragic encephalomyelitis (AHEM). Extensive diagnostic test, including serology and PCR testing of cerebrospinal fluid (CSF) and blood revealed a significant serologic response to HHV-6. HHV-6 DNA was not discovered in CSF of the patient.

Conclusions: Reactivation of HHV-6 is a well-known complication of treatments affecting the immune-system, e.g. in transplant recipients or patients receiving chemotherapeutic agents. However, there is a increasing number of reports on children with primary HHV-6 infections and associated encephalitis. Thus, HHV-6 infections should be in the differential diagnosis of encephalitis, even in healthy children and both molecular and serologic diagnostics should be considered in these patients.

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DETECTION OF FUSOBACTERIAL INFECTION IN A CULTURE-NEGATIVE BRAIN ABSCESS WITH 16S RRNA GENE PCR

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Background and aims: We report a case of *Fusobacterium* mastoiditis complicating brain abscess, in a healthy child.

Methods: A 13 month-old girl presented with a 3-week history of right-ear discharge and pyrexia. She had already received 3 different courses of oral antibiotics following reviews in primary care. Examination revealed drowsiness and lethargy, left-sided gaze, hoarse voice, and increased muscle tone with opisthotonus. Mucopurulent pus was discharging from the right ear-canal. GCS was fluctuating between 12-14/15. An ear-swab obtained a week before, showed polymicrobic growth.An urgent CT revealed a rim-enhancing lesion within the right-cerebellar hemisphere, with skull disruption and bony destruction within the temporal and mastoid bone. There was mass effect with compression of the 4th ventricle and dilatation of the 3rd and lateral ventricles.

Results: Ceftriaxone and Metronidazole were commenced and she was treansferred for neurosurgical care. The abscess was drained and same antibiotic-regimen was continued with significant clinical improvement within 48-hours.Pus cultures were negative however bacterial 16-S-rRNA gene-PCR detected presence of *Fusobacterium species*. A 4-weeks course of the above antibiotics was administered. A repeat brain-MRI revealed residual collection an additional 2-weeks of IV antibiotics was continued, followed by 2-weeks of oral Linezolid.

Conclusions: Fusobacterial invasive infections are rare in children. Usually these patients have received 1-2 courses of oral antibiotics and the likelihood of pathogen isolation is very difficult.The use of 16SrRNA gene-PCR is of vital importance in these cases. Combined surgical and antimicrobial therapy is associated with recovery. However the appropriate duration of antimicrobial therapy remains unclear.

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ACUTE DISSEMINATED ENCEPHALOMYELITIS IN CHILDREN

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Objective: To describe the epidemiologic, clinical, neuroimaging, and laboratory features; treatment; and outcome in a cohort of children with acute disseminated encephalomyelitis (ADEM).

Methods: A 6-year retrospective chart review of children with the diagnosis of ADEM was conducted.

Results: Thirty-six cases were identified. Twenty-two patients (61%) presented in either winter or spring. Twenty-two (61%) had a recent upper respiratory tract illness. Patients presented most often with motor deficits (64%) and secondly with altered consciousness (40%). Spinal fluid abnormalities occurred in 44%. Despite rigorous microbiologic testing, a definite microbiologic diagnosis was established only in 2 child with Epstein-Barr virus disease and 5 patients had elevated immunoglobulin M titers to M pneumoniae.Brain magnetic resonance imaging identified lesions in the cerebral cortex in 80%, in subcortical white matter in 65%, in periventricular white matter in 29%, in deep gray matter in 20%, and in brainstem in 13% of patients. Twenty-seven patients (75%) were treated with corticosteroids, and 25 were treated with intravenous immunoglobulins. 34 patients recovered at discharge and clinical normalization occurred in 31 ,whereas 3/36 (8%) displayed mild, persistent neurologic signs.

Conclusions: Epidemiologic evidence from this study suggests an infectious cause for ADEM. Magnetic resonance imaging was the neuroimaging study of choice for establishing the diagnosis and for following the course of the disease. Prognosis for survival and outcome was excellent.

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ENCEPHALITIS OUTBREAK PRODUCED BY EASTERN EQUINE ENCEPHALITIS VIRUS IN PANAMANIAN PEDIATRIC PATIENTS IN 2010

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Background and aims: Eastern Equine Encephalitis (EEE) Virus belongs to the group of Arboviruses, from the family Togaviridae. Encephalitis produced by this virus causes high mortality and a high rate of neurological sequelae in survivors. The first outbreak of EEE in Panama occurred in the Darien province during 2010. Our aim was to review the clinical characteristics, diagnosis and evolution of this patients.

Methods: We present a retrospective review of the medical history of 23 patients suspected of EEE, who were admitted in the Hospital del Niño at Panamá, Republic of Panamá, between May and July 2010. We registered clinical and epidemiological data.

Results: Most of the patients (95%) came from the endemic area of Darién. The serology was performed in 12 patients with a positive IgM for the EEE virus in 4 patients. Only one referred contact with sick horses. Most common symptoms were fever, vomiting, headache and seizures. There were pathological findings in cerebral TC and MRI in 3 cases. All patients were managed in PICU with supportive treatment, antibiotics, antivirals and anticonvulsants. All of them have slight to moderate neurological sequelae such as psychomotor retardation, swallowing disorders and hemiparesis.

Conclusions:

- In case of encephalitis in an endemic area of EEE, we should suspect it and perform required diagnostic tests.

- As there is no etiological treatment, supportive management, prevention of mosquito bites and vaccination of susceptible horses and laboratory workers should be carried out.

- Fortunately, all our patients survived but with some neurological sequelae.

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INTRAVENTRICULAR VANCOMYCIN THERAPY IN 9 NEONATES WITH CEREBROSPINAL FLUID SHUNT INFECTIONS. MONITORINGS OF CEREBROSPINAL FLUID VANCOMYCIN CONCENTRATIONS

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Background: Intraventricular vancomycin(VCM) therapy is necessary to treat intractable cases of cerebrospinal fluid (CSF) shunt infections. It is suggested that the dose of VCM for children is 10-20mg every 24hrs. But there are few studies about that for neonates and various concentrations are reported. It was the aim of this study to suggest adequate VCM doses and interval for neonates .

Methods: From 2007 to 2010. 9 neonates(12cases) ,who were administered VCM intraventricularly in doses 5mg,10mg or 20mg for therapeutic or prevention purpose in shunt infection, were measured CSF concentrations.

(average age: 54 days;10-102 days, average weight: 3135g ;1326-5127g).

Results: In doses of 20mg/24hr, VCM concentrations were high (average 125µg/mL : n = 6, 98 -168µg/mL) . At 72 to 96hr, they were prolonged high (average 34.8 µg/mL : n = 4, 13.2-72 µg/mL). In doses of 5mg/24hr, VCM concentrations were enough to treat (average 33.4 µg/mL :n = 4, 7-60.2µg/mL).

Conclusion: Because of various concentration , we suggest that VCM monitoring in CSF is important to modify adequate administration of doses. It is reported that CSF VCM concentrations need 5-10µg/mL for treatment. The result of our studies shows that the first dose of 5mg is enough to keep adequate concentrations for neonatal CSF shunt infections.

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HHV-6 & HHV-7 (PCR) IN CSF OF CHILDREN; TEHRAN, IRAN

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Background: The role and frequency of HHV-6 and HHV-7 in central nervous system (CNS) diseases of our children are unclear.

Objective: Searching the DNA-s of HHV-6 & HHV-7 in CSF samples in children with meningoencephalitis.

Methods: A cross sectional study (2007-2009)done in pediatric ward in Rasoul hospital, Tehran Iran. 150 CSF samples obtained from children with meningoencephalitis. Conventional and BACTEC Ped Plus medium; Latex agglutination tests; and in some cases

Bacterial PCR assay used. We searched the DNA-s of HHV-6 & HHV-6 quantitavively by Real time - PCR in 150 CSF samples obtained from children with meningoencephalitis.

Results: Cases was 60.7 %(91) male; 39.3% (59) female; 1-180 months., Fever(>38.5) in 74%; Irritability 70%; Convulsion seen in 53% of cases.

All Herpes virus detected in 12% (18/150) cases. Both HHV-6 & HHV-7 found in 6% of all cases. HHV-6 DNA detected in 4.7% (6) and HHV-7 DNA was detected in 2cases (1.4%) with no correlation with age, sex and clinical signs.

Conclusion: HHV-6 & HHV-7 found in 6% of all studied cases. HHV-6 was slightly more frequent than HHV-7. Our data indicate that herpes viruses is not uncommon causes in children with meningoencephalitis. Our findings presumably may have differed from previous due to epidemiologic and geographic variation (should added to differences in methods, differences in age groups). Its incidence is is lower than other references.

Further studies are needed to define the role of HHV-6 and HHV-7 in neurologic disorders especially in immunocompromised hosts.

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MEDICAL AND NEUROSURGICAL MANAGEMENT OF CITROBACTER KOSERI MENINGITIS

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Background and aims: Citrobacter koseri is a very rare cause of infection in the neonatal period. Neurotropism favors the development of meningitis and brain abscesses in 75% of cases, which carry a mortality of up to 50%.

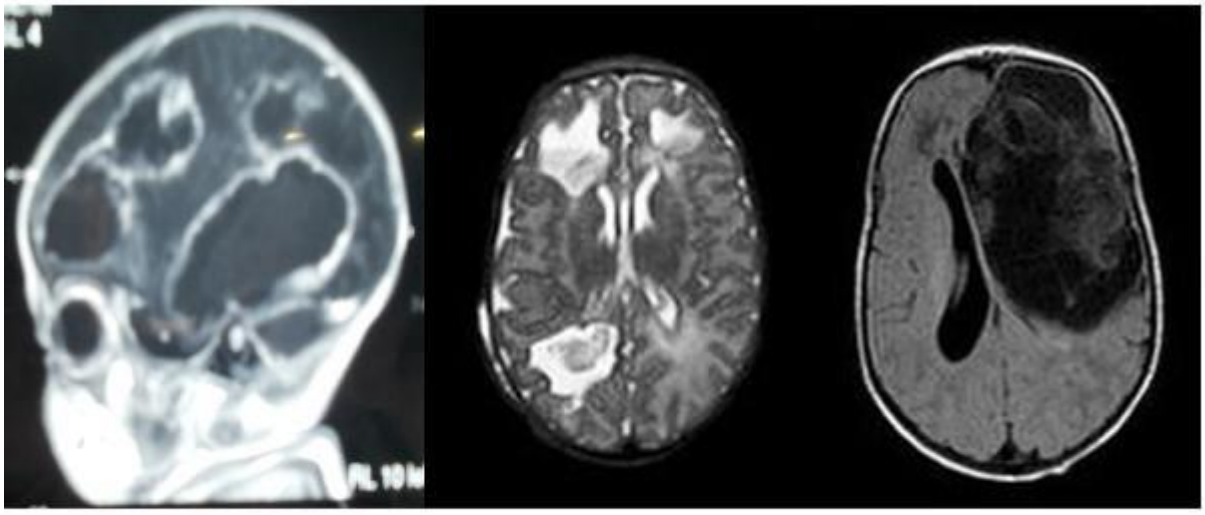
Methods: Clinical course and management of 3 neonates diagnosed of Citrobacter koseri meningitis with brain abscesses are described.

Results: Main data are exposed in table. All 3 patients were male newborns with appropriate weight and were born by vaginal delivery. Lumbar punction and neuroimaging were made after 3 days of admission in case 2. Despite treatment with cefotaxime from admission, case 1 and 3 had very torpid evolution. Case 3 required drainage and aspiration of abscesses up to 3 times. All patients developed hydrocephalus that required placement of ventriculoperitoneal shunt (VPS). All patients survived but with neurological sequelae.

	CASE 1	CASE 2	CASE 3
Age at diagnosis/ Initial clinical manifestations	7 days Fever, jaundice, hypotonia, central apnea	8 days Febricula, jaundice, refusal of feeding	18 days Fever, jaundice, irritability, vomiting
Citrobacter koseri isolation	Blood, CSF, abscess aspiration	Urine, CSF, abscess aspiration	CSF, abscess aspiration
Empiric Treatment/ Especific antibiotic treatment/ Duration	Ampicillin + cefotaxime/ Meropenem+ chloramphenicol. Intraventricular gentamycin/ 9 weeks	Ampicillin + gentamycin/ Meropenem and cefotaxime/ 6 weeks	Ampicillin and cefotaxime/ Meropenem and chloramphenicol. Intraventricular amikacyn/ 9 weeks
Complications	Left cerebral ictus. Multiple cerebral abscesses. Hydrocephalus. Seizures.	Three cerebral abscesses. Hydrocephalus.	Left cerebral ictus. Izquierdo. Two cerebral abscesses. Hydrocephalus. Seizures.
Neurosurgical treatment	Abscesses repited aspiration. External ventricular drainage. Ventriculo-peritoneal shunt placemement	Abscess aspiration. External ventricular drainage. Ventriculo-peritoneal shunt placemement.	Abscesses repited aspiration. External ventricular drainage. Ventriculo-peritoneal shunt placemement.

[Patients with meningitis due to Citrobacter Koseri]

Conclusions: Citrobacter koseri meningitis in neonatal period is a serious infection that predisposes to abscesses development, and early and periodical neuroimagen is needed to detect them.Although the optimal therapeutical approach is still not defined, prolonged antibiotic therapy have to be combined with neurosurgical treatment in all cases.



CASE 1 CASE 2 CASE 3

[Brain abscesses due to Citrobacter koseri]

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ASEPTIC MENINGITIS IN PEDIATRICS: A NEW INSIGHT INTO AN OLD DISEASE

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Background and aims: Aseptic Meningitis is a common infection of the central nervous system in children, for which the diagnosis is based on clinical criteria and conventional laboratory methods. Uncertainty in diagnosis results in prolonged hospitalization and unnecessary use of antibiotics.The aim of this study is to determine the epidemiological, clinical and laboratory characteristics of aseptic meningitis in a portuguese pediatric population.

Methods: Retrospective study of patients admitted to the Pediatric department of a tertiary care hospital who had as discharge diagnosis aseptic or viral meningitis from January 2005 through December 2010.

Results: A total 293 children, median age 4.9±3.7 years, were identified. Most cases occurred during summer. The dominant clinical signs were headache, vomiting and positive meningeal signs in children older than 2 years and fever, anorexia, irritability if younger than 2 years. The median of the cerebrospinal fluid (CSF) cell count was 75 /mm3. Enterovirus RNA was detected in CSF in 213 of 279 (76%) children tested. 101 cases (34.7%) received antimicrobial therapy, and 65.3% did not receive any.

Children with positive enterovirus PCR (polymerase chain reaction) had shorter hospitalization ($P < 0.001$) and shorter duration of antimicrobial therapy ($p < 0.001$) as compared to children who had negative PCR or were not tested. There were no serious complications or deaths.

Conclusions: Enteroviruses are the leading cause of aseptic meningitis in children. Enterovirus PCR reduces the time required for identification of the causative agent and may decrease the use of empiric therapy with antibiotics and shorten hospitalizations.

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BRAIN TUBERCULOMA - A RARE TUBERCULOSIS FORM

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Tuberculosis (TB) is one of the top 10 causes of death among children worldwide. An unique feature in very young children is the imperceptible and often rapid progression from Mycobacterium tuberculosis infection to disease. Brain tuberculoma is a rare feature of extra-pulmonary infection and is considered the most severe.

The authors underline the importance of an early diagnosis of this rare condition.

Clinical report: A six month-old immunocompetent child was admitted with a week-old fever of undetermined origin that didn't respond to antibiotherapy. He had a history of increased head circumference and irritability with a month of evolution. During hospitalization he had seizures and bulging anterior fontanelle was noted. Lombar puncture was performed and abnormal cerebrospinal fluid findings were consistent with TB meningitis. He promptly started empiric anti-tuberculosis medication and steroids. Fundus examination revealed choroidal tubercles and cranial CT scan with contrast showed mild hydrocephalus and space occupying lesions suggestive of tuberculous granuloma. Given the patient risk for increased intracranial pressure he was followed by neurosurgical consult. M. tuberculosis was isolated by polymerase chain reaction tests, microscopy and culture using various clinical specimens.

The infant's diagnosis led to identification of a previously unrecognized TB infection in the mother.

He showed significant clinical improvement one month after starting treatment.

Conclusions: TB disease in children is usually a direct consequence of adult TB, most often of household contacts.

Early diagnosis, prompt institution of anti-tubercular treatment and the clinical stage at which the patient presents are important and deciding factors for final outcome.

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DYNAMICS OF CYTOKINES STATUS IN DIFFERENT CLINICAL FORMS OF ACUTE TICK-BORNE ENCEPHALITIS

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Tick-borne encephalitis (TBE) is one of the most important forms of infectious pathology in Europe and Asia. An estimated >10.000 human clinical cases are reported annually in the endemic countries.

With the aim to research the pathogenetic and diagnostic role of cytokines in TBE we examined the serum concentrations of IL-6, IL-10, IL-12, IFN-α and IFN-γ in pediatric patients with acute forms of serologically confirmed TBE.

A total of 60 sera from 30 patients with different clinical forms of acute TBE were tested. Cytokines' concentrations were investigated semiquantitatively using commercially available ELISA systems (RD Systems, Wiesbaden, Germany). Serology was performed using IgG- and IgM-ELISA and Indirect Immunofluorescence Biochip for confirmation of ELISA results (both Euroimmun, Lübeck, Germany).

In cases of meningoencsephalitic form of TBE the low level of IFN-γ concentration was detected. The maximum IFN - α concentration is revealed in TBE cases with severe neurological disorders. IL-6 and IL-10 showed a higher average level in patients with severe form of TBE than in patients with acute mild infection or febrile forms and increased during regress of clinical manifestations. The IL-12 serum levels were 4 fold higher in acute meningitis patients in comparison with other disease categories.

Acute period of TBE in children is accompanied by change of IL-6, IL-10, IL-12, IFN-α and IFN-γ production, with differences depended on clinical form of disease and age. Changes of the cytokines status reflect current disease severity and it can possibly be used in forecasting disease's currency.

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ENTEROVIRAL MENINGITIS - CLINICAL CHARACTERISTICS AND POTENTIAL USE OF THE BACTERIAL MENINGITIS SCORE. CASE SERIES 2006 - 2010

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Meningitis in children is accompanied by severe morbidity and mortality. While epidemiology and pathogenesis of bacterial meningitis is well understood there is less clinical characterisation of non-bacterial meningitis. Especially in the first months of life and in immunocompromised hosts enterovirus (EV) can cause severe sepsis-like illness.

All children at Prof. Hess childrens´ hospital in Bremen, Germany, from 1.1.2006 - 31.12.2010 who had meningitis and who had been tested for EV infection were included. Hospital ICD-10 data was completed through patient data from the national EV surveillance laboratory where most samples go to for EV-testing by PCR and viral culture.

28 children with proven EV meningitis were included and compared to 25 children with aseptic meningitis tested negative for EV and without defined diagnoses such as neuroborreliosis, or autoimmune-mediated myelitis.

All EV meningitis occurred between June and October; in CSF pleocytosis remained < 700 leucocytes /µl, while protein and was usually normal. In 12 cases viral culture was positive. Children with EV meningitis had higher neutrophils in CSF than EV-negative cases. No short-time sequelae occurred. With the „bacterial meningitis score“ (BMS; Nigrovic et al 2007) 25/28 EV-cases would have been correctly identified as non-bacterial meningitis.

EV meninigits is a common differential diagnosis in children with meningitis in summer and fall; while CSF pleocytosis is dominated by neutrophils and raises up to 700/ul normal CSF protein and glucose suggest non-bacterial origin. Applying the BMS can be useful in order to avoid unnecessary antibiotic treatment and long hospitalisation.

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SURVEILLANCE OF ACUTE FLACCID PARALYSIS IN THE EMILIA ROMAGNA REGION (ITALY): 1996-2010

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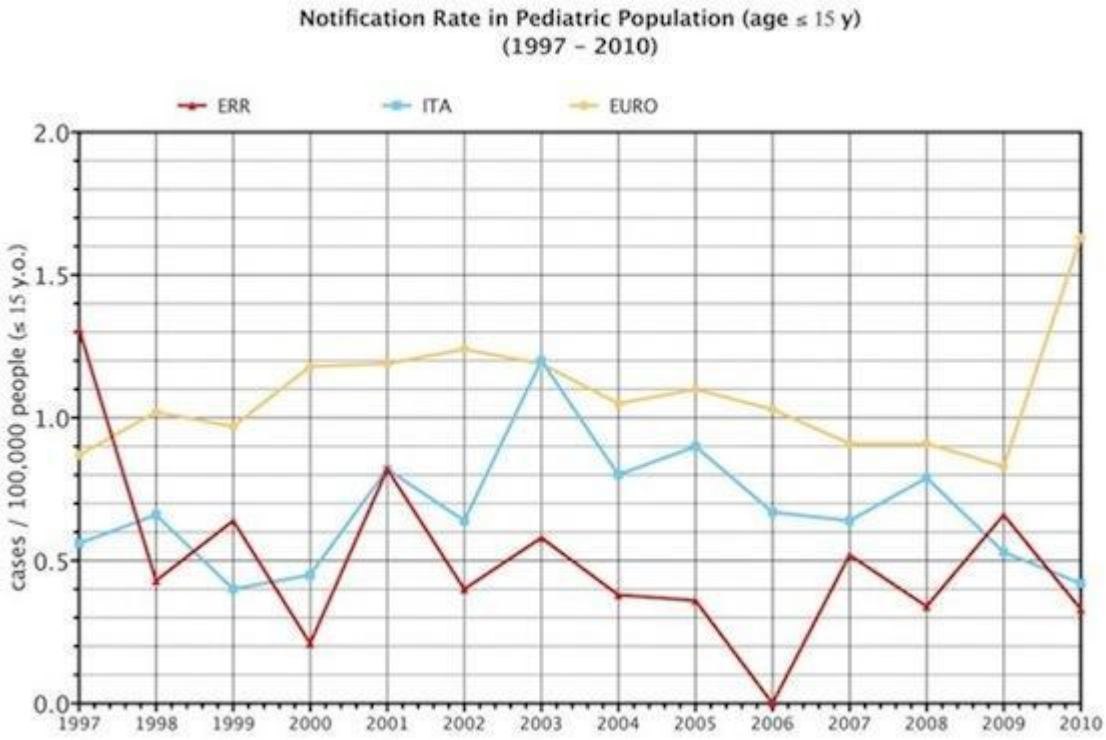
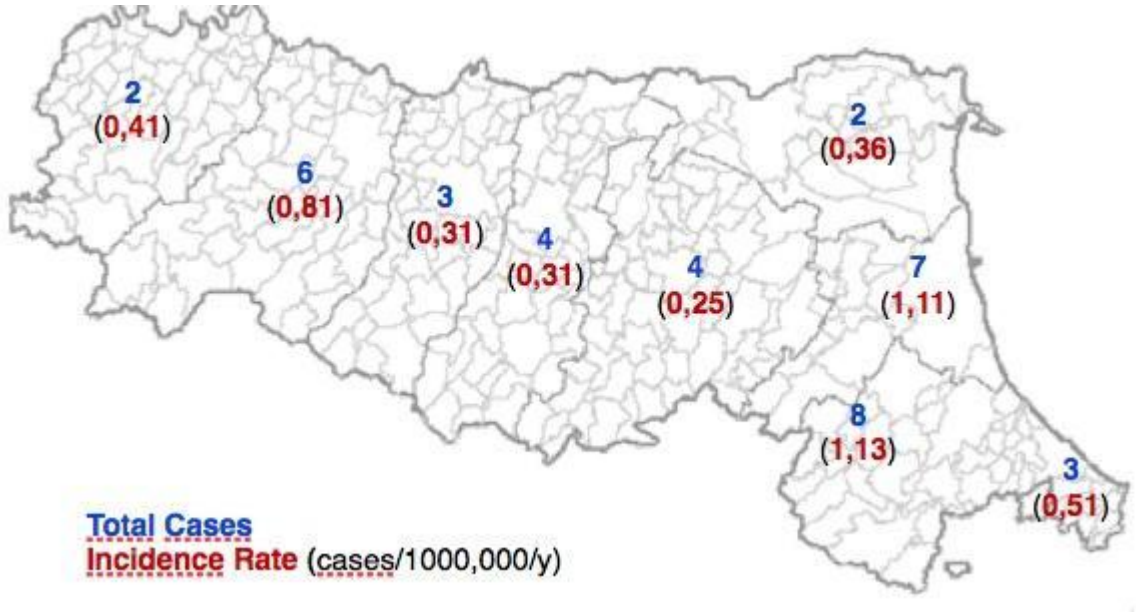
Background and aims: Acute Flaccid Paralysis (AFP) is a clinical syndrome encompassing all cases of paralytic poliomyelitis: therefore, epidemiologic surveillance for AFP cases is of public relevance as an instrument for detecting potential cases and poliovirus infections. Since 1996, the Department of Public Health of Parma University was recognized as regional reference center for Emilia Romagna Region (ERR) for AFP surveillance. Here we present a 15-year summary of the surveillance activity.

Methods: All AFP cases for 1996-2010 with age at notification ≤15 years were retrospectively analyzed, retrieving personal and clinical data from the epidemiological notification forms. Incidence Rates were then calculated from the Italian National Institute for Statistics (ISTAT) data about ERR population.

Results: Overall, 39 AFP were notified (24 males, 15 females) for a mean of 2.6 cases (95%CI:1.82-3.38) on year basis, with a notification rate of 0.51 cases/100,000 subjects/year (95%CI:0.34-0.68). Fever ≥38°C was the initial symptom in 48.7%, and the clinical syndrome was associate with a progressive pattern in 51.3%, with symmetrical paralysis in 59% of cases. Only 5 subjects (12.8%) were affected by a paralysis lasting more than 60 days.



[Image 1. Notification Rate in Pediatric Population]



[Image 2. Geographic distribution of cases]

Conclusions: AFP notification rate in ERR was lower the expected value on national data basis (0.64 cases/100,000 subjects/year 95%CI:0.49 - 0.78). Our results suggest that the continuation of surveillance will need a further sensitization of healthcare workers.

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BEHAVIORAL FUNCTIONING OF CHILDHOOD BACTERIAL MENINGITIS SURVIVORS IN THE NETHERLANDS

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Background and aims: Bacterial meningitis (BM) is a serious infectious disease responsible for high mortality and a high incidence of short and long term sequelae. Cognitive, academic and behavioral problems are reported in at least 20% of the childhood BM survivors. The aim of this study was to determine the incidence of behavioral problems in a cohort of Dutch school age BM survivors using the Strengths and Difficulties Questionnaire (SDQ).

Methods: Three hundred and sixty-one school age BM survivors (200 boys and 161 girls), mean age 8.9 years (range 4.8 to 16.6), selected from the files of The Netherlands Reference Laboratory for Bacterial Meningitis (NRLBM) were included. The mean age at infection was 2.2 years (range 0 to 7.9) and mean interval since the infection was 6.6 years (range 3.7 to 12.4). Parents were asked to fill in the SDQ, a validated questionnaire regarding behavioral issues in children. Assessments scores were compared to an English norm reference group.

Results: Parents of 62 children (17.6 %) reported a total difficulties score in abnormal range compared with 9.7% in the population sample (p-value < 0.001). Except for the conduct problems scale, BM survivors had a higher incidence of abnormal scores compared with the norm population in all the subscales of the SDQ (p-value < 0.05).

Conclusions: The results of this study indicates that, approximately 6.6 year after an episode of BM, there is an increased prevalence of behavioral problems in Dutch school age BM survivors.

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RELEVANCE OF TLR9 POLYMORPHISMS IN THE IMMUNE RESPONSE TO MENINGOCOCCAL MENINGITIS

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Meningococcal meningitis (MM) is a severe infection, leading to neurological sequelae. Genetic variation in immune response genes influences susceptibility and severity of infections.TLR9 recognizes bacterial DNA leading to intracellular inflammatory signaling.

The aim of our study is to associate TLR9 SNPs with susceptibility to and severity of MM.

Two TLR9 SNPs and four TLR9 haplotypes were determined in 390 survivors of MM and compared to 392 healthy controls. Using a novel in silico regulatory SNP technique we assessed potential functional consequences of the TLR9-1237 SNP. Genotype distributions of both SNPs were compared in 13 by literature identified clinical severity parameters.

Carriage of the *TLR9*+2848 mutant was significantly decreased in MM patients compared to controls (p: 0.0098, OR: 0.6, 95% CI: 0.4 - 0.9). TLR9 haplotype I was associated with an increased susceptibility to MM (p: 0.0237, OR 1.3, 95% CI: 1.0 - 1.5). In silico analysis of the TLR9-1237 mutant allele showed increased affinity for pro-inflammatory transcription factors. TLR9 haplotype I, lacking this mutant allele, was associated with meningococcemia (p = 0,001; OR 1,5). Cerebrospinal fluid (CSF) leukocytes/mcl were higher in patients carrying TLR9-1237 TC/CC genotypes (p = 0,024) or TLR9+2848-AA (p = 0,011). CSF/blood glucose ratios are lower in carriers of mutant alleles in the TLR9-1237 SNP (p = 0.017).

TLR9 SNPs are associated with decreased susceptibility to develop MM. We identified an association of TLR9 SNPs with protection against meningococcemia, a prerequisite for meningeal invasion. MM patients showed a better local inflammatory response and lower clinical severity.

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HOST GENETIC POLYMORPHISMS IN THE INNATE IMMUNITY AFFECT THE SUSCEPTIBILITY, SEVERITY AND OUTCOME OF BACTERIAL MENINGITIS

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Clinical manifestations of infection with Streptococcus pneumoniae and Neisseria meningitidis are highly diverse. Some patients are asymptomatically colonized while others develop bacterial meningitis (BM) with life-long sequelae. An adequate innate immune response is essential for defense against BM, but may also lead to permanent neuronal damage.

We have studied how single nucleotide polymorphisms (SNPs) in the pathogen recognition system affect the susceptibility, severity and outcome of BM.

In buccal DNA from 471 survivors of pneumococcal- or meningococcal meningitis in childhood, 12 SNPs in 8 genes encoding for pathogen recognition receptors, including Toll-like receptors (TLRs) and signal transduction peptides, were determined by real-time PCR. Genotype distributions were compared to healthy controls and compared within patients groups classified by clinical severity variables. A prediction model including clinical and genetic markers is being created to identify patients at high risk for sequelae, in particular post meningitis hearing loss.

SNPs in TLR9 are associated with protection against BM and meningococcemia and with increased leukocyte numbers in cerebrospinal fluid in case of BM. In silico analysis of TLR9 mutants showed increased affinity for pro-inflammatory transcription factors.TLR4 is associated with hearing loss, combined carriership with TLR2 SNPs significantly increased this risk ($p< 0,0001$, OR 5,7).

Polymorphisms in the pathogen recognition receptor system contribute to differences in susceptibility, severity, and outcome of BM. SNPs can be valuable markers for identification and customized treatment of high risk patients as illustrated by creating prediction rules, and provides more insight of the immune response in the central nervous system.

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OUTCOMES OF MENINGOCOCCAL SEROGROUP B DISEASE IN CHILDREN & ADOLESCENTS: FINDINGS FROM A LARGE NATIONAL CASE-CONTROL STUDY

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Background: Nations are facing imminent decisions about introduction of new vaccines against meningococcal serogroup B (MenB) disease. Contemporary robust data on sequelae of MenB disease are needed to inform these decisions.

Methods: We present final results from a nationally representative case-control study (UK) of 221 matched pairs aged 3-16 years. Cases were identified through a national database and controls via case GPs. Consenting subjects underwent a standardised assessment. Matched analyses were undertaken using Generalised Estimating Equations (GEE) and conditional logistic regression (CLR).

Results:

	Case	Control	Matched p	Effect size
Verbal IQ	100.7	107.4	<0.0001	-0.46
Performance IQ	98.2	105.0	<0.0001	-0.44
Bilateral Hearing loss <=40db	3.7%	1.0%	0.02	Odds ratio 2.9 (1.2, 7.0)
Cochlear implant	2.4%	0	0.006	-
Working memory	96.4	103.7	<0.0001	-0.44
Executive function	54.7	49.9	<0.0001	0.34
Psychiatric disorder	15%	3.5%	<0.0001	Odds ratio 3.0 (1.2, 7.5)
Amputation with disability	1.2%	0	0.04	-
Epilepsy	2.1%	0.3%	0.04	-

[Outcomes]

Cognitive findings were unchanged when repeated in those without significant HL.

Conclusions: MenB disease is associated with a marked series of deficits in survivors . This is the largest outcome study ever taken. Economic evaluation of these deficits will inform vaccine development and implementation decisions and improved aftercare for survivors.

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IS THE INCIDENCE OF TUBERCULOUS MENINGITIS SUNLIGHT DEPENDENT?

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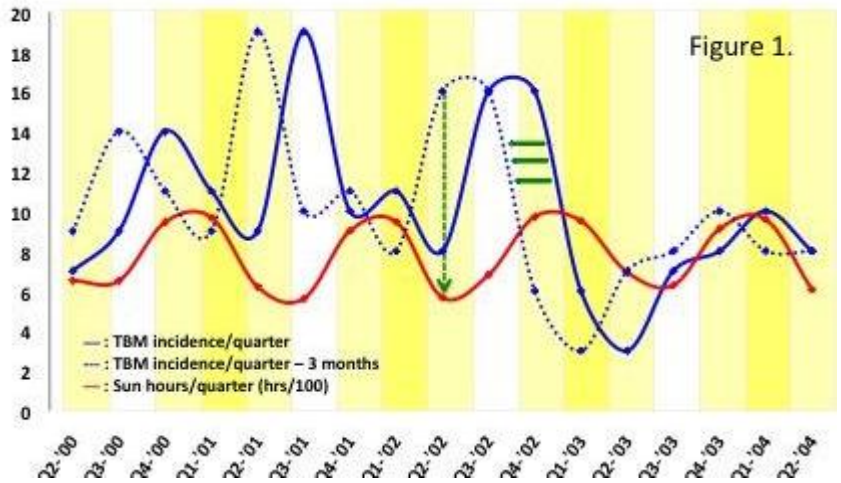
Background and aim: Tuberculous meningitis (TBM) is the most frequent form of childhood bacterial meningitis in the Western Cape of South Africa and is the most severe extra pulmonary complication of tuberculosis. The incidence of *Mycobacterium tuberculosis* infections is suggested to depend on the season. This might be due to sunlight exposure, which plays a protective role in the development of the disease by production of vitamin D in the skin. We therefore hypothesize that there is a sunlight depend seasonal trend in the incidence of TBM.

Methods: Incidence rates from children with TBM were obtained from an ongoing study in a tertiary hospital in Cape Town, South Africa. Daily sunshine hours measured at Cape Town International Airport, were obtained from the South African Weather Service.

Results: In a 5-year period, 189 children (6 months to 12 years old) were diagnosed with TBM.

Poisson regression showed a significant association between the incidence of TBM and sunshine hours 3 months prior to manifestation (IRR 2.43; Z -3,028; 95%CI 0.219 - 26.96; P0.002). Figure 1 illustrates this association.

Conclusions: The association between sunshine hours and TBM incidence strengthens the role of vitamin D in the pathogenesis of TBM. Further prospective research is necessary.



[Figure 1]

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CYTOMEGALO VIRUS AS A POSSIBLE RISK FACTOR FOR NEONATAL GASTROINTESTINAL SURGICAL CONDITIONS

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Background: Cytomegalovirus virus (CMV) is considered as one of the most common causes of congenital infection. The incidence of congenital CMV infection ranges from 0.2 to 2.4% of all live births. Several reports of surgical conditions associated with CMV infection have been published. The aim of the present work is to evaluate the possible causal relationship between CMV infection and gastrointestinal surgical emergencies in neonates admitted to the neonatal ICU and pediatric surgical departments of Assiut University Children Hospital.

Patients and methods: This study included 33 neonate operated upon because of gastrointestinal surgical emergencies in Assiut University Children Hospital during the period from October 2006 to April 2007. Serological detection of CMV IgG and IgM from both mothers and newborns was done for all cases. Surgical specimen was taken from the affected part of gastrointestinal tract of the newborn for histopathologic examination.

Results: Positive serological tests (CMV IgM) were found only in four neonates (3 males and one female). The average gestational age was 34.5 weeks (range 30-38 weeks) and the average birth weight was 3kg (range 2.5-3.8kg). Two had small intestinal atresia, one had meconial perforation and one had high imperforate anus and microcephaly. Maternal CMV IgM was positive only in two cases. All the four surgical specimens showed characteristic CMV nuclear inclusion bodies.

Conclusion: It is necessary to screen all surgical specimens of neonates with surgical conditions for CMV inclusion bodies to minimize the late morbidity in such cases.

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MONTH-BY-MONTH AGE ANALYSIS OF THE RISK OF SERIOUS BACTERIAL INFECTIONS IN HOSPITALIZED FEBRILE INFANTS WITH OR WITHOUT BRONCHIOLITIS

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In a prospective study, we assessed the incidence of serious bacterial infections (SBIs) by month of age in febrile infants less than 3 months with or without bronchiolitis. Overall, SBI was detected in 116 of the 948 (12.2%) infants without bronchiolitis compared with 7 of the 177 (4%) infants with bronchiolitis ($p< 0.001$). However, within the sub-group of neonates aged ≤28 days, there was no difference in the incidence of UTI between those with or without bronchiolitis. Hence, the risk of SBI in febrile infants is significantly lower in the presence of bronchiolitis, but only after the neonatal period.

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CLINICAL AND BIOLOGICAL PARTICULARITIES IN NEONATAL SEPTICEMIA

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Introduction: Neonatal septicemia occurs at premature newborns from the neonatal intensive care units. It is a serious affection with high mortality, even in the presence of a specific antibiotherapy.

Objective: The authors aimed to analyze the risk factors of the disease by grade of premature and starting age, correlated with clinic and biologic signs and with morbidity and mortality.

Material and method: The study was carried out on a period of one year (2008), on a lot of 38 premature newborns, hospitalized, selected by anamnestic, clinic, epidemiologic and biologic criteria. The prevalence was 4,03%.

Results: Neonatal septicemia with early start was present at 14 cases (41%), with extremely serious clinic signs. There were 9 cases associated with maternal-fetal infection (26,47%), 5 cases with rupture membranes at 18 hours (14,71%). The mortality was high in 5 cases (14,71%), at big premature with intrauterine chronic affection and history of maternal-fetal infection. The most present germs: Serratia Marcensens, Pseudomonas Aeruginosa, and coagulaso-negative staphylococcus.

Septicemia with late start was present at 18 cases (52,64%) having a higher prevalence at premature with gestational age lower than 32 weeks and birth weight lower than 1500 g, with long hospitalization and associated malformative pathology . The same germs were involved.

Both groups presented classic signs of septicemia. Beyond positive hemoculture were present: positive PCR with values between 8,92mg/l and 220mg/l, leucocitosys: 17240/mm^3-44000/ mm^3, thrombocytopenia: 15000/ mm^3-120000/ mm^3.

Conclusions: Neonatal septicemia is a serious affection with high mortality (14,71%) at premature newborns even if antibiotherapy was early started.

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LATE ONSET SEPSIS IN PRETERM NEONATES

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Background: Although advances in neonatal intensive care have led to improved survival of preterm neonates, late onset sepsis (LOS, occurring after 3 days of life) continues to be an important cause of morbidity and mortality.

Aim of study: To investigate the frequency, etiology, risk factors and current antibiotic therapy for LOS.

Methods and material: We evaluated 1326 preterm neonates (< 37 weeks of gestations) admitted to the Children Emergency Hospital, Timisoara, Romania between January 2008 to June 2009. Medical data and microbiology reports were reviewed.

Results: Out of 59 (4.44%) newborns diagnosed with neonatal sepsis, 47 (3.544%) had LOS, (mean age: 13.1±2.5 days, 52.47% males), which occurred after 5.7± 4.3 days of hospitalization. The median of hospital stay was 29.5 days. The major culprits identified from blood cultures were Pseudomonas aeruginosa (49.18%), Klebsiella pneumoniae (14.75%), Serratia marcescens (13.11%) and Staphylococcus aureus (8.19%). While Gram-positive bacteria were 100% sensitive to Vancomycin, 75% to Linezolid and 66% to Clindamicyn, Gram-negative bacteria were sensitive to Colistin (93.5%), Imipenem (91.83%) and Ciprofloxacin (90%). Among factors associated with LOS, the most important were invasive procedures such as tracheal intubations and mechanical ventilation (38.98%), and vascular catheters (100%), antibiotics usage (100%) and body weight < 1500g (64.4%). Death prevailed in 8.51% of them.

Conclusions: LOS is a major concern in preterm neonates in our hospital. Therefore, strategies to reduce LOS in preterm neonates are needed urgently.

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CLINICAL CHARACTERISTICS OF CONGENITAL SYPHYLLIS CASES ADMITTED TO THREE INSTITUTIONS IN KOREA, 2000-2010

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Background and aims: Although congenital syphilis (CS) is a serious healthy priority, limited data are available to address this problem in Korea. This study aims to evaluate the pattern and presentation congenital syphilis over a 10-year period as seen in three institutions in Korea.

Methods: Medical records of CS diagnosed at Kyung Hee University Hospital, Kyung Hee University Hospital at Gangdong, and Hanil General Hospital from January 2000 to December 2010 were reviewed.

Results: 20 cases were diagnosed as CS, and 38.5% (5/13) of their mothers had presumed syphilis infection during the first trimester of pregnancy. Among 13 mothers, 4 (30.8%) were foreign born immigrants, 2 (15.4%) were unmarried women. The mean estimated gestational age for 16 identified cases were 37^{+2} weeks (range: 32^{+2} weeks - 40^{+6} weeks), and birth weight was 2,928.4gm (range 1,780gm - 4,010gms). 61.5%(8/13), and 30.8%(4/13) of mothers and 60%(12/20), and 95%(19/20) of babies were positive in non-treponemal test, and treponemal tests respectively. 19 babies were asymptomatic, and 1 baby showed hepatosplenomegaly and jaundice.

Conclusions: Most of the CS cases were born to asymptomatic women through routine surveillance. Thus, promoting awareness about the extent and gravity of CS and mounting effective surveillance is necessary in Korea.

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DO WE ASSESS PROPERLY NEWBORNS FROM THE LUETIC MOTHER?

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Background and aims: The cornerstone of congenital syphilis control is antenatal screening and treatment of mothers with penicillin, which is a cost-effective intervention. However, in large parts of the world, this mother-to-child infection continues to be a significant public health problem. Although it is rare in affluent countries, there has been a resurgence in European countries. Screening should be strengthened among those at high risk, but the interpretation of the results still seems to be a challenge.

Methods: Retrospective study to assess the prevalence of congenital syphilis in our centre between January 2007 and December 2010. Newborns whose mothers where positive for treponemal test (TPHA) during pregnancy controls were included. Demographic, obstetric and clinical data were collected from the maternal records.

Results: Overall 40 newborns were included. The median maternal age was 29,8 years (IQR: 22-41 years) and all mothers were from foreign countries (70% Latin American, 20% African, 10% Eastern European). Only 2 cases presented with mild prematurity. In 11 cases a poor antenatal care was performed. In 7 cases a wrong interpretation of the luetic mothers´ screening tests was done and, therefore, their babies underwent a mistaken treatment with intramuscular penicillin after birth.

Conclusions: We describe the frequency and the problems the clinician faces in a second level Nursery's hospital. Although congenital syphilis is not an uncommon disease, the most usual mistake seems to be the interpretation of the screening tests. Thus, we must be used to assessing maternal serological reactions in order to avoid unnecessary interventions.

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VALGANCICLOVIR TREATMENT OF SYMPTOMATIC CONGENITAL CYTOMEGALOVIRUS INFECTION DIAGNOSED BEYOND THE NEONATAL PERIOD

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Background & aims: Congenital cytomegalovirus (CMV) infection causes progressive sensorineural hearing loss and psychomotor retardation. Despite some infected children are identified after the neonatal period, there are few data regarding antiviral treatment in these patients.

Methods: Multicenter, retrospective case-series analysis of infants with congenital CMV with central nervous system (CNS) involvement who started antiviral treatment beyond the neonatal period.

Results: Fourteen cases were identified, nine confirmed by neonatal dried-blood-spots-PCR and five with suspected diagnosis (positive urine-PCR, suggestive neuroimaging and exclusion of other possibilities). Mean age at diagnosis was 2.8 months, 5/11 had intrauterine growth restriction and 2/14 were premature. Median (range) age at the beginning of treatment was 3 months (1.1-8). All children received oral VGC at 32 mg/kg/day b.i.d., and 4 also intravenous ganciclovir prior to VGC. Median (range) VCG treatment duration was 6 months (3.5-12), only 7 patients developing neutropenia (none required G-CSF). Hearing was tested by brainstem auditory evoked response (BAER) at the time of diagnosis (all patients), 6 (n=10) and 12 months (n=10). Before treatment, 11/14 had hypoacusia (4/11 mild, 1/11 moderate, 6/11 severe). At the 6/12 month BAER-controls, 50%/60% patients remained stable, 50%/40% improved and none worsened. Only 1 patient out of 5 with severe hearing loss at baseline improved, compared to 4/5 with mild/moderate hypoacusia.

Conclusions: Long-term VCG treatment is well tolerated and may preserve or improve hypoacusia in children with late-diagnosed congenital CMV infection and mild/moderate hearing loss at baseline, even when therapy is started beyond the neonatal period.

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THE ROLE OF CONGENITAL CYTOMEGALOVIRUS INFECTION IN THE DEVELOPMENT OF SENSORINEURAL HEARING LOSS IN CHILDREN

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Background: Cytomegalovirus (CMV) is the leading cause of congenital infections, occurring in 0.3-2% of newborns and the most viral cause of hearing loss in children. 84.4% of pregnant women in Belarus are seropositive to CMV. Aim. To study hearing function in children with CMV infection.

Methods: 23 children of early age were under our observation. CMV infection was diagnosed by PCR in saliva, blood, urine, cerebrospinal fluid. The function of hearing was determined by acustic impedansometry, otoacustic emission and acustic evoked patentions.

Results: Median age of children was Me (P25-P75) 3 months (2-6). 19 (82,6%) children were with normal hearing function, in 4 (17,4%) cases was found sensorineural hearing loss. All children with hearing disturbance in the newborn period had following signs of congenital CMV infection: impairment of central nervous system, seizures, periventricular intracranial calcifications, sepsis-like syndrom, congenital pneumonia.

Conclusions: Congenital CMV-infection plays a role in the development of hearing loss in children of early age. The presented data confirm the necessity of audiological screening and monitoring in children with congenital cytomegalovirus infection.

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THE FACTORS WHICH INFLUENCE THE DEVELOPMENT OF SENSORINEURAL HEARING LOSS IN NEWBORN

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Background: Cytomegalovirus (CMV) is the main cause of congenital infection including the impairment of central nervous system. CMV can damage structures of inner ear causing hearing loss in children. 84.4% of pregnant women in our country are seropositive to CMV.

Aim: To estimate reasons of hearing loss in children with congenital CMV infection.

Methods: We analyzed natural history and the course of neonatal period in 4 children of early age with congenital CMV infection who have sensorineural hearing loss. Hearing function was evaluated by acoustic impedansometry, otoacoustic emission and acoustic evoked patentions.

Results: Median gestational age of children was Me (P25-P75) 35.5 weeks (31.5-38), median birth weight - Me (P25-P75) 1910 grams (1650 - 2410). As for their mother´s: during pregnancy they have respiratory syndrome, vaginitis, and intrauterine growth retardation. 2 cases delivered spontaneously (in one case- preterm delivery), 2 - with caesarean section ¬(in one case- preterm delivery). All children in the newborn period had following features of impairment of central nervous system (CNS): seizures, periventricular intracranial calcifications, cerebral ventriculomegaly, and psychomotor retardation. Besides that our newborns have sepsis-like syndrome, congenital pneumonia, jaundice, thrombocytopenia and anemia.

Conclusions: Unfavourable background for development of hearing loss in children in neonatal period with congenital CMV infection are CNS disturbance, low birth weight, premature.

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THE FACTORS WHICH INFLUENCE THE DEVELOPMENT OF SENSORINEURAL HEARING LOSS IN NEWBORN

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Children Infectious Diseases, Belarussian State Medical University, Minsk, Belarus

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Conclusions: Unfavourable background for development of hearing loss in children in neonatal period with congenital CMV infection are CNS disturbance, low birth weight, premature.

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NOSOCOMIAL INFECTION: A THREE-YEAR EXPERIENCE IN A NEONATAL INTENSIVE CARE UNIT

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Background: Nosocomial infections may result in considerable morbidity and mortality among neonates who require intensive care with important short and long term implication.

Aims: Evaluate epidemiological trends and clinical variables of neonates with nosocomial infection admitted in our unit from 2008 to 2010 and compare them with national data.

Methods: A retrospective analysis was performed using a national monitoring health network. We analysed and compared the following aspects: incidence of nosocomial infection, sepsis, infection rate in very low birth weight neonates (VLBW), incidence of central venous catheter (CVC) related sepsis, identification of agent and mortality.

Results: 863 children admitted in our unit; 18,9% VLBW, 17,8% underwent invasive ventilation and 19,6% with CVC. The overall incidence of nosocomial infection was 6/1000 live births (similar do the national database), representing 6,1% of total admissions. The 2 more commom diagnoses were: sepsis (n=45) and necrotizing enterocolitis (n=8). Comparing our results with the national database, we found: incidence of sepsis (5,1‰ vs. 6,0‰); infection rate in VLBW (26.7% vs 41,4%); incidence of CVC related sepsis (19,4‰ vs.17‰) and mortality (0,35% vs 0.30%). In the etiopathogenic analysis, in 66,0% vs 68,6% of cases, the agents were identified. The most frequent bacteria (*Staphylococcus epidermidis* and other coagulase -negative staphylococci) were similar in both groups.

Conclusions: The study shows a great similarity between our results and the remaining units of our country, which can be explained by the standardized care and current efforts in the management of this serious problem.

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CATHETER ASSOCIATED INFECTIONS IN NEONATES WITH PERCUTANEOUSLY INSERTED CENTRAL VENOUS CATHETERS

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Objectives: To determine the rate of catheter - associated infections in neonates with percutaneously inserted central venous catheters.

Patients and methods: 129 neonates in NICU, University Pediatric Hospital in Sofia with 131 percutaneously inserted central venous catheters. We evaluated the rate of catheter related infections and catheter colonization, bacterial isolates from the catheter tip and blood and the dependence of infection rate on the site of catheter placement.

Results: The mean catheter duration was 16,63 +- 8,72 days. The most common insertion sites were the cubital and axillary veins. The rate of catheter - associated infections was 9,1/ 1000 catheter days and colonization rate 28/1000 catheter days. The distribution of the main bacterial isolates was as follows; S. epidermidids 63,9%, K. pneumoniae 9,83% and C. albicans 3,05%. The rate of catheter colonization was highest in catheters, inserted through the jugular vein (66,6%). The highest rate of catheter - associated infections was in the patient group with the catheters, placed through the cubital vein.

Conclusion: Neonates with percutaneously inserted central venous catheters are exposed to significant infection risk . There is possibility to reduce the infection risks, paying attention to the site of insertion and by improving the prevention measures in the high risk patient groups.

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EVOLUTION OF PERINATAL EARLY-ONSET SEPSIS AND GROUP B STREPTOCOCCAL INFECTION IN THE PERIOD2005-2011

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Background: Early-onset sepsis (EOS) and GBS infections cause a high morbid-mortality in neonates. The infection rate varies and our aim was to assess the evolution of infection indexes before and after the implementation of GBS screening (GBS-S) in pregnant women.

Subjects and methods: In a population of 2746 consecutive livebirths (LB), the EOS rate due to any microbe, GBS bacteraemia (GBS-B) rate, positive cord blood culture (P-CBC) and overall CBC done as well as number of VLBW (< 2000 g) have been done in three periods: before starting GBS-S, period I (2005-006), at the beginning of GBS-S, period II (2007 - 2008), and at the full implement of GBS-S, period III (2009 - January 2011).

Results: In periods I/II and III, EOS/1000 LB rate increased steadily (1.16 / 1.86 / 2.32), and GBS-B/1000 LB rate reached an upper level in period II and decreased thereafter (1.0 / 2.1 / 0.9). The rate of (P- CBC) /1000 LB also rose through the three periods (1.2 / 3.8 / 4.9). The overall CBC /1000 LB done also increased in the three periods (1.2 / 3.8 / 4.9) as well as number of VLBW (33/ 101/ 131). There were none death due to EOS.

Conclusions: Over an 6-year period the rate of EOS has risen steadily according to increment of VLBW infant births. Incidence of GBS-B remained at a low rate. Early use of prophylactic antibiotics in neonates with infection risk factors is responsible for the null mortality registered.

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PREVALENCE OF URINARY INFECTIONS AT PREMATURE NEWBORN

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Urinary infections have an important role in newborn's pathology.

Material and method: In the study it was count a number of 74 premature newborn with diagnosis of urinary infections hospitalized in the Premature Department of Clinical Emergency Hospital for Children „L. Ţurcanu" in 2007-2010.

The lot includes:

- newborns with gestational age < 37 weeks; birth weight < 2500 g;
- acute suffering at birth IA=7;
- maternal infectious ci:rcumstances;
- clinical picture relevant for a toxico-septic status;
- paraclinic investigations.

Results and discussions: The urinary infections appeared at premature with birth weight: 2000-2500g, from birth with pathologic evolution. Clinical signs, associated with positive uroculture, were: alteration of general status:-18%, gastro-intestinal phenomena:-42%, neurological manifestations:-72%, dehydration syndrome:-8%, intense jaundice:-30%.

Paraclinic investigations were urine exams that raised the suspicion of urinary infection, confirmed by positive uroculture. The distribution of pathogen germs from uroculture was: E. Coli-86%, Enterobacter-8%, Proteus-6%.

Radiological examination were done at 5 cases (urography confirming 3 cases of congenital hydronephrosis), and ultrasound were done at 16 cases.

Conclusions:

1. urinary infection is more present at premature of 1st degree, female, with Apgar score< 8, from urban environment.
2. the most incriminated pathogen germ is E.coli, followed by Enterobacter and Proteus.
3. the most frequent clinical signs were alteration of general status, gastro-intestinal affections, neurological manifestations, dehydration syndrome, intense jaundice.
4. Ultrasound and urography bring information regarding malformative terrain.
5. 84% of cases had a favorable evolution towards healing and only 16%, raised on malformative terrain, had a stagnation in evolution.

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NEUROSONOSCOPHY AS A DIAGNOSTIC METHOD OF PURULENT MENINGITIS IN NEWBORNS DURING SPINA BIFIDA

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Background and aims: Lumbar puncture is a gold standat of diagnostic Purulent Meningitis.During spina bifida lumbar puncture of spinal cord isn't possible.The aim ofthis work is echographic diagnosis of Purulent meningitis during spina bifida by the Neurosonoscophy.

Methods: Neurosonoscophy and ventricular punction was done from the great fontanella , was staded C-reactive protein (CRP), procalcitonini (PC) in blood, bacteriological culture cerebro-spinal fluid (CSF) and blood in 71 1-2 weeks ages newborns with spina bifida.Was chosen 2 groips 1)29 newborns with meningitis, 2)42 newborns without meningitis.

Results: In the 1st group by Neurosonoscophy was echosymptomatic findings of ventriculitis, all this patient have in the CSF high albumin and citosis-neitrophilosis.Levels of CRP and PC was increased.In the 2nd group Neurosonoscophy findings and CSF analisis was normal.

Conclusions: During Spina bifida, Nurosonoscophy is a good method for diagnosis meningitis with ventriculitis in the early stage of deseases, whan patient doesn't have clinical sings of meningitis.

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VARIATION IN GENTAMICIN AND VANCOMYCIN DOSAGE AND MONITORING IN UK NEONATAL UNITS

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Background: Gentamicin and vancomycin are commonly used in neonatal units for the treatment of life threatening infections. The aim of this study was to describe dosage regimen and approach to therapeutic drug monitoring (TDM) for both antibiotics in units that participate in a UK neonatal network.

Method: Questionnaires were sent to all units across the Extended Neonatal Network (ENN) requesting details of the units dosing, regimen and TDM practice.

Results: 43 (of 114) units replied to the gentamicin and 29 to the vancomycin questionnaires respectively. In total, 10 different gentamicin dosing regimens were used which varied depending on gestational age and weight. Most units (79%) followed British National Formulary for Children (BNFc) dosing guidance regarding vancomycin but there were 9 variations in TDM practice across units.

Conclusions: Standardised dosing regimens and TDM guidance for gentamicin and vancomycin are required to minimise medication errors and optimise efficacy.

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PRELIMINARY ASSESMENT OF THE EFFECTIVENESS OF HEPATITIS B PREVENTION IN CHILDREN WITH MATERNAL EXPOSURE

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Background and aims: In Poland, young women are 10 to 20 times more likely to have been exposed to HBV in early childhood. We have evaluated of the effectiveness of prevention HBV infection in children of women HBsAg positive.

Methods: 67 children (32 girls) of mothers HBsAg-positive from which 20 were infected during childhood. In the other 47 HBV was detected not later than in pregnancy. None of them had acute hepatitis B. HBV DNA was detect in 20 (12 copies/ml to over 580million copies/ml), HBe antigen in 3. Three out of 67 were treated in childhood(interferon, lamivudine or encorton).67 children were vaccinated against hepatitis-B in the first day of life, 59 of them with HBIG.

Results: HBV DNA was detected only once in 9 children:7 between the 2nd and 4th month of life, 1 in the 6th and 1 in the 5th. The last patient was diagnosed with acute hepatitis-B.HBs antigen was found in 1 child (1.5%) with acute viral hepatitis; HBe antigen in 3: 1 with acute hepatitis-B, 1 in the 2nd month of life and 1 in the 2nd and 3rd month. In neither of the last two children HBV infections were confirmed nor HBV DNA in further studies .66 children (98.5%) produced Anti HBs: 3 to 10 IU/L and 6 above1000 IU /L

Conclusions:

1. Prevention of hepatitis B in children from maternal exposure is effective.

2. Maternal transmission of HBV infection is possible despite using prophylaxis, although the risk is low.

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WHEN SHOULD WE SUSPECT CONGENITAL TOXOPLASMOSIS? ANALYSIS OF CASES HOSPITALIZED IN OUR DEPARTMENT AND SYSTEMATIC LITERATURE REVIEW

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Congenital toxoplasmosis when not treated, can result in permanent sequelae therefore early diagnosis is extremely important.

The aim of the study: Summing up our experiences with concentration on clinical symptoms suggesting congenital toxoplasmosis.

Material: 19 patients aged from 5 days to 3 years (including 10 girls) diagnosed in department (2000-2011). Symptoms of congenital toxoplasmosis were: embryonic hypotrophy (5/19), congenital pneumonia (4/19), premature birth (3/19). In 11/19 patients hydrocephalus or ventricular dilatation, in 9/19 calcifications of the brain, in 6/19 hepatosplenomegaly were observed. In 9/19 children active chorioretinitis or postinflammatory retinal scars were visible. Less often symptoms included: anemia, thrombocytopenia, cholestasis, myocarditis, hyperbilirubinemia and microcephaly.

Methods: Review of articles published in English (1960-2010) found in Pubmed with key words: “congenital toxoplasmosis”. Search gave 410 publications. Articles were rated and 27 publications were selected to data synthesis.

Data analysis: Congenital toxoplasmosis occurs in 3-11/100.000 newborns. The majority of newborns are asymptomatic and symptoms of infection appear later, therefore screening during pregnancy and neonatal period is justified. Congenital toxoplasmosis leads to premature delivery in about 40% of infected pregnancies. 2%-8% newborns of mothers infected during pregnancy are born with severe symptoms. Most frequent symptoms are: prematurity, low birth weight, growth retardation, hepatosplenomegaly, jaundice, exanthema, visual problems, muscular hypertonia, pareses, abnormal brain on imaging.

Conclusions: We should consider screening all pregnant women in Poland. Symptoms which should arouse suspicion are: premature birth, low birth weight, jaundice, exanthema at the birth, ophthalmic symptoms, the abnormal brain on imaging (calcifications, the ventricular dilatations) and hepatosplenomegaly.

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WHEN SHOULD WE SUSPECT CONGENITAL CYTOMEGALOVIRUS INFECTION? ANALYSIS OF CASES HOSPITALIZED AT ONE CENTER DURING A 5-YEAR PERIOD

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Congenital cytomegalovirus infection is a major cause of neurologic impairment in children, including hearing and sight impairment and mental retardation.

The purpose of this study was to summarize our own experience in identifying symptoms present in the newborn that suggest congenital CMV infection.

Material and methods: 41 infants (including 22 girls) aged 1 to 16 months (3.5 months average) referred to our department with of congenital cytomegaly suspected from 1999 to 2003.

Results: 26/41 (63,4%) children with congenital CMV infection were identified by means of PCR method. The most common symptoms in children referred to the hospital aiming to screen for the presence of congenital CMV infection were elevated aminotransferases (26/41, 63,4%), anemia (21/41, 51,2%), jaundice (51,2%) and hepatomegaly (20/41, 48,8%). Of the 26 infants with confirmed infection, 17 (65,4%) had elevated aminotransferases, 16 (61,5%), had neurologic abnormalities and 12 (46,1%) hepatomegaly. 14 (53,8%) out of 26 had intracranial calcifications. The presence of petechiae (4/26, 15,4%), microcephaly (3/26, 11,5%), decreased muscle tone (3/26, 11,5%), chorioretinitis (2/26, 7,7%) and thrombocytopenia (1/26, 3,8%) were observed only in children congenitally infected with CMV. Of the 26 neonates with symptomatic CMV disease, 21 (80,8%) were treated with intravenous ganciclovir.

Conclusion: The knowledge about congenital CMV infection should be widespread in medical community. Neonates presenting with elevated liver enzymes, neurological symptoms, cerebral calcifications, hepatomegaly, petechiae, thrombocytopenia and sight anomalies should have excluded congenital CMV infection. Microcephaly, chorioretinitis, petechiae and decreased muscle tone are typical symptoms of congenital CMV infection and highly predictive.

P205

A CASE OF CONGENITAL CEREBRAL TOXOPLASMOSIS RESULTING IN OBSTRUCTIVE HYDROCEPHALUS, MYOCARDITIS AND NEONATAL DEATH

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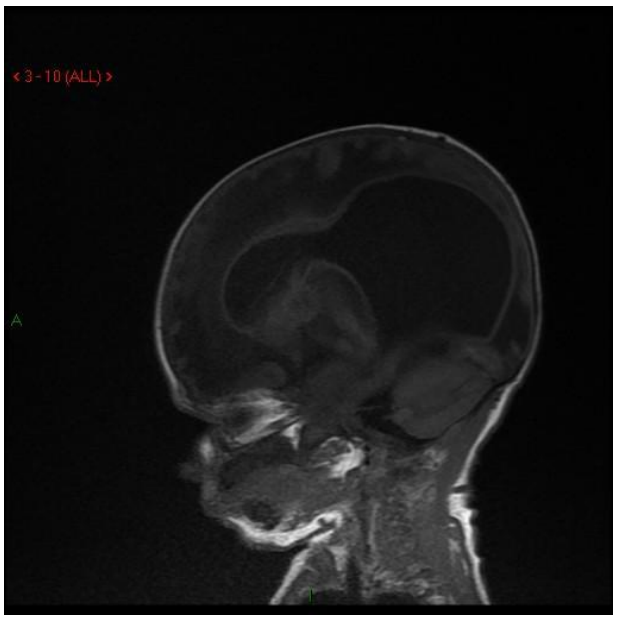
A term neonate was born following surgery for maternal hydronephrosis and subsequent abnormal CTG. Scans at 37 weeks reported a cystic area distorting the falx line with an atrophic cerebral hemisphere and absent cerebellum and cavum septum.

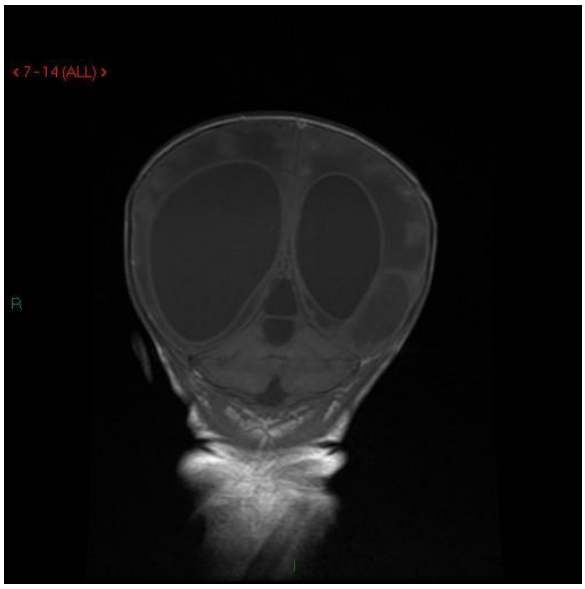
Cranial ultrasound on day 1 showed left unilateral ventriculomegaly with loss of brain parenchyma thought to be a parenchymal cyst. OFC was 32.5cm (2nd centile).

At 3 weeks, a MRI showed multi cystic encephalomalacia and obstructive hydrocephalus secondary to periventricular haemorrhage. OFC was 40cm (99th centile). At 4 weeks he presented to the GP with poor feeding, lethargy and increasing OFC, now 41.3cm (>99th centile). He was noted to be floppy with poor sucking and weak cry. He had a bulging fontanelle and pupils were constricted and poorly reactive. There was seizure activity in the form of facial twitching and bloods revealed hyponatraemia of 120 mmol/l. He received a 3% saline bolus, was mechanically ventilated and transferred to a tertiary PICU.

A CT showed hugely dilated ventricles with abnormal parenchyma with periventricular calcifications. Pupils were non reactive and ophthalmology review suggested retinitis. He became tachycardic and hypotensive despite ionotropes and received a therapeutic ventricular tap. The baby remained hypotensive and subsequently died. Mother´s blood subsequently was positive for toxoplasma IgM, dye test was positive to 4000 IU/ml. At post mortem the cause of death was found to be toxoplasma myocarditis.



[Growth Chart]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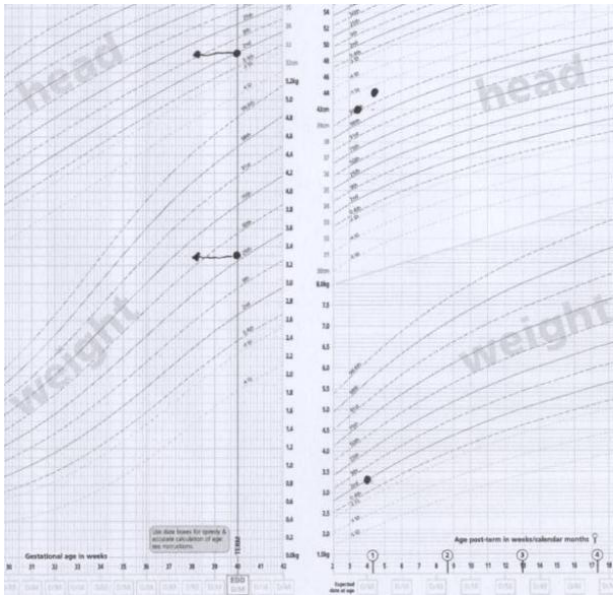
[MRI 2]


head
weight
head
weight
Gestational age in weeks
Age post-term in weeks/calendar months

P206

RIFAMPICIN PHARMACOKINETICS IN AN EXTREMELY PREMATURE LOW BIRTHWEIGHT INFANT WITH CONGENITAL TUBERCULOSIS

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Little evidence is available on pharmacokinetics of antitubercular medication in extremely premature, low-birthweight infants. We report rifampicin pharmacokinetics in a premature infant with congenital tuberculosis. Area under the curve calculations revealed low average rifampicin concentrations at doses of 5mg/kg and 10mg/kg. Evidence from this case suggests 10mg/kg is the minimum dose required.

P207

ETIOLOGY OF BACTERIAL INFECTIOUS DISEASES IN FULL-TERM NEWBORN INFANTS

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Background and aims: Infections are a frequent and important cause of morbidity and mortality in the neonatal period.Newborn infant have quantitativly and qualitativly “imaparied” immunologic system and are less capable of responding to infections. The purpose in this retrospective study was to identifications the bacterial microorganisms caused neonatal infectious diseases in full-term newborns hospitalized in the Center of Neonatology ,during the period of 2002 ,2003 and 2004.

Methods: We used clinical, microbiological, laboratory and radiology methods.

Results: 2086 newborn infants were treated at the Center of Neonatology in Podgorica during the period 2002-2004. 1391 were full term newborn(TNB) and 682 preterm newborn (PTNB).In 626 of all them were proven infections,528 TNB and 98 PTNB.

In 528 TNB were proven infections diseases.Most frequent infection diseases were; omphalitis (44,9%), pneumonia(18,5%), sepsis and/or meningitis (10,9%), cutaneus infections(8,7%), ITU (5,3%), conjunctivitis (5,5%), otitis media (3,8%), mastitis (1,7%) and diarrhea (0,7%). Dominant pathogens in all infections diseases were *Staphylococcus spp.* and *E.coli.* The bacterial agents responsible for sepsis and/or meningitis were: *Staphylococcus aureus* (19%), *Coagulase-Negative Staphylococcus* (41,3%), then with equale incidence SGB, *Streptococcus alfa hemolyticus group A , Streptococcus pneumoniae, Enterococcus and L.Monocytogenes* (1,7%), from Gram negative group *E.coli* is dominant bacterial agents (5,3%) then *Klebsiella pneumoniae , Acinetobacter, Serratia marscensens, Pseudomonas and Klebsiela/Enterobacter (each one 1,7%).*

Conclusions: 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 infections.

P208

GENOTYPE DISTRIBUTION OF CONGENITAL AND POSTNATAL CYTOMEGALOVRIUS (CMV) INFECTIONS IN NEWBORNS

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Background aims and background: Cytomegalovirus (CMV) is the leading cause of congenital infection, with morbidity and mortality at birth and sequelae. Moreover CMV is the most important cause of postnatal infection among preterm infants. The aim of this study is to investigate CMV genotype distribution involved in congenital and postnatal CMV infection.

Methods: 60 postnatally infected infants and 13 infants with congenital CMV infection were included in this study. Genotyping was performed upon amplification and sequencing of the UL55 (gB) and UL144 genes of CMV.

Results: The viral load in the urine samples ranged from $1.55*10^2$ to $4.48*10^8$ copies/ml (median $4.43*10^5$ copies/ml). Genotyping was successful in 70 of 73 patients (95.9%) for both UL55 and UL144. The distribution of UL55 and UL144 genotypes is shown in table 1.

Genotype UL55	1	2	3	4	5	Total
Congenital	6 (46.2%)	2 (15.4%)	3 (23.1%)	2 (15.4%)	0 (0.0%)	13 (18.6%)
Postnatal	26 (45.6%)	12 (21.1%)	11 (19.3%)	3 (5.3%)	5 (8.8%)	57 (81.4%)
Total	32 (45.7%)	14 (20.0%)	14 (20.0%)	5 (7.1%)	5 (7.1%)	70 (100%)

Genotype UL144	1A	1B	1C	2	3	Total
Congenital	4 (30.8%)	1 (7.7%)	0 (0.0%)	3 (23.1%)	5 (38.5%)	13 (18.6%)
Postnatal	10 (17.5%)	2 (3.5%)	1 (1.8%)	19 (33.3%)	25 (43.9%)	57 (81.4%)
Total	14 (20.0%)	3 (4.3%)	1 (1.4%)	22 (31.4%)	30 (42.9%)	70 (100%)

[Table 1. CMV genotype distribution]

All genotypes were represented in our patient population, except for UL55 genotype 5 and UL144 genotype 1C in congenitally infected patients. Congenital and postnatal genotype distributions were largely similar. However, UL144 genotype 1A was more prominent in congenitally infected patients compared to postnatal infections.

Conclusions: Congenital and postnatal CMV infections were conferred by various genotypes. CMV infections were mainly caused by UL55 genotype 1 and UL144 genotypes 2 and 3. Further research is warranted to investigate whether CMV genotypes can be correlated to viral load, clinical symptoms, and/or severity of disease.

P209

EXTREME PREMATURITY - INFECTIOUS COMPLICATIONS

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Introduction: Premature with extremely low birth weight represents a premature with birth weight< 1000g.

Objectives: Authors demonstrate the increased incidence of infections at a lot of premature newborns with extremely low birth weight and existing risk factors.

Material and method: The study was done in the Premature and Neonatology Department of Children Emergency Hospital ”L. Turcanu”, on 98 premature newborns with extremely low birth weight hospitalized in 2006-2010.

Results and discussions: At the studied lot we found 86(87,75%) cases with different forms of infections. Out of these 45(52,32%) presented early onset in the first 3 days of life, 41(47,67%) presenting infection with late onset. Among the risk factors of neonatal early sepsis maternal infection is decisive(45,70%). For late neonatal sepsis existing risk factors are: immaturity of the means against infections at premature, usage of invasive care techniques, long hospitalization.

Depending of hemoculture results we split systemic infection in 3 groups:

Septicemia with germ identified in the hemoculture with present clinical and biological context, 33 cases(38,37 %), septicemia with germ unidentified in the hemoculture or in septic origins where the clinical and biological context is obvious:34 cases(39,53 %), septicemia with germ identified in other origins where clinical and biological aspects are present, hemoculture negative, 19 cases(22,89 %).

Conclusions: Infection is an important factor of morbidity and mortality at the newborn with extreme low birth weight. The incidence is increasing a lot at this newborn category (300/1000 newborns with extreme prematurity) due to long hospitalization and intensive care maneuvers.

P210

ROLE OF C-REACTIVE PROTEIN, LEUCOCYTE AND NEUTROPHIL COUNT IN DETECTING EARLY ONSET NEONATAL GROUP B-STREPTOCOCCAL SEPSIS

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Background: Group B-streptococcus (GBS) remains the most common causative organism in early onset sepsis(EONS). Early detection and treatment are essential for successful management. When EONS is suspected, the current practice is that a septic screen is performed, including blood culture (BC), C-reactive protein (CRP) and full blood count (FBC) followed by treatment with benzylpenicillin/gentamicin. This study aimed to evaluate the role of CRP and FBC as part of a screening for EONS.

Methods: 813 infants born in 2009 with negative BC performed in the first 48 hours of life were identified, from which 236 cases were randomly selected as a control group. White cell counts (WCC), neutrophil counts (NC) and CRP were recorded. Results were compared those in infants diagnosed with GBS-EONS born between 01/2006 and 12/2010. Differences between control and EONS groups were tested with the MANN-Whitney U-test. Sensitivity was calculated for WCC, NC, initial/repeated CRP.

Results: There were 22 cases of confirmed GBS-EONS. Control groups for CRP, and WCC/NC comprised 210 and 215 records, respectively. Sensitivity of initial CRP was 29% in confirmed GBS-EONS. Although not routinely tested during following days, CRP sensitivity was 100% where tested. WCC ($p \leq 0.0026$) and NC ($p \leq 0.0021$) were significantly lower in EONS compared to control group.

Conclusions: CRP tested at the time of initial septic screen is a poor indicator of GBS-EONS, and although CRP tested the following day show high sensitivity/negative predictive value, most infants only have CRP tested at the time of septic screen. CRP should not be included in the routine screening process.

P211

NEONATAL BLOODSTREAM INFECTIONS: A REVIEW OF ANTIBIOTIC TREATMENT DECISIONS AND TIMELINES

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Background and aims: Delays to effective treatment in neonatal sepsis are associated with adverse outcomes. Our aim was to study the information cues leading to changes to antibiotic treatment and measure time intervals as far as introduction of definitive treatment for the episode, to look for any associations with delayed treatment.

Methods: A retrospective chart review of 79 episodes was carried out.

Results: Documentation of results and treatment changes was adequate in most cases.

In 53% cases, at least one regimen change was required from that commenced on day 1. Overall, mean time to definitive treatment was 28 hours (range 0-80 hours).

Excluding episodes of coagulase-negative staphylococcal (CONS) sepsis, the mean time to definitive antibiotic treatment was 23 hours, and there was no significant difference between gram-positive and gram-negative infections. In this group, there was a linear association between the number of information cues available from the microbiology laboratory and the probability of introduction of definitive treatment (r^2 =0.972).

80% of CONS species cultured were resistant to Flucloxacillin. For this reason, mean time to definitive treatment was longer in this group (42 hours).

Conclusions: Despite national microbiological data for neonatal sepsis suggesting a high level of sensitivity to empirical regimens, many episodes of sepsis are treated with two or more antibiotic regimens.

Diagnostic tests providing accurate early information are likely to improve sepsis management, allowing earlier introduction of effective antibiotics.

Awareness of local patterns of sensitivity can improve management.

P212

CMV IGG LEVELS IN PRETERM INFANTS AND THEIR MOTHERS AND RISK OF POSTNATAL CMV TRANSMISSION

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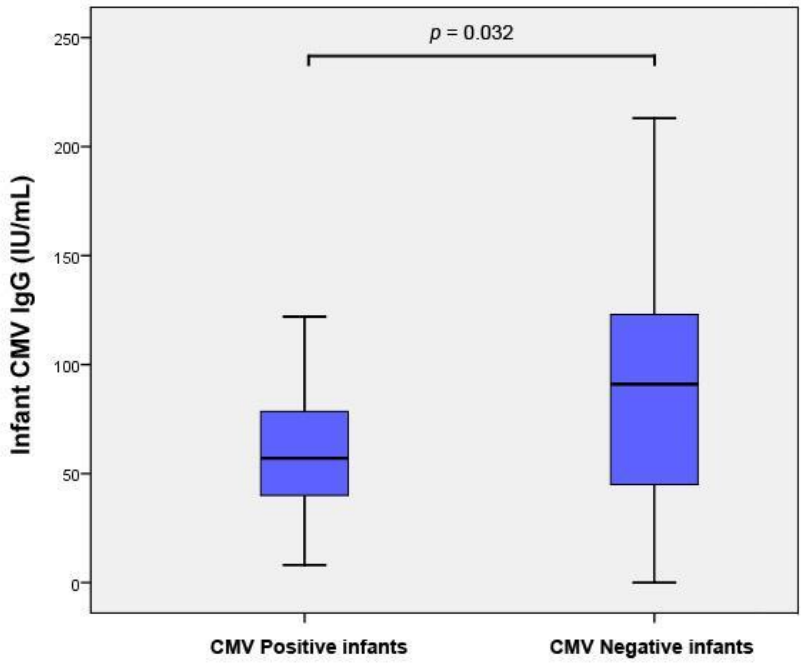
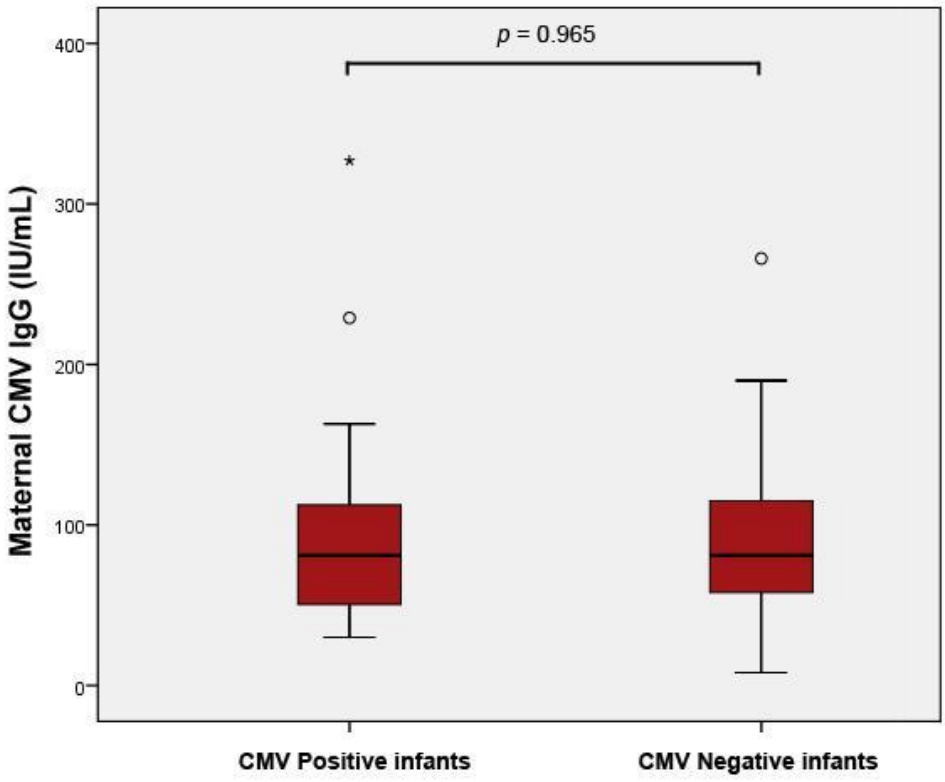
Background and aims: CMV infection is the most common postnatally acquired viral infection among preterm infants. The aim of this study was to assess the correlation between maternal and preterm infant CMV IgG levels and risk of postnatal CMV transmission.

Methods: CMV seropositive mothers and their preterm infants with GA ≤ 32wks were included from April 2003 to July 2009. Blood samples were taken from infants and mothers within 3 days post partum and analyzed for CMV IgG antibodies by enzyme immunoassay (VIDAS). CMV PCR in urine of infants was performed at term-equivalent age to determine postnatal infection. Congenital infection was excluded. Statistical analysis of clinical characteristics of infants (GA, BW) and their mothers (age, ethnicity) was performed. CMV IgG levels in CMV positive and negative infants and their mothers were compared.

Results: CMV IgG was determined in 62 CMV seropositive mothers of 35 infected and 27 non-infected preterm infants. In addition, CMV IgG levels were analyzed in 28 CMV positive and 21 negative infants. Maternal characteristics were not different. GA was significantly lower in CMV infected infants (p=0.01). CMV IgG levels in mothers and infants are shown in graphs.



[Maternal CMV IgG]



[Infants CMV IgG]

Conclusions: Maternal CMV IgG level post partum does not correlate with risk of mother-to-child CMV transmission among preterm infants. Preterm infants with lower gestational age and lower CMV IgG level at birth are at higher risk of postnatal CMV infection.

P213

NEONATAL *FUSARIUM* INFECTION: AN UNCOMMON PATHOGEN

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Among mould infections, *Fusarium* spp. has been increasingly reported in immunocompromised children but not in neonates.

We report the case of an invasive organ *Fusarium* infection in a neonate with esophageal atresia(EA) and tracheoesophageal fisula (TEF).

A 36 week premature neonate had EA and TEF repair on day 3. Malposition of the Rt pulmonary vein complicated surgery and lobectomy of the Rt lower lobe was performed. The post operative course was further complicated by anastomotic leakage, recurrence of the TEF and respiratory complications secondary to aspiration and recurrent pneumonia. Pleural fluid, rhinopharyngeal secretions and chest drain tip cultures grew *Fusarium Complex Solani* sensitive only to Voriconazole. At the time hospital renovation work was undertaken in close proximity to the NICU and although air sampling and other environmental cultures supplied no direct evidence of contamination, it is possible that opening of doors or windows might have allowed the influx of spores from the environment. Additional risk factors might have been the presence of skin breakdown and foreign bodies (chest drains). The patient was treated with voriconazole for 3 weeks with marked clinical improvement.

Emerging fungal infections in neonates are increasingly appearing and reflect the growing population of immunocompromised patients and those recovering from major surgery, as well as changes in treatment strategies such as the use of antifungal prophylaxis. Early suspicion and recognition of uncommon mould infections is of paramount importance and potential hazards of construction works in or adjacent to critical care areas should also be taken into account.

P214

C-REACTIVE PROTEIN AND CBC - THEIR IMPORTANCE IN THE DIAGNOSIS OF MATERNOFETAL INFECTIONS IN TERM AND NEAR-TERM NEWBORNS

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Background and aims: Maternofetal infections are still representing a significant pathology in the neonatal period even in term newborns. Prompt diagnosis and treatment are essential for a good prognosis. According to the data in the literature CRP and CBC have a limited value in the diagnosis of these conditions.

Methods: The study represents a retrospective analysis of maternofetal infection cases diagnosed in the Neonatology Dpt. Sibiu, between 01.01.2010 and 31.12.2010. Anthropometric, hematological parameters, CRP and APGAR score were the data analyzed using SPSS 10.0 for Windows.

Results: The study included 2587 term and near-term infants of whom 43 (1.66%) developed maternofetal infections of different etiologies. In comparison with the newborns with no significant perinatal pathology we have found significant differences only for immature granulocytes (7.76±6.25 vs 3.46±3.69, p=0.001), lymphocyte count (24.24±8.91 vs 29.36±11.33, p=0.019), CRP (50.67±46.86 vs 4.52±3.08), birth weight (3550.12±615.82 vs 3312.98±420.37), and APGAR score (8.14±2.29 vs 9.65±0.74) (p=0.000). No significant differences were found for the total number of leucocytes, mature granulocytes and platelets counts (p>0.05).

Conclusions: When more specific and sensible lab tests and rapid bacteriology tests are not available for a prompt diagnosis and treatment of maternofetal infections, CBC and CRP must be interpreted only in correlation with the clinical signs of infection, maternal and labor history.

P215

NEONATAL ADMISSION AND MORTALITY IN KANOMBE MILITARY HOSPITAL IN RWANDA

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Introduction: Neonatal and Maternal conditions contribute 20-30% of the total burden of avoidable deaths globally. Africa's Neonatal mortality rate is the highest in the world at 40/1000 live births .The major causes of neonatal deaths are infections (31%), Asphyxia (26%) and prematurity (25%). In Rwanda neonatal mortality contributes 25% of infant mortality.

Aim: To identify causes and factors associated with Neonatal admissions and mortality.

Method: Case notes of all admitted neonates from January 2009 to December 2009 were retrospectively reviewed.

Results: A total of 558 neonates were admitted and the commonest causes of admission included neonatal infection 175/558 (31%), prematurity 149/558 (27%) and birth asphyxia 146/558 (26%). Birth asphyxia 28/87 (24%), prematurity 16/87(18%) and severe respiratory distress 13/87 (15%) were the common causes of mortality.The risk of mortality was highest in the first 72 hours of admission (RR: 12.0). Factors associated with neonatal mortality were; severe respiratory distress syndrome (HR=5.0), Low APGAR score < 5 at birth (HR=3.0) and birth asphyxia (HR=3.7).

Conclusion: The causes of neonatal morbidity and mortality were similar to reports from other low resource countries. They can be prevented through effective antenatal, supervised deliveries, appropriate care and early referral of sick neonates.Acknowledgment:The Neonatology staff at KMH.

P216

CONGENITAL RUBELLA SYNDROME: ARE WE GOING TO HAVE AN EPIDEMIC?

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Congenital Rubella Syndrome (CRS) is a trans-placentally acquired congenital Rubella infection which results in multiple organ involvement and protean manifestations including hepatitis, thrombocytopenia, blueberry muffin rash, deafness, eye lesions, cardiac lesions, microcephaly, and mental retardation. Thus it leads to permanent disability in an affected child. However, it is entirely preventable by immunising the mother against Rubella. Exact prevalence of CRS in India is not known, and we report three cases of CRS within a span of two months and feel that prevalence of CRS may be increasing.

All three babies were diagnosed in the first week of life. Growth retardation was seen in 3/3, skin rash in 2/3, microcephaly in 2/3, congenital heart disease in 3/3, buphthalmos in 1/3 and skeletal involvement in1/3. All had thrombocytopenia. Diagnosis was confirmed serologically in all three babies. One baby died at the age of 1.5 months due to congenital heart disease.

This increase in CRS seems to be due to the inconsistent immunisation policies implemented. Boys and girls aged 15 months have received the measles, mumps, and rubella vaccine without policies to attain high vaccination coverage and to protect adolescents and women of childbearing age. It has been stressed that such immunisation practices may lead to an increase in the occurrence of congenital rubella, but this phenomenon has not been previously reported. Vaccination coverage for rubella has remained low, and the proportion of pregnant women susceptible to rubella is gradually increasing, which will lead to paradoxical increase in CRS.

P217

VALUE OF ROUTINE CENTRAL VENOUS LINE TIP CULTURES AT CATHETER REMOVAL: PROSPECTIVE STUDY OF ASSOCIATED RATES OF COLONISATION AND SEPSIS

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Background and aims: Percutaneous central venous catheters(PCVCs) are routinely inserted in NICUs. Lines may become colonised and act as septic foci. We examined the bacteriology associated with PCVC tips at line removal, and associated rates of sepsis and colonisation.

Methods: Prospective study in two UK tertiary NICUs of all PCVCs indwelling for >24h removed during a 14-month period. After disinfecting the skin exit site, the PCVC was aseptically removed and the tip cultured using the Maki Roll technique.

Results: 189 lines were removed, from 142(75%) well and 47(25%) clinically-septic infants. Overall, 36/189(19%) PCVC line tips cultured positive, in 20/47(43%) clinically-septic babies versus 16/142(11%) well babies($p < 0.0001$, X^2 test)(table). 39/47(83%) clinically-septic infants were on antibiotics at line removal and only 23(49%) had a positive blood culture(BC). 7/24(29%) BC-negative septic babies had a positive PCVC tip growth (all coagulase-negative staphylococci).

	Clinically-Septic infants n=20	**Well/colonised infants n=16**
coagulase-negative Staphylococci(CoNS)	18(90)	16(100)
Enterobacter cloacae	1(5)	0(0)
coliforms	1†(5)	0(0)
enterococci	1(5)	0(0)
Data are n(%);†one tip grew both CoNS and a coliform		

[Bacteriology of culture-positive PCVC line tips]

Conclusions: Routine PCVC tip cultures provide a higher yield in babies with suspected sepsis than in well babies. Prior antibiotic treatment may decrease positive BC rates, yet a significant minority of BC-negative babies(29%) nevertheless have a positive PCVC tip culture. PCVC tip cultures may usefully inform the clinical management of septic babies.

P218

NEONATAL INFECTIOUS RISK, LOOKING FOR A C-REACTIVE PROTEIN CUT OFF

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Background and aims : Early onset sepsis is a very serious condition, with challenging timely diagnosis. It has subtle and non-specific clinical findings and a potentially rapid life threatening evolution.

Screening methods for babies at risk generally use C-Reactive Protein (CRP) levels and complete blood count.

Different Neonatal Department, use a wide spectrum of values of CRP (from 1 to 5 mg/dL) for the decision of starting antibiotic treatment.

The authors tried to define a cut-off for CRP value, that help to care all babies at risk, avoiding unnecessary treatment of uninfected newborns.

Methods : All the babies born with infectious risk (N=195) in St Mary Hospital during one year, were evaluated with blood culture, blood count and CRP at 24h of live.

All babies were followed and the infection was confirmed or not with the cultures, serial clinical and analytical evaluation.

Results : All the babies with CRP with less then 2, don't develop serious invasive disease, and this value normalized without antibiotic therapy. Those witch have a CRP higher than 2 have a positive hemoculture or develop clinical signs of infection with CRP elevation until the start of antibiotic therapy ($p< 0,001$).

Conclusions: The authors propose that in infectious risk the CRP at 24h should have a cut off value of 2. This value is the compromise that prevents serious infection and avoids unnecessary treatments.

P219

ASSOCIATION OF VANCOMYCIN AND RIFAMPIN FOR THE TREATMENT OF PERSISTENT COAGULASE-NEGATIVE STAPHYLOCOCCAL BACTEREMIA IN PREMATURE NEONATES

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Background and aims: Coagulase-negative staphylococci (CoNS) are the first cause of late-onset sepsis in premature neonates. The aim of our study was to analyze the efficacy and safety of vancomycin-rifampin association for the treatment of persistent CoNS bacteremia in premature neonates.

Methods: Single-centre retrospective study of cases of persistent CoNS bacteremia in premature neonates admitted at the Hospital-Clinic Maternidad, between April-2006 and December-2010, and treated with the association of vancomycin-rifampin. Risk factors, clinical presentation, laboratory findings, treatment and outcome were recorded in a case-report form. Persistent bacteremia was defined as 3 consecutive positive blood cultures at least 48 h apart or a new positive blood culture after 5 days of adequate antibiotic therapy.

Results: 8 cases were included according to definition. Median gestational age was 25.6 weeks (range 24.4-29.1), all cases had Very-Low-Birth-Weight (VLBW), median 680g. All cases were on parenteral nutrition, 7 had a Peripheral-Inserted-Central-Catheter and 1 an umbilical-venous-catheter, and two were on mechanical ventilation at the time of infection. The most frequent clinical presentations were respiratory impairment, global clinical worsening and hyperglycaemia. CoNS bacteremia was diagnosed at a median age of 8.5 days. All cases were initially treated with vancomycin plus amikacine. Despite vancomycin treatment with proven sensitivity and removal of all sources of infection, bacteremia persisted for a median of 14 days until rifampin initiation. Infection was resolved in all cases on vancomycin-rifampin with no serious side effects.

Conclusions: Vancomycin-rifampin association was effective and safe in VLBW neonates with persistent CoNS bacteremia despite adequate vancomycin therapy.

P220

PROPHYLACTIC PROBIOTICS TO PREVENT DEATH AND SEPSIS IN PRETERM INFANTS IN COLOMBIA

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Background: It has been suggested that probiotics may decrease infant mortality and nosocomial infections due to their hability to suppress bacterial translocation of pathogens in the gut.

Objective: We designed a large multicenter placebo controlled trial testing the use of Lactobacillus reuteri to decrease mortality and nosocomial infection in preterm infants ≤ 33 weeks gestation.

Methods: Prior parental consent, eligible infants were randomized during the first 48 hours of life to either daily probiotic administration or placebo. Infants in the intervention group were administered 5 drops of a probiotic preparation containing 10^8 CFU of lactobacillus reuteri DSM 17938 in the posterior oropharynx or through a nasogastric tube (with 0.5 cc of saline flush) until death or discharge from the NICU.The probiotic was temporarily stopped in infants with a diagnosis of necrotizing enterocolitis and re-started upon initiation of enteral feeds.

Results: A total of 501 infants were included in this interim analysis. A total of 253 infants were randomized in the probiotic group and 248 infants in the control group. Death or sepsis was 15.8% and 19.3% respectively (RR: 0.81, 95% CI : 0.55-1.19); necrotizing enterocolitis was 2.4% and 3.6% (RR: 0.65, 95% CI: 0.65-1.8). Death decreased significantly in both groups compared to historical data (5.9% and 6.8%).

Conclusion: Although we found a higher rate of adverse outcomes in the placebo group, these differences were not statistically significant, No case of sepsis secondary to Lactobacillus reuteri were identified. Randomization of patients has stopped.

P221

THE RELATIONSHIP BETWEEN NEONATAL INFECTION AND INTRAPARTUM MATERNAL FEVER AFTER EPIDURAL ANALGESIA

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Introduction: The relationship between intrapartum maternal epidural analgesia, maternal fever and neonatal serious bacterial infection (SBI) remains controversial.

Objective: To compare the prevalence of neonatal infection between women with intrapartum fever following intrapartum epidural analgesia and women with intrapartum fever without intrapartum epidural analgesia.

Methods: Retrospective cohort study in neonates ≥35 weeks gestational age admitted to the neonatal unit of St. Elisabeth hospital Tilburg, The Netherlands with intrapartum maternal fever (≥38.0°C).

Results: A total of 189 neonates of 185 mothers were included. Of these 185 mothers, 126 (68.1%) received epidural analgesia and 59 (31.9%) did not. Suspected neonatal infection occurred in 7.0% of mothers who received epidural analgesia and in 9.8% of women who did not. Neonates with suspected infection had significantly lower Apgar scores, higher heart and respiratory rates and more often elevated C-reactive protein than uninfected neonates. Neonates of mothers with high grade fever had significantly more symptoms of infection at birth and were significantly more likely to have symptoms of SBI than neonates of mothers with low grade fever.

Conclusion: The prevalence of neonatal infection did not differ between neonates of mothers with intrapartum fever following epidural analgesia and neonates of mothers with fever without intrapartum epidural analgesia. This calls for continued vigilance of the clinician in the evaluation of neonates of women with intrapartum fever following epidural analgesia.

P222

LOOKING FOR CENTRAL NERVOUS SYSTEM INVOLVEMENT IN CONGENITAL CYTOMEGALOVIRUS INFECTION: IS LUMBAR PUNCTURE NECESSARY?

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Background and aim: Neuroimaging studies, including cranial ultrasound, cranial computerized tomography and/or magnetic resonance imaging, audiologic evaluation and funduscopy are well accepted non-invasive investigations for central nervous system (CNS) involvement in patients with congenital cytomegalovirus (CMV) infection. However, clinicians may have to deal with refusal when lumbar puncture for detection of CMV DNA in cerebrospinal fluid (CSF) is discussed with parents. Therefore we wanted to look whether CMV polymerase chain reaction (PCR) on CSF had been useful until now in determining CNS involvement in newborns with congenital CMV infection in whom neuroimaging and sensorineural examinations had been performed.

Methods: We retrospectively reviewed charts of 34 newborns referred to our tertiary centre who had CSF prelevation for CMV PCR in the working-out of their congenital CMV infection. Results of CSF PCR, funduscopy, brainstem evoked response audiometry (BERA) and cerebral imaging (ultrasound and/or computerized tomograpy scan and/or magnetic resonance imaging) were collected.

Results: 7 patients (21 %) showed positive CMV PCR on CSF. In 6 of them one or more abnormalities were found on neuroimaging (6/6) and/or BERA (2/6). In 1 baby classified as no signs of CNS involvement and positive CSF PCR, neurologic working-out had been limited to brain ultrasound and BERA only, while lumbar puncture had been traumatic.

Conclusion: CSF PCR is not likely to contribute to the diagnosis of CNS localization of congenital CMV infection at birth. The less invasive neuroimaging and sensorineural investigations seem sufficient to determine whether or not there is CNS manifestation of the disease.

P223

THE SEVERE CIRCULATORY COLLAPSE WITH GAS EMBOLISM CAUSED BY ESBL KLEBSIELLA PNEUMONIAE IN EXTREMELY LOW BIRTH WEIGHT INFANT

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Background: The extended-spectrum beta-lactamase *Klebsiella pneumoniae* (ESBL-*KP*) is a one of gram-negative cause of nosocomial infection with a serious impact on survival of extremely prematutre infants.

Methods: Thirty two year old pregnant woman with the PPROM and laboratory signs of chorioamnionitis was treated by antibiotics. A female newborn weighing of 870g was born at 25+6 weeks. The postnatal adaptation was uncomplicated. The umbilical venous catheter was inserted subdiaphragmaticaly. On the 3rd day of life (DOL) ESBL-*KP* was cultured from conjunctival swab. A recurrent apnea with intermittent bradycardia was progressively developing on the 5^{th} DOL. Ten hours later the sudden circulatory collapse developed with progressive lactic acidosis. The echocardiographic examination found a poor filling of left ventricle and a dilated right heart with the sign of “snowing”. The mechanical ventilation was started immediately and volume-expanders, epinephrine and bicarbonate were administered repeatedly without any positive response. The complete cardiopulmonary resuscitation was finished after two hours.

Results: The positive blood and pleural effusion culture of ESBL-*KP* was confirmed after the death. A gas containing cavity of 15 mm diameter closely to umbilical vein was discovered in a liver with the positive culture of the same strain. No ESBL-*KP* strain was found in mother's cultures.

Conclusion: The irreversible circulatory collapse with gas embolism caused by ESBL-KP is a rare pattern of gram-negative septic shock. The relation between iatrogenic venous endothelial damage caused by umbilical catheter and invasive ESBL-*KP* with gas production is speculated as the synergic cofactors of this pathogenetic pattern.

P224

NEONATAL INFECTIONS WITH CHILDREN OBSERVED IN DRACEVO AND ITS SURROUNDINGS

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[1]Children Health Department, Polyclinic Dracevo, [2]Pediatric Hospital - Polyclinic Dracevo, Skopje, FYR Macedonia

Introduction: At the Children´s Health Center Dracevo Skopje, all new-born babies in obstetrics as well as new-born babies delivered at homes of rural areas come to a routine check. Giving birth at home is a tradition in the regions of Crni Vrv, Elovo, Kolicani, Dracevica etc.

Aim: To make a comparison of the presence of infections with children delivered at home to those delivered in hospital conditions.

Methods: Statistical treatment of data obtained from medical records, journals of daily record. The following parameters are taken into consideration: The number of deliveries, the presence of skin infections, umbilical infections as well as septicaemia.

Results: The total number of children delivered in hospital in the period 2007-2010 is 1570, while the number of children delivered at home during the same period is 156. Of the new-born babies delivered in hospitals, 700 have suffered from a skin infection, 455 have suffered from an umbilical infection, and 27 have suffered from septicaemia. 45 new-born babies have suffered from a skin infection, umbilical infection has affected 35, and septicaemia has affected 25 of the new-born babies delivered in domestic environment.

Conclusions: The infections during the neonatal period are not uncommon. The skin and umbilical infections are equally frequent when giving birth in a hospital as they are when giving birth in domestic environment. However, sepicaemia with an unsatisfactory outcome is frequent when giving birth in domestic environments, following the traditional manner, without any competent help and in poor sanitary conditions.

P225

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P226

CANDIDEMIA AND RETINOPATHY OF PREMATURITY AMONG VERY LOW BIRTH WEIGHT MECHANICALLY VENTILATED INFANTS

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Background: Retinopathy of Prematurity (ROP) is a serious condition that leads to a long life disability. It is common among the Very Low Birth Weight (VLBW) infants especially when exposed to mechanical Ventilation.

Aim: To study the association of Candidemia with the development of ROP in VLBW exposed to mechanical ventilation.

Subjects: Sixty VLBW with gestational age < 32 weeks and birth weight less than 1500gm exposed to mechanical ventilation. They were divided according to mode of feeding into 20 cases of exclusively infant milk formula fed (EFM), 20 cases of exclusively breast milk fed (EBM) infants and 20 cases who receive both breast milk and infant milk formula (MIB).

Methods: Blood samples from all preterm were cultured periodically and babies were consequently assessed by fundus examination at 4-6 weeks and 2 weeks later. If signs of retinopathy developed they were assessed weekly.

Findings: Overall incidence of ROP was 35 (58%) of all cases studied. ROP incidence was 100% in babies who were positive for candida blood cultures infants. These cases were also deprived of breastmilk and progressed to stage IV and V ROP (9%).

Conclusions: Exposure to mechanical ventilation increases the incidence of candidiasis which in turn increases the incidence of ROP in VLBW. Infants fed on breastmilk have a greater chance of recovery from candidiasis compared to those fed on infant milk formula feeds. Expressed breastmilk feeds should be encouraged in all neonatal intensive care units as a preventive measure against development of invasive infections and progressive ROP.

P227

ILLNESS SEVERITY AT THE TIME GRAM NEGATIVE BACTERIA ARE ISOLATED FROM NEONATAL BLOOD CULTURE

H. Hill[1], T. Neal[2], E. Jacqz-Aigrain[3], **M. Turner**[1], TINN, Treat Infections in Neo Nates

[1]Women's and Chidren's Health, University of Liverpool, [2]Royal Liverpool University Hospital, Liverpool, UK, [3]Robert-Debré Hospital, University Hospital of Paris, Paris, France

Background: Randomised controlled trials of neonatal antibiotics need to account for illness severity at randomisation. However, there are few reports concerning illness severity when neonatal Gram Negative (GN) septicaemia is recognised.

Methods: GN isolates were identified from a routine lab database for a tertiary neonatal unit between 2004 and 2010. Clinical records were consulted to construct NTISS scores (Pediatrics 1992;90:561) at the time of isolation and two days before.

Results: NTISS scores were available in 79 neonates with GN isolates from blood cultures (E. coli 24, Pseudomonas 16, Enterobacter 16, Klebsiella 13, others 10). NTISS scores on the day a GN isolate was identified were median 20, IQR 14 - 25, max 34). NTISS was correlated to gestational age at birth ($r_s = -0.344$, $p < 0.005$) but was not associated with postnatal / postmenstrual age at culture, sex or the nature of the bacteria. Two days prior to the isolation of GN bacteria NTISS had median 14, IQR 11 - 18, max 28 (n=70). The change in NTISS over the two days had median 5, IQR 1 - 8, max 23. Five neonates had lower NTISS scores when positive blood cultures were recognised compared to two days before.

Discussion: NTISS scores can capture illness severity in septicaemic neonates. The NTISS scores two days before GN isolates were recognised suggest that neonates have underlying illness or delayed recognition of GN infection. Some may be improving when septicaemia is recognised. These findings are relevant to the design and analysis of clinical trials.

P228

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P229

SURVEY OF POSITIVE BLOOD CULTURES IN THE NEONATAL UNIT (NOVEMBER 2007 TO OCTOBER 2009)

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Aim: To analyse bacteraemias occurring in our neonatal unit from Nov 2007 to Oct 2009.

Introduction: We use empiric benzylpenicillin and gentamicin for early-onset sepsis, and flucloxacillin and gentamicin for late-onset sepsis. We change to vancomycin for coagulase-negative staphylococcus (CoNS) resistant to flucloxacillin, and a third-generation cephalosporin or meropenem for any Gram-negative isolate.

Methods: As part of service evaluation, we analysed the resistance profiles of isolates over 2 years. An infection episode was defined as one or more positive blood cultures caused by the same organism within a 14 day period.

Results: We had 195 positive blood cultures relating to 154 infection episodes. Of these 154 episodes, 35(23%) were early onset bacteraemia (< 48 hours) and 119 (77%) late onset (>48 hours) bacteraemia.

Of the early onset infections, 20% were due to group B streptococcus, 3% enterococcus, 3% *Staphylococcus aureus* and 3% *Streptococcus viridans.* All organisms were sensitive to either penicillin or gentamicin. The other cultures were likely contaminants: 54% coagulase negative staphylococcus, and 17% micrococcus, diphtheroids or Brevundimonas.

Of the late onset infections, 76% were due to CoNS, 10% Gram negative bacteria (n=12), 5% *Staphyloccus aureus* (n=6, including 2 MRSA), 4% group B streptococcus, and 2.5% Candida. Of the late-onset organisms, 2 MRSA and 3 Gram-negative bacilli were not sensitive to first-line antibiotics. All were sensitive to 2nd-line antibiotics.

Conclusion: Our current empiric antibiotic regimens cover most organisms causing bacteraemia. We have instituted strategies to reduce blood culture contamination.

P230

NEONATES EXHIBIT DECREASED T HELPER TYPE 17-MEDIATED INFLAMMATORY RESPONSES

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Background and aims: Neonates have deficient immunity, critical for host defence against pathogens. T helper type 17 cells (T_H17) lymphocytes produce the pro-inflammatory cytokine IL-17 and are critical for the protection against extracellular pathogens. IL-17 expression and the induction of Th17 lymphocytes have been hardly studied in neonates. In this study, we investigated: a) the expression of IL-17 in the serum of neonates, and b) IL-17 levels and the induction of Th17 lymphocytes following stimulation of neonatal leukocytes with inflammatory agents *ex vivo*.

Methods: Thirteen healthy preterm neonates [birth weight (BW): 1740g (1500-2200), gestational age (GA): 32,5wk (31-34)] and thirteen healthy term neonates [(BW: 2960g (2500-4310), GA: 37,5wk (37-39)] were studied. Six healthy adults were used as controls. Peripheral blood mononuclear cells (PBMCs) were stimulated *ex vivo* with endotoxin (LPS) or ConA. IL-17 in the serum and culture supernatants was measured by ELISA. Percentages of Th17 lymphocytes were examined by intracellular flow-cytometry staining.

Results: Serum IL-17 levels were significantly lower in preterm and term neonates compared to adults ($p < 0,001$). IL-17 was also significantly decreased in LPS and Con-A stimulated neonatal leukocytes ($p < 0,0042$). Percentages of Th17 lymphocytes among stimulated PBMCs were significantly lower in neonates ($p < 0,05$).

Conclusions: Our findings reveal dramatically decreased IL-17 release in the serum of neonates. We also demonstrate that neonatal leukocytes mount decreased Th17 responses following stimulation with inflammatory stimuli. Collectively, our results suggest that deficient IL-17 release in neonates may hamper their host defence leading to overwhelming septicemia and death.

P231

DETERMINANTS OF CATHETER-ASSOCIATED BLOODSTREAM INFECTIONS IN NEONATAL INTENSIVE CARE

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Background and aims: To determine the prevalence and risk factors for catheter-associated bloodstream infections (CABSI) in infants admitted to the neonatal intensive care unit (NICU).

Methods: A retrospective study of infants admitted to the VU University Medical Center NICU in 2007 was conducted.

Results: 196 infants with a total of 369 central catheters and 2824 catheter days were included in this study. A mean CABSI rate of 18.1 infections per 1000 catheter-days (95% CI 13.7-23.8) was found. Risk factors for CABSI were: umbilical catheter dwell-time (r = .41), the use of umbilical venous catheters compared to central venous catheters (RR = 3.5, 95% CI 1.1-11.3) and peripherally inserted central venous catheters (RR = 2.3, 95% CI 1.2-4.6), gestational age less than 32 weeks (RR = 2.6, 95% CI 1.1-6.2) and being born small for gestational age (SGA) for those infants delivered between 32 and 36 weeks gestational age (RR = 4.7, 95% CI 1.2-18.9). Duration of parenteral nutrition and the administration of all-in-one feeding mixture versus parenteral nutrition administered in separate components were not related to CABSI risk.

Conclusions: This study showed that of all central catheter types the umbilical catheter carries the highest CABSI rate and longer umbilical catheter dwell-time increases CABSI risk. The data also suggest that the composition, way of preparation and duration of parenteral nutrition do not influence CABSI risk. In addition the impact of gestational age on CABSI was reconfirmed and SGA infants, born between 32 - 36 weeks, seem to be particularly vulnerable.

P232

EPIDEMIOLOGY OF INVASIVE CANDIDA INFECTION IN A NEONATAL INTENSIVE CARE UNIT IN FRANCE

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Background and aim: The epidemiology and prevention of invasive Candida infections (ICIs) depend largely on risk factors and the role they play in infection control and identifying high-risk patients for prevention. It is important to know local invasive fungal infection data in every neonatal unit to develop an appropriate prophylaxis strategy. We aimed to evaluate the incidence of ICIs in a neonatal intensive care unit (NICU) at the university medical center in Lyon, France.

Methods: We conducted a three-year, laboratory-based surveillance study among all neonates admitted to our NICU from January 1, 2007 to January 1, 2010.

Results: A total of 1,648 newborns, 497 of whom (30%) were under 32 weeks gestational age, were admitted to our neonatal unit. Only four cases of ICIs were identified. Three of these patients were treated with fluconazole. Sixty-nine infants were colonized with Candida albicans. Six of them were treated with fluconazole and one with econazole. Only Candida albicans was isolated and all cultures were sensitive to fluconazole.

Conclusion: The incidence of ICIs in our NICU is low (< 1%). The widespread use of antifungal prophylaxis is not necessary in these conditions. Further research is needed to the subgroup population at high risk of ICIs who may benefit antifungal prophylaxis. Long-term outcomes of neonates with ICIs should be evaluated.

This work is part of the TINN network, which is supported by the European Commission under the Health Cooperation Work Programme of the 7th Framework Programme (Grant agreement n° 223614).

P233

BROAD RANGE16 S RDNA PCR AS AN EARLY DIAGNOSTIC TOOL FOR NEONATAL SEPSIS

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Detection of microbial DNA rather than the microorganisms themselves is a new era has been introduced in diagnostic microbiology. It is suggested to represent a rapid, effective and sensitive method in diagnosing bacterial sepsis in neonates.

Aim of the study: To evaluate the role of PCR amplification of 16 S rRNA in diagnosis of neonatal sepsis and comparing the results of PCR with the blood culture.

Patients and methods: 58 newborn infant with suspected sepsis [41 with early onset sepsis (EOS) (< 7 days) and 17 with late onset sepsis (≥7 days)] were included in the present work. Concomitant blood culture and 16S rRNA gene PCR were done.

Results: Compared to blood culture, the diagnosis of bacterial sepsis in the newborn by PCR revealed 96.4% sensitivity, 66.6% specificity, 72.9% positive predictive value and 95.2% negative predictive value. The sensitivity, specificity, PPV, and NPV of PCR for the diagnosis of EOS were similar to those of late-onset sepsis. 16 mothers (39%) had received antibiotics within 72 hours before delivery and maternal antibiotic drug use did not alter the performance of PCR.

Conclusions: The benefit of PCR is its rapid availability of results with a high negative predictive value. As a tool to ´rule out neonatal sepsis´, PCR can be easily incorporated into the hospital setting. PCR seems to perform well in patients either with suspected EOS or LOS, irrespective of antibiotic drug use in the mother.

P234

PRELIMINARY RESULTS OF THE PERFORMANCE OF IP-10 IN CHILDREN AT HIGH RISK FOR TUBERCULOSIS INFECTION

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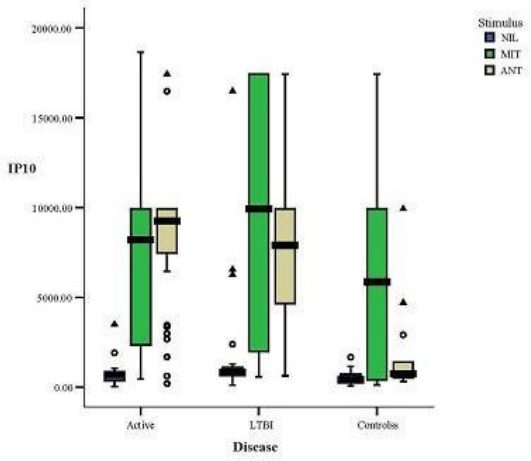
Background and Aims: The diagnosis of childhood tuberculosis (TB) remains complex. Recent, predominantly adult studies have presented the interferon-γ inducible protein 10 (IP-10) as a promising diagnostic biomarker for tuberculosis infection. This study aim to further explore the performance of CXCL10 in pediatric TB infection.
Methods: A study was conducted among 77 children (active disease n=33, LTBI n=27, controls n=17) at high risk of tuberculosis infection. IP-10 concentration was determined using ELISA, in supernatants from whole blood stimulated with Mycobacterium tuberculosis-specific antigens (ANT), mitogen (MIT) and negative control antigen (NIL) obtained from QFT-IT vaccutainer tubes.
Results: Results are illustrated in Figure 1. Stimulation with MIT (positive control) produced a significant increase in IP10 production in all the disease subgroups ($p< 0.01$ in all cases). Stimulation with TB specific antigen resulted in a significant increase in IP10 production in both active disease and LTBI groups but not in the control group (active vs. control $p< 0.001$; active vs. LTBI $p< 0.001$). No significant difference in IP-10 production after ANT stimulation was observed between active and latent infection.
Conclusion: Our results show high IP-10 responses to antigen-stimulated supernatants from children with TB infection, indicating the potential role of CXCL10 as an additional diagnostic TB biomarker. We believe that in combination with IGRAs it could be used to increase diagnostic accuracy in high risk children populations.

Figure 1



ANT; Mycobacterium tuberculosis-specific antigens, MIT; mitogen, NIL; negative control antigen

[Figure 1]

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Dr Virginia Amanatidou)

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COMPARISON OF SEROLOGICAL METHODS FOR DIAGNOSIS OF BRUCELLOSIS

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Brucellosis is one of the most prevalent infectious diseases in Iran. Clinical signs are not specific and laboratory methods are necessary for definite diagnosis. Isolation of microorganism from clinical samples is the most definitive methods,its succession depends on many factors that can not be used in all cases.Standard agglutination test (SAT) and recently Enzyme Linked Immunosorbant Assay (ELISA) are the most important serological tests for diagnosis of brucellosis.

Objective: In this study we compared these two diaghostic methods in patients suspected of brucellosis were appling to laboratory of Emam Khomeini hospital in Mianeh city in 2009-2010.

Materials and methods: In this descriptive study, all patients suspected of brucellosis who referred to Emam Khomeini hospital in Mianeh city from Sep 2009 to Aug 2010 were chosen regardless of age, sex and condition. Their sera were collected and tested by SAT, 2ME and Elisa. 1/80 titer in SAT consider as positive and 2 dilution difference between 2ME and SAT consider as positive IgM.

Results: Overall the sera of 361 patients 215(59%) female and 146(41%) male were tested for IgG and IgM antibodies against brucella. 57(15.8%) samples were positive for IgG + IgM with both SAT and Elisa methods. IgG detected in 141(39%) samples by Elisa method while 97(27%) samples were positive for IgG by SAT. Elisa detected IgM in 26(7.2%) samples while 2ME not able to detecte IgM in this samples.

Conclusion: Sensitive ELISA test for antibodies in the serum of patients that Wright and coombs Wright methods were not able to detect them, is recommended.

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DETECTION OF BRUCELLA BY SERUM PCR AND COMPARISON WITH SEROLOGICAL METHODS IN SUSPECTED CASES

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Background: Brucellosis is a zoonotic disease and specificity of the serology tests is not satisfactory and sensitivity of the culture is low, polymerase chain reaction (PCR) can be an alternative method in making the final decision in some doubtful cases.

Objective: In this study three diagnostic methods were compared in the suspected patients with brucellosis in the endemic area, Mianeh .

Methods: In this study, results of standard agglutination test (SAT), 2ME and specific immunoglobulin (Ig) G and IgM by enzyme-linked immunosorbent assay were compared with PCR results in 100 patients with brucellosis referred to the Imam Khomeini hospital, Mianeh, Iran. Their sera were collected and tested by SAT, 2ME, ELISA and PCR. DNA was extracted from serum samples and examined by PCR involving specific primers for *B. melitensis*, *B. abortus* and *B. suis* based on IS 711 in the brucella chromosome.

Results: PCR technique was applied to serum samples, 30 cases were positive for *B. melitensis* and we were able to isolate more cases compared SAT method and the difference was significant ($P< 0.05$). The sensitivity and specificity of PCR in this study were determined as 83.3% and 86.7% respectively. Six of examined sera samples to PCR were positive for *B. abortus*. Neither of examined sera subjected to PCR were positive for *B. suis*.

Conclusions*:* The results of present study showed that PCR assay is a rapid and sensitive technique for diagnosis of brucellosis compared to SAT method. However it is more valuable when coupled with conventional methods.

P237

ACCURACY OF POLYMERASE CHAIN REACTION ASSAY FOR DNA LOAD IN THE DIAGNOSIS OF EPSTEIN-BARR VIRUS PRIMARY INFECTION IN CHILDREN

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Background: Epstein-Barr virus (EBV) infections are often diagnosed based on clinical features and heterophil antibody testing (HAb) or serology. Nowadays, PCR quantitative assays are extensively used. We evaluated the accuracy of this method in children with suspected EBV primary infection.

Methods: The records of immunocompetent patients < 18 years, who were tested simultaneously for EBV serologies and EBV DNA (PCR assay), over a 42 months period, in a tertiary care hospital, were reviewed. Serologically patients were classified as: primary EBV infection, EBV-seropositive or EBV-seronegative. Infectious mononucleosis (IM) was diagnosed if specified clinical findings and/or positive HAb were present. DNA load ≥500 copies/mL (whole blood) was considered detectable.

Results: One hundred patients were included (median age 38 months; 52 male). Twenty-nine patients fulfilled IM criteria. Twenty-three (96%) of the patients with primary infection had detectable EBV DNA load (median 36.000copies/mL); eighteen fulfilled IM clinical criteria. Sixteen (46%) of the seropositive patients had detectable EBV DNA but viral load was inferior to primary infections (median 2.500copies/mL,p< 0.001); five had IM criteria. Sensitivity, specificity, positive and negative predictive values of clinical criteria versus PCR assay in comparison with serology were, respectively: 79.2% (95% confidence interval,59.5-90.8%) versus 95.8% (79.8-99.3%), 85.9% (76.0-92.2%) versus 77.6% (67.1-85.5%), 65.5% (47.4-80.1%) versus 57.5% (42.2-71.5%) and 92.4% (83.5-96.7%) versus 98.3% (91.1-99.7%).

Conclusions: Clinical criteria are quite accurate in the EBV infection diagnosis. Comparatively PCR assay brings increased sensibility and seems particularly useful when negative, excluding infection. The clinical usefulness of this expensive technique in immunocompetent children should be questioned unless serologies are inconclusive.

P238

PROCALCITONIN IS A USEFUL BIOMARKER IN SUSPECTED MENINGOCOCCAL DISEASE

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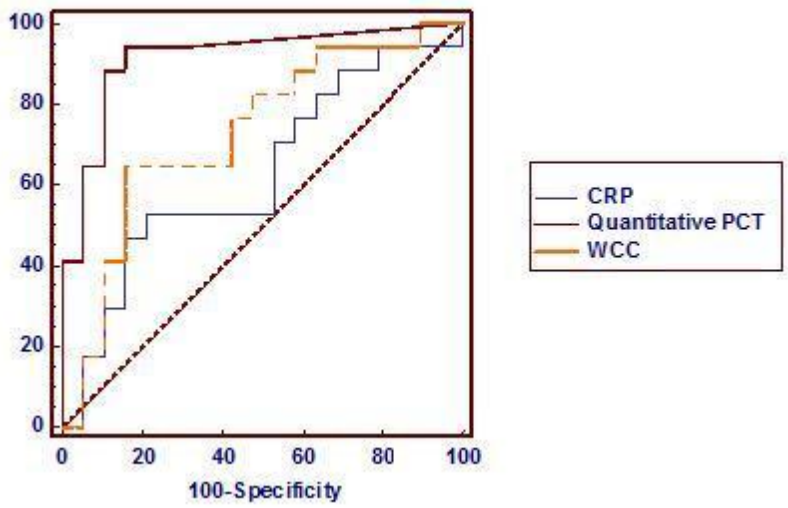
Background: Serum procalcitonin (PCT) is an excellent biomarker for early invasive bacterial disease in children. We present a study evaluating PCT as a diagnostic marker for meningococcal disease (MD).

Methods: Blood was obtained from children presenting to our hospital with suspected MD. Receiver operator characteristic (ROC) curves were used to compare PCT, CRP and WCC as predictors of MD.

Results: 55/104 children presenting with suspected MD had sufficient serum for PCT analysis. 22/55 had confirmed MD. The area under the ROC curve for PCT was 0.92 (95% CI: 0.77 to 0.98), CRP was 0.63 (95% CI: 0.45 to 0.78) and WCC was 0.73 (95% CI: 0.55 to 0.86), Fig 1. The AUC for PCT was significantly larger than either CRP (p=0.005) or WBC (p=0.021). PCT level as a predictor of meningococcal disease had a sensitivity of 82% and specificity of 82%, using a cut-off 1.01 ng/ml and a sensitivity of 68% and specificity of 82%, using a cut-off 2 ng/ml.



[Figure 1.]

Figure 1: Comparative ROC curves for PCT, CRP and WCC for the prediction of MD

Conclusion: In children with suspected MD, PCT is significantly better than CRP or WCC for the prediction of this disease.

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MOLECULAR TESTING OF NASOPHARYNGEAL SPECIMENS HAS POTENTIAL AS A DIAGNOSTIC TEST FOR MENINGOCOCCAL DISEASE

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Background: Molecular testing of nasopharyngeal specimens for *Neisseria meningitidis* (NM) is not widespread because of the risk of detecting asymptomatic carriage. We present our experience of testing nasopharyngeal specimens for NM using Loop Mediated Isothermal Amplification (NM LAMP).

Methods: Children presenting to our hospital with suspected meningococcal disease (MD) have a 'meningococcal pack' of investigations taken including blood for culture, Taqman PCR & NM LAMP and a throat swab for NM LAMP. We compare the results of the throat swab with laboratory confirmed meningococcal disease over a 12 month period.

Results: 160 children had a meningococcal pack completed. 14 had laboratory confirmed MD (14 PCR, 3 blood culture, 1 CSF culture positive). There was one false negative (throat swab negative; blood culture, PCR and clinical picture positive) and one false positive (throat swab positive; blood culture, PCR negative, probable nasopharyngeal carriage). This gives NM LAMP testing of nasopharyngeal specimens a sensitivity of 92.8% (95% CI: 76 to 98) and a specificity of 99.3% (95%CI: 97.7 to 99.8).

	MD	Not MD
TS LAMP +	13	1
TS LAMP -	1	145

[Throat swab result compared with final diagnosis]

Conclusions: LAMP technology is simple and inexpensive and could be applied in the near patient setting. Testing of nasopharyngeal specimens using LAMP has potential as a relatively non-invasive diagnostic test for MD. We believe the potential to diagnose this life threatening disease early outweighs the risk of detecting asymptomatic carriage.

P240

EFFECT OF AGE ON QUANTIFERON-TB GOLD-IN-TUBE (QFT-IT) ASSAY PERFORMANCE AMONG CHILDREN EVALUATED FOR LATENT TUBERCULOSIS INFECTION

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Background and aims: Limited studies have investigated the effect of age upon interferon-γ release assays (IGRAs) performance among children. The study aims were to evaluate the effect of age upon the quantitative and qualitative performance of the QFT-IT method among children and adolescents evaluated for latent tuberculosis infection (LTBI).

Methods: A cross-sectional study was conducted among 769 children (mean age±SD: 7.84±4.68years) evaluated for LTBI between 1/1/2007-1/8/2010. Participants were examined with both TST and QFT-IT and categorized into 4 age groups (infants: < 2years; young children: 2 to < 5years, children: 5 to < 10years; and, adolescents ³10yrs) to evaluate the study objectives.

Results: LTBI (QFT-IT positive) and QFT-IT indeterminate results were detected among 28.7% (n=221) and 3.0% (n=23) of study participants, respectively. QFT-IT indeterminate results occurred more frequently among young children (8.1%; p< 0.0001) and children (2.7%; p=0.025) than adolescents (0.7%). Among LTBI patients, infants had significantly higher mean(±SD) QFT-IT results than adolescents (10.42±5.21 IU/mL vs. 7.49±5.46 IU/mL; p=0.045). Moreover, mean TST size was significantly smaller among infants (11.83±4.90mm; p< 0.0002) and young children (13.45±4.20; p=0.005) than adolescents (15.81±3.50mm). Overall, multivariate logistic regression indicated that QFT-IT positive outcome was not associated with age, but only with mitogen response (OR:1.03; 95% CI:1.01-1.06) and prior BCG immunization (OR:0.46; 95% CI:0.30-0.70). Among LTBI patients, linear regression analysis indicated no association between quantitative QFT-IT result and age (p=0.054).

Conclusion: The quantitative or qualitative (positive-negative) result of the QFT-IT assay is not affected by patient age. However, indeterminate results occur more frequently among younger children.

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A RAPID, COLLECTION-TO-DETECTION PCR SYSTEM FOR THE UNIVERSAL DETECTION OF *M. TUBERCULOSIS*

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Background/aims: *Mycobacterium tuberculosis* (MTB) is a highly transmissible bacterial pathogen with significant morbidity and mortality, particularly in HIV-infected patients. Emergence of multidrug resistant MTB strains has made diagnosis and treatment a high priority, particularly in Africa and developing countries. The 'gold standard' for MTB diagnostics is culture, a method requiring 4-8 weeks for detection. In previous studies, PrimeStore Molecular Transport Medium (MTM) rapidly killed MTB in sputum and facilitated DNA extraction and PCR detection. A rapid, real-time PCR detection assay was: 1) developed for universal species detection of MTB-strains, and 2) evaluated with MTB samples preserved in PrimeStore for DNA preservation at ambient temperature during prolonged shipment.

Methods: A PCR assay was designed from the highly conserved IS6110 gene and integrated into PrimeMix, an all-inclusive, PCR blend. PCR detection was assessed from *M. tuberculosis* DNA preserved/stabilized in PrimeStore MTM from samples collected/shipped from Pretoria, South Africa to San Antonio, Texas, USA.

Results: The PrimeMix Universal-MTB assay is highly specific, detecting 6 of 6 different spoligotyped strains of *M. tuberculosis,* with no cross-reactivity to 5 of 5 non-tuberculosis Mycobacterial strains. The assay is highly sensitive with a limit of detection of 1-10 template copies. Furthermore, MTB DNA and an Internal Positive Control DNA piece present in PrimeStore were preserved/detected by PCR (Ave C_T=15.29 and 28.2, respectively) from samples shipped at ambient temperature for 72 hours.

Conclusion: This Universal-MTB assay could offer significant utility for rapid, point-of-care screening arising from TB infection in patients from rural areas and developing countries worldwide.

P242

THE DIAGNOSTIC VALUE OF SEPTIFAST IN CHILDREN

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Background: Detection of pathogen in sepsis is crucial for adequate therapy. Unfortunately, the gold standard blood culture often remains negative. We aimed to evaluate the diagnostic value of Septifast (multiplex PCR for 20 different pathogens) in comparison to blood cultures (BC).

Methods: Retrospective analysis of all Spetifast analyses in comparison to blood cultures in patients with suspected infection.

Results: 115 specimen were analysed in 79 patients (age at median 6, range 0-20). 87% of all children were diagnosed with one of the following underlying diseases: post liver, kidney or bone marrow transplantation, oncologic disease, cystic fibrosis, pulmonary hypertension. 10 patients were previously healthy. In 101 cases the patients were already treated by antibiotics for at least 24 hours. In 33 specimen (29%) a pathogen could be identified by either one method. A comparison of blood cultures and Septifast results is provided in table 1.

	BC pos.	BC neg.	No BC	total
Septifast pos.	12	14	0	26
Septifast neg.	7	77	5	89
total	19	91	5	115

[table 1]

Pathogens that were solely identified by Septifast were mainly gram-negative bacteria: Enterobacter cloacae, Klebsiella pneumoniae, Stenotrophomonas maltophilia. Results of Septifast testing was available after 6-17 hours; BC took 48-120 hours. Due to positive Septifast results antibiotic therapy was changed in 14 cases.

Conclusion: Septifast multiplex PCR for molecular detection of 20 bacterial and fungal pathogens yielded important additional information in some children with suspected infection. Prospective trials have to validate these results before PCR testing can be recommended on a regular basis.

P243

VEGF, DR5 AND ALCAM LEVELS IN NEWBORNS WITH POSTHYPOXIC BRAIN DAMAGE

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The aim of this research was to investigate the VEGF, DR5 serum level and ALCAM level and to reveal their role in pathogenesis of hypoxic perinatal injury of CNS of newborns.

Materials and methods: 80 newborns with gestation age from 25 to 42 weeks with severe hypoxic damage of CNS were examined. Newborns were divided into four groups: with no structural brain changes; with PVL, IVH, IVH and PVL.

All methods of definition of research factors were based on principle of ELISA.

The procedure was carried out according to standard protocole.

Results: DR5 level exceeded normal in all groups in first day of life. VEGF blood serum level of newborns with PVL and IVH decreased on 7th and 28th days of life. Maximum ALCAM levels were registered in all newborns during the first 48h of life, later ALCAM level started to decrease.

Conclusions:

1) Apoptose brings influence on the formation of severe brain damages of newborns.

2) During transitory changes an increase of VEGF level was noticed before any brain damage was detected. In this case VEGF reflected the following features - the compensatory abilities of the brain and the positive future prognosis.

3) The role of inflammation mechanisms in forming the post-hypoxic brain damage was determined. The fluctuation of ALCAM level can serve as an indicator.

4) The increase of both DR5 and ALCAM levels in newborns reflect the beginning of destructive processes.

P244

VOLUME, CONDUCTIVITY AND SCATTER PROPERTIES OF LEUCOCYTES (VCS TECHNOLOGY) IN NEONATAL SEPSIS

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Introduction: Despite the availability of potent and specific antimicrobial therapy and the recent advances in technology, neonatal septicemia remains a major cause of mortality and morbidity. Early and efficient diagnosis of neonatal bacterial sepsis is essential.

Aim: To evaluate usefulness of the Volume, Conductivity and Scatter (VCS) technology in the early diagnosis of culture proven sepsis in neonates.

Methods: This prospective study was conducted at Sir Ganga Ram Hospital, New Delhi. The study involved 130 neonates (0-28 days), admitted in the neonatal intensive care unit (NICU), who showed symptoms of sepsis like body temperature changes, respiratory distress etc. The neonates were divided in four categories: Culture proven sepsis(25), Probable sepsis(26), No sepsis(44) and Controls(35). The blood samples were taken, sent for culture, C-reactive protein and were also analyzed on the Beckman Coulter LH-750 and LH-755-fully automated hematology analyzers in the Hematology department.

Results: A significant difference was found in the Neutrophil Volume (Standard Deviation, p value= .041), Mean Neutrophil Conductivity (p value-.019), Mean Monocyte Volume (p value-.004) and Mean Monocyte Conductivity. The sensitivity of the MNC, MMV was found to be 72%, 76 % with specificity of 61.4%, 59% at the cut off point of 143.3 and 170.65 respectively. The sensitivity of C-reactive protein was also found to be 72%., specificity was 75%, with a cut off point of 14.

Conclusions: Lower values of MNC, MMC and higher values of MMV can be used as indicators of neonatal sepsis. Further studies are required to explore this relationship.

P245

THE PIPELINE FROM BIOMARKER DISCOVERY TO DIAGNOSTICS: NGAL, GRANULYSIN AND RESISTIN IN MALAWIAN CHILDREN WITH SERIOUS BACTERIAL INFECTIONS

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Background: Identification of reliable biomarkers of infection is crucial to reduce morbidity and mortality from severe infection.Gene expression profiling of patients with sepsis allows the identification of biomarkers involved in the disease process.We aimed to discover biomarkers of serious bacterial infection(SBI) using transcriptomics,and to evaluate their clinical validity using immunoassays.

Methods: We performed microarray analysis on 15 children with SBI, identifying three recognised biomarkers of infection (neutrophil gelatinase-associated lipocalin (NGAL), granulysin and resistin) which were differentially regulated. Real-time PCR validated gene expression.Commercial enzyme-linked immunoassays measured biomarker protein in archived samples, to define their ability to predict SBI.

Findings: Relative gene expression of NGAL and resistin were significantly increased, and granulysin was significantly decreased in cases compared to controls.Relative expression of NGAL, granulysin and resistin were increased in non-survivors compared to survivors, but this was only significant for NGAL.Plasma concentrations of NGAL and resistin were significantly increased in children with confirmed SBI (SBI+) compared to children with signs of severe infection but no confirmed SBI (SBI-), compared to controls (294 v.128 v.62 ng/ml and 193 v.90 v.18 ng/ml, $p< 0.0005$). Plasma NGAL and resistin were significantly increased in non-survivors compared to survivors (316 v.212 ng/ml and 214 v.151 ng/ml, $p=0.02$).Area under the ROC curve for NGAL and resistin in predicting SBI were 0.79 and 0.80 respectively.

Conclusions: We have demonstrated a pipeline from biomarker discovery using transcriptomics through validation to diagnostic testing. NGAL and resistin have been identified as reliable diagnostic biomarkers of SBI in children, which requires validation prospectively.

P246

DEVELOPMENT AND VALIDATION OF A TAQMAN BASED REAL TIME PCR ASSAY FOR DETECTION OF HUMAN ADENOVIRUSES FROM RESPIRATORY TRACT INFECTIONS

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Background: Human adenoviruses (HAdVs) consist of at least 52 serotypes and are responsible for a wide spectrum of respiratory tract infections in both adult and children. The majority of adenoviral respiratroy infections caused by species B, C and E. A simple one step diagnostic method is helpful clinically to promptly offer a result.

Methods and materials: The sequences of HAdVs of species B, C, D and E, obtained from NCBI database, were analyzed. One set of universal primers were designed to target the Hexon region of HAdVs with 120bps of amplicon in size. Two probes against species BDE and C were chosen, respectively. Four representative HAdVs strains (AdV-, -B7, -C1, -D9, and -E4) and a total of 100 stored respiratory HAdV clinical isolates, collected between 2004 and 2008, were analyzed. Fifty prospectively collected throat swabs samples from hospitalized pediatric patients were compared with culture results for validation.

Results: The HAdV PCR assay correctly detected each representative strain and all stored isolates. There was no cross reaction against common respiratory DNA viruses. This assay had a wide dynamic range, detecting from 10^2 to 10^8 DNA copies per reaction. The R^2 ratio of linearity were all > 0.99 for tested species. The HAdV positive rates for 50 consecutive samples by the PCR and culture assays were 10% and 4%, respectively. All the culture positive samples were also positive by the PCR method.

Conclusion: This PCR-based assay enables detection of a broad range of common respiratory HAdVs with good sensitivity and specificity.

P247

SEXUAL TRANSMITTED INFECTIONS AND DIAGNOSTIC METHOD

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Background: Sexual transmitted infections (STIs) have increased in Rwanda and other countries in Africa since the mid-nineties. To obtain a better picture of diagnostic methods used in STI testing institutions in Rwanda, we performed a nationwide survey amongst STI specialists in order to evaluate the quality of STI reports and provide recommendations to harmonize and possibly improve STI diagnostics in Rwanda.

Methods: We asked sentinel physicians and randomly chosen gynaecologists, urologists and dermato-venerologists, about the diagnostic methods used in 2005 to diagnose HIV, chlamydia (CT), gonorrhoea (GO) and syphilis (SY) in a national cross-sectional survey in order to recognize potential problems and provide recommendations.

Results: A total of 739/2287 (32%) physicians participated. Of all participants, 80% offered tests for HIV, 84% for CT, 83% for GO and 83% for SY. Of all participants who performed HIV testing, 90% requested an antibody test, 3% a rapid test and 1% a nucleic acid amplification test (NAAT). For CT testing, NAAT was used in 33% and rapid tests in 34% of participants. GO resistance testing was performed by 31% of the participants. SY testing was performed in 98% by serology.

Conclusions: Diagnostic methods for STI vary highly among the participants. Diagnostic guidelines should be reviewed and harmonised to ensure consistent use of the optimal STI diagnostic methods.

P248

DETECTION OF HCMV INFECTION IN PEDIATRIC PATIENTS UNDERGOING BONE MARROW TRANSPLANTATION

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Human cytomegalovirus (HCMV) can cause serious health problems in immunocompromised patients. HCMV is a well-known cause of morbidity and mortality in bone marrow transplantation recipients. . Early diagnosis of HCMV infection in these patientsis is very important for the appropriate administration of antiviral treatment. Molecular viral detection by PCR has advantages over serological methods especially in immunosuppressed patients, which do not produce specific antibodies. The aim of the study was to compare HCMV identification in peripheral blood and urine of the bone marrow transplanted (BMT) patients. The group of 37 boys and 32 girls positive for HCMV infection either in peripheral blood or urine was selected for the study. HCMV infection were detected by PCR technique using specific oligonucleotide primers for early and late antigen of HCMV genes. CMV infection has been detected in 76 urine samples compared to 31 positive blood samples. In 5 cases CMV has been present in peripheral blood and was absent in urine samples. Using PCR real time technique with SYBR-Green II it was proved that the concentration of HCMV molecules in urine is higher than in peripheral blood. Due to higher concentration of HCMV the urine is more suitable for CMV detection than peripheral blood. On the basis of the obtained results it can be concluded that both urine and peripheral blood samples testing should be recommended for molecular detection of HCMV infection in BMT children.

P249

HOW TO MODEL VITAL SIGNS IN THE PREDICTION OF SERIOUS BACTERIAL INFECTIONS? COMPARING DIFFERENT MODELLING STRATEGIES

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Background and aims: Vital signs are frequently used in the assessment of the febrile child. Clinical preference to use dichotomized parameters contrasts with methodological preference to analyse variables continuously. In this study we compare strategies of modelling vital signs in predicting serious bacterial infections in febrile children.

Methods: Patients' characteristics were retrieved from 1750 febrile children aged < 16 years, visiting the emergency department of the Erasmus MC - Sophia Children's Hospital; 13% serious bacterial infections (n=222). Tachycardia and tachypnea were defined using thresholds for upper limit values of heart rate (HR) and respiratory rate (RR) for age. The association of HR and RR with the presence of SBI was studied using logistic regression models. Four strategies to model HR were compared: the dichotomous variable tachycardia, a normalised continuous value of HR, a continuous value of HR (either linear or transformed) and a model including age and HR and the interaction of age and HR. Performance of models was assessed with the area under the receiver operating characteristic curve (ROC area). The same strategies were applied to RR.

Results: The dichotomised vital signs showed similar predictive ability as the continuous vital signs, either linear or transformed (ROC-area 0.53 (HR) and 0.55 (RR)). A model that also included age performed substantially better (ROC area 0.60 (HR) and 0.63 (RR)), with 8-13% better classification of absence or presence of SBI.

Conclusion: Clinical preferred use of dichotomized vital signs results in information loss, and relatively low predictive ability for the presence of SBI.

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PROCALCITONIN AND C-REACTIVE PROTEIN IN YOUNG FEBRILE INFANTS

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Background and aims: Fever without source (FWS) is one of the most common presenting complaints to pediatric emergency departments. The aim of this study is to determine the accuracy of C-Reactive Protein (CRP) and procalcitonin (PCT) to rule out bacterial infections in children with FWS.

Methods: We conducted a retrospective descriptive study that included all infants younger than 90 days of age with FWS admitted to our ED during 2008- 2010. We included 181 children with at least one blood culture and RCP/PCT determination and urine culture.

Results: BI was documented in 49 patients (27,1%): 45 UTI, 6 bacteremia (3 *Pneumococcus*, 2 GBS, 1 *Enterococcus*); 2 patients had bacteremia and UTI. We analyzed the value of CRP and PCT for predicting bacteremia and UTI. PCT shows larger area in the ROC curves in bacteremia (0,73) than CRP (0,605). The overall sensitivity for PCT in bacteremia was 60% (17-100%) with a cutoff of ≥0,5ng/ml, vs 16,67% (13,1- 46,9%) for CRP with a cutoff of ≥3mg/dl. The overall specificity for PCT and PCR in bacteremia was 84,17 (77,6-90,7%) vs 81,71% (75,99-87,44%). Clinical appearance (well versus toxic/ill appearing) were also recorded, with an overall sensitivity in bacteremia of 66,67% (28,8-100%) and specificity of 86,8% (81,8-91,8%).

Conclusions: PCT showed higher sensitivity and specificity than CRP in young infants with FWS and bacteremia. However, the overall sensitivity of both (PCT and CRP) is low, so we should not underestimate other markers as clinical appearance in children with FWS.

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CHEST RADIOGRAPH AND COMPUTED TOMOGRAPHYFINDINGS IN PEDIATRIC PRIMARY PULMONARY TUBERCULOSIS

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Background: Tuberculosis remains a common public health problem despite the efforts of eradication and control. The diagnosis of primary pulmonary tuberculosis (PTB) in children is often challenging: clinical features are non-specific, sputum is usually unavailable, gastric aspirate difficult to obtain and have a low yield. Since mediastinal lymphadenopathy is considered the fingerprint of PTB the radiographic demonstration plays an important role in confirming the diagnosis.

Aims: The evaluate the radiologic features of PTB in children detected both on chest radiograph (CR) and contrast-enhanced computed tomography scan (CT).

Materials ans methods: One dedicated pediatric radiologist retrospectively evaluated CR and CT findings of children with clinical manifestations of pulmonary tuberculosis, history of contact with smear positive TB patient and positive Interferon-gamma release assay (QFT-G). The imagings were obtained before starting anti-TB therapy that leaded to a complete recovery of PTB in all patients.

Results: We considered 10 children diagnosed with PTB at the pediatric department from 2005 to 2010; 7/10 patients were less than 3 years of age. In 5/10 patients both CR and CT diagnosed hilar lymph-adenopathy with identification of the same side. In the remaining 5/10 children hilar lymphadenopathy was detected only by CT scans. Patchy consolidation was associated with lymph-adenopathy in 1/10 patients and it was demonstrated both by CR and CT.

Conclusions: The radiologic findings of our study, albeit the small number of patients, confirm data reported previously in the literature showing that CT is a more sensitive diagnostic method than CR to detect enlarged lymph-adenopathy in PTB.

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ASSESSMENT OF LYME DISEASES IN CHILDREN

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Background: Lyme disease is an infectious disease caused by a spirochete known as Borrelia burgdorferi. Becouse of the multitude of possible symptoms , a clinical diagnosis is often difficult, especially in the late stages if the information of primary infection is missing.

Aims: The aim of this study was to determine the antibodies with specificity for the in vivo-expressed 22-kDa pG protein as well as the 21.8-kDa lipoprotein LA7 (both from the European Austrian B. burgdorferi sensu stricto strain ZS7) in patients with various stages of Lyme disease.

Methods: The laboratory diagnosis of Lyme borreliosis is based essentially on the detection of Borrelia specific antibodies. Both antigens were expressed as glutathione *S*-transferase fusion proteins and purified by affinity chromatography.

Results: Although there were a great deal of heterogenocity in protein and lipid patterns, several groups based on several major proteins and lipids were identify with different technics and confirmated with Diagnostic Lyme/IgG test Enzygnost.

Conclusions: Lyme Disease is considered to be one of the fastest growing illnesses in the world. Diagnosing Lyme disease can be a very difficult task, which is why so many cases are missed, or patients are diagnosed with another illness entirely. Antibiotics are effective because of their property of selective toxicity.

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PANDEMIC A/H1N1V INFLUENZA 2009 IN CHILDREN: A MULTICENTRIC BELGIAN SURVEY

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Background and objectives: During the 2009 influenza A/H1N1v pandemic, children were identified as a particular “at risk” group. We conducted a multicentric trial to describe pattern of A/H1N1v infection among hospitalized children.

Material and methods: From 01/07/09 to 31/01/10, we prospectively collected all proven (positive H1N1v PCR) and probable (positive Influenza A antigen or culture) pediatric cases of H1N1v infections, hospitalized in four tertiary centers in Brussels.

Results: We reported 215 children hospitalized with proven/probable H1N1 infection. Median age was 31 months. 47% had ≥ one co-morbidity. Febrile respiratory illness was the most common presentation. 36% presented initial gastrointestinal symptoms and 10% neurological manifestations. 35% had pneumonia. Compared to PCR, sensitivity of antigen and culture was low (53% and 59%, respectively). Only 23% of patients received oseltamivir. 21 (10%) children had to be admitted to ICU, of whom seven suffered from ARDS. Rate of co-morbidity tended to be higher among ICU than general wards patients (62%>< 45%,p=0.1). Fatality-rate was 5/215 (2%) and concerned only children suffering from chronic neurological disorders. Children > 2 years old showed a higher propensity to be admitted to ICU (16%>< 1%,p=0.002) and a higher mortality (4%>< 0%,p=0.06). Infants ≤ 3 months showed a particularly mild pattern of infection, with few respiratory and neurological complications.

Conclusion: Although H1N1 infections were globally self-limited, pediatric burden of disease was significant. Compared to other countries experiencing different health care systems, our Belgian cohort was younger and received less frequently antiviral therapy; disease course and mortality were however similar.

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INFLUENZA SURVEILLANCE IN SÃO PAULO STATE: VIRUS DETECTED IN POST-PANDEMIC PERIOD, SP - BRAZIL, 2010

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Background and objectives: In 2009, 12,002 cases and 578 deaths were caused by Flu A H1N1 in SP state, Brazil. On Aug/2010 WHO declared a post-pandemic period, but recommended active surveillance for Flu. The aim of this study is to describe influenza circulation in SP during 2010.

Methods: There are 10 surveillance centers for Flu in SP state to monitor influenza circulation through IFI. This is a descriptive study of virus and Flu strains isolated from patients with ILI in 2010, focused on post-pandemic period, based on registered data in SIVEP-GRIPE and IAL.

Results: In 2010, ILI was responsible by 15% of medical visits, with greater impact in 0-14 y and 25-29 y age groups. Till EW 51, 1,861 samples were collected, and 238 (13%) were lab confirmed (IFI or PCR) for virus; from these, Flu was detected in about 1/3 since April (Flu A =13.5% and FluB =18.9%) B strains predominated till August, and in post-pandemic period Flu A H3 was the predominant one. RT-PCR positivity was higher (22.4%), being 66% of strains positive for Flu B, 23.4% A/H3 and 10.6% for H1N1. Only 89 cases and 15 deaths caused by H1N1 were registered in SP, mostly before the national campaign of immunization with monovalent H1N1.

Conclusions: Co-circulation of Flu B and A H3N2 was detected in SP during pandemic post-period. Influenza surveillance is very relevant to detect clusters and flu strains, and propose the most appropriated measures to control this disease, that cause substantial impact in the community.

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INVASIVE MENINGOCOCCAL DISEASE IN NORTHERN MEXICO: AN ENDEMIC, SEVERE AND PREVENTABLE HEALTH PROBLEM

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Background: Based on Mexican passive surveillance systems, invasive meningococcal disease (IMD) is an infrequent condition with rates not higher than 0.88/100,000 population. The Tijuana, Mexico - San Diego, CA border is the most transited frontier in the planet.

Methods: Between October - 2005 and January - 2011, all patients < 16 years old with confirmed IMD were prospectively admitted at Tijuana General Hospital (TGH). Following culture (blood and/or cerebrospinal fluid) serogroup identification was performed using Latex-agglutination method (Pastorex®).

Results: A total of 27 IMD cases were admitted at TGH. Avg age was 4.6 years old (1 month - 15 years), from which 66.6% were < 5 years of age and 40% ≤ 2 years old. 9 patients had clinical purpura fulminans (CPF) (36%), and 25 (92.5%) had meningitis with/without CPF. Overall mortality was of 18.5%. Serogroup distribution was as follows: “C” - 15 (55.5%), “Y” - 7 (25.9%), “B” - 3 (11.1%) and ignored - 2 (7.4%). *Neisseria meningitidis* was the leading cause of bacterial meningitis, followed by *Streptococcus pneumoniae.* Based on the population-coverage of TGH, estimated rates of IMD are of 3/100,000 population in < 16 years of age and of 7/100,000 in children < 5 years old, respectively.

Conclusions: IMD in the northern border of Mexico is much higher than what is Nationally reported. Serogroup C is the most prevalent. Further strategies are needed in order to implement immunization policies in this region. A National Surveillance System for IMD just started as a result of these findings.

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ARE METEOROLOGICAL PARAMETERS ASSOCIATED WITH HAND-FOOT-MOUTH DISEASE/HERPANGINA CAUSED BY ENTEROVIRUS 71 INFECTION IN TAIWAN?

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Background: In 1998, there was an epidemic of hand-foot-mouth disease/herpangina (HFMD/HA) caused by enterovirus 71 (EV 71) infection in Taiwan. The underlying factors of widespread emergence of viral infection have not been well explained.

Objective: The purpose of the study was to assess the effects of weather variability on cases with HFMD/HA caused by EV 71 infection.

Methods: We analyzed data for HFMD/HA caused by EV 71 infection from national surveillance data and weather variability in Taiwan between 1998 and 2008. Poisson regression models were applied to evaluate the correlation between the incidences of HFMD/HA caused by EV 71 infection and meteorological parameters. The models allow for adjusting of HFMD/HA caused by EV 71 infection for factors such as annual trends, seasonality, temperature, relative humidity. We estimated the effect and the lag structure of both temperature and relative humidity on the base of a distributed a lag model.

Results: During the 11-year study period, the cases of HFMD/HA caused by EV 71 infections varied from 35 to 405 cases per year, peaking in 1998. Seasonal variations in incidence were observed, with an incidence peak during the summer season. HFMD/HA caused by EV 71 infection was correlated with temperature. No clear pattern for humidity effect was observed.

Conclusions: Seasonality of HFMD/HA caused by EV 71 infection can be explained by meteorological influences. The model presented herein is a first step toward predicting epidemic of HFMD/HA caused by EV 71 infection using weather forecast data.

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IMPACT OF CRIMEAN-CONGO HAEMORRHAGIC FEVER ON IRANIAN CHILDREN

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Background and aims: Crimean-Congo Haemorrhagic Fever (CCHF) is a viral zoonosis. The virus is from Nairovirus genus, Bunyaviridae family. Humans are infected by tick bite, handling of infected blood or tissues and nosocomially. The mortality rate could attain 50%. In this study, children´s probable sera for CCHF were analyzed by serological and molecular assays.

Methods: Sera of Iranian CCHF probable children, 1 month to 15 years old, were collected from June 2000 to 2011. They were analyzed by specific Elisa (anti CCHF IgM and IgG detection) and by RT-PCR (gel-based and Real time) in the laboratory of Arboviruses and Viral Haemorrhagic Fevers of the Pasteur Institute of Iran (National Reference Lab).

Results: 47 children (under 15 years old) were confirmed cases for CCHF. Their sera were either IgM positive in Elisa test and/or RT-PCR positive. Most confirmed children were from Sistan-va-Baluchestan province. Among 47 confirm cases, 28 were boy (59.6%) and 19 were girl (40.4%).

Conclusions: Our result showed that the most important hemorrhagic Fever in Iranian children is CCHF. The main way of contamination is contact with tissue or blood of infected livestock, and we observed that confirmed children besides being students work in slaughterhouses, so informing children and their parents about ways of transmission is very useful.

The most infected province is Sistan Baluchestan in the Southeast of Iran neighboring Pakistan and Afghanistan where CCHF is endemic. Our phylogenetic studies have also proven that Iranian CCHF strain is very similar to the CCHF strain of Pakistan (Matin Strain).

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EPIDEMIOLOGY OF PERTUSSIS IN THE MIDDLE EAST AND NORTH AFRICA

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Introduction: DTP vaccination has reduced infant mortality globally but, despite widespread coverage, pertussis remains a problem. Many countries report an increased number of pertussis cases in infants and older age groups along with periodic outbreaks. Whilst information exists on the epidemiology of pertussis in the USA/Europe, the current situation for the Middle East and North Africa (MENA) is unclear.

Methods: A retrospective review of published literature (1990-2010) was undertaken for MENA countries.

Results: Epidemiological data on pertussis in MENA are not widely reported. All 23 countries have implemented a three-dose schedule with high coverage. A fourth dose around 18-months is recommended in 15/23 countries with fewer countries (6/23) implementing a fifth dose (4-6 years).

Country and study period	Population and study sample	Number of deaths/hospitalisations from pertussis
Afghanistan March 2007 – March 2008 Kakar et al. 2009	Surveillance data from 129 sentinel sites; mostly provincial and district hospitals: • 56 outbreaks of pertussis in study period • 2233 suspected cases of pertussis • 718 cases met surveillance definition of the WHO and were reported from patient visits to sentinel hospitals	• 32 deaths (1.4% of suspected cases, 4.4% of cases meeting surveillance definition) • 203 specimens from suspected patients were analysed and *B. pertussis* was culture confirmed in 7/203 cases (~3%)
Iraq June – December 1996 Al-Bargish et al. 1999	Outbreak of pertussis in the general population: • Clinical diagnosis based on WHO criteria • 133 patients presented with pertussis • 64/133 (48.1%) cases were confirmed by culture methods • 53/133 (39.8%) were children <5 years of age	Among the 53 children <5 years of age: • 15 cases lack any immunisation against pertussis: 10 cases aged <2 months and 5 cases aged >1 year Among the 53 children <5 years of age: • 35 were <1 year of age, of whom 16 (46%) were admitted to hospital.
Saudi Arabia 1996–2004 Al-Tawfiq et al. 2007	Retrospective analysis of confirmed cases of *B. pertussis*: • Only cases with a confirmed diagnosis of pertussis infection were included in this study • Confirmed diagnosis of *B. pertussis* was based on positive nasopharyngeal swab cultures or PCR	65/156 confirmed cases (42%) were hospitalised: • Median period of hospitalisation was 5 days (2–21 days) • 63/65 (96.6%) were infants <6 months of age For the infants <6 months of age: • 41/63 (65.1%) had not received any vaccination • 17/63 (27.0%) received one dose • 3/63 (4.8%) had received two doses • 2/63 (3.2%) received three doses • No reported deaths in hospitalised patients
Sudan July 1989 – August 1990 Abdalla et al. 1998	Sudanese children (81 children, 42 cases and 39 contacts aged <15 years) located among 37 households followed for a period of 6 months: • 42 cases made of 11 patients identified initially, with another 26 cases identified during home surveys, and 5 contacts who became secondary cases • Half of the cases were from peri-urban areas and 83.3% were living in crowded households (room index >5) • Primary immunisation rate was low; 2.8%	• Attack rate was higher among unimmunised infants aged <1 year (100%) compared with unimmunised children aged ≥10 years (14.3%, $p = 0.001$) • Male:female ratio of 1:1.6; 20/42 (47.6%) were <5 years of age and 8/42 (19.0%) were infants aged <1 year

[Whitford v3 Table 1]

In 2009 a median incidence of ~0.16 reported cases/100,000 (range 0-18.9) was calculated across the region. Pertussis was identified most frequently in infants who were also most likely to be hospitalised with the disease. Average infant hospitalisation rates of ~43% were seen in two studies (n=100).

Outbreaks occur frequently and were reported for Afghanistan, Iraq and Sudan. In serological surveys 50% of adolescents/young adults showed declining immunity to pertussis despite primary vaccination.

Conclusion: The lack of epidemiological data on pertussis in MENA precludes assessment of disease burden but available published studies confirm greatest morbidity in infants and declining pertussis immunity at older ages.

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CLINICAL ASPECTS OF DENGUE IN CHILDREN IN CENTRAL BRAZIL

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Background and aims: Dengue viruses are the most common cause of arboviral disease in the world. In the Americas, Brazil is leading in cases of dengue reported annually. There is a lack of large studies in children focusing on clinical findings in dengue. The objective of this study was to describe the clinical findings of dengue in children less than 15 years old.

Methods: We performed a retrospective study of all cases of dengue reported to the local Government Health Agency from January 2001 to December 2010 in Goiania, Goias, a city with near 1,300,000 habitants in Central Brazil. Clinical data were analyzed by descriptive statistics.

Results: A total of 113,744 cases of dengue were reported in all ages in that period of 10 years. In children less than 15 years old there were 22,278 cases, in which 9,135 were laboratorial and clinically confirmed on follow up. A total of 7,812 (85.52%) children had fever, 7,440 (81.44%) presented with headache, 6,849 (76.45%) had myalgia and 6,346 (69.47%) was prostrated. Arthralgia, eye pain, nausea or vomiting, rash and diarrhea accounted for 64.02%, 62.70%, 56.95%, 23.05% and 21.75% respectively. Spontaneous bleeding was seen in 768 (8.40%) children and hypotension in 219 (2.40%), shock in 236 (2.58), ascites in 63 (0.69%), pleural effusion in 16 (0.18%) and death in 16 (0.18%).

Conclusion: Clinical findings are the hallmark of dengue in children. In this study fever, headache, myalgia and prostration were the most prominent findings. Few fatal cases were observed.

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PVL POSITIVE S.AUREUS PNEUMONIA IN A CHILD WITH NOVEL INFLUENZA H1N1 INFECTION

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Bacground: Novel influenza type A (H1N1), or pandemic flu was first identified in April 2009 in Mexico and rapidly worldwide. During the period 20 - 26 November, 2009, very high activity was reported in Europe including Latvia, with children up to 15 years of age affected to unusually high degrees.

Aim: The first case in Latvia of Panton-Valentine leukocidin (PVL) positive methicillin susceptible *S. aureus* pneumonia in an adolescent with novel influenza A H1N1 is described.

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

Results: A 15 year old boy was admitted to intensive care suffering from severe respiratory failure with bilateral necrotic pneumonia. The presence of influenza A H1N1 was confirmed by PCR. Invasive *S. aureus* was *spa* type t435 and Panton-Valentine leukocidin gene positive. He was discharged after 58 days in hospital.

Conclusions: Our described case exposes that PVL - positive *S. aureus* with *spa* type *t435* can complicate influenza in otherwise healthy children, with rapid progression to severe pneumonia that needs complicated and long management of the illness.

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TRENDS IN INCIDENCE AND MORTALITY ASSOCIATED WITH W135 MENINGOCOCCAL DISEASE IN SÃO PAULO STATE - BRAZIL, 2000-2010

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Background and objectives: Serogroup C is the most common agent of meningococcal disease (MD) in São Paulo state (SP). Changes in serogroup prevalence are unpredictable, and other serogroups can also cause serious disease. This study analyzed the incidence and case fatality rate (CFR) of emergent W135 serogroup disease by age groups and compared the results with C serogroup MD (the most prevalent at > 80% in 2010).

Methods: MD requires registration in SINAN, and all information regarding serogroup disease incidence is recorded at Institute Adolfo Lutz (IAL), the National Reference Center for MD diagnosis. We selected MD disease data from Jan/2000 till Dec/2010 in SINAN and IAL databanks and analyzed by age group.

Results: The incidence rate of MD in SP state was about 3.1/100,000, with large local variations. Disease rates were higher in the capital (4/100,000 from 10 MD surveillance reference centers) and in Campinas city (3 MD centers). After 2006, W135 MD incidence has grown in all age groups, and in 2010, the CFR associated with W135 MD was 34%, higher than for C MD (~20%).

Conclusions: In SP, the growing incidence and higher CFR of W135 compared with C serogroup is cause of concern. Until Jan/2011, we did not have a vaccine to prevent W135 MD. Therefore, most of people have no protection against W135, and the present low circulation of this serogroup has the demonstrated high potential to spread to those without vaccine-elicited immunity.

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HAEMOPHILUS INFLUENZAE INVASIVE DISEASE IN THE VACCINE ERA

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Introduction: The incidence of Haemophilus influenzae (Hi) type b invasive disease has declined significantly in countries with routine infant Hib immunization. Invasive disease caused by non-type b encapsulated Hi strains (a, c, d, e, f) has been infrequently reported. Invasive disease caused by non-typeable Hi (non-encapsulated), is even less frequent, occurring especially in newborns and immunocompromised children.

Case report: A 32 month-old boy, previously healthy, appropriately vaccinated against Hib (four doses) has been brought to emergency room with a 24 hour history of fever, photophobia and vomiting. On examination, the boy appeared ill and prostrated. Lumbar puncture revealed pleocytosis, decreased glucose, and increased protein levels. Empirical antibiotic therapy with ceftriaxone was started. On day 2 after admission, noted left ptosis; magnetic resonance imaging revealed no ischemic or infectious lesions of the brain parenchyma. Cerebrospinal fluid and blood cultures grew Haemophilus influenzae serotype f. He was discharged after completing 14 days of intravenous antibiotic therapy, with complete resolution of ptosis and no other findings on physical examination, including focal deficits.

Conclusion: Vaccination campaigns revolutionized epidemiology of invasive disease. It has been suggested that the decline in the rate of infections caused by Hi serotype b could have given rise to the emergence of diseases caused by other serotypes, including e and f Hi strains, particularly in the U.S.. Currently there is little information available about the antibiotic susceptibility patterns and clinical significance of the Hi serotype f, thereby emphasizing the importance of epidemiological surveillance and eventual need for Vaccine Research.

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THE COST OF HOSPITALIZATION OF CHILDREN WITH PERTUSSIS: THE IMPORTANCE OF THE INTRODUCING OF COCOON STRATEGY

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The objective was to analyze the pertussis incidence and the duration of hospitalization in children under one year of age in the Czech Republic. The incidence of pertussis in 0-year-olds was declining since the 1950s (3 804.9/100,000 in 1956) and remained below 10.0/100,000 in 1974 through 1999. The incidence rate was fluctuating in four years periods with a peak in 2008 (27.9/100,000). Three deaths were reported in this age group in 2005, 2007 and 2009.

The data about incidence and hospitalization for the study period (2006-2010) were obtained from the National Institute of Public Health, the Institute of Health Information and Statistics, Communicable Disease Information and Notification System in the Czech Republic (EPIDAT). The mortality data were obtained, apart from the aforementioned sources, also from the literature.

During the study period, 108 children under one year of age fell ill on pertussis (the annual incidence 18.7/100,000). The mean age of reported pertussis cases was 2.8 months in this age group. Nearly 86 % of children (92 pertussis cases) did not receive even one dose of vaccine against pertussis. Out 108 children, 86 (79.6 %) were hospitalized. The mean duration of hospitalization was 12.9 days.

The cost to treat one hospitalized child in group under one year of age far outweigh the cost of vaccination of both parents. Vaccination of adults, especially parents, grandparents and other persons caring of the youngest still unvaccinated children should be strongly recommended to protect small children before disease.

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SEVERE BACTERIAL CO-INFECTION DUE TO POSSIBLE IMMUNOPARALYSIS AFTER BORDETELLA PERTUSSIS INFECTION

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Background: Whooping cough is resurgent in the developed world despite high vaccination coverage and has changed its epidemiology, affecting mainly adolescents and adults who play a significant role in the transmission of pertussis to neonates and infants who are particularly vulnerable.

Case report: A 2-month old infant was admitted with fever, feeding problem, paroxysmal cough and worsening respiratory distress over the last 4 days. Physical exploration revealed tachypnea, subcostal/intercostal recessions and hypoxemia. White blood cell count: 73000/microL (neutrophils 30100, lymphocytes 30400), Hb 5.6 g/l; Chest x-ray: bilateral atelectasis. Nasopharyngeal specimen: PCR positive for *B.pertussis*. Respiratory syncitial virus antigen was negative. The patient suffered from progressive respiratory failure needing non-invasive ventilation for 7 days. He developed an *Enterobacter cloacae* sepsis on his fifth day at PICU, 7 days later suffered from a central catheter related abscess due to *Serratia marcescens* and *E. cloacae* requiring surgical drainage. The catheter tip grew methicilin resistant *S. aureus*. He made a full recovery and was discharged in good clinical state after appropriate antibiotic therapy. Immunology studies after clinical recovery revealed normal neutrophil, complement (apart from low Mannose-Binding-Lectin levels being 600ng/ml; normal >1300) and IgG,A,M inmunoglobulin levels for age.

Conclusion: Severe B.pertussis can develop in the very young, the incompletely immunized infants and those with concomitant infections. The classical clinical stages of pertussis might not be present. B.pertussis infection might predispose patients for other viral and bacterial infections possibly due to a transient immunodeficient state (“immunoparalysis”) of the child.

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EMERGENCE OF THE COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* CLONE USA300 AMONG CHILDREN AND YOUNG ADULTS IN ISRAELI AND PALESTINIAN POPULATIONS

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Background: Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections are epidemic in the USA and are caused mainly by a single clone, USA300. In Europe, the prevalence of CA-MRSA is low but increasing and USA300 is uncommon. Data on CA-MRSA in Israel are scarce and these bacteria are still considered to be rare. This report focuses on the appearance of USA300 clone among CA-MRSA strains that have been sent for further classification to the Israeli *S. aureus* Reference Center from various sources.

Methods: All *S. aureus* isolates were sent to the reference center during 2010. CA-MRSA strains were defined as MRSA isolated from individuals in the community or during the first 72h of hospitalization. Staphylococcal chromosome cassette *mec* (SCC*mec*) type, *arcA*, and presence of the genes for Panton-Valentine leukocidin (*pvl*+) were determined by PCR. Sequence types (ST) were assigned by multilocus sequence typing. USA300 strains were defined by pulsed-field gel electrophoresis.

Results: Twelve USA300 isolates were collected from Israeli and Palestinian children and young adults in different regions. Clinical manifestations included skin and soft tissue infections (SSTI´s) and asymptomatic colonization; only one subject had traveled to the USA. All Isolates were SCC*mec* IV, ST8, *pvl*+, and carried the arginine catabolic mobile element. Variable antimicrobial resistance patterns were evident, however all were clindamycin susceptible.

Conclusions: The CA-MRSA USA300 clone, presenting as SSTI´s or colonization, has now been documented among Israelis and Palestinians and may be more widespread in the region than previously perceived. The geographic and antimicrobial resistance variability implicates multiple infection sources.

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PANDEMIC INFLUENZA A (H1N1) VIRAL INFECTION IN CHILDREN HOSPITALIZED AT MANSOURA UNIVERSITY CHILDREN´S HOSPITAL, EGYPT

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Background and aims: Pandemic influenza A (H1N1) has not been systematically studied in Egyptian children. This study was conducted to identify the characteristics of laboratory-confirmed H1N1 infection in children admitted to our hospital from 1 December 2009 to 15 March 2010**.**

Methods: Suspected cases of severe influenza A (H1N1) or mild flu-like illness in the presence of risk factors were admitted to isolation wards. Real-time PCR, chest radiography, complete blood count were done for all patients. Those who confirmed positive for (H1N1) were treated with oseltamivir for 5 days and included in the study.

Results: Thirty-six cases were confirmed positive for influenza A (H1N1), of whom 17 (47.2%) were males. Twelve cases were < 2 years, 11 cases from 2-6 years, and 11 cases from 6-12 years with 50%, 54.5%, and 90.9% co-morbidities respectively. Co-morbidities were found in 24 cases (66.6%) especially bronchial asthma in 8 (22.2%). The most frequent symptoms were: dry cough in 36 (100%), and fever in 33 (91.7%).The most common radiologic finding was bilateral multifocal areas of consolidation in 23 (63.9%). Thirty-three cases (91.7%) recovered after treatment. There were 3 deaths; 2 with co-morbidities and one 4 months girl without co-morbidity.

Conclusion: Influenza A (H1N1) 2009 should be considered during the pandemic in any child with dry cough and fever. Infants < 2 years were affected even without co-morbidities but most of children from 6-12 years had co-morbidities especially bronchial asthma. This population sub-groups should be among the first groups targeted for influenza A (H1N1) vaccine.

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RETROSPECTIVE COMPARISON OF PANDEMIC INFLUENZA A/H1N1 (2009/2010) CLINICAL CHARACTERISTICS VERSUS SEASONAL INFLUENZA A (2007-2009) IN HOSPITALIZED CHILDREN IN BASEL, SWITZERLAND

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Background: 2009, pandemic influenza A/H1N1 (piA) caused significant morbidity and mortality worldwide. Here we compare clinical features and epidemiology of pandemic H1N1 infections to those of seasonal influenza A (siA) infections of the two preceding winter seasons in hospitalized children and adolescents.

Methods: Medical records of all hospitalized patients < 18 years with RT-PCR-confirmed siA (fall 2007 to spring 2009) or piA infections (April 2009 to March 2010) were analysed retrospectively.

Results: 134 patients (piA: N=55, 58% male; siA: N=79, 58% male) were identified; median age was 2.5 yrs (range 0.07-15.5) in piA patients and 1.5 yrs (range 0.04-17.5) in siA patients. Underlying chronic disease was present in 25% (piA) versus 33% (siA) patients. All patients except one had fever; most common other symptoms were cough (piA/siA: 78%/86%), rhinitis (76%/76%) and pharyngitis (67%/68%). Croup syndrome (15%/3%, p=0.02), conjunctivitis (31%/10%, p=0.002) and febrile seizures (26%/13%, p=0.05) were more frequent in piA patients. Overall, 64% (n=35) of piA and 53% (n=42) of siA patients had >1 complication: pneumonia 15%/22%, AOM 13%/11%, CNS complications 29%/18% (all p>0.05). 5 patients (3/2) were admitted to ICU; one 4.8 month old boy with underlying congenital malformations died due to secondary bacterial pneumonia, all other patients recovered without sequelae. Mean hospitalisation duration was 2.9/3.9 days (p>0.05). Influenza immunization rates were 5%/0%). None of siA but 20% of piA patients were treated with oseltamivir.

Conclusions: Although patients with piA infection presented with more febrile seizures, overall severity of disease was not different compared to siA in previous years.

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CLINICAL AND LABORATORY DIFFERENCES ACCORDING TO GENDER AND AGE AMONG CHILDREN AND ADOLESCENTS HOSPITALIZED WITH DENGUE DURING 2008 EPIDEMIC, CEARÁ-BRAZIL

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Backgrounds and aims: Brazil is experiencing epidemiological Dengue Fever (DF) transition with severe cases predominantly affecting pediatric population. We need better knowledge about clinical and laboratory presentation among DF hospitalized children.

Methods: Retrospective observational study including hospitalized children with IgM(+) dengue serology. Study was approved by local ethics committee.

Results: Between January-December/2008, 115 patients were hospitalized, with a mean (range) age of 106.5 (6-226) months [20%(23) < 60 months, 57.4%(66) between 5-13 years], 53.9%(62) female. Right pleural effusion was more frequent in children < 60 months [65.2%(15) vs 35.8%(33); p=0.02, OR=3.35]. Serum albumin ≤3.4 g/dL was more frequent in children < 13 years [56.8%(25) vs 15.4%(2); p=0.008, RR=3.69]. Diarrhea was more frequent in children ≥13 years [57.7%(15) vs 26.9%(24); p=0.003, OR=3.69]. Clinical findings more frequent in males than in females: right pleural effusion [52.8%(28) vs 32.3%(20); p=0.0257, OR=2.35], respiratory distress [45.3%(24) vs 16.1%(10); p=0.0006, OR=4.3] and oliguria [30.2%(16) vs 14.8%(9); p=0.04, OR=2.5]. In children ≤ 59months (n=23), between 60-155 months (n=65) and ≥156 months (n=26), the nadir of leukocytes was respectively: 6399 (3400-13300)/mm^3, 4324 (1000-16900)/mm^3 and 3465 (1700-7700)/mm^3; p=0.00001. The mean (range) of hemoconcentration was 9.03 (0.8-37)%, beeing < 10% in 58.3%(67), between 10-20% in 39.1%(45) and >20% in 2.7%(3). The mean (range) hemoconcentration in males was 10.5 (0.8-37)% and 6.8 (1.1-19.2)% in females; p=0.039.

Conclusions: There were significant variations in clinical and laboratory findings in children and adolescents with DF according to age and gender which must be taken into account in assessing these patients.

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INFLUENZA A H1N1 AND *S .PNEUMONIAE* SEPSIS AFTER MEASLES INFECTION

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Background: Measles is one of the most contagious diseases known and carries a high mortality in developing countries often due to bacterial super infection. Despite the existence of an effective vaccine in Europe, it has not yet been eradicated. We report a child suffering from measles and subsequent co-infection with influenza A virus and *S. pneumoniae* sepsis.

Case report: Eight year old girl with a history of fever, hemorrhagic rash, coryza and conjuntival hyeremia for seven days and increased respiratory distress over the last 24h. She was admitted for suspected measles and possible superinfection. MMR vaccine was not administered. Chest X-ray showed bilateral difuse shadowing. Blood analysis demonstrated marked neutropenia (600/MicroL) and lymphopenia (900/MicroL). Blood culture was positive for penicillin sensible *S.Pneumoniae* and PCR of throat swab revealed Influenza A H1N1. She received penicillin/clindamycin and oseltamivir treatment for seven days. Measles virus grew in urine and throat swabs wheras IgG serology for measles was negative. The patient made a complete recovery. A measles outbreak with 16 was declared in the neighborhood several days later.

Conclusions: Alteration of the oral mucosal immunity is described in children infected with measles virus and may promote bacterial and viral super-infection by organisms commonly found to be carriers of the oral mucosa. The epidemiological overlap in the circulation of two highly contagious viruses such as measles and influenza virus may contribute to more severe disease presentation as it was the case with our patient.

Reference Glennie et al, Trends Microbiol. 201:0:

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INCREASED INCIDENCE OF PERTUSSIS IN A TERTIARY CARE HOSPITAL IN MADRID (SPAIN) 2010. EPIDEMIOLOGICAL AND CLINICAL FEATURES OF THIS DISEASE

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Introduction: Whooping cough is a disease that generates high morbidity and mortality in young children. After universal vaccination was introduced, a decrease of this entity was observed. The aim of this study is to describe the incidence of this disease over the last years.

Material and methods: Epidemiological, clinical and microbiological study; retrospective (2006-2009) and prospective (2010) of paediatric patients hospitalized with whooping cough in a tertiary hospital in Madrid. Diagnosis was made with DNA amplification techniques (PCR) or immunofluorescence (IF) in 2006/07.

Results: 57 patients were admitted with clinical suspicion of whooping cough. Diagnosis was confirmed in 36 patients (63%) with PCR, and no IF was positive. The median age was two months. An increase in annual incidence was observed: 3.4 cases per 100,000 pediatric emergency visits (2006), 11 (2007), 9.2 (2008), 10.2 (2009), 34.2 (2010). 72% of cases occurred in summertime (June-September). The main clinical features were cough (100%), cyanosis (58%), whoop (50%). The average hospital stay was 7 days. 12% of patients were admitted in PICU. The most frequent complication was pneumonia, with a mortality rate of 2.7%. 86.4% of the patients had received less than two doses of vaccination for pertussis. We found household contacts with symptoms consistent with pertussis in 64.8% of patients.

Conclusions: We observed a sharp increased incidence of pertussis in 2010. Most affected patients were infants under three months with incomplete vaccination, with high morbidity. Revaccination in adults should be strongly considered as they may represent important disease transmitters.

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A NOVEL SEVERITY SCORING SYSTEM TO ASSESS SEVERITY OF DISEASE IN AUSTRALIAN CHILDREN HOSPITALISED WITH PERTUSSIS INFECTION DURING AN EPIDEMIC

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Background and aims: Pertussis is the most common vaccine preventable disease in Australia. Despite high immunisation coverage, Australia is experiencing its worst epidemic since introduction of pertussis vaccine into the national childhood immunisation program. The aim of this study was to assess the severity of disease in Australian children hospitalised with pertussis during an epidemic using an objective pertussis severity scoring system designed in Adelaide.

Methods: Variables assessed included length of hospitalisation, frequency of apnoea, level of hospitalisation required, respiratory support, presence of complications and requirement for intravenous fluids (score range 1-18).

Results: Data from 132 children hospitalised in Australia were scored using the pertussis scoring system. 60.6% of admissions scored as mild (score < 7) and 39.4% as moderate-severe (score ≥ 7). 63.6% of moderate-severe cases were in infants < 2 months. The mean severity score for infants < 2 months, 2-< 6 months and 6-12 months was 7.6 (range 2-18), 4.6 (range 2-11) and 7.3 (range 2-16) respectively. For infants < 2 months, 56.9% were assessed as moderate-severe compared to 23.5% in 2-6 month old infants. 55% of Indigenous children scored moderate-severe disease (score ≥7) compared to 38% of non-Indigenous children.

Conclusions: The majority of severe disease occurs in very young infants although severe disease also occurred frequently in children to 12 months of age and Indigenous children. A universal objective scoring system can aid in assessing the impact of pertussis, identifying risk factors for severe disease in children and predicting health resource requirements during an epidemic.

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CHAGAS DISEASE SCREENING OF PREGNANT LATIN AMERICAN WOMEN

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Introduction: Spainis receiving an increasing number of immigrants from South America (SA) due to geographical and historical reasons. The aim of this study is to show the two years experience of Chagas disease screening in pregnants proceeding from SA.

Methods: The study was carried out from February 2009 to February 2011. A enzyme immunoassay (ELISA) was made to all pregnant Latin American women and was confirmed with indirect inmunofluorescence test. Infants born to positive mothers were monitoring by microhematocrit in blood from umbilical cord, PCR, and serology test at both first and eighth month of life.

Results: A total of 598 pregnant women mainly from Bolivia and Colombia were analyzed. We obtained 33 positive tests (5.5%).So far, nineteen children have been studied. One of them was diagnosed as congenital Chagas disease when he was 2 months old (transmission rate: 5.2%) and received treatment with benznidazol during 60 days; *T.cruzi* PCR was negative after 2 weeks of the end of therapy, and seroversion was observed after 82 days. Congenital transmission was discarded in five cases at an average of 8.8 months of life.Thirteen infants continue on study.

Conclusions: The incidence of this sample series is similar to that of other publications fromnon endemicscountries. However, transmission rate is higher. We consider that non endemic countries might to establish guidelines for screening of Chagas diseases in pregnant women proceedingfrom endemic areas.

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OUTCOME OF PEDIATRIC PATIENTS WITH SEPSIS AND MULTI-ORGAN DYSFUNCTION SYNDROME REQUIRING CONTINUOUS RENAL REPLACEMENT THERAPY

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The outcome of pediatric patients with septic shock leading to multiorgan dysfunction syndrome (MODS) is poor. The aim of this study is to document illness severity and look for prognostic factors in children with MODS receiving continuous renal replacement therapy (CRRT).

Methods: From 1990 to 2010 21 pediatric patients with sepsis and MODS were treated with CRRT at the Pediatric ICU.

Results: The mean age of the patients was 5.4±6.1 years, the mean body weight 20±18 kg, 16 males, 5 females. The origin of sepsis was bacterial infection in 14 patients, viral infection in 6 patients, and fungal infection in one patient. The most common causes leading to CRRT were cardiocirculatory failure. Overall survival rate was 52%. Mean arterial pressure was significantly lower for nonsurvivors versus survivors (60±12 vs 54±13 mmHg) at initiation of CRRT. Patients with a fluid overload higher than 20% of body weight had mortality rates of 66 %. Immunsuppressed patients had a mortality rate of 71 % and all patients with additional failure of the GI-tract died. The mean number of OSF and PRISM scores at initiation of CRRT were 4.4±0.6 and 21±9 in survivors and 5.1±0.7 ($p < 0.01$) and 26±11 ($p < 0.01$) in nonsurvivors.

The main reason for mortality was persisting multi-organ dysfunction syndrome.

Conclusion: Despite CRRT persisting MODS results in a high mortality rate, especially in immunsuppressed children. A low mean arterial pressure, and a fluid overload >20% of body weight at initiation of CRRT are also associated with a significantly higher mortality rate.

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ORTHODONTIC BRACKETS AND LEMIERRE'S SYNDROME

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Background: Lemierre syndrome´s incidence is increasing again and estimated at 3.6 cases per million people per year with two population groups at greater risk: previously healthy adolescents (14.4 cases per million per year) and elderly with underlying disease.

Aim: Introduce a new hypothesis for the pathogenesis of Lemierre's syndrome.

Methods: Case presentation and literature review.

Results: A 14-year old female with brackets and gingivitis was hospitalized with classic Lemierre's syndrome, which diagnosis was based on the clinical presentation, blood tests, blood culture growing Fusobacterium nucleatum, and a CT-scan showing internal jugular vein thrombosis. The literature reveals various hypotheses for the rising incidence of Lemierre syndrome: a more selective use of antibiotics to treat pharyngitis, use of antibiotics that lack activity against *Fusobacteria*, contribution of new, more virulent serotypes and early recognition by advanced imaging techniques. However, unclear remains why healthy adolcescents are at greater risk. Explanations may be that one develops protective antibodies during life and an acute first *Fusobacterium* infection at young age is potentially overwhelming or maybe an association exists with *group C Streptococcal* tonsillitis or acute EBV infection that causes temporary T-cell suppression and mucosal damage enabling invasion of *Fusobacteria* into tissues. Our case leads to another hypothesis. Brackets alter the oropharyngeal colonization and increase the load of potentially pathogenic oropharyngeal bacteria, especially *Fusobacteria*, up to 6 months after initiation of treatment which was the case in our patient.

Conclusion: We propose that orthodontic treatment may increase the risk of Lemierre's syndrome in adolescents.

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FIVE CASES OF ATYPICAL PRESENTATION OF RICKETTSIAL INFECTIONS

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Background: *Rickettsia conorii* is the most frequent species of *Rickettsia* in Portugal. In general the disease manifests itself by fever, exanthema, headaches and the presence of an eschar. However atypical forms can be present and physicians should be aware.

Aims: Analyze the atypical presentation of rickettsiosis.

Material and methods: Children admitted from 2000 to 2010. Clinical diagnosis was confirmed by serology and molecular techniques (PCR).

Results: Five cases with a median age of 2 years, were admitted between June and August. The diagnoses were: myositis (1), synovitis (1), cholecystitis (1), orchiepididymitis (1) and meningitis (1). Myositis expressed with functional disability, CPK 9600U/L, lower limbs' edema, hypoalbuminemia (1,6g/dL) and arterial hypertension. Synovitis manifested with functional disability, synovial fluid increase and CRP 16,2mg/dL. The child with cholecystitis had abdominal pain, intra-abdominal fluid increase, leukopenia (1900/µL), thrombocytopenia (75000/µL) and CRP 15,3mg/dL. Orchiepididymitis developed with testicle's inflammatory signs, leukopenia (2900/µL), thrombocytopenia (90000/µL) and CRP 14,45mg/dL. The patient with meningitis, who had pleocytosis (320cells/µL), hyperproteinorrachia (284mg/dL), hypoglicorrachia (36mg/dL), presented only with fever and headaches. The tache noire and the classical triad were present in 3/5 cases. The clinical course was favourable in all cases. Antibodies against *Rickettsia* of spotted fever group were detected in 3/5 cases. In one patient *Rickettsia conorii Malish* strain was identified by PCR and sequencing.

Conclusions: Rickettsial infection may present itself unusually. In a country of high prevalence, especially during summer months and in the presence of an inoculation eschar, it is of the uttermost importance to study the atypical presentations for a possible rickettsial infection.

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OUTCOMES OF HOSPITALIZED PATIENTS WITH PANDEMIC INFLUENZA. EXPERIENCE AT A TERTIARY-CARE CHILDREN'S HOSPITAL

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During the 2009 pandemic of influenza AH1N1 virus, a large proportion of hospital admissions were younger patients, unlike during seasonal influenza. The aim of this study was to evaluate the outcome and complications of children and adolescents who required admission to our hospital.

Methods: This is an observational study of a retrospective cohort composed of patients admitted to a large tertiary care center at Madrid (Spain). Our hospital brings together the care of patients with acute conditions and the management of patients with chronic and complex diseases. The patients included, were hospitalized between April and December 2009 and had pandemic influenza AH1N1-2009 infection confirmed by PCR.

Results: 128 patients fulfill inclusion criteria. The average age at admission was 5´3 years (range 0-18). The proportion of male was higher (65%). 68% had previous medical conditions: asthma was the most frequent, although neurocognitive disease, heart disease and immunosuppression were very relevant. Fever on admission was present in 87% of patients. 93% were treated with oseltamivir. Some patients developed more severe complications and 12% were admitted to critical care units. Three patients died (2.3%). Risk factors for admission to critical care were the underlying heart disease, cognitive impairment, parenchymal condensation on chest radiograph and the need for oxygen therapy at admission.

Conclusions: The flu pandemic of 2009 conditioned a high number of hospital admissions in children and adolescents, mainly in those with underlying chronic diseases. A high percentage of patients progressed to more severe forms, usually severe bronchopneumonia.

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PANDEMIC HUMANH1N1 INFLUENZA INFECTIONS IN KURDISTAN: EPIDEMIOLOGY AND RISK FACTORS FOR SEVERE DISEASE

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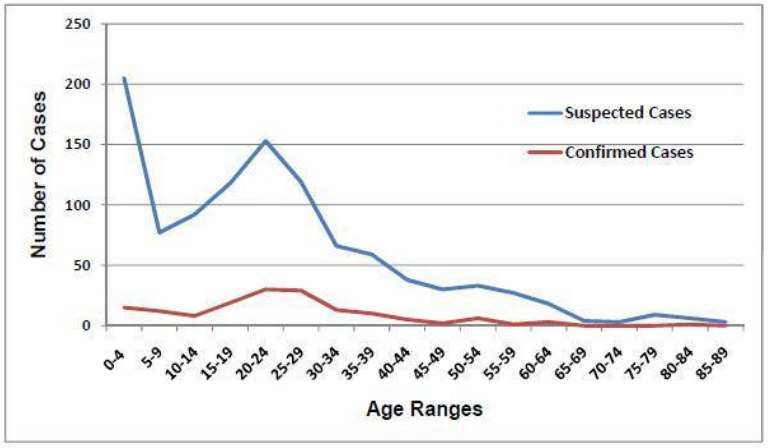
Background and aims: Information on influenza disease burden is essential for policy makers in control programs. Epidemics of swine influenza A/H1N1 virus occurred in many provenience of Iran in 2009 pandemic. Again in 2010, Epidemic of H3N2 killed 13 persons (confirmed Cases). In response the Iran Ministry of Health established the National Avian Influenza Surveillance system late in 2009. The system's mandate was the identification and prompt investigation of suspected human infections in all health-care facilities nationwide.

Methods: A cross-sectional study was carried out in Kurdistan Province. During January 2009 through December 2009, all hospitalized patients presenting with high fever and respiratory symptoms, were investigated. Clinical and demographic data, risk factors and respiratory swab specimens were collected and tested by PCR for influenza. All cases classified according to WHO criteria for Probable and Definitive cases of influenza.

Results: 1060 persons were investigated because of symptoms and signs simulating Influenza (suspected cases), 154 (15%) laboratory-confirmed human influenza infections was identified. Only one influenza - associated death was reported. The mean age of sampled cases (in both groups) was 23 years and 47% were male.



[Age distribution of sampled cases]

Conclusions: Our findings suggest that children and young Adults with human influenza infection are at increased risk for severe disease. The lethality of influenza A (H1N1) 2009 infection were low in our province. Further research on influenza-associated morbidity and mortality using hospital discharge and influenza surveillance databases is needed to inform influenza control policies and support pandemic preparedness planning.

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EPIDEMIOLOGY OF HAND-FOOT-MOUTH DISEASE AMONG CHILDREN IN SHANGHAI BETWEEN 2007 AND 2010

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Background and aims: Hand foot mouth diseases (HFMD) has outbreaked in China since 2008 and costed the life of young children. This retrospective study is to understand the epidemiological features of pediatric HFMD in Shanghai from 2007 to 2010.

Methods: We analyze the epidemiological data of all HFMD cases seeking medical care at the largest-scale pediatric infectious diseases center in Shanghai, which represented about 30% of cases in Shanghai.

Results: 28058 outpatients were diagnosed as HFMD during four years, of whom, 3948(14.07%) were hospitalized, 730（2.60%）severe cases were complicated with neurological involvement and or pulmonary edema/hemorrhage and 11（0.04%）died. The peak season was seen in summer months (May to July). HFMD displayed unprecedented outbreak in 2010. More boys were affected than girls . Since 2008, the major population affected shifted from native shanghainese and day-care center children to migrant and home-care children. 81.88% were children aged 1 to 4 years old. Among 120 severe cases in 2009, EV71 was positive in 119(99.17%); of 431 severe cases in 2010, EV71 was detected in 86.08%. Based on inaptient's surveillance in 2010, EV71 was detected in 54.52% of inpatients in 2010. 12 critically ill cases with pulmonary edema/hemorrhage were infected with EV71.

Conclusion: HFMD has imposed an public health concern. A seasonal peak appears in summer season. Home-care and migrant children have become the predominant susceptible population. EV71 predominance is associated with the outbreak of HFMD and the occurrence of severe and fatal cases.

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EPIDEMIOLOGICAL CHARACTERISTIC OF NOVEL INFLUENZA A H1N1 AND SEASONAL INFLUENZA A AMONG CHILDREN IN SHANGHAI

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Background and aims: Influenza is a common cause of outpatient visits during outbreak. This study focuses on the epidemiological features of novel influenza A H1N1 and seasonal influenza A among pediatric outpatients with influenza-like illness.

Methods: We prospectively collected nasopharyngeal/throat swab from eligible children during Jun 2009 to Jan 2010 in Shanghai. One-step real-time RT-PCR was used for detecting influenza A virus.

Results: 2049 children were enrolled and novel H1N1 were laboratory-confirmed in 169(8.25%) and seasonal influenza A in 278(13.57%). The outbreak of seasonal influenza A were observed from Aug to Sep 2009 and from Sep to Oct 2010. The median age of 280 children infected with seasonal influenza A virus was 29-month-old. 136(48.57%) had exposure history and 87% were exposed to family members. Novel H1N1 was detected between Aug 2009 and Feb 2010, and outbreak between Sep and Dec 2009. novel H1N1 reappeared in Dec 2010 and outbreak in Jan 2011. During pandemic period and seasonal prevalence of novel H1N1, the age and exposure of affected children were distinct (median age: 59 *vs* 35 months; exposure: 55.56% in day-care center *vs* 68.09% in family). Almost all children didn't receive influenza vaccine within one year.

Conclusion: Novel influenza A H1N1 displayed different seasonal pattern from seasonal Influenza A. During pandemic season, preschool and school-age children were most affected. Younger children were most affected with seasonal influenza A. Intrafamily transmission play a major role in spread of seasonal influenza and institutional exposure was the main mode of pandemic transmission.

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IMPACT OF FRENCH ANTIBIOTIC GUIDELINE FOR ACUTE RESPIRATORY TRACT INFECTIONS IN A PEDIATRIC EMERGENCY DEPARTMENT, 2005-2009

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Context: Antibiotic use leads to the emergence and the dissemination of multi-resistant bacteria. Acute Respiratory Tract Infections (ARTI) are the main reason for antibiotic prescription in children. In 2005 the French medicine agency (AFSSAPS) published new guidelines to reduce the misuse of antibiotics in ARTIs.

Objective: To determine the usefulness of the implementation of guidelines to reduce antibiotic prescriptions for ARTI in a Pediatric Emergency Department (PED).

Methods: Retrospective cohort study in a French PED from November 2005 (date of implementation of this guideline in our institution) to October 2009. We retrieved for every child diagnosed as ARTI: date of visit, age, diagnosis, antibiotic prescription.

Main outcome measures: Proportion of ARTI visits that resulted in antibiotics at discharge during and after the implementation of the French guidelines.

Results: During the study 60165 children have been diagnosed as ARTI in our PED. Antibiotic prescription at discharge in our PED was related in approximately 60% to an ARTI visits. The proportion of antibiotic prescription in ARTI visits fell from 29,8% during the first year of implementation of guideline to 19,9% at year 4 ($p< 10^{-6}$). The percentage of antibiotic prescription at discharge decreased for most ARTIs except for Acute Otitis Media and pneumonia for which the percentage remained stable. Amoxicillin/clavulanic acid and amoxicillin were the two most prescribed antibiotic and respectively accounted for 50% and 35% of antibiotic prescriptions.

Conclusions: Antibiotic prescriptions for ARTI declined significantly in our PED with the implementation of French antibiotic guidelines.

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EVOLUTION OF THE MENINGOCOCCAL DISEASE´S INCIDENCE ON PAEDIATRIC NAVARRE´S POPULATION (NORTH OF SPAIN)

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Introduction: The meningococcal disease is a clinical feature of low incidence but with a very important epidemiologic weight, because its high morbimortality

Objectives:

- Analysis about evolution of invasive meningococcal disease´s (IMD) incidence on paediatric Navarre´s population.

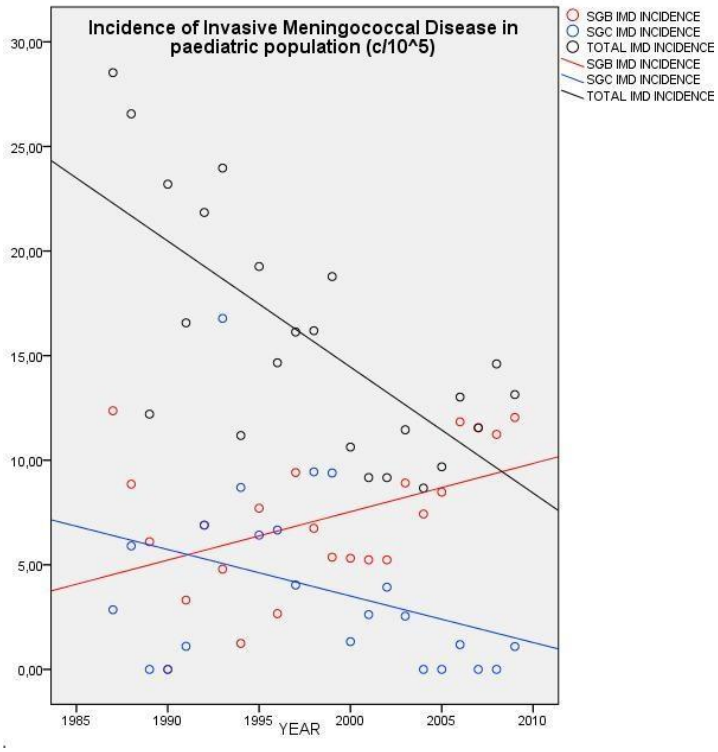
- Evaluate changes on the IMD´s incidence on after introduction of the systematic vaccination against meningococcal C at the last months on 2000 year.

Methods: Population data was obtained from Census of Navarre.

Meningococcal disease data was obtained from the Navarre´s Institute of Public Health from January of 1987 to december of 2009.

Statistical analysis: Student T test, Chi Square test and binary logistic regression.

Results: We observed a global decrease in IMD´s incidence on our population from prevaccinal period(1987-2000) to postvaccinal(2001-2009), from 18,54 to 11,16c/10^5(OR:0,594; CI95%:0,463-0,763). This fall was due to the drop in cases of serogroup C(SGC) from 5,67 to 1,26c/10^5(OR:0,221;CI95%:0,110-0,444) and in non-grouped cases. On the contrary, the cases of serogroup B(SGB) increased on the postvaccination period(from 5,76 to 9,1c/10^5;OR:1,576;CI95%:1,13-2,198). When we stratified by ages and serogroups, we observed an important decrease in SGC incidence in younger groups: 0-5years(OR:0,033;CI95%:0,004-0,237) and 5-9years(from 3.56 to 0c/10^5). In these groups there were not significant rises in SGB incidence. In the other hand SGB incidence increase in older group(10-15years:OR:4,66;CI95%:1.20-18,04) with no significant fall in SGC incidence.



[Incidence of Invasive Meningococcal disease]

Conclusions: After the introduction of vaccination, there was a decrease in IMD´s incidence on paediatric population. However, the important fall of SGC cases on little children has been disguised by the increase of SGB cases on older groups.

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A NATIONAL SURVEY OF THE INCIDENCE AND EPIDEMIOLOGY OF KAWASAKI DISEASE IN IRELAND

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Background and aims: Kawasaki disease (KD) is an acute vasculitic syndrome of unknown aetiology. It is now the commonest cause of acquired cardiac disease in children in the developed world. This study aimed to determine prospectively the incidence and epidemiology of KD in Ireland between 2008 - 2009.

Methods: The Irish Paediatric Surveillance Unit issues monthly notification cards to all paediatricians. Surveillance for KD took place from January 2008 through December 2009. Paediatricians who reported a case were issued with a questionnaire seeking further information..

Results: There were 23 cases of KD recorded during the 2 year study period. 74% were under 5 years which represents an annual incidence of 2.03 /100,000 children under five years. Eleven cases (47%) were classified as incomplete or atypical KD. Average age at presentation was 3 years 2 months (median 4years 6months; range 3.5months- 8years 11months). Median duration of fever prior to therapy was 7 days (range 1 to 28 days). Four children (17%) had coronary artery abnormalities at presentation: coronary artery dilatation, 3; and coronary aneurysms, 1. Twenty cases (87%) received aspirin and IV immunoglobulin. Three cases presented after 3 weeks of symptoms and received aspirin alone.

Conclusions: The incidence of KD in this study is low by international standards. Almost half of cases were incomplete KD, which may be explained by increased awareness of atypical presentations. However, 3 children (13%) were late presenting, suggesting that awareness of KD still needs to be reinforced.

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EXCESS PNEUMONIA AND INFLUENZA (P&I) HOSPITAL ADMISSIONS IN EL SALVADOR 2007-2009

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Background: The burden of influenza is unknown in most Central American countries. However southern seasonality of influenza recently described in El Salvador (2010), allows for application of methods used in in the United States. The aim of this study is to determine excess of cases of hospital admission cases due to P&I occurred in El Salvador during 2007-2009.

Methods: We identified data on weekly hospital admissions for P&I (ICD-10 codes J10-J18) and weekly results of influenza testing collected by the Ministry of Health of El Salvador from January2007-December2009. We defined the epidemic period when the percentage of specimens positive for influenza exceeded 10% for 2 consecutive weeks. We fitted a Serfling model to the hospitalization data. We estimated the number of influenza-associated hospitalizations as the difference between observed number of P&I events and number expected by the model (and 95% confidence intervals).

Results: During the 3-year period from 2007-2009, we estimated a total of 50,320 hospitalizations for P&I in El Salvador, of which 7,751(15%) [95%CI 10,514-5,556] were excess hospitalizations associated with influenza infection. The number and percent of influenza-associated P& I hospitalizations varied from 2,902(16%) [95%CI 1,937-3,888] in 2007, 55(0.5%) [95%CI 0-530] in 2008, and 4,794(23%) [95%CI 3,619-6,096] in 2009.

Conclusions: Our data demonstrate that influenza virus may be responsible for and average of 15% of all hospital admissions for P&I, though varied widely by year in this study, this high influenza disease burden suggests it necessary to strengthen measures in order to protect public health, such as vaccination.

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PERTUSSIS SURVEILLANCE AND SAZONALITY IN SÃO PAULO STATE, BRAZIL - 2000 - 2010

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Background and objectives: In comparison with other countries, Brazil report low incidence rates for Pertussis. Since 2000, São Paulo state developed a model for Pertussis surveillance based on reference centers (n = 33). This study describes the trends and seasonally of pertussis in SP state from 2000 until 2010.

Methods: Pertussis suspected cases are registered in SINAN (national system of information) and investigated by CVE. Lab tests to confirm pertussis are made in IAL, and until 2009 culture was the most relevant criteria for Pertussis´ confirmation. We analyzed confirmed Pertussis cases registered in SINAN by reporting center (included or not in surveillance net), age, year and month of notification.

Results: 1,331 pertussis confirmed cases were identified, 81% in children < 1 y. The reference centers reported almost 40% of cases. Pertussis incidence varied from 0.2/100,000 in 2000, till 0.6/100,000, in 2008 (epidemic year). The majority of cases was confirmed in summer (peak in January), but in 2007 and 2008, the outbreak was announced by a higher number of pertussis cases in winter (July/August).

Discussion: These results showed that the higher number of pertussis cases during winter can point to risk for a new outbreak. As human beings are the only Pertussis reservoir, certainly the disease burden is underestimated when 80% of cases are confirmed in young babies. Medical education and new lab tests to confirm pertussis (PCR and serologic tests) can improve the quality of Pertussis diagnosis and give support for control of this disease.

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REAL-TIME POLYMERASE CHAIN REACTION (RT-PCR) IMPROVED PERTUSSIS DIAGNOSIS IN SÃO PAULO STATE IN 2009/2010, BRAZIL

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

Methods: We studied a total of 932 nasopharyngeal swabs collected between 2009-2010 with culture and RT-PCR. The samples were cultured using standard methods and the RT-PCR reaction was performed in the thermocycler model 7300 from Applied Biosystems including specific primers and probes for detection of toxin gene ptxS1 and the insertion element IS481.

Results: Among 932 swabs analyzed, 67 (7.2%) were culture and RT-PCR (PtxS1/IS481) positive for B. pertussis; 98 (10.5%) swabs were positive only by RT-PCR and the remaining 767 (82.0%) swabs were negative for both techniques.

Conclusions: The introduction of RT-PCR for pertussis diagnosis was an excellent additional method, demonstrating high sensitivity and greater positivity in comparison with culture. The authors concluded that RT-PCR should always be performed simultaneously to culture.

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MEASLES: EPIDEMIOLOGICAL UPDATE IN FERRARA PROVINCE, ITALY

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Background and aims: Description of epidemiological trend of Measles between March 2010 and January 2011 in a population with consistently high and improving immunisation coverage in Ferrara province. Vaccine coverage with one dose at 24 months of age has constantly improved, going from 94.9% in 1999 to 96.7% in 2008. This produced a reduction in the number of notified cases of Measles; however, 24 cases, 20 of which confirmed, were notified in the considered period.

Methods: Notification forms sent to the Department of Public Health of the Local Healthcare Unit of Ferrara have been collected. Since 1999, only those subjects with a laboratory-confirmed diagnosis of Measles (IgM positives) are reported to the regional information system of infectious diseases in Emilia-Romagna.

Results: Between March and May 2010 23 cases, 19 confirmed (14 IgM positive and 5 epidemiologically linked) were notified. One more case was notified on January 28th, 2011, after a free interval lasting 7 months. The mean age of the 20 confirmed cases was 23.3 years. Nin**e** (45%), 4 (20%) and 7 (35%) cases occurred in age classes 0-14, 15-24 and 25-64 years, respectively. Hospitalization was required for 11 patients. One patient suffered from Measles' pneumonia.

Conclusions: Our data confirm how difficult it is to decrease the incidence of Measles below 1/100.000 live births, high vaccination coverage notwithstanding. It is therefore necessary to further increase population immunity and improve surveillance system.

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CHICKENPOX COMPLICATIONS, INCIDENCE AND FINANCIAL BURDEN IN CHILDREN IN ANKARA IN THE PRE-VACCINATION PERIOD

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Background and aims: To determine the complications, financial burden and mortality caused by chickenpox using the data of the region we serve (Ankara) in the pre-vaccination period.

Methods: The study was conducted as a retrospective sectional study at Ankara University.

Results: Of the 65 patients admitted to the our hospital, 34 (52.3%) had been previously healthy, 10 patients (15.4%) had chronic disease and 21 patients (32.3%) were immunocompromised due to hematological/oncological disease. Mean cost per patient for these patient groups were 1260±1445, 627±321 and 918±993 Turkish Lira (TL)(1 TL=0.5 €), respectively. The most common complications of the chickenpox in those patient groups were skin and soft tissue infections (41.2%), hematological complications (50%) and gastrointestinal complications (38.1%), respectively. We found that a total of 105 patients had been treated for chickenpox as inpatients while 3 had died in the 11 hospitals providing inpatient care for pediatric patients in Ankara in 2008. Projecting these data to the age 0-17 general population data for Ankara, we found a 10.6/100000 and 8.7/100000 rates of hospitalization due to chickenpox in Ankara for all children and previously healthy children, respectively. Additionally, the mortality rate for the 0-17 age group was 3.03/1000000 in Ankara. The projected cost related to chickenpox complications for Turkey for all patients and previously healthy patients as 1972500 and 1941660 TL, respectively.

Conclusions: We feel that a national vaccination program for chickenpox will lead to a significant decrease in the overall cost to our country, as observed in other countries with such a program.

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PERITONITIS IN A PEDIATRIC DIALYSIS UNIT: LOCAL PROFILE AND IMPLICATIONS

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Background and aims: Peritonitis is a major complication of chronic peritoneal dialysis (PD). In line with recent recommendations, we analysed peritonitis episodes in our unit to define local microbiological profile and identify local predisposing factors.

Methods: The files of all the children treated with chronic PD during the 10 year period 1997-2007 were reviewed.

Results: Eighty peritonitis episodes were recorded in 29 children (20 male, 9female) aged 0.1-18.5 years(median 11.75) treated with PD for 6-69 months (median 19) for a total 578patient-months. The annual peritonitis rate was 1.66/patient. The main pathogens were coagulase-negative *Staphyloccocus* (32.5%)and *Pseudomonas spp* (16%), which were also cultured in 64-69% of exit sites in the 3 months preceeding peritonitis. No peritonitis ocurred in 31%of patients. All patients less than 5 years old had at least one peritonitis episode.Contaminating conditions(gastrostomy, enuresis, diaper use), found in 44% of the study group and first infection within 6 months from starting PD were significantly associated with an increased peritonitis rate (p=0.01and 0.009, respectively). 18% of patients had to be switched to hemodialysis for recurrent infections. There were no deaths.

Conclusions: Risk factors for peritonitis in our study were: 1st infection within less than 6 months from PD start, Pseudomonas exit site infection, contaminating conditions and young age at thearpy start :< 5 yrs. These susceptible subgroups should be especially targeted during training of caregivers.

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GUILLAIN-BARRÉ SYNDROME: BACKGROUND INCIDENCE RATES IN THE NETHERLANDS

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[1]Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, [2]Departments of Neurology and Immunology, [3]Department of Medical Informatics, [4]Department of Epidemiology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

Background: Guillain-Barré syndrome (GBS) is a (sub)acute polyradiculoneuropathy, which may occur as a Serious Adverse Event following immunisation. To interpret the occurrence of GBS after introduction of large scale immunization programmes, it is important to define recent background incidence rates of GBS.

Method: We used a general practitioner electronic medical record database (IPCI) to assess age specific GBS background rates between January 1996 and April 2008 in the Netherlands. All possible cases of GBS were manually reviewed. Validated incident cases were reviewed by a neurologist for diagnostic certainty using the GBS case definition of the Brighton Collaboration (BC).

Results: In a population of 638,891 persons, we identified 23 validated incident GBS cases (mean age 46 year). The incidence rate (IR) was 1.14 per 100,000 person years (95%CI 0.67-1.61) and was significantly lower for people under 50 years (0.76; 95%CI 0.41-1.32) compared with elderly of 50 years or older (1.80; 95%CI 0.98-3.05). We found no significant differences in age- and calendar year specific IR between men and women. There was no trend in time or season of IR over the years under study. Only 6 cases fulfilled level 1 or 2 of diagnostic certainty of the BC case definition.

Conclusion: The incidence rate of GBS increases with age. Since vaccinations are often targeted at specific age groups, age specific rates should be used to monitor GBS observed versus expected rates after introduction of large scale vaccination programmes.

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BACKGROUNDRATES OF IMMUNE MEDIATED DISORDERS IN THE NETHERLANDS FOR VACCINOVIGILANCE, 1996-2007

N. van der Maas[1], J.P. Dieleman[2], J.M. Kemmeren[1], M.A. Kramer[1], M.C.J.M. Sturkenboom[3], **H. de Melker**[1]

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Background and aims: In 2010 vaccination against human papilloma virus (HPV) infection for 12 year old girls was introduced in the Dutch National Immunisation Programme, preceded by a catch-up campaign for 13-16 year olds. Several immune mediated disorders (IMDs) manifest during this stage of life, therefore sometimes occurring in close time relation with HPV vaccination. Age- and sex-specific background incidence rates (IR) are needed to enable rapid evaluation of safety-signals using observed versus expected analyses.

Methods: We used a general practitioner electronic medical record database (IPCI) to assess age- and sex-specific IRs of autoimmune hepatitis (AIH), type1 diabetes mellitus (type1DM), juvenile rheumatoid arthritis (JRA), myasthenia gravis (MG), encephalitis without an identified microbial cause (ENC), idiopathic thrombocytopenic purpura (ITP), Graves disease (GD), Hashimoto's thyroiditis (HT) and Henoch-Schonlein purpura (HSP) between 1996 and 2007 in the Netherlands. All possible cases were manually reviewed.

Results: Table 1 shows overall IRs and IRs for 10-14 and 15-19 year olds for each IMD. Rates per calendar year showed non significant fluctuation.

IMD	AIH	type1DM	JRA	MG	ENC	ITP	GD	HT	HSP
IR all ages (95%CI)	1.5 (1.0-2.1)	6.0 (5.0-7.2)	1.4 (1.0-2.0)	1.3 (0.9-1.9)	0.6 (0.3-1.0)	1.0 (0.6-1.5)	13.9 (12.3-15.6)	5.5 (4.5-6.6)	3.5 (2.7-4.4)
IR 10-14 y females(95%CI)	0 (0-4.3)	17.7 (9.1-31.3)	3.5 (0.7-11.3)	0 (0-4.3)	0 (0-4.3)	0 (0-4.3)	7.1 (2.4-16.8)	7.1 (2.4-16.8)	7.1 (2.4-16.8)
IR 15-19 y females(95%CI)	1.8 (0.2-8.5)	10.9 (4.5-22.5)	5.4 (1.5-14.5)	1.8 (0.2-8.5)	0 (0-4.5)	3.6 (0.7-11.6)	12.7 (5.7-24.9)	3.6 (0.7-11.6)	3.6 (0.7-11.6)

[incidence rates per 100,000 py for 1996-2007]

Conclusions: For 1996-2007 IRs of several IMDs are rather stable in the Netherlands. There are important age- and sex-specific differences in IRs. These specific IRs are an important tool in vaccinovigilance to address safety-signals arising during mass vaccination campaigns targeting specific age groups.

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BACKGROUNDRATES OF IMMUNE MEDIATED DISORDERS IN THE NETHERLANDS FOR VACCINOVIGILANCE, 1996-2007

N. van der Maas[1], J.P. Dieleman[2], J.M. Kemmeren[1], M.A. Kramer[1], M.C.J.M. Sturkenboom[3], **H. de Melker**[1]

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Results: Table 1 shows overall IRs and IRs for 10-14 and 15-19 year olds for each IMD. Rates per calendar year showed non significant fluctuation.

IMD	AIH	type1DM	JRA	MG	ENC	ITP	GD	HT	HSP
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IR 10-14 y females(95%CI)	0 (0-4.3)	17.7 (9.1-31.3)	3.5 (0.7-11.3)	0 (0-4.3)	0 (0-4.3)	0 (0-4.3)	7.1 (2.4-16.8)	7.1 (2.4-16.8)	7.1 (2.4-16.8)
IR 15-19 y females(95%CI)	1.8 (0.2-8.5)	10.9 (4.5-22.5)	5.4 (1.5-14.5)	1.8 (0.2-8.5)	0 (0-4.5)	3.6 (0.7-11.6)	12.7 (5.7-24.9)	3.6 (0.7-11.6)	3.6 (0.7-11.6)

[incidence rates per 100,000 py for 1996-2007]

Conclusions: For 1996-2007 IRs of several IMDs are rather stable in the Netherlands. There are important age- and sex-specific differences in IRs. These specific IRs are an important tool in vaccinovigilance to address safety-signals arising during mass vaccination campaigns targeting specific age groups.

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AN ECONOMIC EVALUATION OF PEDIATRIC VARICELLA HOSPITALIZATIONS IN TURKEY: A NATIONWIDE SURVEY AT PREVACCINE ERA (VARICOMP STUDY-2)

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Aim: There is a lack of precise information on varicella disease burden and cost's in Turkey.

Methods: We retrospectively evaluated medical records of hospitalized children due to varicella related conditions from 24 tertiary care center of 14 cities (represents 47.2% of children aged between 0-18 years) between October 2008-October 2010.

Results: 640 children (3 days-216 months, 357 boys; 283 girls) have been reported during this time period (325 first year,315 second year). Median age was 36 months and 33% are < 12 months. Most hospitalizations(76.6%) for varicella occurred in children with no underlying medical conditions. Only one child has a history of varicella vaccination. Boys outnumbered girls by a ratio of 1.26. Hospitalizations varied seasonally with a peak in January-February and a second peak in May-June. The annual incidence of hospitalization by varicella in Turkey was 2.73/100.000 children at first year and 2.65 at second year. The highest hospitalization rate was observed in neonates and infants (7.8/100.000 children). Mean hospitalization cost per children was 610$(varies between 124-22266$). Total cost of hospitalization for recent two year by varicella was 397.543$. In our country based perspective, the cost of varicella related hospitalizations (estimated 655 to 1043 cases) in children is 634,439$.

Conclusion: Annual incidence of varicella hospitalization in Turkey was similar with European countries. The annual cost of these hospitalizations reflects only small part of the overall cost, as only limited number of cases requires hospitalization and indirect costs were not included. The disease burden of varicella could be potentially reduced widespread varicella immunization.

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REVIEW OF THE BURDEN OF COMMUNITY AND HOSPITAL-ACQUIRED ROTAVIRUS GASTROENTERITIS IN THE PEDIATRIC POPULATION OF WESTERN EUROPE

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Background and aims: Rotavirus affects 95% of children worldwide by age 5 years and is the leading cause of severe dehydrating diarrhea. The objective of this review was to estimate the burden of rotavirus gastroenteritis (RVGE) in the Western European pediatric population.

Methods: A literature search (1999 -2010) was conducted in PubMed and other sources (CDC; WHO, others). Data on the epidemiology and burden of RVGE among children < 5 years-old in Western Europe -including hospital-acquired disease-were extracted for 16 countries.

Results: 76 studies from the 16 countries were identified. The mean percentage of acute gastroenteritis (AGE) cases caused by rotavirus ranged from 25.3% - 63.5% in children < 5 years of age, peaking during winter. Incidence rates of RVGE ranged from 1.33 - 4.96 cases/100 person-years. Hospitalization rates for RVGE ranged from 7% to 81% depending on the country. Nosocomial RVGE accounted for 47% - 69% of all hospital-acquired AGE and prolonged hospital stays by 4 - 12 days. Each year, RVGE incurred $0.54 - $53.6 million in direct medical costs and $1.7 - $22.4 million in indirect costs. Full serotyping data was available for 8 countries. G1P[8], G2P[4], G9P[8], and G3P[8] were the most prevalent serotypes (cumulative frequency: 57.2% - 98.7%). Serotype distribution in hospital-acquired RVGE was similar.

Conclusions: This is the first review of RVGE burden across Western Europe. It confirms that RVGE is a common disease associated with significant morbidity and costs. A multivalent vaccine protecting against multiple serotypes may decrease the epidemiological and cost burden of RVGE in Western Europe.

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*STREPTOCOCCUS GALLOLYTICUS AND PRETERM NEONATES: R*EPORT OF 8 UNEXPECTED CAUSES OF BLOODSTREAM INFECTION IN A UNIVERSITY HOSPITAL

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Background and aims: In 2006, 5 cluster cases of neonatal bloodstream infection due to *Streptococcus gallolyticus* were notified. One new case in 2008 and two others cases in 2010 that involved *the same pathogenic* were reported in the same neonatal unit. The aim of this abstract is to describe the investigation and the control led to the fall of the cases to characterize the pathogenic, the spring of exposure and the mode of contamination.

Methods: Each time, accurate epidemiological typing was carried out to identify the pathogenic. Infection controls procedures were assessed, workplace practices were observed. Different sampling (environment, mother, healthcare workers) were carried out.

Results: In 2006, all of the preterm neonates were infected with an only strain of *S. gallolyticus susbspecies pasteurianus*. In 2008, S. *gallolyticus susbspecies galloyticus and in 2010, two strains of S. gallolyticus susbspecies pasteurianus, different from those of 2006 were involved.*

No definitive source for the bacteria was found but one of those events plead in favour of cross infection. It was not able to spread the bacterial translocation from the digestive tract to the circulatory system for some of them.

Conclusions: Beyond adapted treatment, standard precautions should be called back to avoid such events. At the same time, paediatricians should keep in mind that *S. gallolitycus* is not so uncommon among neonates. More over, human genitourinary tract carriage could be searched to investigate materno-foetal transmission. Be that as it may, more research is needed to understand epidemiologic patterns of those pathogens in neonates.

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EPIDEMIOLOGY OF HOSPITALIZATIONS DUE TO BRONCHIOLITIS IN CHILDREN UP TO 1 YEAR OLD IN SPAIN (2000-2008)

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Background and aims: This epidemiological survey estimates the burden of bronchiolitis in children up to 1 year old in Spain during a nine year period (2000-2008).

Methods: Retrospective survey by reviewing data of the National Surveillance System for Hospital Data, including more than 98% of Spanish hospitals. All hospitalizations related to bronchiolitis for children up to 1 year old, reported during 2000-2008 period, were analysed. Codes were selected by using the 9th International Classification of Diseases: ICD-9-CM 466. The annual incidence of hospitalization, average length of hospitalization, mortality and case-fatality rate were calculated by using municipal register data.

Results: A total of 122081 hospital discharges in children up to 1 year old were reported during the study period. The annual incidence was 3579.94 cases per 100,000 (CI 95%: 3560.22-3599.66) and decreased during the period in some regions. The average length of stay was 6 (SD 5) days. 109 deaths were reported. The mortality rate was 3.20 deaths per 100,000 (CI 95%: 2.60-3.80) and the case-fatality rate was 0.09% (CI 95%: 0.07-0.11).

Hospitalization and mortality rates were significantly higher in males (4053 vs. 3074 and 3.46 vs.2.91 per 100,000, respectively). Case-fatality rate did not differ by gender.

Annual average cost for National Heath Care System was 257,827,830 € with a mean hospitalization cost of 2,112 €.

Conclusions: Bronchiolitis in children up to 1 year of age pose a significant health threat in Spain. Measures as implementation of specific plans in some regions are helping to decrease the burden of bronchiolitis.

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HOSPITALIZATIONS DUE TO BRONCHIOLITIS IN SPAIN IN CHILDREN UP TO1 YEAR OLD: A SPACE-TEMPORAL APPROACH

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Backaground and aims: Bronchiolitis is currently the third cause of hospitalization in children aged < 1year, with a 7% of all hospitalizations in this age. The objective of this study is to describe the hospitalizations due to bronchiolitis in Spain during 2000-2008.

Methods: We proposed in the bayesian framework a modification of Lee-Carter model, by means of introducing a spatial component and apply it to hospitalizations due to bronchiolitis.

Results: Bronchiolitis-related hospitalization trend did not vary significantly during the period 2000-2008. When studied by age, an increasing trend during three firsts month of life, with differences among gender, is observed. The modification proposed in the model, showed an evident geographic pattern among different regions in Spain, emphasizing in Seville region. Seville show a lower risk of hospitalizations than bordering regions, although they have a high risk of hospitalizations, owing to the implementation of specific plans for bronchiolitis control in 2005.

Conclusions: Bronchiolitis has an evident geographic pattern in Spain. The analysis performed showed an increase in hospitalizations due to bronchiolitis in the first three month of life.

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SAFETY NETTING IN CHILDREN AT RISK FOR SERIOUS INFECTIONS IN PAEDIATRIC EMERGENCY CARE

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Background: As uneventful recovery can never be surely predicted, clinicians use scheduled follow-up. Evidence how to perform follow-up in children at risk for serious infections is lacking.

Aim: Describing characteristics of Emergency Department (ED) revisits for children at risk for serious infections.

Methods: Children with fever, dyspnoea or vomiting/diarrhoea (1 month-16 years) who attended the ED of Erasmus MC-Sophia, Rotterdam (March-December 2010), Netherlands were included. Standardised questionnaires on course of complaints were applied by phone to parents three days after ED-discharge. Sequential ED-visits were defined as 'necessary' if requiring diagnostics, therapeutics and/or hospitalisation. We compared frequencies of necessary, scheduled/unscheduled ED-revisits between three patients groups using Chi-square and univariate logistic regression.

Results: Follow-up data were available for 415/507 children (82%), median age 21months (IQR10-43), 56%boys (n=234). Two-hundred-fifty-seven children(62%) had fever, 81 children (19%) dyspnoea, and 77children (19%) vomiting/diarrhoea. In 10%of the patients (42/132), revisits were scheduled, consisting of significantly more children with vomiting/diarrhoea compared to other complaints (OR3.6 (95%CI:1.8-6.0). In the unscheduled revisits group (n=90;22%) a significant proportion (n=55;13%) was necessary (p=0.045) compared to scheduled revisits. Seventeen(4%) patients with necessary unscheduled revisits were hospitalised compared to 3 (1%) with necessary scheduled revisits.

Conclusion: The ED is dealing with many revisits. Scheduled revisits were mostly seen in children with vomiting/diarrhoea. Unscheduled revisits were significantly more necessary than scheduled revisits. In our ongoing research in developing an evidence based follow-up program after ED-discharge for children at risk for serious infections we will focus on the identification of predictors for complicated clinical course.

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HANDHELD COMPUTERS AS FIELD SURVEILLANCE TOOLS: EXPERIENCE FROM A PILOT STUDY OF ROTAVIRUS SURVEILLANCE IN ERNAKULAM, KERALA STATE, INDIA

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Background: We developed a paper- and electronic-based surveillance system for rotavirus diarrhea in India. Currently, there are limited data on the acceptability and feasibility of handheld computers (also known as PDAs) based data collection for leading infectious diseases in India.

Methods: Rotavirus surveillance was established in and around Kolenchery, Kerala, India and a pilot PDA data entry system was provided in 8 hospitals. We administered a structured questionnaire among current and potential PDA users.

Results: 186 staff completed the survey including 9 current and 177 potential users. Overall, the mean age of current- and potential-users was 38.2 and 29.0 years and 126 (68%) were physicians or nurses. Ninety-two percent (n=172) reported use of mobile phones and 28.5% (n=53) used their phones for e-mail. Eighty percent were comfortable carrying the PDA daily and 85% felt that use of a PDA for routine work was feasible. Most frequently cited concerns regarding use of the PDA for data collection were information accuracy (34% potential vs 56% current users). Sixty-seven percent of current users cited reduction of health-care costs as the most important reason to consider using the PDA while 68% of potential users cited ability to better standardize patient data. Among both groups, the most important barrier to PDA introduction for regular usage was reluctance to accept new technology (56% current vs 42% potential).

Conclusions: Our results suggest that health workers are aware of the PDA for patient data collection and provide important guidance for future PDA data collection design and training.

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CARING FOR INTERNATIONALLY ADOPTED CHILDREN: IMMUNIZATION AND INFECTIOUS DISEASES SCREENING

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Background: During the last years the number of international adoptions has more and more increased in Italy: in 2010 more than 4000 foreign born children were adopted from Italian families. Children involved in international adoption are at high risk of infectious diseases because of their previous life conditions; moreover they were not always adequately immunized against vaccine-preventable diseases.

Methods: From June 2007 to June 2010, 65 adopted children and adolescents (37 males, 28 females, aged from 6 month to 17 years) have been evaluated with a complete sanitary screening in the Department of Infectious Diseases - University of Pavia.

Results: In our cohort most subjects were coming from Latin America (about 33%) and East Europe (26.6%). We detect fifteen cases not fully immunized against poliomyelitis. Just 40% of the screened patients resulted vaccinated against hepatitis B but in two Asiatic children, hepatitis B surface antigen (HBsAg) was detected with impaired hepatic function. Although adequate immunity against tetanus and diphtheria resulted in more than 80% of cases, only 48% of them were fully protected against measles, mumps and rubella.

Multiple intestinal parasites were found in 40% of screened subjects with Giardia lamblia and non-pathogenic amoebae the most frequently identified protozoa; among the worms Hymenolepis nana was mostly detected.

Conclusions: Screening internationally adopted children for infectious diseases even uncommonly encountered in industrialized countries and to assess their immunization status is mandatory in order not only to promote their integration into a new social environment but also to protect the adoptive families.

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MENINGOCOCCAL MENINGITIS C VACCINATION: STRATEGY AND ESTIMATION OF EFFECTIVENESS, PARANA - BRAZIL

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Background and aims: Relevance of Meningococcal Disease (MD) has increased the interest in preventive actions. Brazilian Health Department included the meningococcal C conjugate vaccine for children younger than 2 years of age in 2010. This study performed in Paraná-Brazil aims to estimate the effectiveness of the program with the vaccination strategy adopted.

Methods: Descriptive analysis of data from Parana Public Health Department, including all cases of MD from 2007 to 2009.

Results: There were 326 cases of MD among children and adolescents; meningococcal serogroup was identified in 133 cases (44.5%); 70 (52.6%) was B, 59 (44.4%) C and 3% Y and W135. Evaluation of morbidity showed similar frequencies of fever, headache, vomiting and nuchal rigidity for both serogroups. Frequency of these factors differed for DM caused respectively by B and C: age less than 2 years (60.6% vs. 39.4%), seizures (21.7% vs. 13.6%), coma (10.3% vs. 5.3%) and petechial rash (64.3% vs. 57.6%). Lethality for younger 2 years of age was higher for serogroup C (42.3%) compared to B (35%).

Conclusions: Related to population targeted for vaccination is expected a reduction in lethality taking into consideration that the serogroup C is the main responsible for deaths and a lower impact on the reduction of cases of DM. We can expect a We can expect a reduction in the number of cases for other age groups by herd immunity. These results should be interpreted with cautious considering that 55% of DM cases had not serogroups identified and cases are emerging for Y and W135.

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IMPACT OF ROTAVIRUS VACCINE (RV) IN BURDEN OF DIARRHEAL DISEASE IN BRAZIL

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Background and aims: Rotavirus is the leading cause of morbidity and mortality from diarrhea in children accounting for around 25 million clinic visits, 2 million hospitalizations and more than 600 000 deaths worldwide. In 2006 Brazil introduced the RV (Rotarix^{GSK})in childhood immunization schedule. This study aims to assess the burden of diarrheal disease before and after the introduction of RV.

Methods: This is a descriptive study using national system of Hospitalization data (SIH), Mortality (SIM) and immunization (SI-API/CGPNI).

Results: Among 1,323,875 hospitalizations in children under one year in the pre-vaccine period, 600,635 (45.4%) were due to diarrhea while in the post-vaccination, from 1,120,994 admissions in this age group, 115,259 (10.3%) were due to diarrhea.

There was a 59.2% reduction in deaths from diarrhea in children under 1 year of age between the two periods.

The average cost per hospitalization in 2005 was 175 dollars, while the two-dose regimen costs 21 dollars, equivalent to eight times less the individual cost of hospitalization.

Conclusions: The results show that morbidity and mortality from diarrhea in children under 1 year decreased after the introduction of VR. This certainly reduce spending on hospital admissions and reduce suffering and the rate of potential years of life lost.

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ROTAVIRUS VACCINE (RV) AND GENOTYPES PREVALENT IN BRAZIL

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Background and aims: Oral vaccine against rotavirus (Rotarix â-GSK) was introduced on a large scale in Brazil in 2006. It is indicated to prevent gastroenteritis caused by rotavirus serotypes G1 and the G2, G3, G4, G9.Literature data suggest the possibility that the vaccine is less effective in preventing rotavirus strain G2 P. This study proposes to evaluate the epidemiological data of the disease as well as national data regarding the genotype of the strains circulating in Brazil.

Methods: This is a descriptive study using national system of hospitalization data (SIH) and information from the Central Public Health Laboratories (Lacens).

Results: From 2000 to 2005 there were 4,202,728 hospitalizations of children less than one year of age and 1,962,292 (46.7%) were caused for diarrheal disease. After the introduction of the vaccine, from 1,120,994 admissions in this age, 115,259 (10.3%) were due to diarrhea.

From 903 genotype identified during 2006 to 2010, 63.5% corresponded to G2P4, 8.4% at G9P8, 5.8% to G1P8, 5.1% to G9 and 4.3% to G2. Comparing the percentage distribution between 2006 (305) and 2009 (107) showed that the three most frequent genotypes in descending order were: G2P4, G9P8 and G9 in 2006 (78%) and 2009(58,8). Subsequently appears G1 (7.3%) in 2006 and G6P8 (9.4%)in 2009.

Conclusions: Epidemiological data confirm the reduction of the disease, but the diversity of genotypes indicates the need for investment in research to identify changes in the profile redirecting effective measures to control the disease.

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LISTERIA MONOCYTOGENES: PORTRAIT OF AN OUTBREAK

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Background and aims: *Listeria monocytogenes* causes a variety of diseases, mainly septicaemia, meningitis and perinatal sepsis. Serotype 4b is the main responsible for all major invasive disease outbreaks. Between November 2009 and August 2010, there was an outbreak of listeriosis in Lisbon's metropolitan area. An uncommonly outbreak-associated pulsotype was identified in 19 patients.

Material and methods: Observational analytical study of the patients admitted in our hospital from January 1 to December 31-2010. Detailed information on exposure, symptoms and clinical course was analysed. All *Listeria monocytogenes* isolates were submitted to genetic analysis.

Results: 8 cases were identified, 87,5% males, median age 44,5 years (0-84years); Symptoms started median 5 days (0-120 days) before admission, being fever (71,4%), headaches (57,1%), nausea/vomits (42,9%). Risk factors were present in 87,5% of patients: age above 65 years (2), diabetes mellitus (2), cancer (2) and HIV infection (2). The main diagnosis was bacteraemia (3), septicaemia (5) with meningitis (2). There were complications in 4/8 of the cases: respiratory insufficiency (3), 3 cases of encephalopathy (3) and death (1). All isolates were serotype 4b.

The uncommon outbreak pulsotype was detected in three cases. No epidemiological link was discovered between this 3 cases, but their residency area was precisely the same.

Comments: *Listeria monocytogenes* is ubiquitous in the environment, with a great risk of contamination during food production. Epidemiologic surveillance is the main way for controlling listeriosis outbreaks. Characterization of *Listeria monocytogenes* virulence determinants and comparative genomics are useful tools to analyse community outbreaks.

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THE SURVEY OF HOSPITALIZATION CAUSES OF CHILDREN AT INFECTIOUS PEDIATRIC WARD

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Infectious diseases are among the prevalent diseases that cause the mortality and abundant side effects in different age groups of children. The World Health Organization (WHO) has introduced the infectious diseases to be the sixth mortality cause in developing countries. According to the last accounts, during the month of Mehr 1389 (23rd Sep.-22nd Oct. 2010), infectious diseases have been introduced as the third cause of mortality among children after unintentional events and respiratory diseases in Iran. Considering the ever-increasing prevalence of such diseases and also the role and recognition importance of these diseases in prevention, the present research as a retrospective study has been carried out with the general aim to determine the hospitalization causes at infectious pediatric ward and specific objects of determining the demographic characteristic of hospitalized children at this ward during the first six months of 1389 (21st April-22nd Oct. 2010). Research population was consisting of all hospitalized children at this ward and the required information were collected using the files of such patients. Collected data were analyzed statistically using SPSS software.

The survey of statistical results indicated that, Viral and Bacterial Meningitis, Pneumonia, Kala-azar, Gastrointestinal infection, Skeletal and soft tissue infection, Sepsis, Cervical Lymphadenitis, Disseminated BCG infection, Periorbital Cellulitis and TB with frequencies of 16.6%, 15.9%, 13.6%, 12.1%, 12.1%, 8.3%, 7.5%, 6.8%, 4.5% and 1.5% were among the most prevalent hospitalization causes of children at infectious ward respectively.

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ACUTE OTITIS MEDIA (AOM) DETECTED BY PNEUMATIC OTOSCOPY (PO): AN EPIDEMIOLOGICAL SURVEY IN ITALIAN CHILDREN (0 -6 YRS)

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Background and aims: 33 Italian Family Pediatricians (IFP) of FIMP-MCRN (Medicines for Children Research Network) participated in an observational study to estimate the AOM incidence in children aged 0- 6 years. The AOM clinical diagnosis (AAP recommendations) was supported by PO . Greater cure was given to eardrum position(bulging e full eardrum). Eardrum retraction was one of the exclusion criteria.

Methods: All cases of AOM detected by IFP during 2009-2010 were included. Each IFP had in their care a mean of 426 patients. The population studied totalled 14,048 children.

Results: 583 children [308 Males (52.8%) and 275 Females (47.2%), 33 months median age] showed at least one otitis episode, while the total number of otitis was 683 [unilateral in 519 cases (76%) ; temperature higher than 38°C in 334(48.9%) episodes]. Repeated episodes were found in 80 children (63 had two episodes, 17 more than two). Children with repeated episodes had a mean age of 31 months (std ± 16), not significantly different from the children who had only one episode (34 months,±15) .378(64.8%) children received at least two doses of Pneumococcal vaccination, while 69.6% only one.AOM incidence was 4.1 per 100 person/year and 4.9 per 100 person/year, when considering the total number of otitis.

Conclusions: Annual incidence appeared to be much lower than described in literature, but in this study AOM were diagnosed by narrower clinical criteria; recently, pathology patterns have changed likely because of the introduction of new vaccines, like the pneumococcal one.

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DETERMINATION OF POTENTIAL PARAMETERS EFFECTIVE ON OUTCOME OF ADMITTED CASES WITH PRIMARY VARICELLA INFECTIONS IN ALIASGHAR CHILDREN HOSPITAL (1996-2009), IRAN

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There is a need to study the outcomes of admitted cases with primary varicella in countries in which there is no routine vaccination.

We performed a retrospective study on admitted cases in Aliasghar children hospital, Tehran, since 1996 to 2009;Patients were put in four different groups:

1) patients with acute lymphoblastic leukemia

2) patients with other types of cancer

3) patients who were receiving high doses of corticosteroids

4) previously healthy patients.

Demographic and some indicators of poor general condition on admission were compared; we also looked for ataxia and the time period since the onset of disease up to admission in each group.

88 cases including 24 cases of ALL(27%),9 cases with various types of cancer(10.5%),13 cases who were receiving high dose of corticosteroid were included. Mean age of patients was 6 years(SD=3.5),47 cases(53.4%)were male .Hypotension on admission was significantly more common in patients below four years of age(P value=0.006);Patients in first 3 groups were significantly admitted earlier(P value=0.027); hypotension and ataxia were more significantly seen in previously healthy group(P value=0.01 and 0.04 respectively).Just one case of mortality occurred in a case of ALL during the study period.

We concluded that although immunocompromised cases comprise more than half of admissions , they have been admitted earlier with better general condition on admission. In contrast, previously healthy group specially in cases below four years of age were significantly admitted with poorer general conditions and with more delay ;better educational and management programs are needed for younger age group with primary varicella infections.

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EPIDEMIOLOGY OF PERTUSSIS IN AN URBAN AREA OF POLAND, 2005-2009

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Introduction: In the last decades, an increase of reported incidence of pertussis has been observed in many countries, including Poland, despite a high vaccination coverage among infants and children. Currently pertussis is increasingly reported in older children, adolescents and adults . The objective was to present the epidemiology of pertussis in Mazovian region in Poland in years 2005-2009.

Material and methods: The restrospective analysis of epidemiological data collected by Voievodian Sanitary Station in Warsaw (Poland) was conducted.

Results: 1455 cases of perstussis were reported. The incidence rate of pertussis ranged from 2,4/100.000 in 2006 to 7,91/100.000 in 2008. The incidence rates were highest at two groups : patients younger than 1 year (from 13,27/100.00 in 2005 to 32,68/100.000 in 2007) and at the age 10-14 years (from 68,49/100.000 in 2008 to 11,78/100.000 in 2006). The highest proportion of cases was also ate the age group 10-14 years (from 26,37% in 2009 to 45,98% in 2008). Number of hospitalizations due to pertussis varied from 46 (2006) to 137, while the proportion of cases required hospitalization ranged from 25% (2008) to 37%. 392 (27%) cases of pertussis were reported among patients with negative or not confirmed history of pertussis vaccination.

Conclusions: There is a need to recommend and conduct booster vaccination against pertussis in adolescents and adults in order to limit spreading the disease in these age groups and also to protect unvaccinated newborns and infants for whom older persons may be a sourse of the disease.

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P309

EPIDEMIOLOGY OF RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN HOSPITALISED WITH LOWER RESPIRATORY TRACT INFECTIONS IN MALTA

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Background and aims: Respiratory Syncytial Virus (RSV) is an important cause of hospitalisation in the first 2 years of life. The epidemiology of RSV in Malta, a southern European country with a more tropical climate, has never been described. We aimed to determine the disease burden of RSV in < 2 year old children hospitalised with a clinical diagnosis of bronchiolitis or viral-induced wheeze.

Methods: A prospective observational study was carried out from October 2009 to September 2010. A nasopharyngeal swab was taken from all children aged ≤24 months who were hospitalised with a lower respiratory tract infection (LRTI). RSV was identified by means of a cell culture testing-shell vial system utilising a cell line constituted from a mix of human adenocarcinoma and mink lung cells.

Results: Out of a total of 134 children hospitalised with LRTI, 30 children (22%; mean age 8.2 months) had RSV, with positive viral cultures being detected from November till May and with the highest number of admissions occurring from February to April. The majority of hospitalisations occurred in infants < 12 months old (77%; 23/30), amounting to a hospital admission rate of 5.7 per 1000 infants. None of these children needed mechanical ventilation and there were no mortalities, however, none had any underlying risk factor known to be associated with severe bronchiolitis.

Conclusion: The seasonality of RSV in Malta occurs from February to April, which is later than the December/January peak observed in Northern European countries. The warmer climate in Malta could explain such epidemiological differences.

P310

INCIDENCE OF PERTUSSIS AMONG PATIENTS WITH PROLONGED COUGH VISITING GENERAL PRACTITIONERS IN POLAND, 2009-2010: A PROSPECTIVE ENHANCED SURVEILLANCE STUDY

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Background and aims: Each year, 1500-2000 pertussis cases are reported through routine surveillance in Poland, but the sensitivity of reporting system remains unknown. The aim of the present study was to assess the incidence of pertussis among patients with cough lasting >2 weeks in the general practitioner (GP) setting in Poland.

Methods: The study was performed from July 2009 until September 2010 in the population served by 77 randomly selected GPs (158,596 inhabitants). Inclusion criteria were: age >3 years, cough lasting 2-15 weeks, and informed consent. GPs interviewed each eligible patient, collected a blood sample, and a nasopharyngeal swab. At follow-up 30 days after the initial visit physicians collected a second blood sample and interview. Confirmed pertussis cases were defined as patients meeting the clinical criteria confirmed by laboratory (specific antibody response or PCR).

Results: During the study period, 2,724 patients with cough were admitted to participating GPs, of whom 830 met the inclusion criteria and were recruited into the study. A total of 274 cases were confirmed as pertussis, giving an overall incidence of 1.77 per 1,000 person-years. Extrapolating the present study results to the entire Polish population, we estimated the annual number of GP-referred pertussis cases at 63,742, which is 71-times higher than 896 cases reported by GPs to national surveillance during corresponding period. Underreporting factor ranged from 12 among 3-5 year olds, to 320 among 65-70 year olds.

Conclusions: The present study confirmed the high underreporting rate of pertussis cases seen by general practitioners in Poland.

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DIFFUSION OF PNEUMOCOCCUS SEROTYPES IN CHILDREN. PILOT STUDY IN AN ITALIAN REGION

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Background: The aim of this study is to assess the colonization of S. Pneumoniae in upper airways in healthy subjects. We report the preliminary analysis of this pilot study which will last until april 2011. It is the first italian experience of such analysis in a Region with an optimal PCV7 coverage.

Methods: The study involved 698 children, aged 6-60 months: 349 healthy children and 349 children suffering from upper and lower airways diseases. From each child a pharyngeal swab is collected and the polymerase chain reaction (PCR) is carried out to check the presence of S.Pneumoniae (and other bacteria presents in the upper airways). In case of positivity for S.Pneumoniae, serotypization is carried out.

Results: 698 analysed swabs have resulted in: 367 Pneumococcous (52,6%), 246 H.Influenzae (35,2%), 291 M.Catharralis (41,7%), 118 S. Pyogenes (16,9%) and 161 S.Aureus (23,1%).

Among the 367 isolated Pneumococcus, in 198 cases the serotype has been defined; a great variety of serotypes may be observed (85%of subjects has received anti Pneumococcus vaccine). The most frequent serotypes are: 5(10,9%of children), 19A(4%), 15(3,2%), 33F(2%), 6(1,7%), 18(1%).

Conclusions: These preliminary results show a greater prevalence of emerging serotypes now included in PCV13 vaccine. Future analyses will have to confirm a positive impact of this vaccination on the risk of upper respiratory infections.

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SEROEPIDEMIOLOGY OF MEASLES-SPECIFIC IGG-ANTIBODIES IN GERMANY - RESULTS FROM THE GERMAN REPRESENTATIVE, CROSS-SECTIONAL STUDY (KIGGS) IN CHILDREN AND ADOLESCENTS

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Background: Recently, the WHO European Region confirmed the measles elimination aim and 2015 was set as new target date. To measure progress towards elimination, data on vaccination coverage and incidence and in addition, laboratory confirmation of cases are required. Beyond that, serological surveillance is considered valuable to identify populations for vaccination campaigns. Age-group specific susceptibility targets were established. For the first time representative German data are available.

Method: In 2003-2006 the German Health Interview and Examination Survey for Children and Adolescents (KiGGS) was conducted in a representative sample of 17,641 children aged 0-17 years. In 13,977 children aged 1-17 years blood samples were collected and tested (ELISA) for the presence of measles IgG antibodies, presentation of vaccination cards was requested.

Results: In Germany, the overall prevalence of seronegativity in children aged 1 to 17 years was 10.0% (95% CI: 9.4 - 10.7). Children aged up to nine years met the susceptibility targets. Seronegativity in 10-17 year old children and adolescents was 8.3% (7.6-9.1), each age strata missed the WHO target of < 5%. The proportion of seronegative children was significantly higher if no vaccination card was presented. Seronegativity was especially high in children aged 2-4 and 5-9 years without vaccination cards (24.9% (13.8-40.8) and 22.0 (16.2-29.3) respectively). Interestingly, higher measles IgG-seroprevalence in children for whom a vaccination card was presented was only seen in indigenous children.

Conclusion: German measles vaccination campaigns should focus on older children and adolescents.

Surveillance data only based on presented vaccination cards may underestimate susceptibility.

P313

THE BRITISH PAEDIATRIC SURVEILLANCE UNIT - 25 YEARS OF INFORMING PUBLIC HEALTH POLICY IN THE BRITISH ISLES

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Background: The British Paediatric Surveillance Unit (BPSU) was founded in 1986 as a joint initiative by the Health Protection Agency, Royal College of Paediatrics and Child Health, Institute of Child Health (London), Royal College of Physicians (Ireland) and Health Protection Scotland to provide a single infrastructure for the surveillance of rare childhood conditions, including infections. The BPSU uses active surveillance methods through a monthly reporting card sent to all consultant paediatricians in the UK and Ireland and achieves response rates in excess of 90%. The methodology has been transcribed across the world.

Aims: To review the contribution of BPSU studies to infectious disease control policies in the UK.

Methods: Assessment of BPSU surveillance studies for communicable diseases undertaken since 1986.

Results: Antenatal screening policies have been informed through surveillance of HIV, Herpes Simplex, and congenital infections due to Toxoplasmosis, cytomegalovirus and rubella. The effectiveness of a new immunisation programme was evaluated through surveillance of Haemophilus influenzae type B infections. The childhood burden of emerging, or re-emerging, infections has been assessed through studies of MRSA, Haemolytic uraemic syndrome, variant CJD, and tuberculosis. Recently adverse reactions to H1N1 vaccination in children has been monitored through surveillance of Guillan Barré/Fischer syndromes.

Conclusions: BPSU studies have informed a range of public health policies to control or mitigate the effects of infectious diseases, monitored their effectiveness, and determined the impact of emerging transmissible diseases on children. It provides a simple system for active surveillance of rare childhood conditions and is an important public health resource.

P314

VERY SEVERE CASES OF ROTAVIRUS DISEASE IN GERMANY - A PROSPECTIVE EPIDEMIOLOGICAL SURVEY

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Background: According to the German Infection Protection Act, all cases of rotavirus (RV) disease in Germany are to be reported to the authorities. There are no data concerning the severity of the disease. Aim of study was to prospectively determine the incidence and the outcome in very severe cases of RV disease.

Methods: Cases of very severe RV disease were queried through the collection unit for rare pediatric diseases in Germany (ESPED) using anonymous questionnaires. Data acquisition started in April 2009 for a planned period of two years.

Inclusion criteria were detection of RV in faeces, patient age 0 - 16 years and one or more of the following criteria: intensive care treatment, hyper- or hyponatremia (> 155 mmol/l or < 125 mmol/l), clinical signs of encephalopathy (somnolence, seizures, apnoeas), death due to complications related to RV disease.

Results: 86 cases were reported between April 2009 and December 2010 of which 61/86 questionnaires have been returned. 15/61 cases were nosocomially acquired, 12/15 were in neonatal intensive care.

46/61 cases were community acquired, their mean age was 15.7 months (0 - 83 months), mean hospital stay was 9 days (4 - 38 days). 24/46 patients needed intensive care treatment, 34/46 children had signs of encephalopathy, 24/46 cases had a hyper- or hyponatremia. One death was reported (child with syndromal disease with multiple organ anomalies).

Conclusions: This study shows that RV infections may take a life-threatening course. A substantial number of these cases were nosocomially acquired.

P315

SEXUAL BEHAVIOR AND SUBSTANCE ABUSE OF FEMALE ADOLESCENTS IN BELGRADE (SERBIA)

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Background and aims: The aim of this cross-sectional study was to analyze sexual behavior and substance abuse of female adolescents in Belgrade (Serbia).

Material and method: All female adolescents aged 14 -19 from 3 (Vozvovac, Savski venac and Vracar municipality) of 17 municipality of Belgrade (Serbia) were included in the study. Municipalities were chosen randomly. Data were collected by self-administered questionnaire. For the data analysis chi square test was used.

Results: Of 1130 respondents 293 (25.9%) had vaginal sexual intercourse during life. Of 293 sexually active women 90.8% lived with their parents, 29.7% had irregular sexual partners, 98.3% have consumed alcohol, 83.3% have tried a cigarette, and 33.8% have used drugs during life. Adolescents who were sexually active significantly more frequently consumed alcohol, smoked and used drugs compared to women who did not have sexual relations. Between these two groups there was no significant difference between the age when they first smoked a cigarette (0.079), drank alcohol (0.245) and used drugs ($p = 0.164$). Adolescents who had vaginal sexual intercourse (95.7%) significantly more often had oral sex (0.016) compered to women without vaginal sex (15.2%). However, adolescent without vaginal sex (57.6%) significantly more often had oral sex before the age of 16 (0.054) compered to respodents with vaginal sex (19.4%). Only 33% of female adolescents used a condom during oral intercourse, and 68.5% for vaginal intercourse.

Conclusion: It is necessary to improve and protect reproductive health of female adolescents by developing services for counseling work with young people.

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Conclusion: It is necessary to improve and protect reproductive health of female adolescents by developing services for counseling work with young people.

P317

THE VALUE OF NATIONAL DEATH REGISTRATION DATA IN ASCERTAINING CHILDHOOD MORTALITY FROM INVASIVE *HAEMOPHILUS INFLUENZAE* INFECTION IN ENGLAND

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Background: *Haemophilus influenzae* can cause serious invasive infections, including meningitis, septicaemia and pneumonia. This study aimed to assess the contribution of *H. influenzae* disease to childhood deaths in England using national death registrations data

Methods: The Health Protection Agency (HPA) routinely receives national electronic death registrations data for public health purposes. Records of children aged < 15 years who died in 2009 were scrutinised for any mention of: "*Haemophilus*", "*influenzae*", "Hia/b/c/d/e/f" or "ntHi/ncHi"

Results: Of the 4,436 children who died, only one death certificate recorded "*Haemophilus* bronchopneumonia" secondary to influenza virus infection. Follow-up revealed the *Haemophilus* sp. was isolated from post-mortem lung biopsy but had not been submitted to the HPA for identification and serotyping. During the same period, 14 childhood cases with invasive *H. influenzae* isolates submitted to the HPA were notified to have died, mainly infants aged < 1 year (n=7) and 1-4 year-olds (n=6). Only 6/14 (43%) had any mention of an infection on the death certificate and none recorded the bacterium. Five of the 6 infection-related cases reported "Pneumonia" or "Bronchopneumonia" (including one case each associated with RSV and adenovirus infections), and one other reported "Purulent Meningitis", which was subsequently identified as caused by *Streptococcus pneumoniae*.

Conclusions: Death registrations data do not accurately capture the contribution of *H. influenzae* disease to childhood deaths. This finding emphasises the need for detailed clinical follow-up of reported cases, particularly in the light of a newly licensed vaccine that may prevent invasive *H. influenzae* infections

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ACUTE FLACCID PARALYSIS AND ITS DIFFERENTIAL DIAGNOSIS IN KURDISTAN; 11 YEARS SURVEILLANCE, 2000 TO 2010

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Background and aims: Acute Flaccid Paralysis (AFP) surveillance is a key strategy for monitoring the progress of polio eradication and is a sensitive instrument for detecting potential poliomyelitis cases and poliovirus infection. This study was conducted to describe the characteristics of patients reported with AFP, and to evaluate the performance of the surveillance system using indicators recommended by the WHO.

Methods: It is a simple observational study conducted from January 2000 to December 2010 at Kurdistan center for diseases control and Department of Pediatrics.

Results: 139 children aged younger than 15 years were reported to the Department of Health with AFP. None of the cases were acute poliomyelitis or polio-compatible. In 133 (96.4%) stool samples no virus was isolated. The end diagnoses were as follows: Guillain-Barré syndrome (79 cases), Transverse Myelitis (7 cases) Encephalitis (6 cases), Traumatic Neuritis (2 cases), Viral Myositis (4 cases), Acute Cerebellar Ataxia (3 cases), Myasthenia Gravis (2 cases), Spinal Tumors (4 cases), Toxic Synovitis of Hip (5 cases), Hypokalemic Periodic Paralysis (2 case), others (25 cases).

The WHO defined target of at least 2 AFP case per 100 000 in children under 15 years per year was achieved from 2000 to 2010—from 1.3 to 3.2 per 100 000 population. All except one of the performance indicators consistently met WHO requirements and thus demonstrated the effectiveness of the AFP surveillance program in Kurdistan.

Conclusion: The effective surveillance system and its evaluation may serve as a model for surveillance of other infectious diseases.

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BACTERIAL MENINGITIS IN KURDISTAN: AN OBSERVATIONAL STUDY BASED ON THE NATIONAL SURVEILLANCE SYSTEM

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Background and aims: Surveillance of Bacterial meningitis (BM), including the laboratory investigation of suspected cases, is critical for the early detection of epidemics and formulating an appropriate response, clarifying the burden of disease and evaluating the impact of immunization services.

Methods: An observational study was carried out from 2007 to 2009, estimating the incidence and case-fatality rate by age group and causal pathogens, as well as the seasonality.

Results: The overall number of patients undergone Lumbar Puncture because of Symptoms and Signs Simulating meningitis (suspected Cases) was 1373. We found Pleocytosis of CSF in 80 cases (6%); 71 (5%) of them fulfilled the WHO criteria for Probable cases of BM. *Streptococcus pneumoniae*, and *Neisseria meningitidis* were the main identified agents. Seasonality was evident; most cases of meningitis occured between January and March. No mortality was reported during the period of Surveillance.

The quality of surveillance was evaluated using WHO-recommended indicators.

WHO Indicators of Surveillance Quality	Actual Performance	WHO Targets
-The Percentage of all probable cases for which CSF/blood was obtained for evaluation	95%	≥ 90%
-Percentage of probable cases in which a bacterial pathogen was identified from CSF or blood:		
>Among CSF with 10 or more white blood cells/ml3	12%	≥15%
>Among CSF with 100 or more white blood cells/ml3	12%	≥40%
-Percentage of CSF isolates which are H. influenzae	≥20%	0

[Performance of Bacterial Meningitis surveillance]

Conclusions: The etiologies of an important number of BM still remain obscure in Kurdistan. A nation-wide improvement of the microbiologic facilities may further improve laboratory-based surveillance and clarify the needs for national vaccination programms against Streptococcus Pneumonia and Haemophilus influenzae.

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SHIGELLA FLEXNERI SEROTYPE 6 OUTBREAK AMONG TODDLERS IN JERUSALEM, 2009-2010

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Background: Shigella outbreaks are frequent among toddlers in Israel; Shigella sonnei being the leading serotype for over two decades. A large Shigella flexneri outbreak emerged in Jerusalem during 2009.

Methods: We conducted an epidemiological and clinical investigation. Fecal specimens were collected for culture, serotyping and PFGE.

Results: The incidence of shigellosis in Jerusalem was 150.7/100,000 in 2010, 25.4 /100,000 in 2009 and 100.2 /100,000 in 2008. The *S.flexneri* proportion of all Shigella isolates increased from 3.7% (1990-2008) to 13-19.3% in 2009 -2010. Between January 2010 - June 2010 we investigated 153 patients hospitalized for Shigella infections (*S. sonnei*, n=75, *S.flexneri*, n=78). Most patients were children, 106 (69%) were younger than 6 years (mean age 9.4±16.4 years, median 4.4 years). Hospitalization rates were higher for *S.flexneri* than for *S. sonnei* infections. When patients with S. flexneri infection were compared to patients with *S. sonnei* infection, the proportion of febrile convulsions was similar (24.4% and 21.6%); encephalopathy was more frequent in *S.flexneri* cases than in *S. sonnei* cases (14.1% vs. 5.3%). Hyponatremia was associated with febrile convulsions, 22.7%, vs. 7.7% in patients without convulsions.

Most *S.flexneri* isolates were serotype 6. PFGE analysis revealed three major clusters with over 88% similarity, unique to the outbreak. Antibiotic susceptibility testing disclosed that the recent outbreak strains are more sensitive. In contrast, previous *S.flexneri* 6 isolates were multidrug-resistant.

Conclusions: The current outbreak was characterized by a proportional rise in *S.flexneri* (specifically serotype 6) and by changed clinical presentation. The shift in serotypes deserves further investigation.

P321

DECREASE OF VARICELLA ZOSTER VIRUS - ASSOCIATED PAEDIATRIC HOSPITALISATIONS AND COMPLICATIONS IN BAVARIA AFTER RECOMMENDATION FOR ROUTINE VARICELLA VACCINATION

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Background: In 2004, routine vaccination for varicella was recommended for all children 11-14 months of age in Germany. We investigated the impact of vaccination on the frequency of paediatric hospitalisations and complications associated with varicella (VZ) or herpes zoster (HZ).

Methods: Children < 17 years of age hospitalized with an ICD-10 discharge diagnosis of VZ or HZ were captured by annual data queries in Bavarian paediatric hospitals from 2005 to 2009. Additionally, age, gender, length of stay, and accompanying diagnoses were collected.

Results: 33 (89%) out of 37 hospitals participated; 19 (51%) contributed data for all five years. In total, 1132 VZ and 340 HZ cases were reported. VZ hospitalisations (55% male, median age 3 years, IQR 1-5) lasted 3 days (median; IQR 2-6). HZ hospitalisations (56% male, median age 9 years (IQR 6-13) lasted 6 days (median; IQR 4-8). Specific complications in VZ patients were: 25 (2%) encephalitis, 13 (1%) meningitis, 27 (2%) pneumonia, 329 (29%) other complications; in HZ patients: 10 (3%) encephalitis, 7 (2%) meningitis, 9 (3%) zoster generalisatus, 107 (31%) other complications. The annual incidence estimate of VZ hospitalisations in Bavaria in children < 17 years of age was 13.3-16.8/100,000 until 2007 and decreased from 15.8/100,000 in 2007 (CI 14.2;17.6) to 10.3/100,000 (CI 8.9;11.7) in 2008 and 6.7/100,000 (CI 5.6;7.9) in 2009. For HZ hospitalisations, incidence was estimated as 3.2-4.4/100,000 from 2005 to 2009.

Conclusions: Five years after recommended vaccination, VZ-associated hospitalisations had decreased by >50%. The impact on paediatric herpes zoster hospitalisations needs long-term evaluation.

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ACCEPTANCE AND IMPACT OF ROUTINE VARICELLA VACCINATION IN CHILDREN IN THE AREA OF MUNICH - BAVARIAN VARICELLA SURVEILLANCE PROJECT 2006-2010

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Background: In 2004, routine varicella vaccination was recommended in Germany, with one dose at 11-14 months of age. Since 2009, two doses within the second year of life have been recommended. We investigated annual vaccination coverage and its impact on VZV epidemiology in a defined region during the first years after general recommendation.

Methods: Vaccination coverage was determined by parent surveys in annual random samples of 600 children aged 18-36 months in the area of Munich from 2006 to 2009. Monthly reports of varicella and herpes zoster (HZ) patients < 17 years of age were collected from 2/3rd of Munich paediatric practices between October 2006 and September 2010, covering four varicella seasons.

Results: Coverage with at least one dose increased from 38% in 2006 to 51% in 2007 and to 53% in 2008 and 2009. Varicella cases (n=14,985) decreased from a mean of 6.0 cases per month and practice in the first season to 3.8, 3.3 and 2.0 in the following seasons. The strongest decrease occurred in children < 5 years. Vaccinated varicella cases (usually vaccinated only once) increased from 4% to 9% of all cases. Additionally, 208 paediatric HZ cases were recorded; in the age group < 10 years (n=114 overall) HZ-cases decreased by 50% during the observation period.

Conclusion: Regional surveillance showed positive short-time effects of varicella vaccination. With coverage increasing to 53% by 2009, annual varicella incidence estimates (2007: 78/1000, 2008: 48/1000, 2009: 36/1000 in children < 17 years) decreased by >50%. Long-term effects need further surveillance.

P323

SEASONAL VARIATION OF SEVERE COMPLICATED ENTEROVIRUS INFECTION IN TAIWAN

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Background: Annual surveillance of isolation for severe complicated enterovirus infection (SCEI) has been conducted year-round in Taiwan, a highly endemic area. This study evaluated the seasonality of SCEI epidemic by month from 1999 to 2008.

Methods: We analyzed enterovirus infection reported to the Centers for Disease Control in Taiwan (TCDC) and virology laboratory confirmed data in 19990-2008. The monthly virology isolation rates by viral types were measured. The isolated circulating viruses and weather status were evaluated, including average age-specific, month-specific and virus-specific cases.

Results: During the 10 years of surveillance, 2674 cases were reported to TCDC with 1539 (57.6%) cases confirmed by the virology isolation. Among the confirmed cases, 1325 cases (86.1%) were patients of less than 4 years of age. The confirmed cases were higher in warm months, peaked in June for all ages (n = 338, or 22.0%) and children of less than 4-years (n = 290, or 22.0%). The confirmed cases dropped to 31 cases in all ages and 30 cases (2.2%) in the young children. The SCEI cases significantly associated with the isolation positives of EV71 and coxsackievirus A and B with the relative risk ranged between 1.03 and 1,14 for 1% increase in weekly isolation rate.

Conclusions: The seasonal cycles of isolation positives for EV71 and coxsackieviruses A and B can well predict the development of SCEI cases are likely attributed to changes in atmospheric conditions.

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CHILDHOOD INFECTIOUS DIARRHEA IN A RURAL ZONE IN ROMANIA: A PHARMACOEPIDEMIOLOGIC APPROACH

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Infectious diarrhea is frequent, loose, watery bowel movements resulting from an infection of the digestive system by a bacteria, virus or parasite. Dehydration caused by diarrhea is one of the biggest single killers of children in the modern world and diarrhea itself is one of the major causes of nutritional loss and poor growth. Rehydration is the replenishment of water and electrolytes, lost through dehydration.

Aim: Pharmacoepidemiologic study in infectious diarrhea in children.

Method: This investigation is a part of a larger study that deals with prevalence and pharmacotherapy of gastroenteritis in children in Romania. The study was performed on 205 children with abdominal pain, in a rural primary medical center, during the summer season (between June and August 2010). The investigation consisted of medical sheets analysis regarding the clinical manifestations, causes and the treatment of infectious diarrhea in children.

Results: During the period of the conducted study, diarrhea was reported in 146 children. The most frequent germs that have caused diarrhea were enteroviruses and E.coli bacteria. Dehydration due to diarhhea was observed in 21% of patients, most of these cases requiring hospitalization. Majority of the subjects have received oral rehydration therapy and spasmolytic drugs to improve abdominal pain relief. Antimicrobial medication was prescribed only for 12 cases of infectious diarrhea, because most kids recover on their own. In **conclusion** this study shows that in this family medicine office, oral rehydration therapy is used as a cheap, simple and effective way to correct dehydration caused by diarrhea.

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PHARMACOEPIDEMIOLOGIC INVESTIGATIGATION IN DYSMENORRHEA DUE TO PELVIC INFLAMMATORY DISEASES IN SCHOOLGIRLS

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Dysmenorrhea or painful menstruation may present as an isolated disorder or in association with other conditions. Every month many women suffer from pain around the time of their periods. During menstrual periods, the pain a woman is suffering can be so severe, that she is enable to carry on with her normal activities.

Aim: The investigation of the clinical, epidemiological and pharmacological aspects of menstrual period pain in schoolgirls. This comparative study is a part of a larger study that deals with prevalence, symptomatology and treatment of dysmenorrhea in teenager girls from the zone of the Iasi district, Romania. This exploratory study was performed on 264 volunteer schoolgirls, with ages between 11 and 18, which completed a questionnaire consisting of 21 questions about intensity of menstrual-related distress, measured with the visual analogue scale (range=0-10), systemic symptoms, causes, medical addressability and the drugs used to reduce pelvic pain.

Results: In this study dysmenorrhea was reported in 198 of schoolgirls. 78% of subjects were diagnosed with different pelvic inflammatory diseases, most of them uninvestigated and untreated. The investigation revealed that pain during menstrual period significant influenced the daily life activity of the schoolgirls. Drug therapy plays an important role in pain management. The most alerting aspect of the study was represented by the finding that antibacterial and analgesic therapy was realized especially by self-medication (42%) or according to another person's recommendation (31%).

P326

ALARMING SYMPTOMS FOR SERIOUS BACTERIAL INFECTIONS ARE PRESENT AS TRIAGE CRITERIA AND ASSOCIATED WITH HOSPITALISATION

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Background and aim: A recent systematic review identified alarming symptoms for serious bacterial infections (SBI) in children[1]. Eleven of these symptoms are defined in the Manchester Triage System (MTS) as triage criteria. How often are these alarming symptoms selected at triage and does their presence predict hospitalisation?

Methods: Observational study, including 1770 children with fever (0-16 years) that attended the Emergency Department (ED) of the Sophia Children's Hospital, Rotterdam, Netherlands (Jan 2008-Jul 2009). Triage by the MTS involves selection of one flowchart (major presenting problem) and linked discriminator(s) to determine the patient's urgency level. Numbers of alarming symptoms selected at triage were divided by the maximum number of alarming symptoms available per patient. These percentages were used to identify the association between alarming symptoms selected at triage and hospitalisation by logistic regression.

Results: Median age of patients was 2.2 years (IQR 0.9-4.5), median temperature 38.9°C (IQR 38.2-39.6), 58% were boys. The maximum number of alarming symptoms that could be selected at triage was 8 per patient. Twenty-six percent of patients (n=469) had at least 1 and maximum 4 alarming symptoms scored. The odds of hospitalisation increased with the percentage of alarming symptoms selected (OR 1.04; 95%CI 1.03-1.05). E.g. hospitalisation occurred twice often in children with 20% alarming symptoms selected at triage compared to those without.

Conclusion: Alarming symptoms for SBI are defined in the MTS. Presence of alarming symptoms at triage is associated with hospitalisation. This knowledge can be used to direct patientflows at the ED.

1. Van den Bruel, Lancet 2010.

P327

NOSOCOMIAL ROTAVIRUS INFECTIONS; A META-ANALYSIS OF INCIDENCE AMONG PEDIATRIC HOSPITAL PATIENTS

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Background: Nosocomial rotavirus infections (nRV) represent a significant proportion of rotavirus-associated morbidity. nRV incidence can therefore influence the results of cost-effectiveness analyses of rotavirus vaccination programs. Inconsistent methodology in studies on nRV incidence has resulted in widely varying estimates limiting the application of results.

Aims: To produce a reliable summary estimate of nRV incidence in pediatric settings in Europe and North America that can be used in cost-effectiveness analysis.

Methods: We searched the MEDLINE-database for studies on nRV incidence among pediatric in-patients. To ascertain complete case reporting, only studies describing active surveillance for nRV in their methodology were included. Random effects meta-analysis was performed. Prespecified possible sources of heterogeneity were explored using metaregression.

Results: Seventeen surveillance studies met the quality criteria for inclusion. The overall nRV incidence was 3.6 per 100 hospitalizations (95%Confidence Interval [CI]: 2.1-5.5). Incidence was significantly influenced by the study-months (RV epidemic season only or year-round) and the age-range of included patients. Highest nRV incidence was found for children 3 months-2 years of age, hospitalized during the winter months (5.6/100 hospitalizations; 95%CI: 3.7-7.8). Eleven studies were conducted among high-risk populations inflating the results of the unadjusted estimate. The adjusted year-round nRV incidence estimate without age restriction was 0.4/100 hospitalizations (95%CI: 0.1-2.1).

Conclusion: This is the first meta-analysis summarizing results of surveillance studies on nRV incidence. nRV seems an important problem among hospitalized infants during winter months. The lower, adjusted nRV incidence estimate seems more appropriate for application in burden of disease analysis at population level.

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A CASE OF PURULENT PERICARDITIS CAUSED BY HAEMOPHILUS INFLUENZAE TYPE B

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Introduction: Purulent pericarditis is a rare but life-threatening cardiac emergency. The epidemiology and infectious etiology of the illness have changed over time because of prevention and therapeutic strategies.

Case report: We report a case of purulent pericarditis caused by Haemophilus Influenzae type b in a not immunized 17 months old girl who came from a Roma community.

Based on clinical, radiological and echographic signs purulent pericarditis was suspected on admission and confirmed came by pericardiocentis. We treated the patient with an antibiotic therapy and pericardial drainage with successful results.

Discussion: The aim of this study is to awareness the scientific community on the spreading of severe vaccine preventable infectious diseases among some groups of population. After the widespread of antibiotics and introduction of Hib conjugate immunization in developed countries the annual incidence of Hib invasive disease has greatly decreased from 4.78/100,000 persons to 0.44/100,000 persons among children aged < 5 years. Despite these data a low immunization coverage persists among people with poor socioeconomic status, in particular itinerant populations such as Roma. The reasons of the low access to health care and to immunizations are related to their social conditions and behaviour. To achieve a better and larger coverage immunization we need to improve public health services and to support social services particularly in such population.

P329

CASE REPORT OF CHRONIC INVASIVE FUNGAL SINUSITIS IN IMMUNOCOMPETENT CHILD TREATED WITH SURGERY AND VORICONAZOLE

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Invasive fungal sinusitis is a relatively rare disease and potentially devastating infection, and can be divided into acute fulminant, chronic, and granulomatous invasive fungal sinusitis. The conventional treatment is radical surgery combined with systemic Amphotericin B administration, but the poor prognosis and unestablished treatment options require a better therapeutic strategy [13]. A case report of A 9 years old boy referred to our hospital during January 2008 complaining of protrusion of the left eye since 4 months, associated with headache but no visual disturbances. Clinically ENT examination showed left nostril polypoidal mass with bilateral inferior turbinate hypertrophy with normal ears and throat examinations. Eye examination showed incomplete lid closure, visual acuity of 6/6, normal papillary reaction, extra ocular movement and color vision with nonaxial moderate proptosis of the left eye, normal fundal examination. Para nasal sinuses examination showed opacification and expansion of the left maxillary, ethmoid, and sphenoid sinuses causing mass effect of the left orbit, left medial rectus and optic nerve. FESS (Functional Endoscopic Sinus Surgery) done and the histological examination of the surgical specimen confirmed tissue invasion by narrow septate hyphae, consistent with Aspergillus species. Tissue culture reported as Aspergillus Flavus. He was started on steroid and itraconazole. Steroid dose was tapered over 12 weeks. Condition relapsed after 3 months of itraconazole which was changed to voriconazole, a new antifungal agent, with good responses. Voriconazole administration could form the basis for a new standard treatment for invasive fungal sinusitis

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INVASIVE *CANDIDA* INFECTIONS IN CHILDREN: THE CLINICAL CHARACTERISTICS AND SPECIES DISTRIBUTION AND ANTIFUNGAL SUSCEPTIBILITY OF *CANDIDA* SPP.

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Objectives: The aims of the study were to examine the distribution of *Candida* spp. isolated from sterile body sites, the antifungal susceptibility of the isolates to amphotericin B, fluconazole, voriconazole and caspofungin and risk factors associated with invasive *Candida* infections in children.

Background: The aims of the study were to examine the distribution of *Candida* spp. isolated from sterile body sites, the antifungal susceptibility of the isolates to amphotericin B, fluconazole, voriconazole and caspofungin and risk factors associated with invasive candidiasis in children.

Patients/methods: Thirty-five children with invasive candidiasis between January 2004 and January 2008 were evaluated retrospectively. The antifungal susceptibility of isolated *Candida* species were studied by Etest.

Results: Of the invasive *Candida* infections, 65.7 % was due to *C. albicans*. The second most common isolated species was *C. parapsilosis* (11.4 %). The rate of resistance to fluconazole, amphotericin B and voriconazole were 8.5 %, 2.8 % and 5.7 %, respectively. Caspofungin was the most effective antifungal agent. 22.8 % of the patients died in the first 30 days. In univariate analyses, increased mortality was associated with stay in intensive care unit (ICU), the presence of CVC, failure to remove central venous catheter (CVC) and mechanical ventilation.

Conclusions: The most common causative agent of invasive *Candida* infections was *C. albicans*. Caspofungin was the most effective antifungal agent. Risk factors associated with mortality due to invasive candidiasis were hospital stay in the ICU, presence of CVC, failure to remove CVC and mechanical ventilation.

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VARIATION IN CANDIDA SPP. DISTRIBUTION: REPORT FROM THE SURVEILLANCE PERIOD (2004-2010) IN THE INTENSIVE CARE UNIT (NICU)

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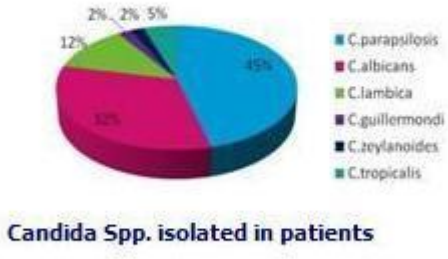
Background and aims: Systemic fungal disease, caused by Candida species, are a much feared complication in NICU,particularly, in VLBW and ELBW infants.

Methods: Infection cases by Candida Spp.and not recorded in NICU of Hospital "G. Martino " of Messina.

Results: The cases were reported 42/1839 (2%) : 21 preterm (G.A. 30.5± 3.78 - Weight 1550.4 ± 906.9), 14 term infants(G.A. 38.42 ± 1.45 - Weight 3128.9 ± 290.8) , 7 pediatric patients.The fungus most frequently isolated was Candida parapsilosis (19/42, 46%).Graph.1-2.About patients studied 7 / 42 died (17%) which 6 / 21 preterm infants (28%), 1 / 7 pediatric patients (14%), no term baby died. We have registered two cases of mycetoma in a preterm baby as a complication of systemic fungal infection.

[Graphic 1 incidence of Candida Spp]



[Graphic 2 Candida Spp isolated]

Conclusions: The increased incidence of Candida parapsilosis is a main cause of infections, linked to fungal adherence ability to prosthetic materials and to proliferate in presence of high glucose concentrations , especially in preterm infants receiving parenteral nutrition,while its aggression is less than C. Albicans. Our study shown the problem of colonization,the selection of resistant strains of Candida in NICU and its new therapeutic options.

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TYPE 1 DIABETIC CHILDREN ORAL YEAST CARRIAGE: A QUESTION OF METABOLIC CONTROL?

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Background and aims: Diabetes is considered a risk factor associated with oral yeast infections. Our aim was to evaluate the yeast oral carriage, in saliva and in oral mucosal of Type 1 Diabetic (T1D) children, and to investigate the relation of yeast carriage with host and environmental factors.

Methods: Yeasts were recovered from stimulated saliva and mucosal surface swabs of 133 diabetic children and 72 control subjects. Diabetic children were grouped according to HbA1c.

Results: Forty percent of the children had no yeasts either in the saliva or in the mucosal surface; only 40% were colonized by yeasts in the mucosa. The number of diabetic patients with no yeasts in the oral mucosa was higher than that of control subjects. Diabetics with a poor metabolic control had a higher number of yeast cells in the mucosa. The most prevalent yeast was Candida albicans; the biodiversity was higher in saliva than in mucosa. Patients inhabiting rural areas exhibited a higher yeast biodiversity. Oral hygiene was found to be determinant on the clearance of non-C. albicans colonizing the mucosa. The T1D children had higher levels of CD4+T-cells in their saliva than control subjects. The higher level of CD4+ cells in the saliva of these patients was correlated with a lower passive colonization by yeast cells.

Conclusions: In children, diabetes per se, does not seem to determine increase in yeast colonization, except when not metabolically controlled. A higher level of CD4+ cells in the saliva is correlated with lower oral yeast carriage.

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FLUCONAZOLE PROPHYLAXIS TO PREVENT INVASIVE CANDIDIASIS - AN OBSERVATIONAL STUDY IN EXTREMELY LOW BIRTH WEIGHT INFANTS BEFORE AND AFTER INTRODUCTION OF PROPHYLAXIS AT A TERTIARY NEONATAL UNIT

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Background and Aims: Invasive fungal infection is an important cause of mortality and morbidity in extremely low birth weight (ELBW) infants. Early diagnosis is difficult and treatment is often delayed.

We assessed the impact of intravenous fluconazole prophylaxis in ELBW infants on the incidence of invasive candidiasis in Neonatal Intensive Care Unit.

Methods: ELBW infants born during the pre-prophylaxis era (Jan 2004 -Dec 2006) were compared with post-prophylaxis era (Aug 2007 -July 2010). Infants born during prophylaxis era received fluconazole prophylaxis for 6 weeks or as long as they had intravenous access. Demographic and clinical data were collected. The two groups were compared for baseline demographics, risk factors for candidiasis and the incidence of invasive candidiasis.

Results: 6 of 53 (11.3%) < 750g infants developed invasive candidiasis during pre-prophylaxis era compared to 1 of 88 (1.13%) during post-prophylaxis era. There was no adverse events or the emergence of fluconazole resistant *Candida* sp. with fluconazole prophylaxis.

	2004-06 Pre-prophylaxis era (Incidence)	2007 - 10 Post-Prophylaxis era (Incidence)
Gestation<27 weeks	6.3% (6/95)	0.8% (1/124)
<750g	11.3% (6/53)	1.13% (1/88)

[Before & after antifungal prophylaxis - comparison]

Conclusions: In the fluconazole prophylaxis era there is a reduction of 83% in invasive fungal sepsis in < 27 weeks gestation infants and in < 750g infants.This study suggests that a targeted fluconazole prophylaxis regimen for ELBW infants is safe and effective in significantly reducing invasive candidiasis.

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CANDIDEMIA IN PEDIATRIC PATIENTS IN A GERMAN UNIVERSITY HOSPITAL: A 10-YEAR STUDY

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Objectives: Candidemia is an important cause of morbidity and mortality in hospitalized patients. The aim of this retrospective study was to analyze epidemiology and outcome of *Candida* blood stream infections among patients at a German university hospital.

Methods: Candidemia episodes in patients admitted to all four pediatric departments between August 1, 1998 and July 31, 2008 were identified through review of the microbiology files and clinical data were extracted from the hospital files. Univariate analysis was performed to determine the relation between potential risk factors and mortality, *Candida* spp., and underlying disease.

Results: During the 10-years period, 32 pediatric patients developed 35 episodes of candidemia (0.47 cases per 100 hospital discharges / 0.60 cases per 1000 inpatient-days). The mean age of patients was 7.50±6.15 years (range, 0-19 years). Cancer (40.6%) and congenital malformations and/or syndromes (25%) were the most common underlying diseases. *C. albicans* accounted for 45.7% (16/35) of the episodes, followed by *C. parapsilosis* (17.2%; 6/35), and *C. glabrata* (14.3%; 5/35). The most frequent risk factors identified for candidemia were use of broad-spectrum antibiotics at onset of the episode (93.9%), central venous catheterization (81.8%) and broad-spectrum antibiotics in the last 2 weeks (69.7%). The 30-day mortality rate was 12.5%. On univariate analysis mortality was associated with neutropenia (p=0.02) and development of severe sepsis or septic shock at diagnosis (p=0.05).

Conclusions: These data demonstrate a lower incidence and case fatality rate of *Candida* BSIs as compared to other pediatric series. Cancer was the most common underlying disease.

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THERAPEUTIC DRUG MONITORING OF VORICONAZOLE IN IMMUNOCOMPROMISD PEDIATRIC PATIENTS

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Background: Voriconazole (VCZ) is approved for management of invasive fungal infections (IFI) in pediatric patients. We analyzed steady-state plasma trough concentrations and their association with endpoints of therapy.

Methods: The cohort included 74 patients (0.2-18y; mean: 10.2y; 32f / 42m) with mostly hematol. disorders (63; 33 post allo-HSCT) who received 101 courses of VCZ for possible (7) and probable/proven (13) IFI, as primary (47) or secondary (32) prophylaxis or as empiric therapy (2) IV (4) and (15)/or (82) PO at recommended dosages until maximum efficacy.

Results: VCZ was administered at a median maintenance dosage of 4.8 mg/kg BID (r, 2.2-17.4) for a median of 40 days (r, 6-1002). Trough plasma concentrations (251; 3.4±4.3/pt) ranged from < 0.2 to 14.9 mg/L with high intra- and interindividual variability and no apparent relation to dose (p=0.074, ANOVA). 22 and 42% of samples were < 0.2 and < 0.5 mg/L, respectively. Increases in transaminases (52 %), bilirubin (24 %) and alk. phosphatase (15 %), skin eruptions (11 %) and neurological AEs (6 %) were mostly ≤ grade II; ten courses (9.9 %) were discontinued due to AEs. Treatment success was observed in 8/20 pts with proven/probable/possible infections, and in 75/81 courses of empiric therapy/prophylaxis. There were no consistent correlations between maximum dose, initial or median trough concentrations and AEs or treatment response, respectively. Proposed threshold values were not discriminative.

Conclusions: VCZ had acceptable safety and was effective in the management of pediatric IFIs. Pharmacokinetic variability was high and no predictable dose-concentration-effect relationships were observed.

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EUROPEAN SURVEY ON ANTIFUNGAL PROPHYLAXIS IN NEONATES

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Background: Neonatal fungal infections are associated to a substantial mortality and morbidity rate. Prophylactic use of fluconazole has been proposed but remains controversial. We aimed to evaluate the use of antifungal prophylaxis in European neonatal intensive care units (NICUs).

Methods: A cross-sectional survey was conducted by means of a structured questionnaire that was to be completed by the heads of level III NICUs over a 7-month period (2009-2010). The survey was part of the TINN neonatal research FP7 European project.

Results: 193 questionnaires from 28 countries were analyzed. Use of antifungal prophylaxis was reported by 55% of the respondents and the most frequently used antifungal agent was intravenous fluconazole (92%). Prophylaxis was primarily indicated because of a low gestational age (< 28 weeks) and weight at birth (< 1000g). Average dose was 3mg/kg in 66% of NICUs with an administration interval of 72 hours in 52% of them. All responders acknowledged the need for additional trials on prophylactic fluconazole's efficacy. Not users of prophylaxis were more likely to be influenced by the local incidence of candidiasis, the risk of increasing antifungal resistances and the absence of a statement by Pediatric Societies in support of routine prophylaxis use.

Conclusions: Current concerns about the use of antifungal prophylaxis include its efficacy, the impact of the local incidence of infection, the risk of emergence of resistant species and the absence of clarified criteria for high-risk neonates. Future studies that address these issues will contribute to a more rational use of anti-fungal prophylaxis.

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ANTI-CANDIDA ACTION OF PROBIOTIC LECTINS IN CONDITIONS OF THEIR PROLONGED CO-CULTURING WITH CLINICAL STRAINS

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Background: Anti-*Candida* action of probiotic bifidobacterial and lactobacillus lectins (BL, LL) on fungal growth on agar was established [1].

The **aim** was to study suppressive action of BL and LL in conditions of their prolonged co-culturing with yeast suspensions of *Candida* clinical strains.

Methods: Clinical strains (*C. albicans, C. tropicalis, C. crusei, C. glabrata*) interacting to antimicrobials were studied. Wells of microplates (GNIIPolimer, Moscow) contained equal volumes of culture (10^8 Cfu/ml) and L (in subagglutinating doses, in dilutions 10-10,000) in 0.9%NaCl. After incubation 24 and 48 h at 37^{o}C, equal suspension samples were transited into plates (*Sabouraud* agar) for growth 2 days at 37^{o}C. Then numbers of colonies were calculated. Controls were free of L.

Results: BL and LL revealed anti-*Candida* effects in all L dilutions tested. Clinical *Candida* strains were ranged in sensitivity to L, and strains of complete suppression by BL or LL were identified. BL revealed some more (prolonged incubation time)-resistant anti-*Candida* action compared to that of LL (BL as more resistant to *Candida* hydrolases).

Conclusions: Inhibition of *Candida* growth by high dilutions of L in conditions of prolonged co-culturing points out signal properties of L, action of BL and LL at earlier steps of *Candida* development. Taken together with the data [1], results indicate prospects of probiotic L as selective suppressors of *Candida* clinical strains also in combinations (BL and LL, L and antibiotics).

[1] M. Lakhtin, V. Alyoshkin, V. Lakhtin, S. Afanasyev , L. Pozhalostina, V. Pospelova. Probiotics & Antimicro. Prot (2010) 2: 186-196.

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SUCCESSFUL TREATMENT OF CANDIDA ALBICANS SEPTICAEMIA IN THREE PRETERM NEONATES

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Introduction: Sepsis is a major cause of morbidity and mortality among neonates. Mortality for candidaemia has been reported to vary between 15% and 59% (Saiman et al, 2000). We report about treatment of three preterm neonates with Candida albicans septicaemia resistant to liposomal amphotericin B.

Patients and results: Patient A.S. (female, 665 g) was born at 24+5 weeks gestation suffering from an amnioninfection syndrome. After recovery she declined on day 13 after live birth and developed hepatomegaly, decreasing thrombocytes as well as increasing CRP values. Candida albicans was detected in blood culture, urine and tracheal secret.

Patient S.M. (male, 820g) was born at 25+3 weeks gestation suffering from an amnioninfection syndrome. After transient recovery he developed low thrombocyte counts and rising CRP values four days after birth. Candida albicans was detected in blood culture, stool and tracheal secret.

Patient D.L. (male, 560g) was born at 27+5weeks gestation suffering from an amnioninfection syndrome. On day 25 after live birth an antimycotic therapy was started because of persisting thrombopenia and hepatomegaly. Candida albicans was found in tracheal secret and urine.

All three patients received liposomal amphotericinB (5 mg/kg/d) and, since they stayed in a poor condition, caspofungin (50 mg/m²/d). Approximately two weeks of treatment blood cultures were negative and hepatomegaly disappeared. Thrombocytopenia rested for five weeks.

Conclusions: To sum up our patients were successfully treated by caspofungin. The main side effect was thrombocytopenia which disappeared approximately two weeks after end of therapy.

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CANDIDIASIS ASSOCIATED WITH MATERNAL DIABETES MELLITUS - A RISK FACTOR FOR THE CONGENITAL CANDIDIASIS?

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Background and aims: Systemic congenital candidiasis is a rare reported condition in newborns - term or preterm.

Methods: The authors report the case of a macrosomic term newborn (40 weeks of gestation) with asymptomatic systemic congenital candidiasis, born by caesarean section because previous caesarean sections.

Results: At 30 minutes of life, the newborn presented mild irritability and hypoglycemia (34mg/dl) treated and stabilized with intravenous glucose and enteral nutrition. The lab tests were normal except CRP, which is continuously increasing to the value of 10,7 mg/dl on the second day, to 42 mg/dl on the third day. Candida Albicans grew up in the blood cultures, sensitive to all usual antimycotics. Under treatment with Fluconazole the clinical course was constantly favourable, repeated blood culture was negative but the CRP decreased slowly. The antimycotic treatment was necessary for 8 weeks, with no adverse reactions. Of note that the mother, with type 1 DM, presented during the whole pregnancy vulvovaginitis with Candida, which could not be eradicated.

Conclusion: As Candida Albicans can penetrate the intact amniotic membranes, it is possible that maternal vulvovaginitis with Candida - especially in mothers with DM - could represent an important risk factor for congenital systemic candidiasis of the newborn. This is important mainly in cases like ours, in which the baby didn't develop any clinical sign of candidiasis - cutaneous or systemic.

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CLINICAL AND MICROBIOLOGICAL STUDY OF SCEDOSPORIOSIS IN PEDIATRICS CASES IN A TERTIARY HOSPITAL 2006-2010

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Background: *S. prolificans* and *S.apiospermum* are opportunistic dematiaceous filamentous fungi which causes serious and therapeutically difficult diseases.

Objective: Study of *Scedosporium spp*. isolation in pediatrics cases in La Fe Hospital during 2006-2010 period.

Material and methods: Study database of Microbiology department and medical records review of patients between 0-17 years with *Scedosporium spp* isolation.

Patients were clasified in fungal colonization, local infection or disseminated infection according clinical variables (table2)

isolation	underlying disease	treatment	diagnosis	predisposing factors	clinical sd.	clinical manif	pathological findings	afected organs	sex/age/outcome
s.prolificans	cystic fibrosis	terbinafine+anphotericine b	colonization localized infeccion dissemi nated infectio n	lung trasplant ation ATB cortycost eroids	osteom yelitis dissemi nated infectio n	lung pain skin lesio n in surg ical wou nd	RM: bone abcess.br onchial byopsy and bone cylinder with fungal structures	lung bon e mar row brai n	fem/17/de ath

[infection cases description]

Results: We obtained 49 isolates; 28(57.1%) corresponded to *S. apiospermum* and 21 (42.8%) were *S. prolificans*, which belonged to 14 patients.

Distribution by age and sex: 0-5 years, 1(7.1%), 6-10 years, 2(14.3%), 11-17 years, 11(78.6%); 7 men and 7 women.

The isolates were grouped into16 episodes (table 1, (cases/year)).Of these 68.7% was caused by *S.apiospermum* and 31.3% for *S.prolificans*.

year	cases
2006	2(12,5%)
2007	3(18,7%)
2008	2(12,5%)
2009	2(12,5%)
2010	7(43,8%)

[cases/year]

Underlying disease such as Cystic Fibrosis was found in15 (93.8%) patients)

Colonization was found in 14 (87,5%)patients, and localized and disseminated infection in 1(6.25%)patient.

Three episodes were treated; they corresponded to *S.prolificans*, colonization, local and disseminated infection in the same patient. .(table 2: infection cases description)

Conclusions: The number of cases has increased in the last year.

Worst prognosis was associated with *S prolificans* isolation.

Treatment of colonization should be assessed in larger studies.

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RESPIRATORY INFECTION CAUSED BY *CANDIDA HELLENICA VAR. HELLENICA* IN A CHILD WITH ACUTE MYELOID LEUKEMIA

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Background and aim: To describe a rare case of *Candida hellenica* infection in a child with acute myeloid leukemia (AML).

Method and results: A 2.5 year-old-girl was diagnosed with AML (M4) and received induction chemotherapy (AML BFM 2004). Twelve days after, she presented with febrile neutropenia with no specific signs or symptoms. Empirical treatment was started with broad spectrum antibiotics and antifungals (caspofungin). Blood, stool and urine cultures were negative repetitively. Thirty days after the initiation of chemotherapy, while the patient was still febrile and neutropenic, she developed lower respiratory system signs of infection (dyspnea, cough, hemoptysis). Chest X-ray showed right pleural effusion and CT scan diffuse pulmonary infiltrates. Consequently, a diagnosis of acute pneumonia was made. Intravenous liposomal amphotericin B (LAmB) was added in combination with caspofungin. Hemorrhagic sputum was sent for examination and after three days of incubation, the yeast was identified as *Candida hellenica.* According to the susceptibility testing, caspofungin was replaced by voriconazole (6mg/kg twice per day) in the combination therapy, while on day 52 amphotericin was discontinued due to clinical improvement of the patient. On day 72, voriconazole was also discontinued as the girl was considered cured from the pulmonary infection and she was released from the hospital. The chest X-ray was completely normal.

Conclusion: The isolation of an uncommon *Candida* strain, which has been described as a human pathogen, in addition to clinical and radiological findings consistent to acute pneumonia, without any other evidence of probable bacterial infection constitute evidence for possible *Candida* pneumonia.

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CRYPTOCOCCUS ALBIDUS SEPSIS IN A PRETERM INFANT: A RARE CASE-REPORT

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Introduction: Cryptococcus albidus is a wide spread fungus in the plants, the water and the skin of animals and humans. We report a rare case of Cryptococcus Albidus sepsis in a premature infant.

Case report: A male 27-weeks gestational age infant was born due to maternal vaginal bleeding with birth weight 1100 grs and Apgar score 3 in 1st and 5 in the 5th minute. The infant was resuscitated in the delivery room and transferred to the Neonatal Intensive Care Unit (NICU). Umbilical vascular catheters were applied in 1st day and neonatal long-line central catheter in the 10th day of life . In the 9th day of life the neonate's clinical status was deteriorated and C- reactive protein (CRP) rose up to 7 mg/dl. Staphylococcus Heamolyticus was identified in blood cultures and antibiotic treatment was modified accordingly. CRP values was further risen in the 28th day of life (up to 28 mg/dl) and Cryptococcus Albidus fungus was isolated in repeated blood cultures. Cerebral spinal fluid analysis revealed no pathological findings. Antifungal agents Ambisone and Fluticosine were added to neonate's antibiotic treatment. In the 25th day CRP values were decreased and significant improvement was observed until his discharge from the NICU in the 40th day of life.

Conclusions: Cryptococcus Albidus is a infrequent infectious specie of the Cryptococcus genus. Most cases attributed to it are referring to skin or ocular infections in immunosuppressed children or adults. We are reporting an extreme rare case of sepsis in a premature neonate.

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CANDIDEMIA IN CHILDREN IN A LARGE TEACHING HOSPITAL: EPIDEMIOLOGY, CLINICAL MANIFESTATIONS, MANAGEMENT, RISK FACTORS AND MORTALITY

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Aims: To investigate the epidemiology and clinical manifestations of candidemia in children, review risk factors and management and assess mortality in a large teaching hospital.

Methods: Data were obtained for all candidemia episodes in children admitted over a 10-year period ending January 2009 (PICU, oncology and pediatric wards), by reviewing the medical files.

Results: We identified 24 candidemia cases, 13 of which occurred in PICU. The median age was 1.6 (range 0.2-14.5) years and median hospital stay prior to the episode was 30 (range 5-615) days. C. parapsilosis accounted for 50% of the isolates followed by C. albicans (45.8%) and C. sake (4.1%).The main predisposing factors were administration of broad-spectrum antibiotics (83.3%), presence of central venous catheters (CVC) (79.1%) and immunosuppression (41.4%). The main presenting symptom was fever while CRP was consistently high in all cases. Amphotericin B was the most commonly used empirical treatment (79.1%), followed by caspofungin (16.6%), fluconazole (8.3%) and voriconazole (4.1%), usually given as adjunct to ampotericin B. CVC was not removed in 5 patients due to problems of vascular access and all of them died with evidence of recurrent or disseminated candidiasis. The overall mortality rate was 45.8% while mortality in PICU patients was 69.2%. Mortality was strongly related with PICU stay (odds ratio [OR] 10.1; p=0.019 and failure to remove the CVC (OR 28.1 p=0.008).

Conclusions: Non-C. albicans species are isolated more frequently than C. albicans in pediatric patients. Prompt CVC removal is essential in management of candidemia. Mortality of PICU candidemia remains high.

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THE STUDY OF ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS IN 52 UNCONTROLLED ASTHMATIC PATIENTS

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Background and aims: Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity lung disease mediated by allergic late-phase inflammatory response to aspergillus fumigatus antigens and might be seen in some patients with asthma.

The aim of this study was finding the prevalence of ABPA among 52 uncontrolled asthmatic patients.

Methods: All uncontrolled asthmatic patients, suspected to ABPA who were referred to Immunology, Asthma and Allergy Research Institute from (December 2006 - January 2009) entered this study. They were screened for ABPA with an A. fumigatus skin prick test. In patients with positive skin test, measuring of A. fumigatus specific serum IgG, IgE, total IgE(by immunocap) ,sputum *Aspergillus* culture, sputum smear study and lung HRCT (high resolution CT scan) were performed and patients were categorized on the basis of Greenberger criteria: ABPA- CB(central bronchiectasis) and ABPA-S(except for the central bronchiectasis).

Results: Twenty eight female and 24 male patients (mean age =33 years) were studied. Eighteen patients (34.6%) had positive skin test and all of them were found to have positive specific IgG and IgE to Aspergillus Fumigatus. In 61% bronchiectasis was seen in the HRCT scan.

The sputum Aspergillus culture was positive in 14 out of 18 asthmatic patients with positive skin prick test. According to Greenberger classification, 39% of patients were diagnosed to have ABPA-S and 61%were diagnosed to have ABPA-CB.

Discussion: This study showed that ABPA-CB was common in uncontrolled asthma and it is recommended physician pays more attention this complication for early diagnosis and treatment in asthmatic patients.

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REFRACTORY INVASIVE ASPERGILLOSIS CONTROLLED WITH POSACONAZOLE AND PULMONARY SURGERY IN A PATIENT WITH CHRONIC GRANULOMATOUS DISEASE

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Chronic granulomatous disease (CGD) is a rare inherited phagocytic disorder resulting in an increased susceptibility to infections including invasive fungal diseases. Among primary immunodeficiencies CGD has the highest prevalence of invasive fungal diseases. Herein, we present a case with CGD who had invasive pulmonary aspergillosis refractory to voriconazole and lipozomal amphotericine B combination therapy that was controlled with posaconazole treatment and pulmonary surgery.

Case: A thirty months old boy presented with swelling and purulant discharge on his back consinstent with abscess formation. Fungal culture from this abscess yielded Aspergillus that was susceptible to voriconazole and amphotericin B but not to caspofungin. Diagnosis of CGD was suggested by the presence of CGD history in the mother's family and the diagnosis was confirmed with the nitroblue tetrazolium test. Voriconazole was given as initial monotherapy and then combined with liposomal amphotericin B because of progression of the lesions on computerized tomography. The combination therapy was given for six months but fungal lesions did not regress and caused costal bone destruction. He underwent chest surgery and his destroyed right upper pulmonary lobe, upper segment of the lower lobe and two necrotic costal bones were resected and antifungal treatment was continued with posaconazole monotherapy. He does not have any fungal pulmonary or bone lesions and complaints in the seven months follow up after surgery. When osteomyelitis occures surgical resection of devitalized bone and cartilage is important for curative intent. Posaconazole is an extended spectrum triazole but dosage in pediatric patients has not been defined.

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SUCCESFULL THERAPY WITH CASPOFUNGIN IN ENDOCARDITIS

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Candida bloodstream infections are increasingly frequent and without adequate therapy may lead to disseminated forms of candidiasis such as endocarditis. Primary treatment regimens of candida endocarditis include liposomal amphotericin B or amphotericin B deoxycholate with or without 5-flucytosine or an echinocandin according to Infectious Diseases Society of America (IDSA) guidelines. Caspofungin is not approved for use in neonates and children below 3 months of age but there is growing evidence in this group of patients. Here we describe a premature baby with endocarditis due to *Candida parapsilosis* treated successfully with caspofungin without valve replacement.

A female infant born at 29 weeks gestation with birth weight 800 g. transferred to neonatal intensive care unit because of respiratory insufficiency. She was intubated and received surfactant replacement therapy. On 12th day sulperazon and netilmycin initiated because of abdominal distension. She could not tolerate full enteral feeding and central venous catheterisation administered for total parenteral nutrition. On follow up her clinical condition deteriorated and laboratory tests revealed thrombocytopenia. Blood cultures from a peripheral vein and central vein catheter both yielded *C. parapsilosis* growth. Catheter was removed and liposomal amphotericin B was started. Echocardiographic examination revealed a 3x2 mm vegetation on the right atrium. After 10 days of therapy, blood cultures were still growing *Candida,* amphotericin B was swithced to caspofungin. Blood culture became sterile after 48 hrs of caspofungin therapy. Serial echocardiographic examinations revealed calcification of the vegetation. Caspofungin was continued for 2 months and she was discharged with oral fluconazole therapy.

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SYSTEMIC CANDIDIASIS CAUSED BY *CANDIDA KEFYR* IN A NEONATE

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Background: Systemic candidia infections are of major concern in neonates, especially in those with risk factors such as longer use of broad spectrum antibiotics. Recent studies showed that also term babies with underlying gastrointestinal or urinary tract abnormalities are much more prone to systemic candida infection.

Methods: We report a very rare case of candidiasis caused by *Candida kefyr* in a term neonate.

Results: Renal agenesis on the left side was diagnosed antenatally and anal atresia postnatally. Moreover, a vesico-ureteral-reflux (VUR) grade V was detected by cystography. The first surgical procedure, creating a protective colostoma, was uneventful. Afterwards our patient developed urosepsis caused by *Enterococcus faecalis* and was treated with piperacillin. The child improved initially, but deteriorated again. A further urine analysis revealed *Candida kefyr* in a significant number. As antibiotic resistance data about this non-albicans candida species are limited, we started liposomal amphotericin B (AMB), but later changed to fluconazole after receiving the antibiogram. Candiduria persisted and abdominal imaging showed “fungal balls” in the right kidney. Since high grade reflux was prevalent we instilled AMB into the child's bladder as a therapeutic approach. While undergoing surgery (creating a neo-rectum) a recto-vesical fistula could be shown and subsequently was resected. The child recovered completely under systemic fluconazole therapy over three months.

Conclusion: Candidiasis is still of major concern in neonates with accompanying risk factors. As clinicians are confronted with an increasing number of non-albicans candida species, knowledge about these pathogens and their sensitivities is of major importance.

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SYSTEMIC CANDIDIASIS CAUSED BY *CANDIDA KEFYR* IN A NEONATE

S. Weichert[1], K. Zahn[2], K. Reinshagen[2], G. Geginat[3], H. Schroten[1], T. Tenenbaum[1]

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Conclusion: Candidiasis is still of major concern in neonates with accompanying risk factors. As clinicians are confronted with an increasing number of non-albicans candida species, knowledge about these pathogens and their sensitivities is of major importance.

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CLOSTRIDIUM DIFFICILE INFECTION IN NEWLY DIAGNOSED PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE - PREVALENCE AND RISK FACTORS

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Introduction: Superimposed infections of pathogenic bacteria may have deleterious effect on the clinical course of inflammatory bowel disease (IBD). Clostridium difficile infection (CDI) is one of them. The aim of the study was to investigate the prevalence and risk factors for Clostridium difficile infection in newly diagnosed pediatric patients with IBD.

Methods: It was a retrospective, observational study evaluating all new diagnosed pediatric IBD patients in 3 pediatric gastroenterology clinic in Poland between the years 2006-2010. All these patients were diagnosed according to Porto criteria, therefore all have been performed screening test for CDI. Potentially risk factors (established for adult IBD patients) for the diagnosis CDI were recorded. This included prior hospitalization and use of antibiotics within 2 months of the CDI detection, colonic involvement, duration of symptoms and others. Diagnosis of CDI was based on a positive stool enzyme immunoassay and/or on the isolation of toxigenic Clostridium difficile strain.

Results: We evaluated 233 patients (108 with Crohn's disease and 125 with ulcerative colitis). The incidence of CDI was 30% CI 95% (24.5% - 36.2%). There was no significant difference in the prevalence of Clostridium difficile infection between Crohn disease and ulcerative colitis (p=0.53). CDI was associated with increasing patient's age (p=0.000057), presence of bloody diarrhea (p=0.000057) and longer duration of IBD symptoms (p=0.0265). There was no significant difference in antibiotic exposure, prior hospitalization or disease activity between IBD patients with and without CDI.

Conclusion: The prevalence of Clostridium difficile infection in newly diagnosed IBD patients was 30%.

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BURDEN OF ACUTE GASTROENTERITIS IN SANTIAGO ISLAND, CAPE VERDE

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Background and aims: Acute gastroenteritis (AG) is responsible for >700million cases/year in < 5year olds in developing countries. Our aim was to evaluate the burden of AG in children in a developing country where there are no previous studies.

Methods: Retrospective analysis of the records of all children ≤10years with AG admitted to the short stay unit (SSU) and ward of Agostinho Neto Hospital, Praia, Cape Verde, from 01/01 to 31/12/2008. This hospital covers an estimated 42000 children ≤14years.

Results: During the study period there were 4019 children with AG observed in the Emergency Service (ES) (12% of all observations), 39% during July-September. 352children (9%) were admitted to the SSU or ward. Of these, the median age was 6months (9days-10years): 42% < 6months and 99% < 5years. The median duration of stay was 7days(0-57). Only 21% of the notes described dehydration, being moderate-severe in 59%. Of the 167children admitted to the ward, 31% had weight ≤P3; 4/16 stool cultures were positive (3 *Salmonella*,1 *Shigella*); 80% were treated with antibiotics. 9 children died.

Conclusions: AG has a high morbidity in this population. Almost all cases occurred in children < 5years and mostly < 6months. The peak during rainy season may suggest a bacterial rather than viral aetiology. The number of ES observations is probably an underestimate of the burden of disease since a non-quantified proportion of cases will not present to healthcare. This study underlines the need for measures to prevent AG including improvement of hygienic and sanitary conditions as well as immunization.

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RETROSPECTIVE EVALUATION OF ACUTE GASTROENTERITIS (AGE) AND ROTAVIRUS GASTROENTERITIS (RVGE) INCIDENCE IN AN ITALIAN POPULATION FOLLOWED UP BY FAMILY PAEDIATRICIANS

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Background and aims: Rotavirus infections play a major role in disease among children < 5-years-old. Data on RVGE incidence in community-care setting are limited because no systematic testing for rotavirus is needed at this level. The aim of this study was to estimate RVGE incidence at the community level based on *Pedianet´*s data (an Italian family pediatricians research network) over time and by age-group.

Methods: All children of the Pedianet cohort ≤ 12 years (2002-2008) who experienced an AGE were considered. A probabilistic model, based on data from the REVEAL study including children < 5 years was developed using the c-index and allowed to estimate the burden of RVGE in children < 5 years. Correction for under-reporting of symptoms was applied.

Results: 35,000 AGE cases were reported in more than 120,000 children ≤ 12 years (mean incidence: 72 x 1000 p-y) and 70% occurred in children < 5-years. Among children < 5-years, proportion and incidence of RVGE were 19.4 % and 22.7 (x 1000 p-y). The highest incidence was reported from age 6 to 23 months, the lowest in patients < 6 months. AGE and RVGE episodes showed a winter peak.

Conclusions: *Pedianet* database is a useful tool for collecting information about AGE episodes at the primary care level. Estimated proportion of RVGE episodes in the AGE database was in agreement to previous European data. Epidemiological result showed consistent RVGE incidence over years in children < 5 years.

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VIRAL ETIOLOGY, PROGNOSTIC FACTORS AND OUTCOME OF FULMINANT HEPATIC FAILURE IN CHILDREN

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Fulminant hepatic failure (FHF) is a catastrophic syndrome which may progress to death. In developing countries viral hepatitis is common etiology. Our aim is to identify the viral etiology, determine the prognostic factors and outcome of FHF

Methods: All patients with FHF with suspected viral etiology, admitted to a tertiary care hospital over a 3-year period were included. FHF due to drugs, autoimmune or metabolic liver disease were excluded. Grade of encephalopathy, viral markers, coagulation profile, liver function test and serum potassium levels were recorded.

Results: 108 children were identified with FHF due to viral hepatitis.Median age was 5 years. Forty were due to hepatitis A, 11 due to non A -G viral hepatitis, 13 due to hepatitis B,1 hepatitis E while 4 were having co-infection. 53 patients survived, 38 expired while 18 LAMA. Children with grade IV encephalopathy had 77% mortality, while those with grade 1 had 100 % survival. Delay between the first symptom and the onset of hepatic encephalopathy (within 10 days vs > 10 days), low albumin (< 2.5 g/dL), PT > 60 seconds & hypokalemia (< 3.5 mmol/dl) on admission were more likely to die.($P < 0.05$).

Conclusions: Hepatitis A and B were the most common viruses causing FHF. Children with severe coagulopathy, hypoalbuminemia and hypokalemia on admission and prolonged duration of illness before the onset of hepatic encephalopathy are more likely to die.Timely and proper vaccination against hepatitis A and hepatitis B can reduce the mortality and morbidity due to these viruses.

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BENEFICAL EFFECT OF LACTOBACILLI IN TIGHT JUNCTION INTEGRITY

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Background and aims: Probiotics are considered to reduce diarrhoea duration in clinical. Disruption of the epithelial barrier was affected by pathogens. We have previously shown that Lactobacilli provide anti-inflammation in vitro. The aim of this study was to investigate whether Lactobacilli may limit epithelial damage induced by lipopolysaccharide (LPS).

Methods: *Lactobacillus. rhamnosus* GG (LGG), *L. paracasei* and *L. johnsonii* were added on inflamed Caco-2 cells exposed to *Salmonella* LPS for 1, 6, or 24 hours. To identify the damage of Caco-2 cells monolayer was evaluated with epithelial permeability by transepithelial electrical resistance (TEER). The expression of tight junctional protein-1 was measured by immunofluorescence microscopy.

Results: Compared to LPS-pretreated controls, TEER of the polarized Caco-2 cell monolayers co-cultured with LGG, *L. paracasei* or *L. johnsonii* was significantly increased after 24 hours. Tight junction in control cells without any supplementation markedly curvy but the cells seemed larger after LPS exposure. The curvy junctions and the size of the cells appeared to be better preserved than in cells co-cultured with LPS alone.

Conclusions: Lactobacilli increase epithelial barrier function as measured with TEER and might reinforcing barrier of the epithelium exposed by LPS. In addition, Lactobacilli were suggested to strength disrupts epithelial tight junction structure, including tight junction protein-1 in Caco-2 cells monolayer. Therefore, Lactobacilli may stabilize tight junctions and prevent damage of the epithelial monolayer barrier function in host cell morphology.

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ROTAVIRUS GASTROENTERITIS IN POPULATIONS WITH DIFFERENT SOCIO-ECONOMICAL STATUS

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Background and aim: In our country RV vaccine is not included in national immunization program.

We evaluate the impact of socio-economical disparities on RV immunization status and disease aspects in Romanian children.

Material and methods: Case series analysis and questionnaire for parents, in two urban hospitals: Life Memorial Hospital (LMH-private hospital) and Institute for Mother and Child Care (IMCC-tertiary referral state hospital).

Results: In IMCC 405 stool cultures (SC) and 235 viral antigen detection (VAD) tests were performed. Tests investigated 367 [64.5% admitted patients] and 215 [7.36% of 2922 outpatients] children with diarrhea. In LMH 136 SC and 155 VAD were performed: 120 [70.59% of 170 admitted patients] representing all children with diarrhea.

All proven RV cases in December 2010 were evaluated by questionnaire.

In LMH were treated 18 RV (15% of diarrhea cases), in IMCC were 62 RV cases: 44 admitted, 18 outpatients (26.67% admitted diarrhea cases and respectively 0.62% of all outpatients).

Only 7 patients were vaccinated. Being vaccinated was more frequent associated with private hospital admittance (OR-11.54[95% CI 2.013-66.137]).

Vaccination was associated with high socio-economical status (OR-10.97 [95% CI 4.809-25.03]) but not with educational status of parents.

Severity was: Vesikari score 5.6 in LMH, 6.2 out-patients from IMCC 10.3 in admitted patients IMCC.

Conclusions:

1. RV gastroenteritis represents ~1/4 diarrhea admitted children during winter.

2. Vaccination rate for RV is low (13.5%) in private-insured patients, and even lower in state hospital patients (1.41%).

3. Socio-economical higher status was associated with higher vaccination rate but marginally with severity.

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CLUSTER OF NEUROLOGICAL MANIFESTATIONS OF ROTAVIRUS INFECTION IN CHILDREN

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Aim: To describe a cluster of children infected with rotavirus presenting with neurological symptoms and discuss the potential clinical implications.

Methods and results: Over a four-week period, four children presented to our hospital with various neurological symptoms and were subsequently found to have rotavirus in their stool (summarised in table). All four children made a complete recovery, and were well when reviewed at six weeks.

Case	Age and sex	Presenting history	Clinical examination	Blood results	CSF results	Stool virology	Imaging	Treatment
1	1 year old girl	Vomiting, 2 episodes of unresponsive-ness	Febrile, irritable, neurology normal	HCO3 ↓ Lactate ↑ Culture negative	Microscopy & chemistry normal Culture & HSV negative	Rotavirus positive	EEG normal	Ceftriaxone
2	3 year old girl	Diarrhoea, vomiting, multiple afebrile seizures	Normal	CRP ↑ HCO3 ↓ Lactate ↑ Metabolic acidosis Culture negative	Failed LP	Rotavirus positive		Ceftriaxone, azithromycin, aciclovir, phenytoin, lorazapem
3	2 year old boy	Diarrhoea, vomiting, 1 febrile seizure 4 afebrile seizures	Febrile, neurology normal	CRP ↑, Culture alpha-haemolytic streptococcus	Microscopy & chemistry normal Culture & HSV negative	Rotavirus positive	CT brain normal	Ceftriaxone, aciclovir, phenytoin
4	2 year old boy	Vomiting , drowsiness, 1 febrile seizure, diarrhoea	Reduced GCS, otherwise normal	Normal, Culture negative	Microscopy & chemistry normal Culture & HSV negative	Rotavirus positive	CT and MRI brain normal	Ceftriaxone, aciclovir

[Summary of cases]

Conclusion: Rotavirus infection in children in the resource-rich countries is usually benign but complications are rarely reported. This is the first reported cluster of children with neurological symptoms associated with rotavirus gastrointestinal infection. Potential mechanisms for how rotavirus causes its rare neurological complications are discussed.

Although the neurological manifestations of rotavirus infection are rare, given the extremely high incidence of rotavirus infection this case series has important clinical implications. Three of the four children described here were started on aciclovir for possible encephalitis. Although this should remain standard practice as diarrhoea is a common childhood symptom, we suggest that in a child with neurological symptoms who improves rapidly, detection of rotavirus in the stool may assist clinicians in the decision to stop aciclovir early, especially if there is no CSF available.

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PARENTAL BURDEN OF ACUTE GASTROENTERITIS AMONG CHILDREN YOUNGER THAN 5 YEARS OF AGE IN THE UNITED ARAB EMIRATES

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Background: Acute gastroenteritis (AGE) affects about two billion children worldwide annually and imposes a financial and a work loss burden on parents. Currently, there is a lack of studies reporting the burden of AGE on families in the Middle East.Method.

Methods: A cross-sectional survey was conducted through face to face interviews in the Emirate of Abu Dhabi, United Arab Emirates (UAE) from March 13 to April 20, 2010. Parents of children less than five years of age who had suffered from acute gastroenteritis in the preceding three months were included in the sample. Direct and indirect financial burden of AGE on families was assessed.

Results: A total of 500 parents were interviewed. Parents sought medical care for their children during 87 percent of the AGE episodes. Among those, 10 % required hospitalization. When medical care was sought, the average cost per episode incurred by families was AED237 (US$64), 4.5 times higher than the AED53 (US$14) average of those not seeking medical care. Nearly 60 percent of this difference was attributable to insurance co-payments and the cost of medications. Among those who sought medical care, 69 percent took oral rehydratation solution, 68 percent antiemetics, 65 percent antibiotics and 64 percent antidiarrheals. Overall, 38 parents per 100 episodes missed work for an average of 1.4 days due to their children's gastroenteritis.

Conclusions: AGE has an important economic and productivity impact on parents in the UAE. To reduce this burden, efforts should be made to prevent acute gastroenteritis and to optimize its treatment.

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HOW TO PREDICT HOSPITALISATION IN CHILDREN WITH ACUTE GASTROENTERITIS

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Background: Acute gastroenteritis (AGE) is one of the most common reasons for visiting the emergency room in young children. In young children the most common cause of acute gastroenteritis is Rotavirus, which can cause severe dehydration.

To reduce morbidity and mortality due to dehydration it would be helpful to identify children who will fail oral rehydration.

Our aim is to identify predictors for hospitalisation in children 1 month- 5 years of age with acute gastroenteritis (AGE).

Methods: Data were retrospectively collected from a database containing all children who visited the emergency room at Sophia Children's Hospital in 2008.

Included were all healthy children 1 month- 5 years of age with acute vomiting and/ or diarrhea. Exluded were children with chronic diarrhea (> 7 days), severe dehydration with hypovolemic shock, fever with another focus and children with a chronic underlying disease.

The primary outcome was hospitalisation. Variables associated with hospitalisation were evaluated using logistic regression analysis.

Results: Results are based on 177 children, 60 % male, mean age 1.5 years, range 0.1- 4.8 years. 58% of a total of 24 hospitalised children received oral or intravenous rehydration on the emergency department.

Predictors for hospitalisation were young age (1-6 months) (p 0.023) and level of MTS-urgency ($p < 0.01$). Abnormal values for heart rate and temperature, defined according to PRISM-criteria, did not predict hospitalisation.

Conclusion: Predictors for hospitalisation in children with acute gastroenteritis are young age (1-6 months) and MTS-urgency level. PRISM definitions of vital signs are not useful in predicting hospitalisation.

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HIGH PREVALENCE OF HUMAN G8 ROTAVIRUS STRAINS DURING 2008-09 IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Background and aims: Rotaviruses are the world's leading cause of severe rotavirus diarrhea in children < 5 years of age and form a major public health problem. However, limited regional and country specific data on rotavirus diversity is available from sub-Saharan Africa. This study aims to determine the genetic diversity of group A rotaviruses detected during 2008-2009 in the Democratic Republic of the Congo (DRC).

Methods: In this study a total of 218 fecal specimens were collected in the pediatric ward of three hospitals in Kisangani (University Hospital, General Referral Hospital of Kisangani, Village de Pédiatrie) and screened by an immunochromatographic antigen test (Rota-CIT, BioConcept, Belgium) for the presence of group A rotavirus antigen. In total, the G and P-types of 68 rotavirus-positive samples were characterized by reverse-transcription polymerase chain reaction and sequencing.

Results: The predominant G-type was G8 (detected in 37% of specimens) and the most predominant P-type was P[8] (60%). A total of 9 different G/P-combinations were found: G8P[8] (32%), G1P[8] (23%), G2P[4] (15%), G1P[6] (9%), G12P[6] (9%), G9P[8] (5%), G8P[6] (3%), G8P[4] (2%) and G2P[6] (2%).

Conclusions: The high prevalence of the G8 VP7 specificity in the DRC, which is believed to be of bovine origin, highlights the need for continued surveillance of rotavirus diversity in the DRC. Based on these data, rotavirus vaccines will be challenged with a wide variety of different RV strain types in the DRC.

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COMPLETE GENETIC CHARACTERIZATION OF HUMAN G2P[6] AND G3P[6] ROTAVIRUS STRAINS

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Background and aims: Human rotavirus (HRV) strains bearing genotype P[6], in association with a variety of G-types, have been detected in Africa. However, the relative frequency of P[6] HRV strains outside Africa is low. Recently, a number of P[6] HRV strains in combination with G3 have been isolated for the first time during the 2008-2009 rotavirus season in Belgium and a G2P[6] was isolated in the United States in 2006. This study aims to describe complete genomes (11 segments) of these recent P[6] HRV strains isolated outside Africa and analyze their relationship to other known RV strains.

Methods: To investigate the evolutionary relationships of these strains, we sequenced the complete genomes of 3 P[6] HRV strains, 2 strains isolated in Belgium and 1 strain in the United States, and compared them with the genomes of other RV strains.

Results: Our genetic analysis revealed that most of the 11 gene segments of these 3 strains belonged to genotype 2 (DS-1-like). The genomic comparison of the 2 Belgian G3P[6] strains revealed that all 11 segments were identical. The American G2P[6] strain was phylogenetically closely related to the Belgian P[6] strains and to other recently isolated HRV strains.

Conclusions: These data suggest that reassortment(s) involving VP7 have occurred recently. The rise of the P[6] genotype needs to be closely monitored especially because this genotype is not included in the currently available RV vaccines.

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CLINICAL EFFECTIVENESS OF HIGH DOSE THREE-COMBINATION PROBIOTICS (BIO-THREE®) THERAPY IN PEDIATRIC PATIENTS WITH INFECTIOUS GASTROENTERITIS

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Background: Including our previous report, several studies have shown that rotavirus infection and salmonella infection are the leading causes of infectious gastroenteritis. The primary aim of the study was to evaluate whether the addition of high dose probiotics to the routine treatment would reduce the severity and time course of infectious gastroenteritis in pediatric patients.

Methods: A single-center, open-label, randomized, controlled trial was conducted to collect 268 patients aged 3 months to 14 years and hospitalized with infectious gastroenteritis between February 2009 and October 2010. After written informed consent was obtained, subjects were randomized to receive conventional treatment or add-on treatment of the probiotics to the conventional treatment.

Results: The result of the trial showed that the percentage of patients with severe diarrhea (Vesikari scale ≥11) reduced after probiotics treatment. Patients in the Rotavirus group showed significant improvement from day 1 after probiotics treatment ($p=0.001$). Patients in the Salmonella group were significantly improved at day 5 and 7 ($p< 0.05$, respectively). Patients in the Other AGE group also showed significant improvement at day 3 ($p< 0.0001$). All the patients in the probiotic group revealed improvement at day 3 after treatment and would further demonstrate significant improvement at day 5 and 7 ($p< 0.05$, respectively).

Conclusions: Seven days of high dose Bio-three were highly efficacious and safe in infants and children for treating severe gastroenteritis and the incidence of severe gastroenteritis was significantly reduced in the rotavirus group.

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TRENDS IN THE PREVALENCE AND ERADICATION RATES OF H PYLORI INFECTION IN SYMPTOMATIC CHILDREN: A SINGLE CENTER STUDY

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Background: Helicobacter pylori is one of the most widespread bacterial infections worldwide. The prevalence of H pylori infection in children from developed countries has been steadily declining over the last decade as a result of the socioeconomic status improvement and probably also as a consequence of the frequent use of antibiotics.

Aims: To evaluate retrospectively the dynamics of the prevalence of H pylori infection among gastroscopied symptomatic children over the last decade and to establish the succes of its eradication after the first line therapy.

Methods: We studied 802 consecutive symptomatic children (494 girls, age range 6 months - 18 years) referred for the first gastroscopy for various reasons, during the past decade (2001-2010). H pylori was assessed before and 4 weeks after treatment by urease test and histopathology. Socioeconomic status, eradication rates of H pylori after the first line therapy were evaluated.

Results: Overall, H pylori infection was documented in 467 of the 802 symptomatic children (58,22%). Its prevalence varied from 56,16% in 2001 to 50,63% in 2010, with an unexpected increase between 2006 and 2008, from 77,77% to 67,70%. The colonization rate was inversely correlated with the socioeconomic status ($p< 0,005$). Overall, the eradication rate of H pylori infection after the first treatment was 70,73%, with a decrease from 83,61% in 2001 to 71,18% in 2010.

Conclusion: Our data suggest that the prevalence of H pylori infection in symptomatic children was only non-significantly lower during the past decade. The eradication rate of H pylori after the first line therapy decreased gradually.

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ROTAVIRUS GENOTYPING DATA IN LITHUANIA DURING FOUR ROTAVIRUS SEASONS

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Background and aims: Rotaviruses (RV) are a major cause of acute gastroenteritis in Lithuanian children. There have been no comprehensive studies made on molecular rotavirus epidemiology in the country. As a member of the European Rotavirus Surveillance Network, EuroRotaNet, Lithuania committed to provide rotavirus genotyping data during several RV seasons. This is the first comprehensive report of rotavirus genotypes circulating in Lithuania.

Methods: Faecal samples, positive for group A rotavirus antigen, were collected between 2005 and 2010 at Vilnius University Children's hospital. All rotaviruses were genotyped according to EuroRotaNet protocol.

Results: A total of 1880 rotavirus positive samples were characterised. Most common were human rotavirus genotypes G1P[8], G2P[4], G3P[8], G4P[8], and G9P[8], their incidence varied from 84.7 to 94.7% among seasons. Potential zoonotic or human-animal hybrid strains occurred no more frequently as in 4.2% of cases. During 2009-2010 RV season, the emergence of G6P[9] strains was observed, is was found in 10 (2.0%) cases. Mixed rotavirus infections represented from 2.4% to 11.3% of depending on the season. Reassortant of human RV strains were detected in all seasons and occurred in 0.4 % to 5.7% of cases.

Conclusions:

1. Most common rotavirus genotypes in Lithuania were G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8].

2. Reassortant between human and animal rotavirus strains or potential zoonotic rotavirus strains represent a small proportion of all rotavirus strains which infect humans, but are found every season representing a potential for emergence of new strains.

3. The distribution of genotypes differs among seasons.

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THE BURDEN OF ROTAVIRUS DISEASE IN DENMARK 2009-2010

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Background: This study sought to determine the incidence and the burden of severe diarrheal disease in Denmark with emphasis on rotavirus disease.

Methods: This study was designed as a national prospective disease surveillance of children< 5 years of age hospitalized for acute gastroenteritis in Denmark during March 2009 to April 2010, using rapid rotavirus and adenovirus antigen detection.

Results: A total of 3100 hospitalizations annually among Danish children < 5 years can be attributed to acute gastroenteritis and 1210 (39%) of these to rotavirus disease. The majority of RV-associated hospitalizations occur among children ≤24 months of age (RV-associated hospitalization rate: 7.7/1000 children ≤24 months-of-age and 3.8/1000 children< 5 years-of-age). Although the well-known seasonal pattern of rotavirus was evident with a peak during the spring months of March to April, our active surveillance demonstrated RV-associated hospitalizations throughout the year. Genotyping of a subset of RV-samples demonstrated high frequency of G1 (39%) and G4 (32%). Adenovirus was detected in 350 AGE-associated hospitalizations (11.2%).

Conclusion: In conclusion, of the 3100 annual AGE-associated hospitalizations among Danish children < 5 years, 1200 are RV-associated (39%). Rotavirus is indeed ubiquitous in the population; despite a marked seasonality it is associated with hospitalizations year round and can be considered a major health burden among young Danish children.

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ESTIMATES OF HEALTHCARE AND NON-HEALTHCARE COSTS DUE TO SEVERE ROTAVIRUS INFECTIONS LEADING TO HOSPITALIZATION IN SWEDISH CHILDREN (< 5 YEARS)

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Introduction: Estimates of economic benefit of rotavirus vaccination depend on the accuracy of calculated country-specific costs related to rotavirus gastroenteritis (RVGE). Transmission of disease to family members adds to the economic burden through loss of caregiver productivity. The aim of this study was to assess costs related to *severe* RVGE.

Material and methods: A prospective, observational study was conducted in a large hospital in the Stockholm region, serving a population of 66,222 children < 5 years. RVGE related health care resource use and time off work were collected from a sample of families with hospitalised children due to community- and nosocomially-derived RVGE (n=153). Health care related costs were calculated using 2008 DRG reimbursement for acute diarrhoea and productivity loss using self reported absence combined with 2008 Swedish average cost for a working hour (€28) from SCB/Statistics Sweden.

Results: Median age of hospitalised children was 15 months. For caregivers, average workday loss due to children's, siblings or own disease was 4.2 days and 1.2 days, respectively. Estimated average total cost per child was €3227, €1949 (60%) for health-care related costs, €1186 (37%) productivity loss and €92 (3%) due to other indirect costs.

Conclusions: Economic burden of RVGE is primarily driven by costs related to in-patient care, sensitive to unit cost used. However, loss of productivity is also significant in spite of generous parental allowance in Sweden, 12-18 months per child. A limitation of this study is that productivity loss from care for non-hospitalized children and its household members was not assessed.

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ADHERENCE OF TREATMENT OF ACUTE DIARRHEA TO WHO RECOMMENDATIONS AND NATIONAL GUIDELINE IN GEORGIA

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Despite national guidelines few children suffering from acute diarrhea receive low osmolarity oral rehydration solution (ORS) and zinc. The aim of this study was to analyze practitioners´ prescriptions for acute diarrhea for adherence to WHO recommendations and Georgian National guideline.

A questionnaire-based, cross-sectional survey was carried out in Georgian regional hospitals and out-patient clinics. Special questionnaire was elaborated based on IMCI guideline, covering issues of diarrhea identification, assessment of dehydration severity, rehydration therapy, use of antibiotics, Zinc and low-osmolarity ORS.

Totally 350 questionnaires were analyzed, 95 from hospitals and 255 from out-patient clinics. About 90% of medical staff uses ORS during diarrhea, but most of them (78%) haven't even heard about low osmolarity ORS and its benefits, despite this most of them frequently used low osmolarity ORS without knowing about it. In hospitals in case of moderate dehydration 38% of physicians use intravenous rehydration. In 45% antibiotics were used without indication, in 35% antiemetics were prescribed. 21% of interviewed persons have heard about Zinc and its benefits during acute diarrhea, but only in few cases was Zinc used during acute diarrhea.

This study demonstrated better results then 2 years ago, but still there is low adherence to standard treatment guidelines for management of acute diarrhea in children. Key public health concerns were the no use of zinc and the high use of antibiotics and antiemetics and intravenous fluids. To improve case management of acute diarrhea, continuing professional development program targeting the practitioners is necessary.

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ADHERENCE OF TREATMENT OF ACUTE DIARRHEA TO WHO RECOMMENDATIONS AND NATIONAL GUIDELINE IN GEORGIA

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THE RELATIONSHIP BETWEEN H.PYLORI INFECTION IN CHILDREN AND FAMILY HISTORY OF PEPTIC SYMPTOMS

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Background and aim: It is well known that H. pylori can lead to gastroduodenal inflammatory and neoplastic diseases.

The purpose of this study is to investigate the relationship between the presence of H.pylori infection in children and their parental history of dyspeptic symptoms.

Methods: A total of 201 children (106 male, 95 female, median age 9.0 years, range 2 months-18 years), who underwent diagnostic oesophagogastroduodenoscopy, were tested for H. pylori infection between 2002 and 2004. The presence of parental dyspeptic complaints were questioned. The diagnosis of H. pylori infection was made if urease test and histological examination of gastric biopsies obtained during endoscopy were both positive. The relationship between H. pylori infection in children and parental history of dyspeptic complaints was reviewed retrospectively. For statistical analysis, independent t-test and Pearson´s chi-square test were used.

Results: 71 of (35.3%) 201 children had H. pylori infection. The difference between H. pylori infection rate in children with and without gastric symptoms was insignificant ($p = 0.549$). On the other hand, 52 among the parents of 201 (25.9%) children had a history of gastric complaints. H.pylori infection rate was higher in children with parental history of dyspeptic complaints compared to those without (31 of 52, 59.6% vs 40 of 109, 26.8%), this difference was statistically significant ($p< 0.001$).

Conclusion: Our findings suggest that it will be useful to screen for H. pylori in those children with a parental history of gastric symptoms even if they themselves don't describe any gastric complaints.

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PROBIOTIC LACTOBACILLUS REUTERI SHORTENED THE COURSE OF ACUTE ROTAVIRUS DIARRHEA

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Background and aims: Acute infectious diarrhea is a major cause of childhood morbidity and economic burden for families.

Aim: To evaluate the efficacy of the probiotic Lactobacillus reuteri as an adjuvant to oral rehydration solution in shortening the duration of acute rotavirus (RV) diarrhea in hospitalized children under 2 years old.

Methods: The study involved children with mild or moderate RV diarrhea admitted to University Hospital "St. Anna", Sofia for the period January - December 2008. Stool samples were tested for RVs by enzyme immunoassay (ELISA) and were also cultured to exclude the presence of enteropathogenic bacteria. On admission most of the children were given the probiotic Lactobacillus reuteri for 3 days.

Results: Rotavirus was identified in 132 of 153 (86 %) children tested with diarrhea. Fifteen cases were excluded from the study because of severe diarrhea. As a total, 117 children eligible for the study were evaluated (59 without probiotic Lactobacillus reuteri and 58 with probiotic Lactobacillus reuteri given). The mean age of the children was 18 months. The mean duration of diarrhea was 4, 2 days in a subgroup not received the probiotic and 2,7 days in a subgroup received it ($p < 0,05$). The administration of antimicrobials before inclusion did not make any differences. In no patient diarrhea persisted longer than 4 days.

Conclusion: Lactobacillus reuteri as an adjuvant to oral rehydration solution in children less than 2 years old with mild to moderate RV diarrhea decreased the duration and reduced the risk of prolonged diarrhea.

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GASTRODUODENAL BY HELICOBACTER. PYLORI (H. PYLORI) INFECTIONS

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Bαckground and aims: H. pylori is able to cause chronic inflammation (gastroduodenitis etc) and is considered to be peptic ulcer's main cause. Many children, younger than 5-6 years old, are infected by Helicobacter, while infection's frequency increases with age. A pediatric patient's case with gastritis, duodentitis caused by H.pylori is described.

Methods: History: chronic abdominal pain with periodical nature (since2 years, 1-2 periumbilical pain episodes weekly with reflection to the back, without accompanying symptoms). Perinatal period: normal, family history: mother with duodenum ulcer.

Physical examination: Abdominal soft, painless, without organomegaly, rest systems: normal. Hematological- biochemical tests, urine test- culture, Mayer, abdominal U/S: normal.Urea Breath Test (UBT) was made, gastroscopy, biopsy-histological examination, Campylobacter Like Organism (CLO) test, as well.

Results: UBT: H.pylori infection, gastroscopy: esophagus:normal, stomach(fundus:normal, body- antrum: micronodular, erythymatous mucosa), duodenum(1st part: mucosal pale, inflammated, 2nd part:normal) - H.pylori gastritis- duodentitis findings. Esophageal biopsy: vascular branches chorionic papillae's hyperemia, biopsies- part of body's mucosal, from the border body-pylorus- : chronic active gastritis, serious grade lesions with lymphnodules formations, regenerative epithelial hyperplasia, focal, hemorrhagic filtrations coexistence, duodenum biopsies: chronic duodenitis lesions, focal hemorrhagic pervasions coexistence. Histochemical control: big grade H.pylori.,CLO test: H.pylori infection positive. After administration of Clarithromycin 500mg twice daily, amoxicillin500mg 3 times daily and omeprazole 20mg twice daily, for 2 weeks, H pylori eradication was achieved (confirmation with UBT a month after treatment).

Conclusions: In differential diagnosis for children with abdominal pain, with duration of 2 weeks or more, H.pylori infection must be included.

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CHARACTERISTICS OF CO-INFECTION WITH SALMONELLA AND ROTAVIRUS IN HOSPITALIZED CHILDREN IN SOUTHERN TAIWAN- A 6-YEAR ANALYSIS

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Background and aims: This study aimed to analyze the characteristics and severity of acute gastroenteritis related to rotavirus (group R), non-typhoid Salmonella (NTS) (group S), or both (group B) of children in Taiwan.

Methods: Medical records of children admitted from October 2002 to September 2008 for acute gastroenteritis related to rotavirus, NTS, or both, were collected and analyzed.

Results: Among 2,040 medical records being reviewed, 40 patients were identified to be infected by both pathogens, while 501 cases by rotavirus alone, and 189 by NTS alone. The age at admission did not show significant difference between the three groups ($p=0.4717$). Age distribution of cases revealed that the age between 12 and 24 months comprises the largest proportion of cases in every group. There were 442 males and 288 females in this study, and the gender ratios did not differ significantly among the three groups ($p=0.9661$). Higher positive rates of fecal leukocyte and fecal pus cell, higher incidence of seizure, and longer hospitalization were observed for group B, as compared with that of group S ($p< 0.05$) while clinical severity in group B were significantly higher than that in group R ($p< 0.05$). A proportional association was found between the monthly case number of rotavirus infection with mean temperature difference in southern Taiwan ($r=0.9248$; $p< 0.0001$).

Conclusions: Positive fecal leukocyte and fecal pus cell might be a valuable marker indicating a co-infection of NTS and rotavirus in children. The addition of rotavirus infection in Salmonella infection does not worsen the clinical manifestation.

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CHANGES OF BONE METABOLISM IN HCV-INFECTED PAEDIATRIC PATIENTS

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Background: Several studies have demonstrated bone disorders in HCV-infected adults, most frequently during the advanced stages of the liver disease. The changes in bone metabolism occurring over time in children and adolescents who acquired HCV infection *in utero* or by blood transfusion in early infancy have not been thoroughly studied yet.

Methods: Data regarding biochemical markers of bone metabolism (serum levels of calcium, inorganic phosphate, alkaline phospatase, osteocalcine as bone synthesis index and C-terminal telopeptide of type 1 collagen as bone resorption index) and ultrasonographic bone densitometry have been collected in a cohort of 18 HCV-infected children and adolescents (8 males, 7 females).

Results: The serum levels of calcium, inorganic phosphate and bone specific alkaline phosphatase were normal in all cases; by ultrasonographic densitometry low bone mineral density values (compared with control subjects of the same age) were detected in 7/18 subjects (38%). Osteopenia was diagnosed in 5 vertically-infected children (3 of whom born to HIV-coinfected mothers) and osteoporosis in two, aged 11 and 21 years respectively, the former of whom born to HIV-coinfected mother too. The serum levels of osteocalcine resulted increased in all cases of osteopenia but just in one case of osteoporosis.

Conclusions: In our cohort the ultrasonographic densitometry proved to be the most sensitive test for early diagnosis of bone turnover alterations in subjects otherwise healthy, with normal or just poorly alterated liver function. A periodical evaluation of bone metabolic rate in chronically HCV-infected children and adolescents is mandatory in the aim to better assess these alterations.

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CLINICAL FEATURES OF GASTROENTERITIS (RGE) CAUSED BY ROTAVIRUS G4P8 SEROTYPES IN MINSK, BELARUS

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In Minsk we marked annual changing of the season peak (February-April) dominant rotavirus serotype: 2005 - G4P8 (69%),

G1P8 (11.3%),

G2P4 (9.9%),

G3P8 (4.2%); 2008 -

G4P8 (53.3%),

G2P4 (22.9%), G1P8 (14.3%), G3P8 (9.5%); 2009 - G2P4 (46.7%), G4P8 (31.2%), G1P8 (13.3%), G3P8 (2.2%); 2010 - G4P8 (60.0%), G2P4 (29.1%), G1P8 (7.3%), G3P8 (3.6%). Vaccination against rotavirus doesn't is a routine in Belarus. The aim was to study clinical features RGE caused by G4P8 serotypes in children who were treated in the Paediatric Infectious diseases Minsk City Clinic (PIDCC).

Materials and methods: The research was performed at the PIDCC at 2005 and 2008. The diagnosis RGE were confirmed by detection of a rotavirus antigen in stools (EIA and serotypes by PCR).

Results: We observed 28 children with RGE at the age of 6 - 60 months Ìå (Ð25-Ð75) 19 (12-34). They were admitted at the Clinic at 1-4 day from the disease beginning Ìå (Ð25-Ð75) 1.0 (1.0-2.0). RGE severity (Vesicary's scale) were Ìå (Ð25-Ð75) 12.5 score (10.0-14.0). The body temperature was Ìå (Ð25-Ð75) 38.4ºC (37.9-39.0). The dehydratation was Ìå (Ð25-Ð75) 1.0 degree (1.0-2.0). 22 from 28 patients had different catarrhal symptoms. Children younger than 6 month old had more specific clinical symptoms (n=2). All patients had basic therapy (rehydratation, diet). After the treatment the improvement of the condition was observed (diarrhea disappearance 3.5 (3.0-4.0) days, vomiting discontinuance 1.0 (1.0-2.0) day; temperature normalization 2.0 (2.0-3.0) day.

Conclusion: RGE caused by G4P8 serotypes has moderately severe. Serotypes control is important for epidemiology.

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ISOLATION OF *VIBRIO CHOLERAE* SEROGROUPS O1 FROM WATER OF KAROON RIVER IN AHVAZ CITY, SOUTH WEST OF IRAN

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Background and aim: Vibrio species are one of the main bacterial groups in the environment that are known as opportunistic bacteria. Cholera is a major cause of illness in the developing world. The World Health Organization reported in 2006 that 236,896 cases of cholera occurred in 52 countries, a 79% increase over 2005. The cholera bacterium may also live in the environment in brackish rivers and coastal waters.

The aim of this study was to investigate isolation of *Vibrio cholerae* serogroups O1 from Water of Karoon River in Ahvaz, Iran

Methods: During 4 months between April 2010 to july 2010), 100 sample were collected from water Karoon River in Ahvaz, Iran. The study period the recorded river temperature was about 25-28°C and pH ranged from 7 to 8. The samples were cultured onto Thiosulfate Citrate Bile salts Sucrose and MacConkey agar, and incubated at 37oC for 24 hours. The via colonial morphology compatible with *Vibrio* were characterized by oxidase test and agglutinated with antiserum for serotype and biochemical tests.

Results: In this study, 100 samples of water Karoon River in Ahvaz, Iran, 8 (8%) sample were positive for *Vibrio cholerae* strains. The all *Vibrio cholerae* isolated from water Karoon River in Ahvaz, Iran, were *V. cholerae* serogroup O1 serotype Inaba.

Conclusion: *V. cholerae* existed as the natural habitat in estuary water of the River and showed obvious genetic diversity. The priorities for cholera are improved control public health for water, sanitation, and surveillance and further development of appropriate vaccines.

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VIRAL GASTROENTERITIS IN CHILDREN HOSPITALISED IN LVIV, UKRAINE

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Introduction: Rotavirus and more recently norovirus are recognized as main causes of moderate to acute gastroenteritis in children less than 5 years of age. Salmonella, Enterobacter and Rotavirus are most commonly encountered bacterial and viral pathogen in Ukraine, the role of other enteric pathogen in childhood gastroenteritis has rarely been estimated.

Methods: During a winter & spring periods (2009-2010) 264 children < 3 years old admitted at Lviv Infection Diseases hospital were investigated. Demographic and clinical data were collected.The diseases severity was estimated using Vesikari scores. Stoll bacteriology investigation & ELISA for virus pathogen were used.

Results: All children had gastroenteritis symptoms during admission. Rotavirus antigen was detected in 31,4%, the rate of norovirus was 36,6%. 79% of norovirus infections and 90% rotavirus infections were symptomatic. In 58,1% rotavirus infected children and 67,4% norovirus infected baby virus infection viral-bacterial coinfection were found. The virus-virus coinfection were found in 25% case, more often norovorus-rotavirus coinfection were observed. With regard to clinical severity, rotavirus resulted in longer hospital stay, higher rate of vomiting, stool occult blood, leukocytosis, lower rate in stool pus cell, and C-reactive protein elevation more than 5 mg/dL as compared with norovirus.

Conclusions: The highs prevalence rotavirus and norovirus infections as a cause of acute viral gastroenteritis in infants and young children were established. No statistical differences in illness severity were found between mixed infection and monobacterial or monoviral infection.

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PARVOVIRUS B19 INFECTION ASSOCIATED WITH ACUTE HEPATITIS

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Parvovirus B19 (PvB19) has been documented in serum samples of patients with acute hepatitis (AH) without etiological diagnosis. In a pediatric series of fulminant AH, 4 out of 21 children had PvB19 infection and other small pediatric series showed that PvB19 was present in 50% of AH of unknown origin. We describe a child with AH, of unknown origin initially, caused by PvB19.

A 10-years-old boy, previously healthy, attended our institution because of vomiting, loose stools, diffuse abdominal pain and choluria during the last three days. He had presented an erythematous malar rash which was diagnosed as erythema infectiosum by the primary care pediatrician the previous week. A new rash appeared in the last day. In the physical exam the patient had conjunctival jaundice and an exanthema with macular lesions on trunk and legs with petechiae on feet. In the laboratory studies he showed: bilirrubin 5,3 mg/dL (3,7 mg/dL conjugated), AST 115 IU/L, ALT 238 IU/L and INR 1,3. Serologic exam for HVA, HBV, HCV, CMV, EBV and Toxoplasma was negative. IgM PvB19 was positive (1:40) and PvB19-DNA was detected by means of PCR procedures. Supportive care was carried out. He reached full recovery in the fourth week.

AH is a rare manifestation of PvB19 infection. This infection must be considered in case of AH of unknown origin, after exclusion of usual causes.

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HERPES SIMPLEX TYPE-1 ESOPHAGITIS IN A IMMUNOCOMPETENT HOST

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Infectious esophagitis is generally seen in immunosuppressed patients. We report a case of *Herpes simplex* virus (HSV) esophagitis in an immunocompetent host.

An 11-year-old male, without previous relevant or recurrent infections, presented with a 3-day history of high grade fever, right hemi-abdomen pain, leukocytosis, neutrophilia and PCR 87 mg/L. Ultrasonographyc exam of the abdomen ruled out focal infections and was highly suggestive of mesenteric adenitis. At the fourth day, abdominal complaints disappeared and a retrosternal pain began. The chest radiograph and EKG were normal. Omeprazol was started. 24 hours later, pain was intensified, with mild odinophagia, and high grade fever persisted. A non-purulent exudate on left tonsil, without oral lesions, was seen. On endoscopic image, 4 ulcers with raised edges and a diffuse erythematous mucosa with superficial erosions was seen. The histological picture was of viral esophagitis and immunohistochemical staining for Herpes virus was positive. IV acyclovir was started. Fever disappeared immediately. Pain and odynophagia improved in the first day and completely disappeared in 4 days. An elevated IgM HSV type 1 was documented. HIV antibody was negative and CD4, CD8, immunoglobulins and complement levels were normal.

Herpes esophagitis is a rare, but well-defined entity. There are about 20 paediatric cases reported. Probably is an underdiagnosed condition. A high degree of suspicion and a prompt endoscopic examination is required for the diagnosis. It is usually a self-limited infection. There is no evidence to support acyclovir therapy, but early antiviral therapy may hasten the resolution of symptoms.

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SERUM NEOPTERIN CONCENTRATION AS A MARKER OF VIRAL DIARRHEA IN INFANTS

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Background: Serum neopterin concentrations is elevated in a lot of diseases in which cellular immunity is activated. Gastroenteritis in infants is a major causative factor of childhood mortality and morbidity all other the world. The great majority all the infantile diarrhea cases is caused by viruses. Evaluation of serum neopterin concentration is known as a cheap, quick, sensitive method of indentifying viral infection in children. Introduction of serum neopterin concentration measurement to the diagnostic process of infantile diarrhea can be a cost-effective method of identifying viral etiology of the disease.

The aim of the study was to evaluate whether serum neopterin concentration can act as a marker of viral infantile diarrhea.

Methods: Fifty five infants, aged from 0.1 to 12 months entered the study. All of the patients presented with symptoms of diarrhea. Rotavirus or adenovirus infection was diagnosed. The control group consisted of 95 healthy infants. The serum neopterin concentration was evaluated by ELISA method.

Results: Serum neopterin concentration in the study group was from 5.85 to 160 nmol/L (median 25.4 nmol/L) and it was significantly higher than in the control group (from 2.73 to 16.7 nmol/L; median 4.23 nmol/L) ($P < 0.001$). Neopterin concentration was above the normal value (>11 nmol/L) in 53 children from the study group and only in 4 from the control group. There was no significant difference between infants with rotavirus and adenovirus infection ($P=0.32$).

Conclusion: Eelevated serum neopterin concentration can be used as a marker of viral diarrhea in infants.

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ACUTE CHOLECYSTITIS IN THE DIFFERENTIAL DIAGNOSIS OF CHILDREN WITH ABDOMINAL PAIN - CLINICAL CASE

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Background and aims: Abdominal pain is a major cause of urgency demand in Pediatric age. It is often difficult to differentiate an ordinary pain from an emergency.

Acute acalculous cholecystitis is an uncommon gallbladder disease, rarely seen in children and, therefore, frequently underdiagnosed.

We shouldn't forget to consider cholecystitis in the differential diagnosis of pediatric patient with jaundice and/or abdominal pain in the right upper quadrant.

Clinical case: 4-year-old boy presented with abdominal pain and vomiting for 48 hours. In the past 3 months, he had already been admitted twice to the emergency room because of the same symptoms and was discharged with symptomatic medication.

On admission, he presented afebrile, hemodynamically stable, generalized abdominal tenderness, stronger in the right quadrants, with guarding and positive Blumberg.

Laboratory results revealed neutrophils leukocytosis and negative C-reactive protein. *Salmonella spp* was isolated in stool.

Abdominal ultrasound suggested acute acalculous cholecystitis, so he was started on analgesia and intravenous antibiotics. On D3, despite clinical improvement, he began an anallitical padron of cholestasis; a second ultrasound hypothesized a choledocal cyst. He was then transferred to the Surgery department H.D.Estefânia, where completed 14 days of *ev* antibiotics, with clinical and laboratory improvement and was discharged asymptomatic. He was submitted to elective cholecystectomy, and the histology confirmed a choledochal cyst.

Conclusions: With this case the authors underscore the importance of including acute cholecystitis in the differential diagnosis of children with abdominal pain and emphasize the value of clinical symptoms and ultrasound for the correct diagnosis.

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PAEDIATRIC INTENSIVE CARE TREATMENT IN 60 CHILDREN WITH ROTAVIRUS INFECTION

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Introduction: Rotavirus infection (RVI) is the leading cause of severe acute gastroenteritis in children throughout the world. Even in well developed countries with good medical treatment options like in Austria severe and fatal cases can be observed.

Patients and methods: We analysed children admitted to our paediatric intensive care unit (PICU) due to proven RVI between 1990 and 2010. Patients with severe underlying diseases have been excluded.

Results: 373 patients had to be admitted to the ICU due to metabolic and electrolyte disorder, 60 of them where tested positive for RVI; 25 females (41%) and 35 males (59%). The mean age was 16 months (median 10, minimum 2, maximum 190). In 7 patients (11%) intubation was necessary. One Patient died in spite of all efforts, in 59 patients a combination of oral and parenteral rehydration led to a stable fluid balance and total recovery. The mean duration of stay at the ICU was 4±6 days.

Discussion: Although RVI is a common cause for hospitalisation of small children, severe complications under appropriate therapy are uncommon. In spite of all therapeutic efforts a severe progression can be observed in single cases with fulminant dehydration, metabolic disorder and the need for intensive care.

Conclusion: Rotavirus infections have still a substantial morbidity in well developed countries with modern therapeutic possibilities and can turn to a life threatening event in unrecognised cases.

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THE HOMEOPATHY TREATMENT STOPS ACUTE DIARRHEA IN INFANTS AND TODDLER TREATMENT OF ACUTE INFANTILE DIARRHEA

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Background: Previous studies suggest that homeopathic treatment might be useful in acute childhood diarrhea.

Aim: To evaluate the therapeutic efficacy and safety of homeopathy in treating acute diarrhea in infants and toddlers.

Methods: Randomized, double blind, placebo-controlled, prospective, multicentre, parallel group, clinical trial of phase ll. 113 infants and toddlers between 2 and 47 months of age with acute diarrhea were randomly allocated to either the homeopathy group (55 patients) or the placebo group (58 patients). The primary outcome measure was reduction in stool to ≤ three watery or loose stools in 24 hours over a period of at least 2 consecutive days. Secondary outcome measures were response rate, stool consistency, abdominal pain, cramps, body temperature, frequency of vomiting, occurrence of adverse events and tolerance to the study medication. The participants were assessed until ascertainment of response, 10 days at maximum.

Results: Statistical testing revealed that the homeopathy treatment was significantly superior to that of the placebo in terms of time to response (p = o.ooo7). The medial time to response was 2.5 days in the homeopathy group and 4.8 days in the placebo group. Treatment with homeopathy shortened the duration of diarrhea by 2.3 days. In total diarrhea was stopped in 52/55 patients (94.5%) in the homeopathy group and 29/58 patients (50%) in the placebo group within 10 days. Fourteen patients dropped out the trials because of unsuccessful therapy.

Conclusion: Homeopathy showed a significant superiority to placebo in the treatment of acute diarrhea in infants and toddlers.

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MOLECULAR EPIDEMIOLOGY OF ROTAVIRUSES IN ESTONIA IN 2007-2008

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Background and aims: Rotaviruses are major causes of acute gastroenteritis in children ≤5 years worldwide. Two vaccines have been licensed against rotavirus: Rotarix (G1P[8] strain) and Rotateq (serotypes G1-4 and P[8]). Knowing circulating rotavirus strains in the geographic area is important for recommendation of vaccines. The purpose of our study was to describe rotavirus genotype distribution in Estonian children aged < 5 years during 2007-2008.

Methods: 671 children with laboratory confirmed rotavirus gastroenteritis from three major paediatric hospitals of Estonia were prospectively enrolled. Rotavirus G-/P-genotypes were detected from randomly selected 124 stool samples by semi-nested reverse transcription-PCR.

Results: The study population for genotyping resembled the whole population in median age of 15 and 17 months, respectively, and in Clark score of 13 and 12 points, respectively. The commonest G-genotypes were G2 (37.1%) and G4 (33.9%), yet the prevalences of G1, G9 and G3 were considerably smaller - 13.7%, 6.5%, 3.2%, respectively. The dominant P-genotype was P[4] (40.3%), but P[8] occurred in somewhat lower rate - 25%. Genotypes P[6] and P[11] both accounted for 0.8% of cases, but as many as 30.6% were P-untypeable. The prevailing strain was G2P[4] (34.7%), causing significantly more gastroenteritidis than G4P[8] (12.9%), G1P[8] and G9P[8] (both 4.0%), G3P[8] (1.6%). Mixed infections occurred in 4% of cases.

Conclusions: The distribution of rotavirus genotypes in Estonia does not resemble that in Europe, although we should keep in mind fairly large proportion of P-untypeable samples. Nevertheless, considering heterotypic immunity vaccines induce, efficacy of immunization can be expected high.

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ISOLATION OF ENTEROINVASIVE *ESCHERICHIA COLI* (EIEC) FROM DIARRHEAIN CHILDREN BY POLYMERASE CHAIN REACTION (PCR) TECHNIQUE

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Background and objectives: Enteroinvasive *Escherichia coli* (EIEC) strains include a group of diarrheagenic *Escherichia coli* (DEC) and are known to cause shigellosis-like symptoms in both adults and children. They belong to a limited number of serotypes and their somatic (O) antigens are identical with, or related to, certain Shigella antigens. EIEC strains are confirmed by demonstration of invasiveness by polymerase chain reaction (PCR) for detection of the *ipaH* (invasive plasmid antigen H *)* gene that is specific for these strains among DEC. Because of that in our country,Iran, have not been carried out very study for detecting of these strains, aim of this study was detection of EIEC in diarrheal under 5 year old children in Tehran.

Materials and methods: During the descriptive study, 300 stool samples were collected from children with diarrhea visited in Ali Asghar Hospital and children medicinal center of Tehran during 4 month(April-Jul 2008). *E.coli* species were isolated by standard bacteriological and biochemical tests. Presence of invasive plasmid antigen H (*ipaH*) gene in confirmed colonies was investigated by PCR technique.

Results: Among 300 stool specimens studied using culture method and biochemical tests, 39(13%) *E.coli* species were isolated. Among these 39 strains, 7(2.3%) strains containing *ipaH* gene (EIEC) were detected by PCR technique.

Conclusions: Enteroinvasive *Escherichia coli* (EIEC) in our country, Iran, may be as bacterial pathogen causing childhood diarrhea. Therefore we should use of new techniques for investigation of these strains.

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PREVALENCE OF HELICOBACTER PYLORI INFECTION IN CHILDREN IN SANANDAJ (WEST OF IRAN): A CROSS-SECTIONAL STUDY

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Background and aims: Helicobacter pylori are associated with duodenal ulcer and gastric carcinoma. It colonizes over 50% of the world population. Colonization is usually acquired during childhood. High prevalence occurs in developing countries. A study was conducted to determine epidemiology of the infection among children in Sanandaj.

Methods: The study was cross-sectional in design. Four hundred fifty eight stool samples were collected randomly from children of 6 different age groups including 4 months, one, 2, 5, 10, and 15 years old. The Helicobacter stool antigen test was used to detect infection.

Results: There were increasing prevalence rates of Helicobacter Pylori infection with increasing age in all age groups (p value< 0.0001; Likelihood Ratio=64.6). We found significant increase in infection rate as the family size enlarged (p value< 0.005, Likelihood Ratio=10.44). We investigated the rate of *H. pylori* infection and the duration of breast-feeding. There was no significant decrease in infection rate as the duration of breastfeeding prolonged (p value>0.05).

Conclusions: We found widespread H. pylori infection in children in our community. Infection with H. pylori is acquired as early as 4 months of age and earlier, as by 4 months of age at least 43% of children were positive for H. pylori antigen. It seems that the prevalence of *H. pylori* infection in children in Sanandaj is very high and is cumulative with increasing age.

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OPTIMISATION OF DIAGNOSIS AND THERAPY IN CHILDREN WITH ACUTE GASTROENTERITIS

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Background: In our laboratory we perform stool sample testing for invasive bacteria in children with acute gastroenteritis; we rarely use viral etiology tests. Aims. 1.To improve the diagnostic and therapeutic management in children admitted for acute gastroenteritis; 2.To conceive a diagnostic and treatment algorithm in cases with acute gastroenteritis; 3.To reduce hospitalization costs for patients with acute enteritis.

Methods: We've analyzed all patients admitted in pediatric clinic for acute gastroenteritis during 6 months period. Inclusion criteria: children under 5 years of age; sterile urine specimens; no previous antibiotic treatment; fever. Included patients were evaluated for “C” reactive protein (CRP) serum levels. Stool samples were tested for viral etiology (Rotavirus/Adenovirus- R/A) and for invasive bacteria (Salmonella, Shigella, Yersinia, Campylobacter, E.coli). For bacterial confirmation we used mediums, biochemical tests, latex agglutination and for R/A identification immunocromatographic tests. Data was analyzed statistically (independent sample T test).

Results: 82 children were included: 30 cases with R/A (mean CRP 3,97mg/l), 6 children with bacterial infection (mean CRP 53,14mg/l). Cut-off CRP value for viral etiology was 6,68. There is statistical significant difference between mean CRP levels in viral versus non-viral cases (p value 0,010).

Conclusions: All confirmed viral enteritis were associated with low CRP serum levels. Diagnosis and therapeutic algorithm: step 1: selection of patients according to inclusion criteria; step 2: serum CRP evaluation; step 3: for low CRP level it's recommended R/A testing; patients with high CRP value need bacterial identification tests; step 4: no treatment in viral etiologies.

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CLINICAL MANIFESTATIONS OF ROTAVIRUS INFECTION IN YOUNG INFANTS HOSPITALIZED AT NEONATAL CARE UNITS

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Purpose: To define the clinical manifestations of rotavirus (RV) infection in neonates and young infants hospitalized in neonatal care units.

Materials and methods: From October 2008 to September 2010, a total of 153 stool specimens positive for rotavirus were detected in 104 episodes from 100 young infants hospitalized at neonatal care units of our hospital. Demographics and clinical presentations of these infants were analyzed.

Results: Of the 104 episodes, 76 (73%) were hospital acquired. 58 (55%) were male. The mean age of onset was 29 days. The most common presentations were loose stool passages (53%), abdominal distension (52%), blood or mucus in stool (42%), and unstable vital signs (33%). Watery character in stool passage was identified in 13% of the infants and vomiting in 23%. A picture suggestive of necrotizing enterocolitis was identified in 22 episodes (21%), 12 of which were stage II or above. The infants in hospital-acquired group had a significantly higher rate of blood or mucus in stools (52.6% vs. 14.3%, $p< 0.01$), and unstable vital signs (39.5% vs. 14.3%, $p=0.02$) while a lower rate of watery diarrhea (9.2% vs. 28.6%, $p=0.04$) and fever (13.8% vs. 42.9%, $p< 0.01$). There were five deaths, but all of them had major diseases.

Conclusion: Bloody, mucoid stools and unstable vital signs are commonly seen in neonates and young infants with rotavirus infection. A substantial proportion of these infants may present as necrotizing enterocolitis. Once introduced, rotavirus appears to become a troublesome problem of hospital-acquired infections in the neonatal care settings.

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ROTAVIRUS GENOTYPES DISTRIBUTION IN TWO SUCCESSIVE PERIODS (2008-2010) IN GREECE

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Background and aims: Rotavirus (RV) is the most common cause of acute gastroenteritis (AGE) among preschool children worldwide. Aim was to evaluate the diversity of RV genotypes among children in Greece during two consecutive seasons.

Methods: Fecal samples from children ≤5 years of age who visited emergency units of 15 Pediatric Hospitals with AGE between September 2008-August 2010 were tested for RV Group A antigen with immunochromatography. Positive samples were G and P typed through RT-PCR and sequencing using specific primers for the VP7 and VP4 genes respectively.

Results: A total of 696 samples were genotyped; 63% belong to children ≤2 years old, 1.3% of children with RV had been received at least one vaccine dose. Seasonal peak of RV infection was March-May in 2008/2009 and January-March in 2009/2010. The most predominant types in both seasons were G4P[8] (60%, 57%), followed by G1P[8] (17%, 20%), G2P[4] (11%, 10%), G9P[8] (3%, 1%) and G3P[8] (1%, 1%). In 2009/10 a potential reassortant strain G12P[8] accounted for 4% of the samples. Mixed or uncommon infections were account for 8 and 7% respectively. No association was observed between RV genotypes and hospitalization, geographic location or gender. Mean age of children with G2P[4] was higher.

Conclusions: Five most common human RV strains circulating worldwide and covered by current vaccines are predominant in Greece; their proportion vary from 92% to 89% among seasons. Constant RV surveillance is necessary to detect changes in strain distribution and monitor possible introduction of escape mutants during the post vaccine era.

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BLASTOCYSTIS HOMINIS IN STOOL OF SYMPTOMATIC AND ASYMPTOMATIC CHILDREN

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Blastocystis hominis is an obligate anaerobic protozoon with faecal-oral transmission. Current data regarding clinical manifestation are not available in Germany. In this study we investigated

(1) if B. hominis causes gastrointestinal symptoms,

(2) if there exists a correlation between B. hominis numbers and clinical symptoms, and

(3) if a seasonal accumulation occurs. From 2006 to 2010 stool samples of 892 children showing gastrointestinal symptoms and 54 without symptoms were investigated microscopically following Lawless and chlorazole staining. In 196 of the symptomatic children (22.0%) and 4 of the asymptomatical children (7.4%) B. hominis was found in stool specimens. No significant correlation between the quantity of the protozoons and the clinical symptoms was detected. B. hominis was found more frequently during the summer months (133 cases) compared to the winter half-year (63 cases). The significantly increased confirmation of B. hominis in symptomatical children argues for B. hominis as an obligate pathogenic protozoon. The augmented detection of B. hominis during the summer months could be explained with seasonal nutrition habits and summerlike outdoor activities.

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PHYLOGENETIC ANALYSES OF ROTAVIRUS OP354-LIKE P[8] STRAINS INDICATE A RAPID SPREAD IN THE HUMAN POPULATION

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Background and aims: Rotaviruses (RV) are the main etiological agent of gastroenteritis in young children causing approximately 600.000 cases per year. Two recently introduced life oral vaccines, Rotarix™ and RotaTeq™, have been proven highly efficacious against all major circulating genotypes in humans. OP345 is the reference strain for a recently described P[8]-lineage, which has been increasingly reported and has emerged in Africa, Asia, Europe and the Middle-East. Moreover, OP354-like P[8] RV strains have been found in combination with virtually all VP7 genotypes commonly found in humans.

Methods: OP345-like P[8] RV strains were collected from various continents and the sequence of the complete VP4 gene was determined. Phylogenetic and pairwise comparison analyses were applied to establish the evolutionary relationships among OP345-like P[8] RV strains.

Results: Phylogenetic analyses showed that OP345-like RV strains clustered close together and displayed more than 96% similarity on a nucleotide level. In contrary, OP345-like P[8] strains were only 89-90% similar to the P[8] genotypes of both Rotarix™ and RotaTeq™.

Conclusions: OP345-like P[8] RV strains have been detected on several continents. However, the limited diversity among OP345-like P[8] RV strains indicated that they have been circulating in the human population for a relatively short time span, and must have spread swiftly. The combination of i) distinct antigenic properties compared to the P[8] genotypes in vaccines and ii) the fact that they have been found with Wa-like as well as DS-1-like backbones, which are well adapted to infect humans, could make them a potential threat to future vaccine efficacy.

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GENETIC ANALYSES OF THE VP7 AND VP4 GENES OF CIRCULATING ROTAVIRUSES IN BELGIUM REVEAL ANTIGENIC DISPARITIES WITH ROTARIX™ AND ROTATEQ™

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Background and aims: Two rotavirus (RV) vaccines, Rotarix™ (G1P[8]) and RotaTeq™ (G1-G4, P[8]), have recently been successfully introduced in many countries around the world, including Belgium. The RV vaccine parental strains were isolated approximately 30 years ago in France (G4 parental strain in RotaTeq™) and the US (all other parental strains). At present, little is known about the relationship between currently circulating RV strains and vaccine strains.

Methods: In the present study, we determined the complete sequences of the RV genome segments encoding the outer capsid proteins VP7 and VP4, of currently circulating RV strains in Belgium. VP7 and VP4 both contain antigenic domains that induce neutralizing antibody responses.

Results: Several amino acid (AA) differences between wild-type RV and RV vaccine strains were observed in multiple antigenic domains for every G- and P-genotype. However, the highest variability was observed among G1P[8] RV strains and the G1 and P[8] components of both vaccines. Phylogenetically, the circulating RV strains clustered in three distinct P[8]-lineages. In particular the RV strains of the P[8]-lineage 4 (OP354-like) showed a significant number of AA differences with both vaccines mainly in VP8*. Circulating G3 RV strains were found to possess an extra N-linked glycosylation site compared to the G3 strain in RotaTeq™.

Conclusions: These results indicate that the antigenic domains of RV strains contained in the vaccines differ substantially from those of the currently circulating RV strains in Belgium. Over time this might result in selection for strains that escape the RV neutralizing-antibody pressure induced by vaccines.

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CLINICAL AND MOLECULAR EPIDEMIOLOGICAL SURVEILLANCE OF NOROVIRUS DIARRHEA AMONG OUTPATIENT CHILDREN IN FIVE METROPOLITAN CITIES, CHINA

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Background and aims: Norovirus has been recognized as a common pathogen of childhood diarrhea. The purpose of this study was to understand the epidemiology of norovirus associated-diarrhea among Chinese children and characterize genotypes of circulating norovirus.

Methods: We conducted a prospective investigation among outpatient children with acute non-dysentery diarrhea between August 2008 and July 2009 in Shanghai, Hangzhou, Guangzhou, Chongqing and Tianjin. One step real-time RT-PCR was used for screening norovirus GI and GII. The genotypes were classified based on sequences of partial capsid. Group A rotavirus was also tested.

Result: Among 5091 fecal samples, 1563 (30.7%) were rotavirus-positive. Of 3528 rotavirus-negative samples, 1049 (29.7%) were norovirus-positive. The incidence of norovirus-associated non-dysentery diarrhea is estimated to be over 20.6% (1049/5091). 1036 (98.7%) noroviruses were GⅡand 16(1.5%) were GⅠ. Among 444 strains sequenced, GII.4 (70.7%) was most common with 97.1% clustered into GII.4 2006b, followed by GII.3 (21.4%). GII.2, GII.6, GII.7, GII.12, GII.14,GII.13, G11.16, GI.3,GI.4 and GI.5 were also detected. 91.8% children with norovirus-diarrhea and 92.5% children with rotavirus-diarrhea were ≤2 years old. Norovirus usually predominantly prevalent between July and October in Shanghai, Hangzhou and Chongqing, but from November to April in Taijin. However, norovirus was detected more frequently in other seasons than spring in Guangzhou. Rotavirus diarrhea peaks during October to January.

Conclusion: Norovirus are the major causitive agents for childhood diarrhea. Nevertheless, the seasonality of norovirus diarrhea was diverse in the different areas. GII.4 2006b variants were prevalent in China.

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CONGENITAL HYDRONEPHROSIS AND NEED FOR ANTIBIOTIC PROPHYLAXIS

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Background: A majority of the infants with congenital hydronephrosis remain infection free, and without structural defect such as Vesicoureteral reflux (VUR). Even so, they receive antibiotic prophylaxis. We hypothesize that all infants need not be put on routine antibiotic prophylaxis.

Method: Data was collected on infants born in the year of 2006 and 2007 with the history of congenital hydronephrosis by retrospective chart review. The data on ultrasonography study, antibiotic usage, frequency and timings of voiding cystourethrogram (VCUG) and presence of VUR, was gathered along with demographical information. Statistical analysis was conducted using Graphpad software.

Results: A total of 204 patients with congenital hydronephrosis were identified. Hundred and forty eight (72.5%) of the infants were male. 171 patients received amoxicillin prophylaxis until normal VCUG was obtained at 6-8 weeks of ages. Out of 204, VCUG was obtained on 197 patients, and of those 162 (82.2%) had normal initial VCUG (95% Confidence Interval 73-88). 35 infants (17.7%) showed Grade I-V VUR. 19 out of 35 infants (54.2%) had Grade I-II VUR which resolved by 30 months of age. Of 16 children (45.7%) with high grade reflux and 3 underwent surgical intervention. Febrile UTI was documented in only 9 (8.6%) children.

Conclusion: In conclusion, patients with congenital hydronephrosis have low incidence of VUR (17.7%). According to our study 181(88.7%) children who received prophylactic antibiotic during their first 4-8 weeks of life, did not need it. Thus, all infants born with hydronephrosis may perhaps not require prophylactic antibiotics routinely.

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NEONATAL CANDIDURIA: DOES IT JEOPARDISE THE OUTCOME OF NEONATES AT RISK IN NEONATAL INTENSIVE CARE UNITS (NICUS)?

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Background: There is limited information on neonatal candidal urinary tract infection (UTI). Predisposing factors are prematurity, antimicrobial agents , and prolonged hospital stay.

Objectives: To discuss the prevalence and features of candiduria among neonates at risk.

Patients and methods: We prospectively studied 50 neonates at risk (with GA 30-39weeks) from NICUs of Cairo University between September, 2009 and May 2010. Urine was collected by sterile urethral catheterization for Candida culture. Cases were divided to:

1) **Group I (with candiduria)** (n= 16) {10 fullterm(FT) and 6 preterm (PT).

2) **Group II (without candiduria)** (n= 34). Blood cultures, Kidney function tests and renal ultrasound were ordered for certain cases to exclude candidiasis.

Results: Candiduria incidence among neonates ***at risk*** was 32%.

There was no significant difference between the two groups as regard GA,sex ,duration of either hospital stay, or antibiotic therapy .However, certain antibiotic combinations showed higher incidence of candiduria.

Conclusion: Neonatal candidal UTI, may be associated with morbidity and mortality. Routine urine analysis (especially for neonates with risk factors) is recommended to start antifungal therapy. Protocols of antibiotic therapy mandate further periodic re-evaluation.

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CHARACTERISTICS OF CHILDREN BORN TO HIV-INFECTED MOTHERS IN EQUATORIAL GUINEA

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Introduction: Equatorial-Guinea had an estimated prevalence of HIV-infection in pregnant woman of 7,3% in 2008. Not much is known about the children born to HIV-infected mothers in the country. The aim was to describe the characteristics of HIV-exposed children in a country without virological-diagnosis.

Methods: We retrospectively analized the HIV serostatus of children born to HIV-infected mothers in Bata, Equatorial-Guinea from june 2008. Diagnosis was made through rapid tests based on WHO recommendations for countries without virological tests.

Results: 71 patients were included. 46% of the mothers received antiretroviral treatment (ART) during pregnancy, treatment most used in mothers was Zidovudine, Lamivude and Nevirapine; 36% of the newborns received antiretroviral-prophylaxis, the regimen most commonly used was single dose of nevirapine. 95% of the children were born vaginally; 4 children received mixed-feeding and all the others were exclusivelly formula fed. 31 patients abandoned follow up. Forty patients completed the follow-up, 12 children were infected (30%)(12/40), 6 children died before definitive diagnosis and 22 were antibody-free at 18 months. The transmission rate of children born to mothers that received ART was 15% (2/13) versus 37% (10/27) of the children born to mothers that did not receive ART. There were no infections in the fifteen children that received prophylaxis and that their mothers were on ART.

Conclusions: In our cohort, ART in HIV-infected pregnant woman decreased HIV-vertical transmission but the rate of mother to child transmission is still very high. Many children were lost to follow-up so methods to increase it are needed.

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CHARACTERISTICS OF CHILDREN WITH HIV-1 INFECTION, RECEIVING HAART. A CROSS-SECTIONAL STUDY

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Introduction: Since 1996, when HAART became available, there has been a change in the course of HIV-infection, becoming a chronic disease. Our aim was to describe the characteristics of the children followed in our hospital.

Methods: A cross-sectional study was performed on 32 HIV-infected children, followed until December-2010, at the University-Hospital de Getafe, Spain.

The evaluation of patients collected clinical and laboratory information from the last visit. A frequency analysis for SPSS version-15 was carried out.

Results: Thirty-two children with HIV-1 were evaluated, 29 infected through vertical-transmission. The median age was 14 years. According to CDC-classification, 53% of children were on category A, 31% B and 16% C. Immunological-class was 3 in 73% of children, 12% class 2 and 16% class 1. The median nadir of CD4 was 337 (12%). The median current CD4 was 749 (31%). Only one adolescent had a CD4% below 15% due to lack of adherence. The median viral-load was < 20 copies/ml, Median time on antiretroviral treatment was 10 years. Twenty-six patients had undetectable viral-load, all of whom were on HAART. The combination more frequently used was 2 nucleoside reverse transcriptase inhibitors (NRTI) and a protease inhibitor (PI). Two children received salvage regimens including raltegravir, 1 tipranavir and 5 darunavir. The prevalence of metabolic complications including hyperlipidemia and lypodistrophy was 52%.

Conclusions: Most of our patients are receiving HAART, with good virological and inmunological control. The prevalence of metabolic abnormalities was high. Strategies to improve adherence and decrease toxicities are needed in perinatally-acquired HIV-infected children.

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USEFULNESS OF RESEARCH OF CARDIAC INVOLVEMENT IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN CHILDREN

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Objectives: Assessing the importance of cardiac involvement induced by human immunodeficiency virus infection (HIV infection/AIDS) in children.

Methods: Patients, 51 children (2 -16 years old) with HIV infection/AIDS in various stages of evolution, with evidence of heart involvement. Evaluation of patients: clinical, ECG, Chest X ray, echocardiography (echo). Staging of HIV infection / AIDS by clinical exam and CD4 lymphocytes values.

Result: 60% of patients were included in group P2f clinical staging:. Signs of cardiac involvement: heart failure (11 cases), tachycardia (20), deafness of the heart sounds ± gallop rhythm ± systolic murmur of mitral regurgitation (12), dyspneea (14), non-symptomatic (14) or with signs of others diseases. ECG : disturbances of ventricular repolarisation, sinusal tachycardia. RxCT: cardiomegaly (30% cases) ± aspects of pulmonary infections. Echo exam: cardiac involvement in 66% cases: dilated cardiomyopathy, the most severe changes (14 cases), pericarditis (10 cases), isolated dilation of the left and right ventricle (6), LV diastolic dysfunctional (14), pulmonary hypertension (6). The severity and incidence of cardiac disease was associated with significant reduction of CD4 value < 400/mmc. Hystological exam performed in 28 patients died by pulmonary infections: aspects of myocarditis, pericardial and myocardial inflammatory infiltration, necrotic lesions.

Conclusion: The high incidence (66% of Cases) and severity of clinical manifestations, cardiac suffering during HIV infection / AIDS is one of the most important problems of these patients. Cardiological evaluation of patients, especially by echocardiography is necessary in all the stages of the infection, even non-symptomatic, for the diagnosis and follow-up of evolution.

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SINGLE CENTRE EXPERIENCE OF MOTHER-TO-CHILD HIV TRANSMISSION PREVENTION: YEARS 2005-2010

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Introduction: Constanta is one of the counties most affected by HIV in Romania. Over the last years we have noticed an increasing number of children exposed to HIV through mother-to-child transmission (MTCT).

Objective: To assess the mother-to-child transmission rate of HIV infection over a period of 6 years (January 2005 - June 2010).

Material and method: Relevant parameters in children: duration and type of antiretroviral treatment given as PMTCT medication, viral load (VL) at birth. Relevant parameters in mothers: type of delivery, ARVT received previously delivery, VL in the last trimester of pregnancy.

Results: 104 children and 100 HIV+ mothers have been monitored. Out of the 104 children, 5 were HIV+, and 99 were HIV-. Out of the 104 children studied, only 3 died in their first month of age (VL undetectable in 2 cases, and VL=130 copies/ml in one case). 2 children (one HIV+ and other HIV-) didn't received ARVT after birth. 97 children received ARVT in first 24 hours of their life for 6 weeks, 4 children (2 HIV+) received ARVT after first week of their life and 3 didn't received ARVT. Only 5 infants were breast feed (3/5 of HIV+ and 2/99 HIV-). Among all deliveries 23 were vaginal (4/5 of HIV+, 19/99 HIV-). Out of all 100 HIV+ mothers, 90 received ARVT during pregnancy. In third semester of pregnancy VL was undetectable in 71 cases.

Conclusions: The overall MTCT rate was 4.8%. The lack of HIV diagnosis in pregnant women was the major risk of MTCT.

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HYPOPHOSPHATEMIA AND HYPOKALEMIA SIGNS OF TUBULAR DAMAGE IN HIV INFECTED CHILDREN RECEIVING TENOFOVIR DISOPROXIL FUMARATE (TDF) PLUS PROTEASE INHIBITORS (PI)

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Objective: Our aim is to assess renal function in HIV infected pediatric patients on antiretroviral therapy (ART) investigating the role of TDF co-administered with PI on the tubular damage.

Methods: Forty nine patients were included. Twenty-three were treated with regimens containing both TDF and PI (TDF+PI), ten with PI, eight with TDF and eight without either TDF or PI (Other Treatment (OT)). The children tested in each group didn't differ in age, gender or percentage of CD4+. Phosphorus, potassium and estimated Glomerular Filtration rate (eGFR) have been evaluated at baseline, one year and two years of therapy.

Results: A reduction in eGFR showed to be significant after two years control (p=0.008) in the entire cohort. No significant variation has been found in the different therapy groups. Phosphorus was significantly decreased after one year control (p=0.03) and at two years (p=0.002) in the entire cohort, and in the TDF+PI group after two years control (p=0.02). In the multivariate analysis we found a significant variation in the potassium level matching the TDF group versus OT group (p=0.02). Four on five patients who developed at least grade 2 DAIDS hypophosphatemia event were treated with both TDF and PI.

Conclusions: According to our data the role of PI seems to be predominant in the tubular damage induced by TDF. The eGFR reduction does not seem to be associated to TDF, PI or both of them. Phosphorus and potassium showed to be sensitive test to detect early tubular damage.

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DRUG RESISTANCE IN HIV CHILDREN INFECTED BY VERTICAL TRANSMISSION, CAMPO GRANDE - MS, BRAZIL

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This study aimed to estimate the magnitude of viral resistance in children and adolescents infected with HIV through vertical transmission according to the antiretroviral regimen. Data were collected from medical records of all patients aged between zero and 19 years old infected with HIV through vertical transmission and attended between 1996 to 2009 at two referral units in the city of Campo Grande - Mato Grosso do Sul, Brazil. It was excluded exposed children who seroreverters, exposed children without indication to treatment and exposed children with indication for treatment who refuse to make use of antiretroviral. Study was conducted from 90 patients and eight were excluded. Among patients enrolled, 76 (92.7%) were alive, five (6.1%) were deaths and one (1.2%) had unknown situation. Over 75% of surviving patients were between six and 15 years. Regarding genotyping, 33 patients (40.2%) had this test performed, five were sensible to all drugs tested, 17 showed resistance to two classes of antiretroviral drugs and five were resistant to three classes. Enfuvirtide and raltegravir were not included in the genotyping assays. The laboratory findings included increased resistance to Nucleoside Analog Reverse Transcriptase Inhibitors (47.3%), mainly lamivudine, zidovudine and didanosine, followed by the Non-nucleoside Reverse Transcriptase Inhibitors (32.7%). Greater sensitivity was identified in relation to protease inhibitors. Considering there are reports of the apparent association between resistance to three classes of antiretroviral drugs and the risk of disease progression and death, early detection of treatment failure and rapid reassessment of the patient is necessary.

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COMBINATION NEONATAL PROPHYLAXIS (CNP) FOR INFANTS AT HIGH RISK OF MOTHER-TO-CHILD TRANSMISSION (MTCT) OF HIV-1

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Background: Preventive interventions have led to MTCT rates of HIV-1 < 2% in Western countries. However, the use of CNP remains controversial.

Aims & methods: The Madrid cohort is a multicentric prospective observational study of HIV-1-infected pregnant women and their children. We selected the mother-infant pairs at higher risk for MTCT (maternal detectable viral load at delivery, lack of antenatal ARV prophylaxis) and describe their characteristics.

Results: Ninety mother-infant pairs were identified. 40 women (43%) received HAART during pregnancy. 20 out of 50 women not on HAART did not receive intrapartum ZDV either. Mean delivery GA was 38 weeks (36% preterm). Median (IQR) viral load at delivery was 10,000 copies/ml (1480-50001). Median birth weight was 2775 g (2115-3198), 37% < 2500 g. All infants received prophylaxis (20 ZDV, 17 ZDV+3TC, 9 ZDV+NVP, 44 ZDV+3TC+NVP), which was well tolerated, without serious adverse events.

Tables 1 and 2 present hematological values at two months.

	ZDV (n=14)	CNP (n=57)
Median Hb (g/dL)	10.6	9.8
25th percentile	9.7	9.2
75th percentile	11.1	10.4

[Table 1]

	ZDV (n=13)	CNP (n=42)
Median neutrophil count (cells/mm^3)	2090	1646
25th percentile	1194	1304
75th percentile	2716	2103

[Table 2]

Conclusions: CNP is frequently prescribed in Spain as post-exposure prophylaxis in high-risk infants and it is well tolerated.

P400

USE OF NEONATAL ENFUVIRTIDE (T20) AS PART OF PREVENTION OF MOTHER TO CHILD TRANSMISSION (PMTCT) - A CASE SERIES

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Background and aims: To evaluate the use and therapeutic drug monitoring (TDM) of Enfuvirtide in 5 neonates born to 4 HIV-infected mothers with multi-drug resistance and/or detectable viral load (VL).

Methods: A standardised questionnaire was developed and data collected on maternal VL and antiretroviral therapy, neonatal drugs used in PMTCT, serious adverse events (SAE) and Enfuvirtide TDM in 5 neonates.

Results: The mothers had CD4 cell counts ranging from 9-522 x10^12/L, all had detectable VL within 2 months of delivery. Three mothers had multiple NRTI, NNRTI mutations, no PI mutations. Four were premature and 4 delivered by caesarean-section.

Three babies received Enfuvirtide subcutaneously and 2 intravenously, all at 2mg/kg twice daily for 2-14 days. Neonatal regimens also included Zidovudine, Didanosine, Kaletra or Nevirapine.

Five SAE's reported in 4 neonates, 2 transient hyperbilirubinaemia, 1 elevated creatinine, 1 thigh abscess due to Staphylococcus aureus and 1 lactic acidosis.

Trough levels of Enfuvirtide measured on day 1 ng/ml in three infants were 864, 1136 and 2607 ng/ml (therapeutic range 2600-3400 ng/ml). Further trough levels measured 2145 ng/ml day 11 in one infant and 8161 day 7, 8551 ng/ml day 14 in a further infant.

All have at least 3 negative HIV-PCR's.

Conclusions: Adverse events were common, only 1 probably Enfuvirtide related. All resolved without sequelae. Interpretation of TDM is difficult due to variation in administration, timing of TDM and likely inter-patient variability. A protocol is needed for using Enfuvirtide when infants cannot take oral medication and mother has multi-drug resistant virus.

P401

NEW HIV-1 CRF, ISOLATED FROM CHILD BORN TO HIV-INFECTED MOTHER

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Introduction: More than 75 % of HIV/AIDS cases are connected with the heterosexual rout in Belarus. Annually about 200 children born to HIV-infected mothers, despite on preventive therapy of 10 % of them become a HIV-infected.

Methods: RT-PCR, PCR, “ViroSeq HIV-1 genotyping system v.2.0”, sequencing ABI Prism 3100 Avant genetic analyzer, SeqScape, BioEdit sotware, HIV Drug Resistance Database Stanford Universyti, MEGA4.1.

Results: In April 2010 we are investigated blood sample from patient Ìos., 6 years old girl, born to HIV-infected mother. The conducted researches have not revealed HIV-1 resistance. The average p-distances between sample Ìos. and reference sequences of A subtype from Russia, Ukraine and consensus IDU-A have made of 0.068, and with reference sequences of B subtype 0.094. Average p-distances between isolate Ìos. and reference sequences CRF03 have made 0.090. The comparison of sequences in gene gag p17/p24 region of isolate Ìos. with reference sequences HIV-1 A subtype show average p-distances 0.129, and with reference sequences B subtype - 0.075. The analysis of isolate Mos. sequences on V3 loop gp120 gene env region HIV-1 has shown that average p-distances with reference isolates subtype B have made 0.323, and with A subtype - 0.155.

Conclusion: Thus, it has been shown that Ìos. isolate is recombinant form ÀÂ, but differs on genome structure from earlier described CRF03_ AB ($A^{gag}B^{pol}B^{env}$). The new variant of CRF ÀÂ having the following structure: $B^{gag}A^{pol}A^{env}$. Sequences of new HIV-1 variant in gag, pol and env genes were submitted to EMBL/Genbank/DDBJ under accession numbers: FR775442.1,

FN995656.1., FR775442.1

P402

MATERNAL ANTIRETROVIRAL USE FOR PMTCT: DOES SELECTION OF PI VS NNRTI REGIMEN INFLUENCE PREMATURITY RATE?

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Background and aims: Choice of ARV treatment during pregnancy has been reported to influence prematurity rate. To examine this, we analysed infant outcome from a previously described 10 year cohort of HIV exposed infants.

Methods: Prospectively gathered data from HIV exposed live births 1/1/99-31/12/08, including maternal ARV use, indication, agent choice, duration, and gestation at delivery were analysed. Analysis was confined to mothers treated only for PMTCT. Prematurity rates for NNRTI vs PI based regimens were compared (Chi square, Fishers exact test, two tailed).

Results: 964 HIV exposed infants, median gestational age 39 weeks (range 24-44), were identified. 89(9%) were delivered < 37 weeks gestation, of whom 36 were < 34 (4%) and 7 (0.7%) < 28 weeks gestation. Of 964 infants, 50 mothers did not receive ARVs in pregnancy, 145 (15%) were on treatment pre-conception and 769 (80%) received ARVs for PMTCT. Of these 769, 220 (29%) received NNRTI and 461 (60%) PI based regimens (205 lopinavir/ritonavir, 148 nelfinavir). 88 received NRTIs alone (mono or dual therapy). The mean and median gestation at delivery for both the NNRTI and PI regimens were 39 weeks. 15/220 (7%) NNRTI exposed vs 42/461 (9%) PI exposed infants were delivered at < 37 weeks (p =0.38). Similarly 6/220 (3%) vs 16/461(3%) and 1/220 (0.45%) vs 2/461(0.43%) were delivered at < 34 and < 28 weeks respectively.

Conclusion: In this cohort the incidence of prematurity was similar to that for the general population and no difference between PI and NNRTI regimens was found.

P403

HIGH PREVALENCE OF LOW VITAMIN D IN HIV VERTICALLY INFECTED CHILDREN LIVING IN IRELAND

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Introduction: In addition to its key role in bone mineral metabolism, Vitamin D has important immunomodulatory and antiinfective properties. Development of clinical rickets in a 14 year old boy on HAART (FTC/TDF/EFV) prompted an audit of Vitamin D status in our HIV infected cohort.

Methods: Cross-sectional study of vertically HIV infected children attending the National Centre for Paediatric HIV in Ireland. 25 (OH) Vitamin D levels were defined as: deficient, ≤27.5nmol/L; low, >27.5-75nmol/L and normal, >75nmol/L. Parathyroid hormone (PTH) levels < 65ng/mL were considered normal.

Results: Data were available on 63 children (32 male). Ethnicity: African, 50; Caucasian, 10; and mixed African-Caucasian, 3. Forty-nine children were receiving HAART (TDF, 19; EFV, 19; and 8/19 both TDF and EFV). Median Vitamin D level was 43nmol/l (range, 7.8-101). Vitamin D levels were: deficient, 15 (24%); low, 42 (66.5%); and normal, 6 (9.5%). Median PTH level, 65ng/mL (range, 15.8 - 804). PTH levels were elevated in 9 (15%). Seven children (11%) were Vitamin D deficient with elevated PTH levels, 3 with associated hypocalcaemia and hypophosphatemia. Two received EFV; 1, TDF; and 3, TDF/EFV containing HAART. Urea, Creatinine, Urinary Calcium/Creatinine and Protein/Creatinine ratios were normal in 42 of 43 (98%) children. One child had pre-existing HIV nephropathy.

Conclusion: The majority (57/63, 90.5%) of our cohort of vertically HIV infected children have low Vitamin D. PTH levels were elevated in 15%. In the absence of demonstrable renal dysfunction, further study of additional mechanisms eg. inadequate intake, decreased absorption, drug-effect, insufficient sunlight, ethnicity is warranted.

P404

PREVENTIVE INTERVENTIONS IN MTCT OF HIV-1 AND CHANGES IN VERTICAL TRANSMISSION RATES

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Introduction: Preventive interventions for mother-to-child transmission (MTCT) of HIV-1 have resulted in transmission rates of less than 2%.

Objectives: To describe patterns in the management of HIV-1 infected-women and their newborns and to analyze the changes in the MTCT rates over time.

Methods: The Madrid cohort is a multicenter prospective observational study of HIV-1 infected-pregnant-women and their babies. Two periods were considered: 2000-2003, cohort period 1 (CP1) and 2004-2007, cohort period 2 (CP2).

Results: 803 HIV-infected-women and their infants were included, 427 in the CP1. A decrease in access to antenatal care in CP2 was observed ($p < 0.05$), but this change was not attributed to maternal origin. More women received HAART in CP2 ($p< 0.05$). Starting HAART in the first trimester of pregnancy was more frequently observed in CP2 ($p < 0.05$), which was not explained by differences in CD4-cell-counts. Significantly more women in CP2 had undetectable levels of viral-HIV-RNA at delivery. No differences in trends in mode of delivery were observed. 90% of women delivering vaginally had undetectable HIV-RNA, without differences during the two periods. Combined-antiretroviral prophylaxis in newborns was most used in CP2 ($p< 0.05$).Thirteen children (1.6%) were HIV-1 infected by vertical transmission. Viral-load was not fallen to undetectable levels during pregnancy in 12 cases. No changes in MTCT-rates were observed over time.

Discussion: Despite the improvement in the interventions, no changes in MTCT rates were observed. No timely access to antenatal care in CP2 was the main limitation to develop all preventive interventions available nowadays.

P405

MOTHER TO CHILD TRANSMISSION OF HIV-1 AND RISK FACTORS ASSOCIATED

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Indroduction: Preventive interventions for mother-to-child transmission of HIV-1 have resulted in transmission rates of less than 2%. Maternal high viral load before delivery has been described as the main risk factor of HIV-1 vertical transmission. The use of HAART during pregnancy has increased the number of women who achieved undetectable viral load.

Objectives: To analyze the risk factors of vertical transmissionof HIV-1.

Methods: The Madrid cohort of mother-infants pairs is a multicenter prospective observational study of HIV-1 infected pregnant women and their babies. This analysis includes deliveries between January, 2000 and December, 2007.

Results: 803 HIV-infected-women and their infants were included. Thirteen children (1.6%) were HIV-1-infected by vertical transmission. In the analysis, no antiretroviral therapy during pregnancy, detectable maternal viral load before delivery, and prematurity were the main risk factors for HIV-1-infection. Eight women did not receive antiretroviral therapy during pregnancy. Four women received HAART, but they could not achieve an undetectable-viral-load. Only in one case (0.12%) HIV-1 infection occurred despite of undetectable viral load at delivery. HAART was started in pregnancy at week 25. Adherence is not well controlled during pregnancy and acute-caesarean-section was performed at week 38. Rupture of the amniotic membranes was during labour. Infant was not breastfed and received combined therapy prophylaxis. Positive RNA-HIV-1 infant-test was observed in the first week of life.

Discussion: As described previously, maternal viral load was the best predictor of the risk of vertical transmission of HIV-1. Unsustained control of viral load could be associated with residual transmission of HIV-1.

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MOTHER TO CHILD TRANSMISSION OF HIV-1 AND RISK FACTORS ASSOCIATED

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Discussion: As described previously, maternal viral load was the best predictor of the risk of vertical transmission of HIV-1. Unsustained control of viral load could be associated with residual transmission of HIV-1.

P407

HIV CHARACTERISTICS AND EDUCATIONAL ACHIEVEMENT OF A COHORT OF HIV INFECTED ADOLESCENTS DUE TO VERTICAL TRANSMISSION

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Objectives: To assess immunovirological situation, psychosocial profile and educational achievement in a cohort of HIV vertically infected adolescents followed in 5 hospitals in Madrid.

Methods: Cross-sectional descriptive study. Data related to HIV infection were obtained every 3 months in routine visits. Patients and their parent/tutors were interviewed using a semi-structured questionnaire designed to evaluate adherence and psychosocial profile. The Strengths and Difficulties Questionnaire (SDQ) was also administered.

Results: 95 adolescents (median age 16.5 years (12.4, 20.6), 97% Spanish, 10% hepatitis C). Fifty four % of their mothers acquired HIV infection by using injection drugs. Thirty four % were on C3 CDC category(18% had encephalopathy). CD4 nadir ≤ 15% (63%). Median age at HIV diagnosis (0.59 years (0, 12.2)), at the beginning of antiretroviral (3 years (0, 14.5)) and of HAART (5.7years (0.6, 18)); 42% had received ≥ 3 HAART based regimens.Nowadays, 97% of patients have CD4 ≥15% and 72% viral load ≤ 50copies/ml. Adherence ≥95% doses (48 %). Regarding educational achievement, 90% were at school or college, 19% had lost ≥ 2 years. Most common psychosocial problem concerning SDQ was hyperactivity (33%).There weren´t relationship between academic achievement and CDC stage, CD4 nadir, encephalopathy, adherence and HAART regimens; however it was related to the educational profile of their parents.

Conclusion: Although current immunovirological situation of our adolescents is good, they had a long history of failures and change of antiretroviral. An important percentage have academical difficulties but it hasn´t been related to HIV parameters; however, parent´s academic profile seems to be very important.

P408

DRIED BLOOD SPOT POLYMERASE CHAIN REACTION DNA FOR HIV IN PREVENTION OF MOTHER TO CHILD TRANSMISSION PROGRAMME IN NIGERIA

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Background and aim: Nigeria bears 30% of the global burden of MTCT of HIV. Early infant diagnosis of HIV using DBS PCR DNA is a standard of care for HIV exposed infants. The aim is to describe the outcome of a PMTCT programme.

Methods: HIV PCR DNA reports of 218 infants tested between 2007 and 2010 in a tertiary institution were retrieved and analyzed.

Results: 38% (82/218) of HIV positive mothers started highly active anti-retroviral therapy before pregnancy, 45% (97/218) started HAART during pregnancy, 10% (22/218) did not receive ART, 6.4% (14/218) had unknown ART status. 1.4% (3/218) had zidovudine for > 4 weeks.

52% (112/217) of HIV exposed infants were females, 48% (105/217) males. 12% (26/216) had DBS at 4-5 weeks of age, 7% (15/216) at 6 weeks, 32% (72/216) at 7-12 weeks, 48%(94/216) at >12 weeks of age. 85% (184/217) were healthy at testing. 9% (20/218) had repeat test 6 weeks after cessation of breastfeeding, 3% (6/218) repeated PCR following problems with first test. 45% (97/218) of these infants received AZT/NVP for 6 weeks, 17% (37/218) didn't receive any, 9% (20/218) and 19% (42/218) received NVP and AZT respectively. 42% (90/217) of infants were ever breastfed.

91% (198/218) of infants had negative PCR DNA test results. 8% (18/218) had positive PCR DNA. 1% (2/218) was indeterminate.

Positive DNA PCR was associated with no ARV in pregnancy and unknown ARV status in pregnancy.

Conclusion: PMTCT is efficacious and requires urgent scale up in Nigeria.

P409

SUCCESFUL TREATMENT OF 6 YRS OLD HIV EXPERIENCED CHILD WITH RALTEGRAVIR AND DARUNAVIR

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There is currently acute need for new drugs for treatment experienced children failing on their HAART. Most of the new drugs approved is currently licensed to be used in adults and not children. We report here, a case of 6 yrs old with successful treatment both in virological and clinical after combination use of both raltegravir and darunavir.

This unfortunate girl was diagnosed to be infected at 5 months and antiretroviral (ARV) of zidovudine, didanosine and ritonavir started. Her baseline viral load (VL):>750,000 copies/ml and CD4:789 cells. She was asymptomatic except for having hepatosplenomegaly.

Ten months later she was not fully suppressed. Her VL:35,000 and CD4:1617 cells.Compliant was good and there was no clinical failure.Since no new ARV was available, HAART was not changed.

In January, 2010, she was admitted with acute history of fever, seizure and mental changes. Examination showed an ill child who was pale, febrile with no cutaneous lesion.CNS examination was abnormal.She was treated as meningoencepalitis .

Her CD4:114 cells and VL: 487, 852 copies/ml. She was initially treated with antifungal and antiviral and treatment adjusted after cultures known.

New HAART regime of tenofovir,lamivudine,darunavir ,ritonavir and raltegravir was started (HIV resistance study in Nov,2008 showed few TAM's and multiple PI mutations).One month after starting, VL drop to 1353 and CD4 went up 662 cells and after 9 months,viral load not detected and she is back to her normal self.Even new ARV when used as salvage therapy showed good response.

P410

PENICILLIUM MARNEFFEI INFECTION: CASE REPORT ON VARIED CLINICAL PRESENTATIONS IN TWO HIV INFECTED CHILDREN

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Penicillium marneffei is a dimorphic intracellular opportunistic fungus causing a systemic disease, in both immunocompetent and immunocompromised patients. It has emerged as an important opportunistic pathogen in HIV-infected patients in Southeast Asia and has been considered an acquired immunodeficiency syndrome (AIDS)-defining disease. Tough this infection is more common in adults, about 5% of HIV infected children suffers from P. marneffei infection.

We report first two HIV infected children with disseminated or systemic P. marneffei infection. First patient presented with abdominal mass mimicking lymphoma and second patient presented with molluscum like cutaneous lesions and central nervous involvement.

The first patient had organism isolated from blood and tissue culture. Skin biopsy specimen from the second patient showed histological evidence of P. marneffei and tissue culture grew P. marneffei.

Amphotericin B is the treatment of choice in P. marneffei infection. The first patient had good clinical response and outcome following Amphoterecin B and Itraconazole for 10 weeks. Unfortunately the second patient succumbed because presented very late with disseminated disease.

Although rare among children, Penicillium marneffei infection should be considered in the differential diagnosis of opportunistic infection in HIV infected children.

P411

TWIN PREGNANCIES IN HIV INFECTED WOMEN: RESULTS FROM THE GREEK HIV BIRTH COHORT STUDY, 1990 -2010

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Background and aims: To evaluate occurrence of adverse pregnancy outcomes and rate of mother to child transmission (MTCT) in twins born to HIV positive women.

Methods: Using data obtained from the Greek HIV birth cohort we assessed retrospectively pregnancy outcomes and HIV status according to implemented interventions in twin pairs in pre- and post- HAART period, before 1996 and after 1996 respectively.

Results: Overall 3.6% (7/191) of all deliveries were twins. Most mothers (71.4%) had foreign nationality. Only 1 twin- pregnancy occurred before 1996. In the period from 1997 to 2010, 2/6 mothers had a known HIV(+) status before pregnancy, 3/6 were diagnosed antenatally and 1/6 postnatally. Late intrapartum diagnosis was associated with foreign nationality.

The delivery route was caesarean section in all cases. All except one children weren't breastfed. Rate of prematurity was 42.8% and mean birth weight 2405gr and for first- and second- born child, respectively. One infant died due to congenital cardiac disease.

In 2/7 pregnancies that newborns received no neonatal prophylaxis, 3/4 infants became infected. In the rest of twin-pregnancies, even when maternal HIV status was diagnosed intrapartum, appropriate interventions according to time of diagnosis were implemented and transmission rate was 0%.

Conclusions: Transmission in high risk twin-pregnancies is reduced when appropriate interventions are implemented, however emphasis should be given in early detection of mother's HIV status. Further multicentre prospective studies are necessary to assess the risk of prematurity and other adverse pregnancy outcomes in twins born to HIV positive mothers, in the era of HAART.

P412

HIV-POSITIVE WOMEN PRISONERS ANTIRETROVIRAL THERAPY ADHERENCE AND MEDICAL FOLLOW-UP IN PREVENTION OF HIV-INFECTION IN THEIR CHILDREN

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Background and aim: Women prisoners and their children are one of the most socially-disadvantaged HIV-infection risk groups. The aim of the study is to assess high risk behavior, adherence to treatment and medical follow-up in HIV-positive women prisoners with and without children.

Methods: Analysis of women prisoners with and without children medical records observed at the regional HIV-center.

Results: Women prisoners typical social-medical characteristics are obtained: young age - 25-40 years old (86.4%), unemployed (74%), secondary school education (86%), unmarried or living in unregistered wedlock (77.6%), 87.4% are intravenous drug users, chronic viral hepatitis C diagnosed in 89.6% cases. Half of women have had more than 2 years convictions.

More than half (63.8%) of women prisoners have children: 82.6% have one child. Children were born after HIV-infection diagnosis of mother in 42% cases. Only 43% of women with previous detention history got full perinatal transmission prevention. Mother-to-child transmission of HIV-infection has been verified in 10.4% of children.

Only women prisoners with children: 35% after release and 63.4% diagnosed at leisure came for the medical observation to the HIV-center. 55.6% had interrupted observation for more than a year, 64.7% were non-adherent to the therapy.

Conclusion: This group of patients - women prisoners and their children - demands multidisciplinary team approach and constant psychological and medical support for re-socialization to decrease high risk behavior, increase adherence to therapy, health condition improvement and secondary HIV-infection prophylaxis.

P413

HIV-POSITIVE WOMEN PRISONERS ANTIRETROVIRAL THERAPY ADHERENCE AND MEDICAL FOLLOW-UP IN PREVENTION OF HIV-INFECTION IN THEIR CHILDREN

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Methods: Analysis of women prisoners with and without children medical records observed at the regional HIV-center.

Results: Women prisoners typical social-medical characteristics are obtained: young age - 25-40 years old (86.4%), unemployed (74%), secondary school education (86%), unmarried or living in unregistered wedlock (77.6%), 87.4% are intravenous drug users, chronic viral hepatitis C diagnosed in 89.6% cases. Half of women have had more than 2 years convictions.

More than half (63.8%) of women prisoners have children: 82.6% have one child. Children were born after HIV-infection diagnosis of mother in 42% cases. Only 43% of women with previous detention history got full perinatal transmission prevention. Mother-to-child transmission of HIV-infection has been verified in 10.4% of children.

Only women prisoners with children: 35% after release and 63.4% diagnosed at leisure came for the medical observation to the HIV-center. 55.6% had interrupted observation for more than a year, 64.7% were non-adherent to the therapy.

Conclusion: This group of patients - women prisoners and their children - demands multidisciplinary team approach and constant psychological and medical support for re-socialization to decrease high risk behavior, increase adherence to therapy, health condition improvement and secondary HIV-infection prophylaxis.

P414

BREASTFEEDING AND HIV TRANSMISSION: CURRENT KNOWLEDGE AND GUIDELINES REALITIES AND CHALLENGES IN A HIGH HIV PREVALENCE RESOURCE LIMITED SETTING

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Background: Dramatic reductions in Mother to Child Transmission (MTCT) risk of HIV have been reported in High Income Countries (HIC) none breastfed populations. Guidelines regarding feeding options and HIV in RLS have led to confusion and debate which needs to be guided by evidence of child survival.

Objective: To describe under 5 child mortality in a breastfed cohort in Zimbabwe

Methods: Better Health for the African Mother and Child (BHAMC) study was initiated in 2002 to assess the role of single dose Nevirapine (sdNVP) in reducing MTCT of HIV before Highly Active Antiretroviral Therapy (HAART) was readily available in the country. Pregnant women were enrolled from 3 peri-urban maternal and child health clinics at 36 gestational weeks. Mother and child pairs were followed up from birth, 6 weeks, 4 and 9 months and 6 monthly thereafter.

Results: A total of 1050 (479 HIV infected and 571 HIV uninfected) pregnant women were enrolled and gave birth. More than 90% of the infants in this cohort were breastfed regardless of maternal HIV status with less than 10% among the HIV exposed infants having been exclusively breastfed for at least 6 weeks. Child mortality over 5 years was 24 % for the HIV exposed 7 % for the HIV unexposed and 68% for the HIV infected. Not having been breastfed was the most significant risk factor of this mortality regardless of maternal HIV status.

Conclusion: Breastfeeding improves child survival regardless of maternal HIV status in RLS.

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AMYLOIDOMA ASSOCIATED WITH INCORRECT USE OF ENFUVIRTIDE IN AN ADOLESCENT WITH AIDS-CASE REPORT

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Enfuvirtide has been used in AIDS patients in salvage regimens, providing control of viral replication and immune recovery. It is associated with frequent application site reactions like pain, erythema, induration, and transient nodules.

We describe a case of amyloidoma in the site of application of enfuvirtide associated with incorrect use in an HIV-infected adolescent.

A male, vertically infected adolescent, C3, aged 15, started 3TC, lopinavir / r, enfuvirtide and efavirenz. After 12 weeks, viral load was undetectable. After 20 months of use, a single nodule in the anterior right thigh with 5 cm in diameter without signs of inflammation, soft and well demarcated, was identified. The caregiver stated many applications in this same place, without making turns. The ultrasonographic evaluation revealed a solid isoechogenic masss, oval, septated circumscribed, measuring 6.5 x 3x 4.5 cm in the subcutaneous tissue. A needle puncture revealed solid, brittle and yellowish content. Histopathology revealed chronic inflammatory process organized around amorphous material with foreign body granulomas. Amyloid deposition was suggested by Positive Congo red staining and the presence of and emerald-green structures at polarized light suggested amyloid deposition. In the literature, only one case of amyloidosis related to medication was reported. It was a man of 47, with extensive induration, pain with fragile epithelial surface at all sites of application and spontaneous bleeding in the subcutaneous tissue. Pathological analysis revealed deposits of protein material consistent with amyloid. The main feature of this patient was the single nodule, covered by normal skin with no signs of bleeding.

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DISCLOSURE OF HIV DIAGNOSIS TO CHILDREN IN A PAEDIATRIC HIV CLINIC, UK

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Background: The Children's HIV Association (UK) (CHIVA) recommends that disclosure of HIV diagnosis is made to children by 11 years. We audited the age at disclosure at a paediatric clinic.

Methods: 50 HIV positive children aged 10 years or over were identified. Retrospective data was collected from all case notes.

Results: Of 50 children (≥ 10 years) 29 (58%) had full disclosure. Forty percent (n=12) had disclosure by 11 years, 70% (n=20) by 12 years.

Of the 29 children with disclosure median age at diagnosis was 7.5 years (IQR 5-12 yrs). There is correlation between age at diagnosis and age at disclosure; those diagnosed later were older at disclosure. Of those with disclosure after 12 years (n=9) all were diagnosed later (>10 years, median 13 years). Disclosure was by the consultant in half of cases and parents in a quarter. There was no correlation between age at disclosure and person disclosing.

There were 21 children with minimal knowledge of their HIV status. One third of the cohort are ≥ 12 years. Median age at diagnosis was 5 years (IQR 2-7), significantly younger than children with full disclosure; p=0.005 (Mann Whitney U). Most common reason for non-disclosure was parental resistance (43%).

Conclusion: There is a need for improved disclosure of HIV diagnosis by 11 years. There is a significant difference in median age at diagnosis and disclosure. This suggests that work around disclosure needs to take place with families from an early age. Parental reluctance was a common reason for delay.

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UNDETECTABLE VIRAL LOAD AFTER ADDITION OF RALTEGRAVIR IN A 36 WEEK PREGNANT ADOLESCENT WITH HIGH-LEVEL HIV VIRAEMIA

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Obtaining undetectable viral load (VL) during pregnancy is crucial for the prevention of mother to child HIV transmission (PMTCT), particularly in vertically transmitted adolescents with multiple treatments. Raltegravir is an effective treatment which can induce a rapid VL decline in pregnant women with good tolerability and few interactions.

We report the case of a 17 year old woman diagnosed at 18 months with vertically transmitted HIV-1/HCV infection who initiated treatment at age 5, with didanosine plus stavudine and switched one year later to AZT, 3TC and amprenavir with early viral failure due to poor adherence and intolerance.

She maintained sustained HIV replication despite treatment with regimes including DDi, D4T, efavirenz and nelfinavir. From age 10 to 18, ART was suspended with VL maintained between 2000 to 3879 copies, CD4 34%. Genotypic resistance test showed high resistance to nevirapine and efavirenz.

She consults at 15 weeks of unplanned pregnancy with 518 CD4 T cells/mm3 and a VL of 4282 copies/mL. Lopinavir/ritonavir 400mg/BD, AZT and 3TC is immediately started with persistently high VL (1902 copies/mL) and 633 CD4 cell/mm3 at 36 weeks due to poor adherence. Raltegravir (400 mg BD) was added at this point with an extremely rapid decrease in VL, undetectable by week +3. Vaginal delivery took place after 4 weeks of raltegravir and the newborn was treated with standard PMTCT regimen. Although additional data is still needed, this case adds preliminary data that raltegravir could potentially be a safe and effective drug used in late pregnancy.

P418

ADHERENCE TO ANTIRETROVIRAL THERAPY IN A COHORT OF HIV-INFECTED CHILDREN AND ADOLESCENTS

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Background: Adherence to antiretroviral therapy is particularly difficult among either HIV-infected infants and adolescents depending on dose administration and its relationship with meals, lack and unpleasant taste of pediatric formulations, but also side effects and refusal of the infection itself. We evaluated adherence in vertically infected children and adolescents.

Methods: In our study 26 vertically HIV-infected patients (7 children aged 3-12 years and 19 adolescents aged 13-19 years) are considered. 19 of them are on HAART regimens with protease inhibitors (PIs), while three are treated with a non-nucleoside reverse transcriptase inhibitor (NNRTI) regimen. The mean number of doses was 5.7/day. We investigated the cases of virological failure caused by poor compliance and we explored the role of psychosocial determinants that may affect their adherence to medication regimens.

Results: Perfect adherence was reported in 73.3% of patients living with their biologic parents or relatives. The four cases of therapeutic failure were all treated with PIs regimens and none with NNRTI. For three of them (aged 17-19 years) the poor adherence resulted from a full awareness of their status of infection. Moreover their parents demonstrated to be unable to understand the problem of their children and to help them to deal with it.

Conclusions: Perfect adherence is an essential component of successful antiretroviral therapy. In our experience the adolescence (corresponding to full awareness of the infection status) and the life with HIV biologic parents in virological failure themselves may be independent factors increasing the risk of poor adherence to antiretroviral therapy.

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NEW TENDENCIES IN APPROACHING HIV PATIENTS SURPASSING THE FALSE DICHOTOMY "CURATIVE TREATMENT VERSUS PALLIATE CARE"

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Introduction: The chronic nature of HIV and the burden more and more oppressive of morbidity caused by it, correlated with the toxicity of the treatment, are new challenges in caring for the patients on the long term.

Method: 120 patients from the palliate department of the Infectious Diseases Hospital Constanta were studied**.**

Results: More then 50% of the total number of patients received both ARV treatment and second and third gear opioid treatment; 20% either refused the ARV treatment, either they presented side effects that determined them to stop the therapy in order to treat the side effects and other infections; 2% of the patients in advanced stages have received, in the last 7 days of their lives: triple ARV therapy, opioid and symptomatic treatment . The prevalence of symptoms in the advanced stages of HIV infection has showed us that the most frequent symptoms in these phases are: tiredness 85% of cases, followed by pain 76%, nausea and vomiting 56%, depression 40%, dyspnea 34%. Amongst the patients who received third gear opioid treatment, 80% have been diagnosed with lymphomas in stages where oncology chemotherapy was surpassed.

Conclusions: It is reasonable to ask ourselves if it has any therapeutic sense to continue the ARV treatment for a patient in terminal phase. In these situations, the ARV will not have any visible effect and probably will bring more therapeutic confusion to a dying patient if the aggressive therapy is being continued.

P420

SYSTEMIC LUPUS ERYTHEMATOSUS IN A TEENAGER WITH PERINATALLY ACQUIRED HIV

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Background and aims: We have encountered a case of an 11 year old girl who was known to have perinatally acquired HIV and presented with arthritis around the initiation of HAART. Although immune reconstitution syndrome was considered, in view of her normal nadir CD4 count, strongly positive ANA, dsDNA, low complement levels and splinter nail haemorrhages she was diagnosed with systemic lupus erythematosus (SLE). This was the first case of SLE in an HIV positive patient we have encountered so far and we have carried out a literature search to assess the frequency of SLE in HIV positive children.

Results: In the literature we found 6 cases of SLE in HIV infected children. A recent study of HIV infected adults reported SLE in 3/888 patients, eg significantly more than overall incidence of SLE of 40/100 000. Other studies noted a relative increase of SLE and rheumatoid arthritis after the introduction of HAART. The cases presented at any stage of illness but were sometimes triggered or exacerbated by immune reconstitution. With a low CD4 count the symptoms of SLE usually resolved.

Conclusion: The literature on SLE in paediatric HIV infected patients is scarce but adult literature shows an increased incidence of SLE in HIV infected patients. Although SLE is more prevalent in adulthood, it is possible that some paediatric cases are missed. Similarity between these two conditions should prompt us to test all SLE patients for HIV and consider SLE in HIV infected patients presenting with symptoms suggestive of SLE.

P421

IMPROVING ANTIRETROVIRAL THERAPY ADHERENCE IN HIV-INFECTED CHILDREN. PILOT STUDY

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Introduction: Poor adherence to antiretroviral treatment (ART) is the commonest cause of treatment failure in children and adults living with HIV, and this is especially important during adolescence. Therefore, any analysis of ART effectiveness in children should include an evaluation of adherence to ART. The aim of this study is to assess the usefulness of an ART adherence monitoring program in an HIV-infected pediatric population.

Patients and methods: A pilot study, observational and cross-sectional, was performed, within the framework of the "Health Education Program for Optimizing Adherence in Pediatric Patients with HIV", which is part of the "I am not alone" project. Adherence was assessed simultaneously by different methods: personal interview, therapeutic drug monitoring, pharmacy dispensing records and evolution of viral load and CD4+ lymphocyte count.

Results: Twenty patients were included (50% female, median age 14.5 years). Percentage of self-reported full adherence was 90% (95% CI: 70-97.2%); however, the median adherence percentage according to pharmacy dispensing records was significantly lower (83.3%, SD=32.88). The average of drugs and dosage forms per day were 3.5 (SD=0.83) and 5.5 (SD=2.72), respectively. There was an inverse relationship between the number of dosage forms per day and adherence scores ($F=13.8$; $p=0.002$). No single method was statistically related to adherence, although therapeutic drug monitoring showed a trend towards significance.

Conclusions: Global adherence to ART was high and was favored by simple regimens. Self-reported adherence overestimated real adherence to ART in our cohort. The simultaneous use of different methods to assess adherence is recommended in HIV-infected children.

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HYPERLACTATEMIA IN INFANTS BORN OF HIV-INFECTED MOTHERS EXPOSED TO ANTIRETROVIRALS. OPEN PROSPECTIVE COHORT STUDY (2004-2007)

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Introduction: In developed countries, most children born of HIV-positive mothers are exposed to antiretroviral (ARV) agents perinatally. Various studies have related ARV exposure to hyperlactatemia.

Aims: To determine the incidence of hyperlactatemia, lactic acidosis and associated neurologic manifestations in children of HIV-infected mothers and HCV-infected mothers during the first year of life.

Patients and methods: Prospective comparative cohort study from 2004 to 2007 with 40 patients per group. pH, lactic acid, and alpha-alanine levels were determined at 1, 3, 6, and 12 months of life. Pathological hyperlactatemia: lactic acid >2.1 mmol/L and alpha-alanine >435 µmol/L.

Results: 79 patients were studied (39 in the ARV-exposed cohort, 40 in the control cohort). Maternal demographic characteristics were similar in both groups. 89.7% of pregnant HIV-infected mothers received HAART and 10.3% AZT-monotherapy; 54% had undetectable viral load and 20% CD4+ count < 350/mm^3. 31 neonates received AZT monotherapy and 8 combined therapy. Twelve patients (5 exposed and 7 non-exposed) presented some neurologic abnormality and 4 (5.1%) (1 and 3) neurodevelopment alterations (p=0.34). Pathological hyperlactatemia was seen in 56.4% (95% CI, 39.6-72.2) and 57.5% (95% CI, 40.9-73.0) of patients, respectively (p=0.92), with more cases in premature patients (p< 0.05). HIV and ARV-related variables were not associated with pathologic hyperlactatemia. Hyperlactatemia was not associated with neurologic abnormalities.

Conclusions: In utero and perinatal ARV exposure was not associated with the development of hyperlactatemia. Only prematurity was related to a higher incidence of this condition. There was no association between hyperlactatemia and the development of neurologic symptoms.

P423

EMERGENCE OF THE HIV INFECTION IN THE CHILD IN ALGERIA

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In Algeria the prevalence of the HIV is 0.1% in general population, 150 children would be infected with of which the half is in Oran.

Objective: To highlight the reality of the HIV infection problem in the child in our area, to describe the principal epidemiologic aspects and private clinics which encourage with tracking and finally to point out the means of the prevention.

Materials and methods: Retrospective study of 73 children infected by HIV in 1997-2008.

Results: 78.43% less than five years (mean: 26 months ± 2 months),and sex ratio: 1.51. The vertical transmission was 94.5%, the breast-feeding was noted at 63 cases (86.3%). The chronic diarrhoea 41 (56.1%), tuberculosis 17 (23.28%), lost of weight 29 (39.72%), adenopathy 47 (64.38%), molluscum contagiosum 19 (26%), oral candidosis 42 (57.5%), bad teeth 26 (35.6%), unexplained fever 18 (24.6%), lymphoid pneumonia interstitial 14 (19.1%), chronic parotitis 9 (12.3%), otitis 26 (35.6%), neurological signs 7 (9.5%), were the most evocative signs. The HAART was founded in 34 children (46.5%), 27 (37.6%) died and 19 (26%) were lost sight of the fact.

Conclusions: Virus transmission was vertical, children become symptomatic in an age 26 months. Lost weight, generalized lymphadenopathy, the respiratory signs, chronic ORL and digestive were the most frequent signs. Chronic parotidis, *molluscum contagiosum* and multiple- early dental decays were signs which characterized these children. 26% of them died. In front of a chronic clinical signs in the child, we must to think of tracking and interest the prevention.

P424

SUSTAINED VIROLOGICAL SUPPRESSION WITH PROTEASE INHIBITOR (PI) MONOTHERAPY: AN ONGOING OBSERVATIONAL STUDY IN FIVE CHILDREN

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Background: Simplification of HIV treatment by switching to protease inhibitor monotherapy after virological suppression with HAART can reduce pill burden, side effects, drug interactions, medication cost and may enhance adherence as well as preserve future treatment options.

Methods: Ongoing observational study. HIV-infected children treated in our hospital with consecutive HIV-1 RNA < 20 copies/mL during at least 6 months while on HAART and no PI mutations were switched to monoboosted lopinavir/r (mLPV/r) or atazanavir (mATZ/r). Primary endpoint was the proportion of children with HIV-1 RNA < 20 copies/ml. Secondary objectives included safety, adherence, immunologic response and pharmacokinetic PK studies of mLPV/r and mATZ/r.

Results: Five out of 25 HIV infected patients (pt) on HAART were changed to mPI/ (4 mLPV/r and 1 mATZ/r). Mean CD4 cell counts during the last 6 months on HAART were as follows: pt1: 567; pt2: 426; pt3: 798; pt4: 430; pt5: 1118. Currently at a mean of 70.2 weeks (range 64-80), none of the five children showed progression of their disease. All patients maintain HIV-RNA viral loads (VL) of less than 20 copies/ml. Mean blood CD4 cell counts/microl on mIP/r was: pt1: 826; pt2:406 ; pt3: 796 ; pt4:577; pt5:1166. Mean serum concentration (mcg/ml) of LPV: pt1: 12.4; pt 2: 9.2; pt3: 5.2; pt4: 8.2; and ATZ: pt4: 2.6. **Conclusion:** Viral suppression at a mean of 70.2 weeks was sustained in all five children using PI/ritonavir monotherapy as simplified maintenance therapy. Randomized studies of simplified mPI/r therapy in children are needed to evaluate our observation.

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NORMAL BONE MINERAL CONTENT AMONG HIV-UNINFECTED CHILDREN PERINATALLY EXPOSED TO ANTIRETROVIRALS

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Background: A decrease < 2% in HIV mother-to-child transmission has occurred upon the implementation of prophylactic measures. Most HIV-uninfected infants are perinatally exposed to antiretrovirals, and potential long-term adverse effects of such exposure remains of concern. Low bone mineral content (BMC) is a recognized complication of HIV infection that has been noted more frequently in the era of highly active antiretroviral therapy (HAART), but very scarce data on this issue are available for children perinatally exposed to antiretrovirals.

Materials and methods: We performed a cross-sectional study in a cohort of HIV-uninfected prepubertal children born to HIV-infected mothers and perinatally exposed to antiretrovirals that are followed up in tertiary-care pediatric hospital in Barcelona (Spain). The following exclusion criteria were used: age at birth below 35 weeks, birth at weight >3SD or < 3SD, chronic conditions and long-term use of corticoids. BMC was measured by dual energy X-ray absorptiometry. Clinical, anthropometric data and dietary intake of calcium (mg/day) were obtained at the time of assessment.

Results: BMC was measured in 70 prepubertal children (51% females; mean age: 6.8 years, range: 4-9 years). Mean (range) daily calcium intake estimations were 820mg (600-1350mg). Mean (range) BMC Z-score values were -0.08 SD (-1.99 to +2.15) and were not different from a population norm Z-score. When exposure to antiretrovirals (type and time of exposure) and other perinatal variables (exposure to other drugs, ethnicity, weight at birth or prematurity) were taken into account, differences were neither observed.

Conclusions: HIV-uninfected prepubertal children perinatally exposed to antiretrovirals show normal BMC values.

P426

LONG-TERM RESPONSE TO HEPATITIS B VIRUS VACCINATION IN HIV-INFECTED CHILDREN; IMPLICATIONS OF HAART INTERRUPTION

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Background and aims: Response to vaccines is poorer in HIV-infected children. We describe the role HAART interruption plays in the long-term response to hepatitis B virus (HBV) vaccination.

Methods: Cross-sectional study within a cohort of HIV-infected children who received a complete HBV vaccination series. The following thresholds defined response to vaccination: optimal seroprotection, >100 IU/l; seroprotection, 10-100 IU/l; and no seroprotection, < 10 IU/l. Seroprotection levels were compared to different clinical, treatment and biological variables, including immune situation at the time of vaccination and at the time of assessment, and HAART interruptions.

Results: Seventy-six patients were included (60% females, 81% vertical transmission, 26% with AIDS); 60% of the children had received HAART as first antiretroviral treatment and 3 of them remained antiretroviral naive. Median number of HAART regimens was 3; 42% of patients had interrupted HAART at least once, for a median time of 36 months.At the time of assessment, all patients were symptom-free, none of them presented with severe immunosuppression and viral load was undetectable in 72%. Optimal seroprotection, seroprotection and no seroprotection were observed in 20%, 13% and 67% of the children, respectively. Having interrupted HAART was associated with a poorer seroprotection level against HBV (any seroprotection: 21% versus 42% of the patients; p=.06).

Conclusions: Despite vaccination, 67% of the patients in our cohort show no seroprotection against HBV. HAART interruption seems to associate a poorer seroprotection level against HBV.

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OCCULT HEPATITIS SCREENING IN THE CATALAN COHORT OF HIV-INFECTED PEDIATRIC PATIENTS (CORISPE-CAT)

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Background and aims: Occult B and seronegative C hepatitis can be missed in immunocompromised patients when using regular screening methods, leading to an increased risk of severe liver damage in case of reactivation. The implementation of occult HBV and seronegative HCV markers in the regular laboratory screening in HIV-infected children may allow the detection of co-infected patients at risk of hepatic decompensation.

Methods: Cross-sectional study to assess the prevalence of occult HBV and seronegative HCV infection within CoRISpe-CAT Cohort. Demographic, clinical, immunologic and virologic data, as well as antiretroviral treatment and vaccination status were collected. Occult HBV and HCV infection markers (HBsAg, anti-HBs, anti-HBc IgG and IgM, and PCR DNA test for HVB; ELISA and RIBA antibodies and PCR-RNA tests for HCV) were performed.

Results: Overall 105 patients were included (57.9% female, 62.1% Caucasian, median age 14 y, most of whom vertically-infected, 83%). At assessment, one third met AIDS criteria, 77% showed undetectable viral load and median CD4 cell count was 983/mm^3.

Neither occult HBV infection markers nor acute HBV infection were detected. Two patients (1.9%; 95% CI: 0.2-6.7) showed chronic infection markers (positive HbsAg and antiHBc IgG), and 4 children presented the anti-HBc alone pattern (3.8%; 95% CI:1.1-9.5). Three patients (2.9%; 95% CI: 0.6-8.1) had seronegative HCV infection.

Conclusions: Occult HBV infection does not represent a serious problem in our Cohort. The anti-HBc alone pattern does not seem to be more common than previously described. As previously reported, HCV evaluation in HIV-infected children must include viral genome detection.

P428

COMPLIANCE TO ANTIRETROVIRAL TREATMENT IN CHILDREN IN SÉGOU

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The ARV therapy is at present one of the main responses against HIV infection. *To* assess adherence to antiretroviral therapy in children aged 0-15 years infected with HIV in NGO-WALE Segou.

Our study, transversal and driver with a prospective collection of data took place from 1 October 2009 to March 31, 2010 at the NGO WALE Segou and covered thirty-six (36) children. The mean age of the sample was 5 ± 3.3 years with extremes of 2 years and 14 years. The sex ratio was 1.1 for boys. Over the past 6 months 93.3% of children were watching with good rates ranging from 88.9%, 97.2%, 94.4%, 91.7% and 91.7% respectively from T0 to M6.The cause of noncompliance were the most frequent: the refusal of the child, forgetfulness, unavailability of the person to the custody of the child and side effects. The types of the noncompliance most represented were taken and disrespect missed dose. The regimens have been most effective in our study is secondary (AZT/3TC/NVP) with 34.3%. Patients on the protocol 2 NRTI and NNRTI were most numerous with 94.4%, the treatment protocol remained unchanged at 94.4% of children. Treatment failure was the sole reason for change protocole.33, 3% of persons having custody of the children expressed difficulties. The good compliance rate of 92% of children under 7 years old was higher than 90.90% of more than 7 years. The rate of adherence to ART in children in WALE is encourageant.The results are the benefits of therapeutic education.

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LIPID ALTERATIONS IN HIV-INFECTED CHILDREN WHO RECEIVED ANTIRETROVIRAL THERAPY

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Background and aims: Hyperlipidemia has been noted to occur in HIV-infected individuals, particularly when receiving antiretroviral therapy (ART). The aims of this study are to describe lipid profile in HIV-infected children after initiating ART and to study the relation between lipid alterations and therapeutic regimes.

Methods: Retrospective review on clinical files of HIV-infected children consulted in Hospital Pediátrico de Coimbra, throughout 2010.

Results: There were 21 HIV-infected children consulted, all of them were on ART. Median age was 11,6 years, 76% were male. Thirteen out of 21 children (62%) had hypercholesterolemia and 7 (33%) had hypertriglyceridemia. Median cholesterol levels were 4,52 mmol/L and median triglyceride levels were 1,58 mmol/L. Individuals were split between three groups: one medicated with nucleoside reverse transcriptase inhibitor (NRTI) and non-nucleoside reverse transcriptase inhibitor (NNRTI), where the prevalence of hypercholesterolemia was 28% and 14% had hypertriglyceridemia; another one medicated with NRTI and protease inhibitors (PI), where the prevalence of hypercholesterolemia was 73% and hypertriglyceridemia was 36%; and the last one medicated with NRTI, NNRTI and PI, where all children had hypercholesterolemia and 67% had hypertriglyceridemia. Statistically significant differences (p=0.030) in cholesterol levels were found between groups whose regime included PI and those who not. No statistically significant differences were found regarding triglyceride levels.

Conclusions: Lipid alterations must be closely monitored in HIV-infected children on ART, because of the high prevalence of hypercholesterolemia and hypertriglyceridemia. These lipid alterations can be related with the type of drugs used. One must take this under consideration when choosing therapeutic regimes.

P430

HIV-VPR VARIANTS VERSUS DISEASE PROGRESSION

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Background and aims: The biological functions of HIV-1 Vpr have been involved in the replication and pathogenesis of the virus. Infants with perinatal acquired HIV-1 infection have widely variable courses, the long-term non-progressors and fast progressors. The aim of this ongoing work is to study the correlation, in a population of perinatal infected children, between the Vpr variant present and disease progression.

Methods: In this study 27 perinatal HIV-infected children have been included, since 2005. The HIVvpr gene was amplified and sequenced. The children were clinically evaluated the disease progression evaluated by several clinical markers such as haematological parameters, viral load, development delay, opportunistic infections, other pathophysiological conditions.

Results: The analysis of Vpr sequences in 27 patients showed that 10 carried the mutation R77Q. At the time of first medical appointment the children infected with the Vpr variant carrying the mutation showed lower viral load than children with no mutation. During the period considered (2005-2010) all the children with the R77Q mutation children remained with no clinical signs of disease except one that developed Burkitt Lymphome. All the children are under HAART.

Conclusions: We believe that with this study it will be possible to identify Vpr as a bio-marker of disease progression.

P431

CLINICAL OUTCOMES OF PEDIATRIC HIV CASES IN AN UNIVERSITY HOSPITAL, TURKEY, 2000-2010

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Background and aims: Turkey has an estimated 3.900 people living with HIV infection. Of these nearly 75 (1.9%) are estimated number of infected children under 15 years. The aim was to describe the clinical outcomes of pediatric cases with HIV who were admitted to the Pediatric Infection Department University Hospital between 2000 and 2010.

Methods: Data were recorded, including clinical presentation, transmission, HIV staging, CD4 counts, total lymphocyte count (TLC), opportunistic infections (OI).

Results: Twenty-two patients 54% males and 46% females with a median age of 2.5 were recorded, of which 59 % (n:13) were acquired through mother-to-child transmission (MTCT) of HIV. Antiretroviral (ARV) prophylaxis was given to 13 infants after birth.

Twelve infected patients are now on HAART. The median CD4 count was 16% (range of 4%-45%) with a median TLC of 1790 (range 680-3000). Six Of 12 patients was in stage 2 and 2 patients were in stage 3 upon their initial presentation to the clinic using the WHO HIV staging. The most common complaints were chronic cough, dermatitis, chronic diarrhea and failure to thrive. The three most prevalent OIs were oral candidiasis, pulmonary TB and herpes zoster. Prevalence of OIs increased with lower CD4 counts. Two patients with stage 3 are dead in the first six months after initiation of HAART.

Conclusions: Highly active antiretroviral therapy was well tolerated, but earlier referral for ART initiation may reduce mortality.

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EFFECTS OF SIMPLIFICATION OF HAART IN HIV INFECTED CHILDREN

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Background and aims: HAART has improved survival in HIV-infected patients but may be associated with important adverse events. Simplification of HAART may improve adherence and metabolic alterations. The aim was to describe virologic, inmunologic, clinical and lipid profile outcomes in HIV-infected children after simplification.

Methods: Prospective, multicenter study of children from the 310 HIV-infected children and adolescents in the Madrid Cohort since 2003. Fifty-six simplifications were studied in 44 patients. The simplified regimens included protease inhibitor withdrawal (type 1), pill number decrease(type 2), change from BID to QD (type 3), change in nucleoside-analogs to decrease toxicity (type 4) and use of a “combo” with FTC+ABC+EFV(type 5).

Results: Median age at the time of simplification was 13.6(10.6-16.6) years; 18 (40.9%) were clinical category C and 11(25%) category B. In 13 patients (23.6%) simplification was type 1, 33(60%) type 2, 24(43.6%) type 3, 24(43.6%) type 4 and 18 (32.1%) type 5.

No patients experienced severe clinical events. Two patients developed an increase in viral load. The median baseline CD4% was 33.8%(SD 6.3), and increased at 6 (34.9%; p=0.021), 12(36.3%; p=0.005), 18(35.2%; p=0.050) and 24 months (34.8% p=0,074).

Median baseline lipids were: cholesterol 186(SD 44.6), triglycerides 157(SD 106), which decreased at 6(160 cholesterol; p< 0,01, 128 triglycerides; p=0.014), 12 (163 cholesterol; p=0.06, 108 triglycerides; p=0.04), 18(168 cholesterol; p=0,36, 116 triglycerides; p=0,3) and 24 months (163 cholesterol; p=0.021, 105 triglycerides 0.093).

Conclusions: In our cohort simplification was safe and well tolerated. Furthemore, the immunological function and lipid profile of these children improved.

P433

VACCINATION HISTORIES AND SEROLOGY IN CHILDREN WITH HIV/AIDS

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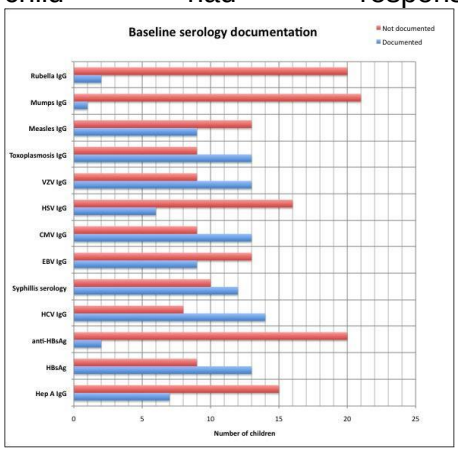
Background and aims: To audit baseline serological testing and documentation of immunisation history in HIV-infected children.

Methods: Case notes of 22 HIV-infected children in active follow-up in our Paediatric HIV clinic were reviewed to establish baseline serology, immunisation history and re-immunisation schedules. If serology was not documented, the hospital's electronic results system was searched. Documentation was compared against national standards.[1]

Results: Children were median 6 years old; 59% were male and 68% born abroad. Only 3 children (14%) had documentation that immunisation records had been reviewed. 4 children (18%) had no documentation of the immunisation schedule followed. Of 286 possible serological results (in 22 children), documentation was present for 114 (40%). Serology was better documented for hepatitis B, hepatitis C, CMV, syphilis, VZV and toxoplasma (59%, 64%, 59%, 55%, 59%, 59% children, respectively), than for mumps, rubella, hepatitis A and HSV (5%, 9%, 31%, 27%) [Figure 1]. 5 (23%) children underwent re-immunisation but no child had response to re-immunisation recorded.



[Baseline serology documentation]

Conclusions: Documentation of immunisation history and serology is suboptimal in HIV-infected children. We recommend use of baseline and 'annual review' proformas to prompt review of immunisation status annually. 2011 PENTA vaccination guidelines will clarify re-immunisation of HIV-infected children and repeat serological testing.

References: 1. Children's HIV Association: Base Line Investigations for Children with HIV (2009). http://www.chiva.org.uk/health/guidelines/suspected-hiv.

P434

EARLY INFANT DIAGNOSIS - GATEWAY FOR SURVIVAL OF HIV INFECTED INFANTS

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Transmission of Human Immunodeficiency Virus (HIV) in infants and children below 18 months is a significant global problem as it can be transmitted from an infected mother to her child during pregnancy, at childbirth and through breastfeeding. 90% of 370,000 new infections were acquired through mother-to-child transmission of HIV.

To curb this problem in India, National AIDS Control Organization (NACO) initiated the Early infant Diagnosis (EID) project in April 2010. This project involves conducting HIV-1 DNA PCR to detect HIV-1 proviral DNA from blood specimens collected onto filter paper or dried blood spots (DBS) and whole blood samples within 2weeks of testing a positive DBS. HIV antibody testing cannot identify infection in children < 18 months.Hence HIV-1 DNA PCR is the test of choice in NACO's HIV care and treatment program.

In India, along with our laboratory, six other laboratories are engaged with EID. By the end of December our laboratory received 867 DBS specimens out of which 124 (14.3%) were positive. Out of 124 positive patients, whole blood specimens were procured from only 70 patients which is the biggest lacuna & challenge of EID program. High HIV percentage positivity was observed in specimens from Gujarat (66/437, 15.10%), followed by Mumbai (55/397,13.8%) and Madhya Pradesh (03/33,9.09%).

In conclusion, early diagnosis by HIV-1 DNA PCR followed by prompt Anti Retroviral Therapy (ART) is critical to save significant number of innocent lives, a vital intervention, which allows countries to provide essential health services and progress in keeping children alive and healthy.

P435

POSTNATAL DEFICIENCY OF ANTIBODIES TO RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN OF HIV-INFECTED MOTHERS

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Background and aims: As the most common cause of lower respiratory tract infection in young children worldwide, respiratory syncytial virus (RSV) infects almost all children by the age of two years. We present a group of HIV-infected mothers and their respective infants under six months of age (34 mother/infant pairs) for whom serum antibodies to respiratory syncytial virus were assayed.

Methods: Births of the HIV-exposed but uninfected children were from April, 2006 to February, 2007. All were followed monthly in the HIV outpatient pediatric unit at Federal University of São Paulo, Brazil

The study was approved by the institution ethic committee, and written, informed maternal consent was required to participate. Mother/infant blood samples were collected upon admission. All samples were centrifuged and frozen at -70° C until analysis. Serologic testing for RSV (RIDASCREEN RSV IgG) was performed to evaluate protection levels conferred by mothers to their babies. Results were interpreted as negative (< 11.0 U/ml), indeterminate (11.0-20.0 U/ml), or positive (>20.0 U/ml).

Results: Thirty-one of 34 mothers (91.1%) were anti-RSV seropositive, compared with 19 children (61.0%). One infant tested positive, while the mother did not, suggesting postnatal RSV exposure and mounting of its own humoral response.

Conclusions: Our results may indicate that children born to HIV-infected mothers are compromised in terms of RSV protection, due to fewer maternal antibodies transferred during pregnancy. Further study is needed to evaluate the clinical and epidemiologic consequences of these findings.

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HEPATITIS A ANTIBODIES IN HIV-INFECTED ADOLESCENTS EIGHT YEARS AFTER PRIMARY IMMUNIZATION AND ITS ASSOCIATION WITH THE IMMUNOLOGICAL PROFILE

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Background and aims: HIV infection is associated with reduced immune response to vaccination and accelerated decay of antibodies. We analyzed the persistence of protective hepatitis A virus (HAV) antibodies eight years after primary immunization in HIV-positive patients and its association with the immunological profile.

Methods: 29 vertically HIV-infected adolescents (median age:12.9y) were studied in 2010. All had seroconverted after two HAV vaccine doses in 2002. HAV antibodies were measured by electrochemiluminescence. Lymphocyte immunophenotyping was performed by flow cytometry. Statistical analysis employed Mann-Whitney and Fisher's exact test.

Results: Among the 29 patients studied, 23 (79.3%) remained immune (HAV antibodies>20mIU/mL) 8 years after primary immunization. Age, gender, clinical progression of HIV infection, median viral load and antiretroviral therapy were similar between immune and susceptible groups. HAV susceptible group, in comparison with HAV immune group, had lower median CD4+T cells/mm3 (200 versus 634, p=0.004), lower median B cells/mm3 (103 versus 335, p< 0.001), lower median NK cells/mm3 (67 versus 209, p=0.002), lower median percentage of naive CD4+ T cells (20% versus 30%, p=0.026), lower median percentage of naive B cells (52% versus 68%, p=0.009), higher median percentage of activated memory B cells (19% versus 7%, p=0.004), higher median percentage of activated (CD38+HLADR +) CD8+ T cells (51% versus 22%, p=0.002) and higher median cell percentage of memory B cells in exhaustion (23% versus 8%, p=0.031).

Conclusion: Persistence of HAV antibodies occurred in 79.3% of patients and was associated higher CD4+ T, B and NK cell numbers and lower immune activation.

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NEPHROGENIC DIABETES INSIPIDUS ASSOCIATED WITH TENOFOVIR ADMINISTRATION: CASE REPORT

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Background and aims: Renal toxicity of tenofovir has been reported in the adult HIV population. Reports in children are very rare. Toxicity has also been described in association with other antiretrovirals. We present a paediatric case of nephrotoxicity associated with tenofovir with didanosine, emtricitabine and lopinavir/ritonavir coadministration.

Methods: Case report.

Results: A 12-year-old girl with AIDS (clinical stage C) with a multidrug resistant virus and several treatment failures initiated emtricitabine, tenofovir, didanosine, and lopinavir-ritonavir in 2008 with good tolerance. Her viral load became undetectable and CD4 count normal.Two years later she presented generalized weakness, polydipsia and polyuria. On physical examination she was dehydrated. Her vital signs were stable. She had lost 5% of her weight in the previous week.Urinalysis revealed a urine gravity of 1.000, osmolality 150 mOsm/Kg, absence of proteinuria or glucosuria. The blood analysis showed osmolality 289 mOsm/Kg, normal values of glucose, creatinine, urea, sodium, potassium, chloride and calcium. A water restriction test followed by desmopressin administration confirmed the diagnosis of nephrogenic diabetes insipidus. Tenofovir and didanosine were stopped and abacavir was added. The patient was treated with a thiazide diuretic and salt restriction. There was good clinical evolution and no relapses.

Conclusions: Toxicity can limit the use of successful antiretroviral regimens. Tenofovir is nephrotoxic and should be used with great caution and the coadministration of didanosine avoided whenever possible. However, treatment options are frequently very scarce in antiretroviral experienced children with multidrug resistant virus. They present complex therapeutical challenges that need a careful clinical and laboratory follow-up.

P438

EFFECT OF HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY ON SERUM LIPOCALIN-2 LEVELS IN HIV-INFECTED CHILDREN

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Background: Lipocalin-2 or Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a 25-kDa glycoprotein belonging to the lipocalin superfamily of proteins. Although this protein may play a pivotal role in the innate immune response, in acute kidney injury and lipodystrophy, there are few data on NGAL levels in patients with human immunodeficiency virus (HIV)-infection. In this study we aimed to investigate the effect of highly active anti-retroviral therapy (HAART) on NGAL levels in children with HIV infection.

Patients and methods: Sixteen HIV-positive children were included in the study, while 22 children matched for age and sex served as controls. NGAL levels were determined by an immunoassay (BioPorto Diagnostics A/S Gentofte Denmark) in patients before and one year after HAART and in controls.

Results: Before initiating HAART, the HIV-infected children had significantly decreased serum NGAL levels compared to healthy controls (18.8±9.9 vs 67.5±11.4 microg/L, respectively, $p< 0.001$). During HAART, we observed a pronounced fall in virus load expressed as HIV-RNA copies and a marked increase in $CD4^+$ T cell counts. These changes were accompanied by significant increase in NGAL concentrations reaching levels comparable to those in healthy controls after 12 months of therapy (68.1±47.5 vs 67.5±11.4 microg/L, respectively, $p>0.950$).

Conclusions: We found decreased serum NGAL levels in HAART untreated HIV-infected children, which normalized during HAART. These findings suggest that dysregulated NGAL levels should be added to the list of abnormalities that characterize HIV-infected patients. Whether these abnormalities are due to innate immune response, HIV-associated nephropathy and/or lipodystrophy needs further investigation.

P439

IMPAIRED T-CELL DEPENDENT AND INDEPENDENT MEMORY B-CELL FORMATION IN HIV-INFECTED CHILDREN

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Background and aims: Patients infected with the human immunodeficiency virus (HIV) display multiple defects in their B-cell compartment, even under antiretroviral (ART) treatment. Since most studies were performed in adults, we studied the effects of vertically acquired HIV infection on the build-up of the B-cell compartment in children.

Methods: We studied 58 ART-treated HIV-infected children and 115 age-matched healthy controls. Patients were characterized by CD4+ T-cell numbers and serum HIV RNA levels (RNA copies/ml). Furthermore, the absolute numbers of 2 naive, 6 memory-B-cell subsets and CD21low B-cells were determined by 8-color flowcytometry in peripheral blood.

Results: All HIV-infected children had near normal CD4+ T-cell numbers. Most patients had undetectable or low serum HIV levels (< 1,000 RNA copies/ml), and only a few patients had a serum HIV level >15,000 RNA copies/ml. Most memory-B-cell subsets were reduced in young HIV-infected children (< 5yr), normal at 5-15yr and again reduced in 16-20yr as compared to healthy controls. Interestingly, T-cell independent CD27-IgA+ B-cell numbers were severely reduced in all age categories. In contrast, IgM-only memory-B-cell numbers were increased until 5-9yr of age and normal in older children. Patients with detectable serum HIV RNA showed increased CD21low B-cell numbers that lacked CD24 expression.

Discussion & conclusion: Our results demonstrate impaired build-up of both T-cell dependent and independent memory-B-cell subsets in HIV-infected children despite ART-treatment. Furthermore, our results suggest direct effects of HIV on the development of the aberrant CD21low B-cell population. We are currently further studying the nature of the CD21low B-cell population.

P440

A STUDY OF PULMONARY TUBERCULOSIS AMONG PEOPLE LIVING WITH HIV/AIDS

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Tuberculosis (TB) is an infectious disease caused by *Mycobacterium*. It is a leading public health problem particularly in the developing countries. The HIV epidemic has increased the global tuberculosis burden. TB is commonest opportunistic infection and leading mortality of People living with HIV (PLHA).

Objectives: To determine prevalence of Pulmonary Tuberculosis among HIV positives attending HIV clinics in Eastern Nepal.

Methodology: Cross-sectional prospective study was carried out among HIV positive attending different VCT and HIV clinics from Sunsari Morang and Jhapa district of Eastern Nepal. Face to face interview performed and sputum sample were collected using convenience sampling technique. Out of total 242 PLHA, 75.2% were males and 24.8% females; around half of them (48.8%) were in the age group of (30-39) yrs, 23% in (25-29) yrs, and 15.7% in (20-24) years. Prevalence of pulmonary tuberculosis was found to be 27.3% (n=66).

Conclusion: Prevalence of PTB is very high among PLHA attending VCT & HIV clinics of Eastern Nepal. There is urgent need of active case finding and treatment through DOTS among people living with HIV/AIDS of this region.

P441

KAPOSI´S SARCOMA IN A HIV-INFECTED ADOLESCENT IN SÃO PAULO, BRAZIL

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In non-endemic countries, Kaposi´s Sarcoma (KS) is still rarely reported among pediatric patients.

This report regards the case of an adolescent of 15 years old, HIV infected by vertical transmission. The patient denied any prior sexual activity. He was admitted to the hospital, complaining of cephalgia, nausea and vomiting for the previous 2 days. A cranial CT scan revealed a brain lesion suggestive of toxoplasmosis, for which he was treated with sulfadiazine, folinic acid and pyrimethamine. There was clinical improvement; however, on the 15th day, hyperemia occurred on the right hemi face with an eyelid edema. A control cranial CT scan showed regression of the brain lesion. On his admission, the patient already displayed a reddish lesion, smaller than 0.3 cm, on his face; he said it was a blemish that had appeared 15 days earlier. Facial cellulites was considered and systemic antibiotics were then introduced. The lesion evolved with rapid growth, and another purplish lesion appeared on his right arm. Biopsies of lesions and blood samples were collected for analysis. Biopsy diagnosis was KS, and Human Herpesvirus 8 was detected in peripheral blood. A lesion suggestive of KS occurred in the sigmoid colon. Chemotherapy was initiated with daunorubicin every 15 days. Lesions progressively diminished in size and became virtually imperceptible after 6 months.

Despite its rarity among pediatric patients KS should be researched. It responds well to chemotherapy.

P442

CAUSES OF DEATH IN HIV-1 INFECTED CHILDREN DURING THE HAART PERIOD IN SÃO PAULO, BRAZIL

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Brazil have implemented a national antiretroviral drugs distribution program, which have been providing medical care and no-cost antiretroviral therapy to HIV-infected patients since 1990.

The present study aimed to assess the number of HIV-infected children who died between June 2005 and June 2009, as well as the main causes of death among children treated at Instituto de Infectologia Emilio Ribas, São Paulo, Brazil.During the observation period, 18 children died, 8 girls and 10 boys, at an average age of 13,3 years.

The average death rate was 4 deaths per year and mortality rate were 1,35 deaths per 100 person-years.Fifteen of eighteen patients had CDC AIDS-defining. Gastrointestinal diseases and end-stage AIDS were the leading causes of death. The leading gastrointestinal cause was chronic diarrhea due to Cryptosporidium infection. Oral candidiasis recurred in the majority of patients. Six children had Citomegalovirus infection; two girls became infected with Cryptococcus. JC virus was present in the blood and cerebrospinal fluid of two boys. Hodgkin´s lymphoma was observed in one boy. Three deaths were not related to AIDS: one boy died from a severe ceftriaxone-induced hemolytic reaction, and another boy died from surgical complications; one girl died from a severe Epstein-Barr virus infection.

There certainly was a significant decline in the death rate since the introduction of antiretroviral therapy; however, better adherence and new therapeutic options for opportunistic infections remain necessary.

P443

AIDS RELATED NON HODKGIN LYMPHOMA (NHL). FIFTEEN YEARS EXPERIENCE AT A PEDIATRIC ITALIAN CENTER

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Introduction: Burkitt's lymphoma (BL) is the most common AIDS related lymphoma in childhood. The incidence of cancer in children with AIDS is 2,5%. Despite the advent of highly active antiretroviral therapy (HAART) the observation of AIDS related NHL remain stable. We report five cases of BL in HIV infected children.

Methods: We reviewed all medical records and histopathologic tissues of patients with BL observed from 1995 to 2010 at the Children Hospital Bambino Gesù in Rome.

Results: On 130 HIV vertically infected children (< 18 yrs) followed from birth at our center we observed five cases of BL (3,8%, 5/1892 patient-yrs). All were males. At the diagnosis mean age was 11,2 years, three patients had CD4 cell count between the range 105-822/mm³(mean value 414), four had viral load between 80-460.000 copies/ml (mean value 135.816) and the median months of HAART were 6,6 for three patients. Epstein Barr Virus (EBV) was detected in three cases. All patients performed chemotherapy according to the Italian Association of Pediatric Hematology Oncology (AIEOP) protocol for NHL combined with HAART. One patient presented a relapse after 26 months and was treated with R-ICE protocol followed by autologous stem cells transplantation. The survival at 15 years is 80% with a median remission of 36 months.

Conclusions: Immunodeficiency, cumulative HIV viremia and detection of EBV are considered major risk factors for BL in HIV infected patients as observed in our cohort. Further studies are necessary to evaluate the most sensitive predictors of AIDS-related lymphoma among HIV infected children.

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OCULAR TOXOPLASMOSIS MISDIAGNOSED AS CMV RETINOPATHY IN AN HIV INFECTED PATIENT

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Introduction: Ocular manifestations can occur in up to 50% of human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) patients. Retinal microvasculopathy and opportunistic infections, mainly cytomegalovirus (CMV) and Toxoplasma gondii retinitis, are the most common manifestations, even in the era of highly active anti-retroviral therapy (HAART). Immune recovery vitreitis (IRV) can occurs in patient with CMV retinitis initiating ARV therapy. Ophthalmologist findings are at the basis of diagnosis with laboratory tests. In immunosuppressed patients CMV retinochorioiditis can be similar to ocular toxoplasmosis disease.

Case report: We report a 21 years old Hiv positive female suggestive of CMV retinopathy on the ophthalmologist examination and then diagnosed as toxoplasmic retinochoroiditis based on serologic test. She presented a one month history of decreased vision and her CD4 cell count was 20/mm³ with 367.632 copies/ml hiv viral load (bDNA). Fundus examination of the right eye showed a vitreous inflammatory reaction associated with an opaque yellow-white infiltrate with trace of hemorrage suggestive of CMV retinochorioiditis. We did not perform vitreous biopsy. Laboratory tests revealed the detection of IgM for toxoplasma gondii and a negative blood culture for CMV. On the basis of ophthalmologist features and antibodies titers, antiparasitic therapy was started with pyrimethamine and sulfadiazine combined with HAART.

Discussion: In immunocompromised patients with necrotizing retinochoroiditis differential diagnosis including herpes virus and toxoplasma gondii infections should be performed. In atypical cases in addition to laboratory tests and fundus examination vitreous biopsy with cultures should be considered.

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HUMAN ANTIMICROBIAL PEPTIDE LL37 INHIBITS BIOFILM FORMATION OF *STAPHYLOCOCCUS EPIDERMIDIS* ON POLYURETHANE CENTRAL VENOUS CATHETER

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Biofilm-associated catheter infection is a common complication in neonatal intensive care. Premature birth, low birth weight and long hospital stay are significant factors for this condition. *Staphylococcus epidermidis*, which is known as commensal, has emerged as the most common cause of devise-related infection. *S. epidermidis* cells are extremely capable of adhering to catheters and forming a multilayered structure called biofilm. Biofilm formation increases the resistance of bacteria to host defense mechanisms as well as to antibiotic therapy.

LL37 is the only member of the cathelicidin host defense peptide family expressed in humans, considered to be antimicrobial as well as to have anti-biofilm effect.

The aim of this study was to investigate possible inhibitory effect of LL37 on biofilm formation on polyurethane central venous catheter. Biofilm formation was performed in vitro by incubating pieces of catheters in liquid bacterial cultures of the laboratory strain ATCC35984 in the absence and presence of LL37. 1 mg/l and 16 mg/l peptide-concentrations were used. Biofilm was analysed by scanning electron microscopy (SEM). Quantitative analysis was also done according to Weibel et al. (1979).

The biofilm mass was weaker and the bacterial number reduced on the catheter surface at 1 mg/l compared to conditions in the absence of the peptide, as judged by SEM. More bacterial inhibition was found at the higher LL37 concentration. Similar results are obtained with polystyrene microtiter plates.

This study suggests that human cathelicidin peptide LL37 could be a new candidate in diminishing devise-related infections caused by *S. epidermidis*.

P446

IMPAIRED HUMAN-BETA DEFENSIN 2 RESPONSE IS ASSOCIATED WITH FULMINANT NECROTIZING ENTEROLOCOLITIS IN ELBW

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Background: Human beta-defensins (hBDs) are antimicrobial peptides involved in the innate host defence which might be impaired in extremely low birth weight infants (ELBW) with necrotizing enterocolitis (NEC).

Methods: During April 2008 and December 2009 ELBW with a gestational age of up to 27+0 weeks and a birth weight of < 1000g were included in this study. Fecal samples were obtained every other day and in case of abdominal surgery intestinal samples were taken and analysed for hBD2, MD2 and TLR4 expression.

Results: ELBW who eventually developed severe NEC (n=6) did not show an hBD2 response in fecal samples before or during NEC. Accordingly, hBD2 expression in intestinal samples of ELBW with severe NEC was extremely low on protein and mRNA level, comparable with healthy children (n=28) and significantly lower compared to children with Crohn´s disease (n=32). Intraindividual analysis of two ELBW who survived severe NEC showed 10, 5 and 3fold higher mRNA levels for hBD2, TLR4 and MD2 at term during stoma closure. Whereas hBD2 concentration in meconium was high in all ELBW, it then dropped in healthy ELBW reaching a nadir at day 14 followed by a steady increase from thereon.

Conclusion: ELBW with severe NEC do not show an hBD2 response possibly due to insufficient MD-2 and TLR-4 expression suggesting an insufficient LPS sensing in response to luminal bacteria. High hBD2 concentrations in meconium probably reflect hBD2 found in the amniotic fluid conferring a protective effect against NEC on ELBW during the first week of life.

P447

GENOME WIDE ASSOCIATION STUDY PROVIDES FURTHER SUPPORT FOR THE TLR4 PATHWAY IN CHILDREN WITH *HAEMOPHILUS INFLUENZAE* B (HIB) VACCINE FAILURE

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Background: We have recently shown in a candidate gene study that a functional single nucleotide polymorphism (SNP) in *Mal/TIRAP*, an intracellular adaptor molecule downstream from the TLR2/4 receptors, was strongly associated with non-meningitis cases of invasive *Haemophilus influenzae* serotype b (Hib) disease in previously immunised children.

Methods: A genome wide association study (GWAS) was performed in the same cohort of 174 children with Hib vaccine failure and compared with 4,703 Caucasian controls from the Wellcome Trust Case Control Consortium datasets. Primary analysis comprised score-based tests modelling the effect for a trend-per-copy of the minor allele. SNPs showing $P < 1.00 \times 10^{-4}$ were considered suggestive evidence of association. All score-based tests were accompanied by an unguided 2 d.f. genotype test to ensure no deviation from the trend model.

Results: The GWAS identified a significant association between the Asp299Gly functional SNP on *TLR4* and Hib vaccine failure, in terms of minor allelic frequency (0.11 vs. 0.056; odds ratio (OR)=2.00; 95% confidence interval (CI)=1.41-2.85; $P=7.8 \times 10^{-5}$), and genotype distribution (0.799/0.190/0.011 vs. 0.891/0.106/0.003; $P=6.8 \times 10^{-4}$). Moreover, the minor allele frequency was strongly associated with non-meningitis cases (0.139 vs. 0.059; OR=2.4; 95% CI=1.5-3.7; $P=1.5 \times 10^{-4}$) but not with meningitis cases (0.098 vs. 0.059; OR= 1.7; 95% CI = 0.97-2.8; P=0.064).

Conclusions: The association between non-meningitis cases of Hib vaccine failure and the Asp299Gly SNP on TLR4, which has been associated increased susceptibility to Gram-negative infections and septic shock, provides further support for the importance of the TLR4 pathway in invasive Hib disease among previously immunised children.

P448

CANDIDA BEHAVIOR AS COMMUNICATIVE BODIES WHICH CONTROL AREA: SYMMETRICAL LANDSCAPES ALTERED BY ANTIFUNGALS

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Background: Probiotic lectins of lactobacilli and bifidobacteria (LL, LB) of human origin can destruct pathogen biofilms. The aim was to study behavior of *Candida* in response to antifungals.

Methods: Clinical *Candida* clinical strains were isolated and identified by standard methods. Fungal growth was in dishes (*Sabouraud* agar) in the presence of disc-antifungals.

Results: The behavior of *Candida* as the whole body was compared in conditions of continuous surplus (or not) growth (body I or II) and discontinuous growth (body III). I was looked like as a real body (4 main features). II and III acted as communicative ones. Results point out area control by *Candida*: center and border, near center and near border areas, left and right areas in sectors. Symmetrical area marking-out by *Candida* depended on primary antifungal localizations. During normal and stress conditions the area symmetry was altered and converted into asymmetrical images. II and III were decreased (mosaic excision saving whole architecture) in near border area (earlier and stronger, in responce to LB) and near center area (later and lower, in responce to LL). The way to rich critical size of *Candida* body (level of whole body architecture disruption) was to use simultaneously synergic combinations (LB, LL, and/or antimycotics).

Conclusions: The body functioning helps *Candida* in survival. It seems, *Candida* bodies (like III) communicate in/between biotopes in human organism. They recognize early surrounding antifungal signals (also as changing and increasing in stress conditions images that serve as fungal memory). *Candida* behavior is important for drug strategy choice.

P449

GLUCOCORTICOID RECEPTOR POLYMORPHISMS ARE ASSOCIATED WITH *STAPHYLOCOCCUS AUREUS* COLONISATION AND ATOPIC DERMATITIS IN CHILDHOOD. THE GENERATION R STUDY

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Background and aims: Nasal *Staphylococcus aureus* colonisation, which is associated with atopic dermatitis (AD), is common in children. In adults, glucocorticoid receptor (GR) single nucleotide polymorphisms (SNPs) were associated with *S. aureus* colonisation. The aim was to assess whether GR SNPs are associated with *S. aureus* colonisation until age 3 and whether the association between *S. aureus* colonisation and AD depends on GR variants.

Methods: This study was embedded in a birth cohort. DNA was obtained from cordblood samples and assessed for five GR polymorphisms: *Bcl*I, *TthIII*I, GR-9β, N363S and ER22/23EK. Nasal swabs for *S. aureus* isolation were obtained in 1,079 children at 1.5, 6, 14, 24 and 36 months. AD symptoms were questionnaire-derived at age 4.

Results: Six haplotypes were distinguished. GR haplotypes were not associated with *S. aureus* colonisation during infancy. At age 3, however, four haplotypes were significantly associated with reduced nasal colonisation; haplotype 1 (OR 0.46 95%CI 0.25-0.85 as compared to wildtype), 2 (BclI, OR 0.46 95%CI 0.25-0.85), 3 (*Bcl*I+TthIIII, OR 0.40 95%CI 0.20-0.79) and 4 (GR-9β+TthIIII, OR 0.47 95%CI 0.24-0.93). However, the odds of AD were highest for those children with frequent *S. aureus* colonisation holding 2 of the 5 minor GR haplotypes compared to children holding two copies of wildtype (aOR 2.89 95%CI 1.03-8.07).

Conclusions: Several GR-haplotypes were associated with reduced *S.aureus* colonisation rate at age 3, but not in infancy. Yet, the children with non-wildtype GR-haplotypes were prone to develop AD symptoms given prior *S. aureus* colonisation. A gene-environment interaction seems to exist.

P450

IMMUNOGENICITY AND PROTECTIVITY OF *STAPHYLOCOCCUS AUREUS* AND *STREPTOCOCCUS PNEUMONIAE* PROTEINS IN RELATION TO NASOPHARYNGEAL COLONIZATION AND VACCINATION

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Background: Colonization rates of *S. pneumoniae* and *S. aureus* are inversely correlated and seem to shift after pneumococcal conjugate vaccination (PCV-7). We decided to study the natural humoral response against pneumococcal and staphylococcal surface proteins in relation to carriage with both pathogens in PCV-7 immunized and non-immunized children.

Methods: During a RCT(NCT00189020), we obtained nasopharyngeal samples at 6, 12, 18 and 24 months and sera at 12 and 24 months of age. We analyzed IgG against 40 staphylococcal and 18 pneumococcal proteins using flow cytometry (n~130 per group) and studied immunogenicity and protectivity of these antibodies.

Results: In children previously colonized with *S. aureus* IgG levels were significantly higher against the proteins ClfA, Efb, SCIN, SEH and SSL_5 ($p < 0.01$), whereas in children previously colonized with pneumococci IgG levels were higher against all proteins when compared to non-colonized individuals ($p < 0.001$).Increasing age was associated with a higher response against almost all pneumococcal proteins and a lower response against more than half the staphylococcal proteins ($p < 0.01$), which correlates with colonization dynamics. None of the pneumococcal or staphylococcal antibodies seemed to protect against colonization with the homologous or heterologous species in the following year. Finally, there were no differences between vaccinated and non-vaccinated children in antibody levels.

Conclusions: Pneumococcal and staphylococcal proteins appear immunogenic in infants. Unfortunately, at 12 months of age neither of the anti-protein antibodies showed to be protective nor cross-protective against pneumococcal and staphylococcal colonization, respectively. No effect of PCV-7was observed on natural immunity against both pathogens.

P451

HOST-PATHOGEN INTERACTION IN CHILDREN SUFFERING FROM OTITIS MEDIA

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Background: Since viral infections may result in Eustachian tube dysfunction, increased adherence of bacteria to epithelial cells and may modulate host immunity, we investigated the effect of bacteria and viruses on the inflammatory response in the middle ear of children suffering from OM.

Materials and methods: Children < 6 years of age, suffering from recurrent or chronic OM and scheduled for tympanostomy tube insertion, were enrolled in a prospective study. Middle ear fluids (*n*=116) were collected during surgery, and qPCR was performed to detect known bacterial and viral otopathogens (*Streptococcus pneumoniae*, *Haemophilus influenzae, Moraxella catarrhalis* and 15 respiratory viruses among which rhino-, adeno- entero- and (para)influenzavirus). To measure the inflammatory cytokine response, concentrations of IL-1β, IL-6, IL-8, IL-10, IL-17a, TNF-α and INF-γ were determined.

Results: Viruses (28%), bacteria (27%), bacteria and viruses (27%) or no otopathogens (19%) were detected in middle ear fluid, with *H. influenzae* and rhinovirus being predominant. Surprisingly, no cytokine differences were found between patients with viruses alone versus no otopathogens. In contrast, the detection of bacteria was associated with a significantly elevated inflammatory cytokine responses compared to when no bacteria were detected. This increase strongly correlated with the bacterial load. Finally, no synergy was observed for viral-bacterial co-infection compared to infection with bacteria alone.

Conclusion: In the middle ear of patients with recurrent or chronic OM, the presence of bacteria, but not viruses, is associated with an increased inflammatory response. This finding suggests that bacteria are an important factor determining the inflammatory process during OM.

P452

A NOVEL ROLE FOR APOPROTEIN-A1 AND HIGH DENSITY LIPOPROTEIN-C AS ACUTE PHASE REACTANS DURING INFECTIONS

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Aim: To evaluate alterations in the concentrations of apoAI, apoE and HDL-C, during infection and to investigate a possible correlation between them and CRP.

Material and methods: 20 children, 3-7 yrs old with bacterial pneumonia were examined. The diagnosis established by typical clinical manifestations confirmed by positive chest X-ray and/or positive blood cultures. ApoE, apoAI, HDL-C and CRP levels were measured on admission and three weeks after their discharge from the hospital. All patients were treated with antibiotics and had uncomplicated course. To perform the statistical analysis we used paired t-test and correlation statistical analysis between CRP and the other parameters.

Results: The mean values of the parameters tested between the acute and convalescent phase were: CRP: 173. 25 ± 28.45 mgr/lt vs 3 mgr/lt, HDL-C: 24.4 mg/dl ± 13.07 vs 53.5 mg/dl ± 9.84, apoAI: 79.50 mg/dl ± 23.17 vs 138.21 mg/dl ± 12.53 and apoE: 6.11 mg/dl ± 1.24 vs 5.31 mg/dl ± 1.39. Statistically significant difference was observed between the acute and convalescent phase for HDL-C (t= -11.938, p-value= < 0.001), apoAI (t= -18.71, p-value= < 0.001) and apoE (t= 2.53, p-value= 0.020). A significant correlation was detected between CRP and HDL-C (r= -0.494, p-value= 0.027) and apoAI (r= -0.622, p-value= 0.003).

Conclusions: Significant differences in the mean concentrations of apoAI, apoE and HDL-C were detected between the acute and convalescent phase. A significant correlation was observed between CRP and HDL-C, apoAI. The latter observation raises the possibility these molecules to act as acute phase reactants.

P453

PRESCHOOL WHEEZE: THE ROLE OF REGULATORY T CELLS AND BACTERIAL COLONISATION

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Background: Wheeze is a common symptom among preschool children. Nevertheless, there is a lack of knowledge about the underlying pathophysiology. The role of bacterial infection/colonisation and regulatory T cells (Treg) in preschool wheeze is largely unknown.

Aims:

- To investigate whether wheezing preschool children differ in bacterial infection and colonisation with airway pathogens and Treg compared to healthy controls.

- To study whether wheezing children with bacterial colonisation have lower levels of Treg compared to colonised controls.

Methods: We recruited 252 children (aged 2-4 years) with (n=202) and without (n=50) recurrent

wheeze. Proportions of Treg were quantified by flow cytometry ($CD4^+CD25^+CD127^-$).

Nasal- and throat swab were analysed for colonisation with *Streptococcus pneumoniae* and *Haemophilus (para)influenzae*. Serology for *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* was analysed in venous blood.

Results: Positive serology for *Mycoplasma pneumoniae* was mildly elevated in preschool wheezers compared to non-wheezers (10.9 vs. 2.4%, p=0.09). No significant differences were found in amounts of Treg between wheezers and non-wheezers. In wheezing children colonised with *Streptococcus pneumoniae* elevated levels of Treg compared to colonised children without wheeze were found (7.4 vs. 6.4%, p=0.03).

Conclusions: Wheezing preschool children colonised with *Streptococcus pneumoniae* had elevated levels of Treg. We hypothesised, however, to find lower levels of Treg in colonised wheezers reflecting impaired immunity. We might conclude that in preschool wheezers Treg are stimulated upon colonisation with typical airway pathogens. Possibly these Treg have a defective function and can not prevent an inflammatory airway response leading to wheezing symptoms.

P454

PNEUMOCOCCAL POLYSACCHARIDE CAPSULE INCREASES SUSCEPTIBILITY OF *STREPTOCOCCUS PNEUMONIAE* TO HUMAN NEUTROPHIL ELASTASE AND CATHEPSIN G MEDIATED KILLING

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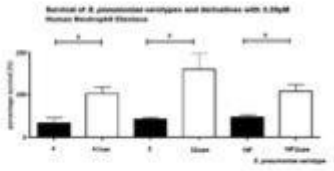
Background and aims: *Streptococcus pneumoniae* are an important cause of severe infections in children. *S. pneumoniae* expresses a polysaccharide capsule (>90 serotype variants) which is a major virulence factor with anti-phagocytic and anti-opsonic properties. Neutrophil granulocytes play an important role in controlling infections caused by *S. pneumoniae.* Activated neutrophil serine proteases have been shown to be primarily responsible for the killing of bacteria. *In vitro* purified human neutrophil elastase or cathepsin G is sufficient to kill *S. pneumoniae* in a serine protease dependent manner. The present study assessed whether capsule affects *S. pneumoniae* susceptibility to serine protease mediated killing.

Methods: *In vitro* bactericidal assay: encapsulated *S. pneumoniae* type 2, type 4 and type 19F strains and their isogenic unencapsulated derivatives were incubated with the purified human neutrophil serine proteases elastase or cathepsin G followed by quantitative culture.

Results: We found a significantly higher susceptibility of encapsulated pneumococci to *in vitro* killing by the purified human neutrophil serine proteases elastase and cathepsin G (elastase data see fig 1).



[Effect of pneumococcal capsule on elastase killing]

Conclusions: In summary, our results demonstrated that capsule does not protect *S. pneumoniae* against human neutrophil serine proteases. In contrast, neutrophil serine proteases demonstrate increased activity against encapsulated *S. pneumoniae.*

P455

BACTERIAL CELL WALL COMPONENT MURAMYL DIPEPTIDE SYNERGIZES WITH RESPIRATORY SYNCYTIAL VIRUS IN CYTOKINE PRODUCTION

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Hospitalizations due to respiratory syncytial virus (RSV) have been associated with respiratory bacterial co-infections. The mechanism behind this synergy is thus far unknown.

The bacterial cell-wall component muramyl dipeptide (MDP) is recognized by the intracellular pattern recognition receptor NOD2. NOD2 is a modulator of signals transmitted through TLRs. RSV can be recognized by TLR3, TLR4 and TLR7/8. Our hypothesis is that RSV induced TLR activation is enhanced by NOD2 stimulation.

Human PBMCs were stimulated for 24hrs with RSV-A2, purified TLR ligands and MDP. Subsequently cytokines were measured.

Stimulation with RSV-A2 or MDP resulted in low cytokine responses. However, a combination of both stimuli resulted in high cytokine responses. Ratio's were calculated; [RSV+MDP]/[RSV]+[MDP]. The combination of both stimuli resulted in a 2.0±0.28, 3.8±1.07, 2.2±0.30 fold increase in respectively IL-6, TNF and IL-1beta production.

Stimulation of PBMCs with specific ligands for TLR3 and TLR 7/8 in combination with MDP did not show synergy. Viral ssRNA and dsRNA are therefore not the viral ligands that cause the synergy. This excludes TLR3, TLR7 and TLR8 as potential receptors involved in the crosstalk with NOD2.

Blocking TLR4 internalization with dynasore induced a 3.5 fold increase of the synergy in cytokine production when MDP and RSV were combined. This suggests that the crosstalk between RSV and MDP is TLR4 dependent and TRIF independent.

We show a synergy between MDP and RSV for the induction of cytokines which is independent of intracellular TLR recognition and therefore most likely TLR4 dependent. Ongoing experiments have to confirm this conclusion.

P456

PULMONARY TUBERCULOSIS OUTBREAK IN A PREDOMINANTLY PEDIATRIC POPULATION

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According to the WHO, global tuberculosis (TB) epidemics result in nearly 2 million deaths and 9 million new cases of the disease annualy. Community-based outbreaks of TB are uncommon in the United States but represent a dramatic type of epidemic that can lead to considerable investigations.

In February 2007, infectious pulmonary TB was identified in a 45-year-old African-American grandmother who frequently provided care for her grandchildren and other children of her family. The index case was reported to the Genesee County Health Department, who carried out investigations to identify family and social contacts.

This study highlights the need for education in the public, and the crucial role of early diagnosis of infectious cases.

We reviewed past medical records of contacts, and prioritized them for evaluation based on period of exposure to the index case. Health department staff screened contacts using clinical evaluation, tuberculin skin test, and radiography of the chest when indicated. Results were reviewed, and data was analyzed using descriptive inferential, and epidemeological statistics.

A total of 66 contacts were identified, thirty three were under 18 years of age. Skin testing was perforrmed in 61 contacts, and was positive in 23 of them. Active TB was diagnosed in 13 contacts, ten of them were under 10 years-old.

Community based outbreaks of TB continue to occur, and transmission in this aforementioned setting can be very efficient. Early diagnosis, and screening of exposed vulnerable contacts such as children in order to avoid progression to active disease and its associated complications.

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KNOWLEDGE AND USE OF ITNS FOR MALARIA CONTROL AMONG MOTHERS OF UNDER-5 CHILDREN ATTENDING PRIMARY HEALTH CENTRES IN ILE-IFE,NIGERIA

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Background and aims: In Nigeria as in other parts of Sub-Saharan Africa, malaria is the leading cause of under-five (U-5) mortality rate contributing 33% of all childhood deaths and 25% of infant mortality.

Effort made to control malaria was the launching of Roll Back Malaria (RBM) initiative at a summit of African Heads of States held in 2000 in Nigeria. At this summit, a declaration was made to halve the burden of malaria by the year 2010. One of the targets set for the first five years was to ensure that under-five children and pregnant women have access to and sleep under insecticide-treated nets (ITNs).Aim of our study is to assess knowledge of and use of ITNs among mothers of U-5 in the study area.

Methods: The study was carried out among randomly selected 245 mothers of U-5 attending all the existing 13 primary health centers in Ife Central Local Government Area (ICLGA) in Ile-Ife, SW Nigeria. A pre-tested semi-structural interviewer's administered questionnaire was used in collecting the data from the volunteered respondents.

Results: From the results, despite the fact that most of them (83.7%) have heard about ITNs, a few (16.7%) of them are always using it . The common reason for not using it was that it was not readily available (27.1%) .

Conclusion: From the results in the study, we recommend that ITNs should be made available at affordable cost in order to promote a wide scale use of it for malaria control in Nigeria.

P458

ASSESSMENT OF INCIDENCE AND RISK FACTORS OF VENTILATOR ASSOCIATED PNEUMONIA

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Background and aims: With increasing use of ventilation in tertiary care hospitals, there is an increase in incidence of Ventilator Associated Pneumonia (VAP) and associated mortality. The aim of this study was to assess the incidence and risk factors associated with VAP.

Methods: Prospective study conducted which included children aged ≥1 month and ≤12 years and requiring mechanical ventilation (M.V.) for ≥48 hours with parental consent. For diagnosing V.A.P., National Nosocomial Surveillance System (NNIS), criteria of 1996 were used.

Results: Using NNIS criteria, the incidence of VAP was 36.2% (n=38), 86.8% within 4 days of M.V. and 13.2% after 4 days. Those who developed VAP had statistically significant higher frequency of endotracheal suctions in last 6 hours, reintubation after 72 hours of extubation and more number of attendants at the time of recruitment as compared to controls. Risk factors that were statistically significantly associated with V.A.P. were positive bacterial culture of endotracheal aspirate (O.R. 4.46, 95% CI: 1.43,14.65, p value 0.003) and positive bacterial culture of endobronchial aspirate (O.R. 2.81, 95% CI: 1.13,6.99 p value 0.013). Common bacteria isolated in endotracheal and endobroncial cultures were Klebsiella in 25.0% and 20.5% and Staphylococcus aureus in15% and 12.8%, respectively, while other isolates were of Pseudomonas aeruginosa, E.coli, Acinetobacter, Candida, Bacillus cereus and Enterococcus.

Conclusion: Since almost one third of ventilated patient develop VAP, care has to be taken to ensure optimizing the number of endotracheal suctioning and minimizing the number of reintubation and number of attendants taking care of the patient.

P459

IMPACT OF PREVENTION ON HOSPITAL ACQUIRED ROTAVIRUS INFECTIONS IN BELGIUM

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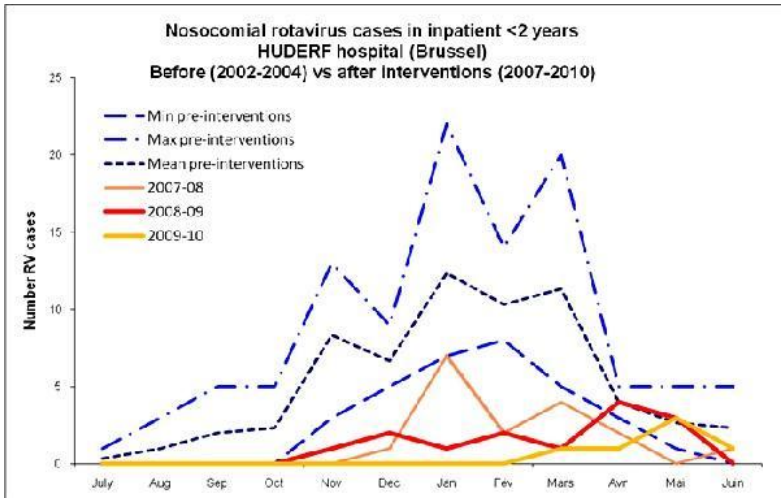
Background: Rotavirus is one of the most common cause of hospital-acquired (HA) infections in pediatric wards. Data on impact of hand hygiene education are scarce. And Moreover, virtually no data are available regarding rotavirus vaccine impact on HA rotavirus Infections (HARVI).

Aims and methods: We analysed the impact of
(1) improvement of hand hygiene compliance measured during 3 national campaigns starting in 2005 and
(2) rotavirus vaccine universal use, which started in October 2006 (with 88% coverage in 2007 in Belgium), on HA rotavirus incidence in a 30-beds infant ward in Brussels University pediatric hospital.
HARVI episodes were collected prospectively between 2002 and 2010. HA Rotavirus was defined as acquired after 48 hours admission or within 72 hours re-admission.
Results: Hand hygiene compliance significantly increased from 39.5% in 2005 to 53% in 2006 and reached 75.6% in 2009. The proportion of HARVI among RV gastroenteritis decreased up to 2006 (p=0.0002), then increased post-vaccination due to declining rotavirus incidence in the community. Impact of these combined interventions between 2007 and 2010 is presented in the Figure.
Conclusion: Our results show a dramatic decrease of HARVI infections after a multimodal intervention has been implemented involving hand hygiene campaigns and universal rotavirus vaccination. The reduction of rotavirus disease and seasonal pattern change is similar to what has been observed for community-acquired infections after universal vaccine introduction.



[HARVI cases before and after interventions]

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DAY OF INFECTION IN A NICU VERSUS SURVEILLANCE DATA

J. Christoph[1], F. Schwab[2], E. Kattner[1]

[1]Neonatology, Kinderkrankenhaus auf der Bult, Hannover, [2]Institute for Hygiene and Environmental Medicine, Charité-University Medicine, Berlin, Germany

Background: Surveillance systems for neonates provide data on pathogen frequency, device application and infection rates, subdivided into birth weight groups. An adjustment of infection rates by the day of life is possible in the surveillance system NEO-KISS.

Question: Is the temporal occurrence of device associated infections in our NICU different from the other departments in NEO-KISS -surveillance?

Methods: Surveillance data analysis of our NICU's Bloodstream infections (BSI) (N=136 BSI) and the NEO-KISS database (N=4572 BSI after deduction of our data) for the years 2005 - 2009 on the first day of sepsis, stratified by the devices CVC, PVC and none.

Results: The percentiles P25, P50 and P75 of the day of first CVC-associated infection in our NICU are significantly later than in the other surveillance participants (p = 0.001), in PVC this shift is not significant (p=0.087), whereas in premature infants without device the time course is nearly indistinguishable from the other units.

Device	institution	N	P25	P50	P75	p
total	NEO-ADB	4572	11	17	30	0,045
	ADB	136	12	18	39	
CVC	NEO-ADB	2132	11	16	25	0,001
	ADB	29	15	25	49	

[First day of sepsis]

The stratification into birth weight categories of < 500g to 1500g in 250g increments shows no significant birth weight dependencies.

Conclusion: In addition to unit-specific device utilization rates, the interval in time to the first day of an infection can indicate risk factors which should be observed.

P461

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INFECTION CONTROL IN HOSPITALIZED CHILDREN: CONCERNS OF OFF-LABEL PAEDIATRIC USE

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Paediatric medicines (PM) pose a challenge due to heterogeneity of the age groups and the difficult extrapolation between adults and children. Many medicines used in paediatric care are not authorized or are prescribed outside the product license (off-label) especially in hospitals where critically ill children are more exposed to several medicines. Our objective was to investigate the nature and extend of pediatric off-label use in infectious diseases treatment in Portuguese hospitals.

Methods: Cross Sectional observational and descriptive study in Portuguese hospitals. Survey to 109 hospitals on all existing uses of PM. Off-label use was defined as the utilization at an indication, dosage, frequency or route of administration different from the specifications in Summary of Product Characteristic.

Results: In total, 1031 medicines were reported for paediatric use from 23 out of 109 hospitals. 17.6% were antinfectives: 65.9% for systemic use and 13.2% antimycotics were the main classes. Amoxicilin and Clavulanic Acid was the medicine more frequently reported followed by Flucloxacillin. 24.4% of the total PM was used off-label and 30/252 (12%) were antinfectives being ciprofloxacin more frequently reported. 4.2% of the total PM were unauthorized.

Conclusion: Despite European and American initiatives promote awareness and research in the paediatric population, there is still off-label medicines use in infectious diseases treatment, underlining the need to stimulate scientific data collection by experimental studies or outcome research. Although off-label use is a complex issue and is not synonymous with inappropriate use, more efforts are needed to increase rational medicines use in children.

P463

INFECTION CONTROL PRACTICES AND MRSA DECOLONISATIONIN UNITED KINGDOM NEONATAL UNITS

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Prevention of nosocomial infection is a key part of good neonatal care. In particular, Meticillin resistant *Staphylococcus aureus* (MRSA) is an important pathogen with screening for colonisation now commonplace. There appear wide variations in infection control practices in UK neonatal units.

Aims: The aim of this survey was to determine the impact of infection control problems, and to evaluate the differences in infection control/hygiene practices.

Methods: We undertook a structured telephone interview of all neonatal units in the United Kingdom between July 2009 and February 2010. 198 Neonatal units were identified and 172 (87%) agreed to take part.

Results: 12.2% of units had been closed due to an infection control issue in the last year, of these, 48% were Level 3 units and 32% surgical units. 14.1% of units had a current infection control concern, of these, 36% were due to MRSA, 24% multi-resistant Gram negative organisms, and 20% viral infections. Surgical units were more frequently affected (40% vs 11.1%). There was a wide variation in the hygiene measures utilised (eg. surgical scrubs, aprons and gloves). There were also considerable differences in hand hygiene practices. Infants identified as colonised with MRSA were routinely decolonised in 73.8% of units. De-colonisation regimens varied with more than 15 different regimens. Degree of isolation after successful de-colonisation also varied.

Conclusions: Neonatal units in the UK are faced with significant infection control issues and there are considerable variations in infection control practices. There is a need to develop an evidence base to underpin practice.

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SEPSIS UPDATES IN NURSERY PGMI LRH PESHAWAR, KPK PAKISTAN

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Government of NWFP Health Deptt., Peshawar, Pakistan

Study was carried out in Nursery PGMI Lady Reading Hospital January 2009 -December 2009.

A major tertiary care hospital situated in Peshawar.

Aims and objectives:

1. The incidence of NNS in admitted to nursery patients.
2. The relative frequency in male compared to female.
3 outcomes of neonates with sepsis
4.To determine etiologic agents

Materials and methods: Hospital born, community patient included.. Detail history & physical examination done.
Cultures through aseptic techniques , with all precautions.
The patients comprises all neonates ,both sexes were included.
A random sample of community ,hospital born patients
Study design: Descriptive ongoing study .
Results: Out of total 3172 admissions 14.18 % (450) were confirmed cases of sepsis.
266 male, 184 female, male to female ratio being 3:2
Full term 370 (82 %), premature 80 (18 %),
Patient expired due to sepsis 155 (34.4 %).
Patient discharge 276 (61.33%).
Left against medical advice12 (2.66%)
Discharge on will 07(1.55%)
Escherichia coli found in 178 cases (39.5%),
Staphylococcus aureus with 119 cases (26.4%),
Pseudomonas in 103 cases (22.88%),
Klebsiella in 32 pts (7.11%) and
Proteus in 18 cases (4%).

comparison
Study
Incidence
Mortality
E.Coli/Gram -ve
S.Aureus/Gram+

Conclusions: Treatment of maternal infections, minimal handling of newborns and totally aseptic invasive procedures if needed.
Prompt institution of antibiotic therapy and supportive care will save most of the cases of neonatal sepsis.
Monitoring and keeping active records of neonates with sepsis.

P465

EXPERIMENTAL TRANSMISSION OF HEPATITIS B VIRUS BY TEARS USING MICE WITH CHIMERIC HUMAN LIVERS

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Background: Body fluids from HBV carriers such as saliva, semen, urine, sweat, and tears, are potential sources of HBV transmission. The infectivity of tears from HBV carriers was investigated.

Methods: Thirty-nine children and 8 adults (Age range, 0-47 years; median age, 9 years) who were chronically infected with HBV were enrolled. Of the 47 patients, 39 were positive for HBeAg. From the 47 patients, 19 urine samples, 38 saliva samples, 11 tear samples, and 9 sweat samples were collected. Real-time polymerase chain reaction was used for the quantification of HBV DNA.

Results: HBV DNA was detected in 73.7% (14/19) of urine samples, 92.1% (35/38) of saliva samples, 100% (11/11) of tear samples and 100% (9/9) of sweat samples. The levels of HBV DNA levels in the urine, saliva, tears, and sweat (mean ± SD) were 3.2 ± 1.9 log copies/mL, 5.4 ± 1.5 log copies/mL, 6.2 ± 0.7 log copies/mL, and 5.2 ± 0.6 log copies/mL, respectively. A statistically significant correlation was observed between HBV DNA in serum and that in saliva/tears ($r = 0.56$, $p < 0.05$). Tears from a child with chronic HBV infection were injected intravenously into two human hepatocyte-transplanted chimeric mice. One week after inoculation, both chimeric mice became positive for serum HBV DNA.

Conclusion: The levels of HBV DNA in tears from young children were high. Tears were confirmed to be infectious using the chimeric mice. Strict precautions should be taken against direct contact with body fluids from HBV carriers with highly viremia.

P466

HEALTH CARE-ASSOCIATED INFECTIONS DETECTED IN MARMARA UNIVERSITY HOSPITAL PEDIATRIC UNITS FROM 2008 TO 2010

C. Kuzdan[1], A. Soysal[1], G. Çulha[2], G. Altınkanat[3], G. Söyletir[3], M. Bakır[1]

[1]Pediatric Infectious Diseases, [2]Hospital Infection Control Comitte, [3]Microbiology, Marmara University Medical Faculty, Istanbul, Turkey

Objectives: Health care-associated infections (HCAIs) increase morbidity, mortality and costs. In developing countries, are seen more frequent of HCAI because of inadequate infrastructure. There is not enough data regarding the epidemiology of HCAIs of pediatric patients in Turkish hospitals. Owing to this we aimed to analyze the annual incidence and the antibiotic resistance patterns in our pediatric ward.

Materials and methods: All hospitalized patients in the pediatric ward were assessed with regard to HCAIs from 1st January 2008 to 1st November 2010. Data was prospectively collected according to standard protocols of the National Nosocomial Infections Surveillance System (NosoLINE).

Results: During the study period of three years 16.5% of all hospitalized patients developed HCAIs. The most frequent HCAIs were urinary tract infection (UTI) (29.3%), bloodstream infection (27%), pneumonia (21%). While the most frequent agent isolated from UTI were *Escherichia coli* (26%), the most common agent is *S. epidermidis*(30.4%) for bloodstream infections. Vancomycin resistance was found in 73.3% of all *Enterococcus faecium* strains. Production of extended-spectrum β-lactamase was detected 58.3% of *Klebsiella pneumoniae* and *Escherichia coli* isolates.

Conclusion: HCAI surveillance is important to provide the basic data with regard to determination of HCAI rate, treatment and prevention of HCAIs.

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P468

THE USE OF ROUTINE HOSPITAL DATA TO MEASURE NOSOCOMIAL INFECTION RATES IN PAEDIATRIC UNITS AND ASSESS TRENDS OVER TIME

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[1]Paediatric Infectious Diseases Unit, [2]Department of Clinical Microbiology, St. George's Hospital, London, UK

Background: Hospital-acquired infections are associated with significant morbidity and mortality, but validated criteria for measuring nosocomial infection rates have not been established.

Objectives: To assess the use of routine hospital data to measure nosocomial bacteraemia rates between the neonatal and paediatric units in a London tertiary hospital and to assess trends over time.

Methods: The Microbiology Department at St. George's Hospital uses a standard pro-forma to document clinically significant bacteraemia. Nosocomial bacteraemia was diagnosed if the blood culture was taken ≥72 hours after hospital admission in a child with clinical and/or laboratory features of infection.

Results: Of all the routine hospital data assessed, number of discharges was the most consistently available parameter for the 9-year period (2001-09). During this time, although the number of nosocomial bacteraemia episodes were similar for neonatal (n=254) and paediatric (n=224) units, nosocomial infection rates were 11.6-fold (95% CI, 9.8-13.9) higher for the neonatal unit (5.8 vs. 0.50/100 discharges, respectively). Analysis of trends revealed a significant reduction in nosocomial bacteraemia rates between 2001 and 2009 for both the neonatal unit (7.8 to 2.5 episodes/100 discharges) and the paediatric wards (1.2 to 0.4 episodes/100 discharges), which were mainly related to a decline in venous catheter-related staphylococcal bacteraemia following the introduction of new catheter care policies to reduce the burden of MRSA infections.

Conclusions: Hospital discharge rates provide an effective method for measuring nosocomial infection rates within hospital units and over time, and, after adjusting for case mix, could be use to compare rates between hospitals.

P469

EPIDEMIOLOGY AND CLINICAL CONSEQUENCES OF EXTENDED SPECTRUM BETA LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACEAE IN A PAEDIATRIC HOSPITAL

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[1]ULB-Huderf, [2]CHU-Brugmann, [3]CHU-Tivoli, Brussels, Belgium

Background and aims: The prevalence of extended spectrum beta-lactamase producing gram negative pathogens (ESBL-GN) is increasing worldwide. Few data have been published on ESBL in paediatrics. We describe the clinical epidemiology of children colonised and/or infected with ESBL producing strains in a 170-beds paediatric teaching hospital.

Material and methods: Patients with ESBL producing GN were recorded prospectively by the infection control team. Epidemiological and clinical data were completed retrospectively for the years 2006-2009. Our results were compared with a previous study performed between 2003 and 2005 in the same hospital.

Results: 394 children (aged 0-18 years) were colonized and/or infected by an ESBL-GN during the study period (154 in 2009 compared to 53 in 2003). 232 (59%) were already ESBL positive on hospital admission (versus 44/142 (31%) for the years 2003-2005); 203 (52%) were from North Africa. 283 (72%) stayed in PICU. 63 patients (16%) presented 67 infections with an ESBL-GN. UTI were the most frequent infections (54% in our study, compared to 3/17 (18%) in 2003-2005; p=0.008); there were 13 pneumonia and 8 bloodstream infections. No child died from an ESBL infection. 487 different ESBL-GN organisms were isolated from the 394 children during the study period : *E. coli* increased from 16/53 (30%) in 2003 to 86/154 (56%) in 2009 (p=0.001).

Conclusion: Number of ESBL-GN has been increasing since 2003. UTI became the most common ESBL-GN infection, associated with a change in ESBL-GN pathogens distribution, predominantly an increased frequency of ESBL positive *E coli*.

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METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* INFECTION AND COLONISATION IN PEDIATRIC OUTPATIENTS

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Background and aims: Screening for colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) represents the key aspect of infection control, for limiting the spread of this organism. The aim of our study was to determine the prevalence of MRSA, isolated from paediatric outpatients, and their associated resistance patterns.

Methods: We collected 18115 pathological samples from paediatric outpatients from Timisoara (Romania) during April 2009 - June 2010. Identification of germs and extensive antimicrobial tests (by dilution antimicrobial susceptibility tests) were performed with the help of the automatic Vitek2 System (bioMerieux France), using Vitek 2 GP and Vitek 2 AST P594 cards.

Results: We isolated 2514 microbial strains, from which, 404 strains were *Staphylococcus aureus,* respectively, 26,48% (107 strains) MRSA. All these MRSA strains associated other resistance phenotypes (amynoglicosides, fluoroquinolones, etc.). Most of the patients (91,58%) were colonised with MRSA (isolated from nasal swabs), only 9 patients (8,42%) being infected (with MRSA isolation from sputum, wound secretions, pus, throat swabs, conjunctival discharges, ear discharges).

Conclusions: The high prevalence of incidence in MRSA, implies a rational policy in prescribing antibiotics.

Acknowledgments: These data are part of the PNII 42121 project: “Molecular characterization of multidrug resistant strains, hospital or community acquired, collected from south-west Romania”.

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NOSOCOMIAL ROTAVIRUS GASTROENTEROCOLITIS IN A LARGE PEDIATRIC HOSPITAL IN WARSAW, 2006-2009

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Background and aims: Rotaviruses are the leading cause of community-acquired and nosocomial gastroenterocolitis in children. There is little data concerning the epidemiology of nosocomial rotavirus gastroenterocolitis (NRVG) in Central European countries, including Poland. The aim of our study was to analyze the epidemiology of NRVG in a large tertiary hospital in Warsaw.

Material and method: We analyzed retrospectively data of 49 697 children aged 0-18 years hospitalized in period 2006-2009. NRVG was defined as acute gastroeneterocolitis (> 3 loose, or looser-than normal, stools in 24 hours and/or vomiting), confirmed with rapid immunochromatographic test (BioMaxima, Poland), if symptoms developed > 48 hours after admission.

Results: The total number of 469 cases of NRVG was diagnosed. The cumulative attack rate of NRVG was calculated 0.97% (CI 95% 0.86-1.02), the cumulative incidence density was 2.07/1000 bed-days (CI95% 2.01-2.13). The mean proportion of NRVG among all rotavirus infections was 23.9% (CI 95% 22.03-25.81). The highest rates of NRVG were noted at wards where the mean duration of hospital stay was longer than 5 days. 67.5% cases of NRVG were diagnosed in the autumn and winter period, 71% children with NRVG were younger than 2 years, the mean age of a patient with NRVG was 16.2 months. The mean duration of hospital stay of children with NRVG was longer than the average duration of hospitalization (11.5 vs. 4.5 days, p< 0. 01).

Conclusions: Our study showed a relevant incidence of NRVG, which can prolong the children's hospital stay and increase costs.

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HOSPITAL-ACQUIRED ROTAVIRUS GASTROENTERITIS (HARVGE) AT THE UNIVERSITY CHILDREN'S HOSPITAL OF NORTHEASTERN POLAND: A 5-YEAR RETROSPECTIVE STUDY

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Background and aims: In Poland like in other developed European countries HARVGE is considered a great economic and health problem. The aim of this study was to assess the incidence of community- and hospital-acquired rotavirus infections in children hospitalized at the University Children's Hospital in Bialystok, Poland. The voluntary, chargeable rotavirus vaccination has been used in Poland since autumn 2006 year. Vaccination coverage in our region rose from 1.1% in 2007 to 11.3% in 2009.

Methods: Retrospective analysis of data obtained from the hospital statistics and Nosocomial Infection Control Team dataset was performed for the years 2006 - 2010. All children discharged with first-line diagnosis of RVGE (ICD code: A08.0) and children infected with rotavirus while hospitalized were recorded.

Results: In the whole study period, 1053 out of 97237 (1.1%) hospitalized children were diagnosed with RVGE. In 722 out of 1053 cases (68.6%) the rotavirus infection was community-acquired (CA) whereas 331 (31.4%) of children were infected while hospitalized. The highest HARVGE incidence rate per 1000 patient-days was recorded in 2009 - 1.18, the lowest in 2006 - 0.68. Sporadic and outbreak HARVGE cases have occurred in all hospital units with the highest frequency (45%) in the Department of Paediatrics, Allergology and Gastroenterology. 73.7% of children with HARVGE vs 54.6% with CARVGE were aged < 2 year ($p < 0.05$).

Conclusions: HARVGE constitutes a challenge for Nosocomial Infection Control Teams in children's hospitals. The universal RV vaccination could reduce HARVGE and should be considered in cost-effectiveness analyses in Poland.

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AN EPIDEMIOLOGICAL STUDY OF COAGULASE-NEGATIVE STAPHYLOCOCCI ISOLATES DEMONSTRATING HOSPITAL-ACQUIRED INFECTION

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Introduction: Coagulase-negative staphylococci (CoNS) are recognized as the most frequently isolated organisms from blood cultures. *Staphylococcus epidermidis* has been the dominant species. The high prevalence of this infection on neonatal unit of our hospital led us to look for cross infection by typing the blood culture isolates from these patients. The staff were also examined to see if they acted as a reservoir

Methods and materials: One hundred two isolates of CoNS were obtained from cultures of blood from premature neonates. The species of the isolates were determined by biotyping methods, susceptibility was measured by the agar diffusion method, and PFGE was performed with 0.9% agarose gels in Tris-borate-EDTA buffer.

Results: Among the neonates there were 89 episodes of CoNS bacteremia in 55 patients. The distribution was 75.3% *S.epidermidis.* Susceptibility testing demonstrated that 35 isolates were resistant to penicillin, ampicillin, methicillin, netilmicin and gentamicin, while they were sensitive to ciprofloxacin, erythromycin, fusidic acid, rifampin, and vancomycin. PFGE applied to the isolates of *S. epidermidis* generated two clusters of isolates (type A and type B) on the neonatal ward. Staff screening identified PFGE type A isolates on the hands of four nurses and two doctors from the neonatal ward. PFGE type B on the hands of two nurses.

Discussion: PFGE demonstrated two clusters of isolates of S. epidermidis (type A and type B) on the neonatal ward. Combining the results confirmed cross infection. Types A and B concurrently isolated from the hands of the staff of the appropriate unit.

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EVOLUTION OF AN EPIDEMIC OUTBREAK OF *SERRATIA MARCESCENS* IN A THIRD LEVEL NEONATAL INTENSIVE UNIT

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Introduction: *Serratia marcescens* is a cause of serious nosocomial infections in Neonatal Units. Its incidence as an opportunistic pathogen has been documented in recent years, causing outbreaks.

Objectives: To describe an epidemic outbreak of *Serratia marcencens* derived from an index case in a third level Neonatal Intensive Care Unit (NICU).

Methods: Setting: 8 intensive care and 12 intermediate care unit at University Hospital Joan XXIII of Tarragona (Spain). Follow-up period: December 2009 (diagnosis of index case) - January 2011. Prospective surveillance control was conducted with weekly collection of rectal swabs for detection of colonization and infection reporting. An environmental microbiological study was done to detect the original source of cases.

Results: The index case was a premature newborn with an early diagnosis of sepsis by *Serratia marcescens*. 29 infants with positive culture of stools were detected in the period from January to October 2010. Prevalence of infection was 30.8%: 2 bacteraemia (6.8%), 2 urinary tract infection (6.8%) and 5 conjunctivitis (17.2%). No new cases were detected in the last 2 months. Environmental microbiological study was negative. In a first phase, contact isolation of cases was implemented as a prophylactic measure and a cohort of cases was followed-up. Despite of these measures the outbreak was not controlled. Universal contact isolation was necessary with an update of the procedures applied to staff and parents.

Conclusions: The probable cause of this outbreak was due to contact transmission. The implementation of universal contact isolation by professionals and relatives was proven as very effective.

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NOSOCOMIAL INFECTIONS IN GENERAL PEDIATRIC WARDS OF A TERTIARY CARE HOSPITAL IN TURKEY

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Background and aims: The aim of this study is to determine the prevelance, type and clinical features of nosocomial infections (NIs), etiological distribution and antibiotic resistance patterns of responsible organisms in hospitalized children at general pediatric wards in a three-year period.

Methods: Nosocomial bacterial infection episodes of 1 month-18 years old patients between 2005 to 2008 were evaluated retrospectively. The Hospital Infection Control Committee (HICC) NI surveillance reports for the study period were used as database. Nosocomial infections were defined on the basis of Center of Disease Contol (CDC) criterions.

Results: Nosocomial infection was detected 171 (2.25%) of 7594 hospitalized patients. Some of these patients experienced more than one episode, so total NI episodes were 229. Patients age varied in 1-144 months olds (14.5 ±23.6 months). Nosocomial infections were diagnosed in 3-180 days of hospitalization (19.2 ±21.5 days). Nosocomial infection rate was 3.02%, NI density 3.17/1000 patient day. The frequency of NI's were respiratory system infections (49.8%), blood stream infections (21%) and urinary tract infections (20%). Nosocomial infection rate was inversely proportional to the age. The majority of NIs (88%) was seen in patients younger than 2 years old. Gram negative microorganisms were more frequently isolated (79.8%) than gram positive microorganisms. We found that 27.5% of patients with NI died.

Conclusions: High mortality rate in our patients was considered to be due to not presence of pediatric intensive care unit for critically ill patients, common association of concomitant diseases, high rate of mechanical ventilation use and invasive Pseudomonas aeruginosa infections.

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WHETHER THERE IS A DIFFERENCE OF CNS IN NEONATAL CENTRE AND IN MATERNITY HOSPITALS?

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Background and aims: CNS (coagulase negative staphylococci) have emerged over recent years as etiologic agents in a series of infections of the newborns. Neonatal center and maternity hospitals deal with infants with different status of health. The aim of this investigation was comparison of the species and strains of CNS caused the infections of the newborns in Kulakov scientific centre for obstetrix, gynecology and perinatology of Moscow (SCOGP) and in the maternity hospitals (MH) of Nizhniy Novgorod.

Methods: For identification of 102 CNS isolates we used sequencing of *tuf* and *gap* genes fragments. Multilocus sequence typing (MLST) scheme of Thomas J.C. et al. was applied for S. epidermidis strains differentiation. For distinguishing S. haemolyticus strains we developed MLST scheme, including *mvaK*, *rphE*, *tphK*, *gtr*, *arcC*, *tpiA*, *aroE* genes.

Results: 5 CNS species were detected both in SCOGP and MH. One more species *S. capitis* was isolated from hospital environment in MH. *S epidermidis* was most frequently isolated in SCOGP and *S. haemolyticus* - in MH. Some of *S. haemolyticus* strains were isolated from children with clinical evidence of pneumonia.

From 24 revealed ST (sequence type) of *S epidermidis* ST59 was isolated as in SCOGP so in MH. 11 ST were detected for *S. haemolyticus*. All *S. haemolyticus* ST were closely related.ST3 was isolated in four MH. ST5 и ST11 circulated in SCOGP four month.

Conclusions: Neonatal centre with intensive therapy and MH differed in species compositions and strain ST of CNS - etiologic agents of infections of the newborns.

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BACTERIAL CONTAMINATION OF INTENSIVE CARE UNITS (NICU) AND DETERMINATION OF ANTIBIOTICS RESISTANCE PATTERNS IN ISOLATED BACTERIA IN HAMADAN HOSPITAL

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Background and aim: Bacterial contamination in hospitals is one of the major problems in hospitals that cause serious damage to human and society. The aims of this study was the evaluation of bacterial contamination of intensive care units (NICU) and determination of antibiotics resistance patterns in isolated bacteria in Fatemihe hospital , west of Iran.

Methods: This was a cross-sectional study that 400 samples were randomly collected from environments and apparatus of neonatal intensive care units of Fatemihe hospital in Hamadan. The places which were tested were washing sink, floor of wards, beds of patients, suction, oxygen mask, incubator, infant scale and staff fingers. The samples were inoculated into EMB and Blood agar by sterile wet swabs and transferred to medical laboratory for identification. Strains were tested for antibiogram by NCCLS protocol. The antibiotics disks were consisted of: ampicillin, imipenem, ceftriaxone, ceftizoxime, erythromycin, vancomycin, gentamicin, cephalexine, cefepime and ciprofloxacin.

Results: The average rate of bacterial contamination of NICU of was 79.5%. The most contaminated places were washing sink (98%), suction (74%) and the lowest was oxygen mask (44%). The most bacteria isolated were as follow: *Staphylococcus epidemidis* (17%), *Bacillus subtilis* (12.5%), *Acinetobacter baumannii* (11.3%) and *E. coli* (8.2%). Most of isolates (60%-90%) were sensitive against imipenem, ceftriaxone, vancomycin, cefepime and ciprofloxacin, whereas most of them were resistant to ampicillin, gentamicin, erythromycin and cephalexine.

Conclusion: Our results showed the considerable bacterial contamination (79.5%) of NICU in particular with *Acinetobacter baumannii* and the high drug resistance in strains isolated from Fatemihe hospital.

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PREDICTING BACTEREMIA IN CHILDREN WITH CANCER AND FEVER IN CHEMOTHERAPY-INDUCED NEUTROPENIA. RESULTS OF THE PROSPECTIVE MULTICENTER SPOG 2003 FN STUDY

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Aim: To develop a score predicting the risk of bacteremia in pediatric patients with cancer and fever in neutropenia (FN), and to evaluate its performance.

Methods: Pediatric patients with cancer presenting with FN induced by non-myeloablative chemotherapy were observed in a prospective multicenter study. A score predicting the risk of bacteremia was developed from a multivariate mixed logistic regression model. Its cross-validated predictive performance was compared to that of published risk prediction rules.

Results: Bacteremia was reported in 67 (16%) of 423 FN episodes. In 34 (8%) episodes bacteremia was known only beyond reassessment after 8-24 hours of inpatient management. Predicting bacteremia at reassessment was better than prediction at presentation with FN. A differential leukocyte count did not increase the predictive performance. The reassessment score predicting future bacteremia in 390 episodes without known bacteremia used four variables: hemoglobin ≥90 g/L at presentation (weight 3), platelet count < 50 G/L (3), shaking chills ever observed (5), and other need for inpatient treatment or observation according to the treating physician (3). Applying a threshold ≥3, the score - simplified into a low-risk checklist - predicted bacteremia with 100% sensitivity, with 54 (13%) episodes classified as low-risk, and a specificity of 15%.

Conclusions: This reassessment score, simplified into a low-risk checklist of four routinely accessible characteristics, identifies pediatric patients with FN at risk for bacteremia not yet known. It has the potential to contribute to reduction of antimicrobials, and to shortening of hospitalizations in pediatric patients with cancer and FN.

P480

VISCERAL LEISHMANIASIS REVEALING CHRONIC GRANULOMATOUS DISEASE IN AN INFANT

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Objective: To report a case of an infant with disseminated leishmania Donovani (LD) and Chronic Granulomatous Disease (CGD).

Method: Retrospective report of the data on a six months old infant who presented with multiple skin lesions and fever since second week of life.

Result: He had indolent fever since the second week of life associated with skin lesions on the face, neck and the limbs. He came from an area where both visceral and cutaneous leishmaniasis is an endemic disease. Skin biopsy showed leishmania Donovani bodies and the culture revealed Staphylococcus aurous and serratia marssisinse on two different occasions. His immune work up confirmed CGD and living related bone marrow transplantation was successful but complicated with cerebro vascular accident.

Conclusion: Although few case reports had been reported regarding this subject but up to my knowledge this is the first case to be reported in infant with CGD and disseminated VL. As the prognosis of CGD is poor, with high morbidity and mortality and infantile leishmaniasis also adds on high rate of morbidity and mortality if not treated early. Establishing an early diagnosis has important practical implications in the successful treatment of these patients. The description of this case and a brief review of the current literature are provided to familiarize physicians mainly in the endemic areas with the relatively rare presentations of these tow conditions together.

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EVALUATION OF *PNEUMOCYSTIS JIROVECI (CARINII) (PCC)* PROPHYLAXIS AMONG PEDIATRIC ONCO- HEMATOLOGIC PATIENTS: ARE ALTERNATIVE REGIMENS REALLY JUSTIFIED?

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Background: Although Trimetroprim-Sulfamethoxazol (TMP-SMX) is the recommended first line agent for PCC prophylaxis, the use of alternative regimen seems to increase.

Objective: Assessment of the use and the relevance of alternative regimen for PCC prophylaxis in a pediatric onco-hematology centre.

Methods: We retrospectively reviewed regimen for PCC prophylaxis in 2000, 2005 and 2010. The medical charts of patients not receiving TMP-SMX were reviewed to determinate the relevance of the use of an alternative regimen. An alternative regimen was considered as justified in cases of TMP-SMX allergy; intolerance; elevation of LFT; neutropenia. When TMP-SMX had been discontinued for neutropenia, it should have been reintroduced since the patient received 100% of the chemotherapy dosage on time (LAL and solid tumor), and 3 months after resolution of the neutropenia (HSCT).

Results: Among the 544 patients on PCC prophylaxis, 135 (24.8%) received an alternative regimen. It represented 11% of the cases in 2000, 26% in 2005 and 33% in 2010. The reasons involved for not using TMP-SMX were neutropenia 48.9%, allergy 19.2%, intolerance 11.8%, elevated LFT 5.9%, and others 14.1%. According to our criteria, the decision of delivering an alternative prophylaxis for PCC was justify for 93 patients (69%).

Conclusions: An increase use of alternative prophylaxis for PCC was observed in the children treated for cancer in our institution. This practice was justified for only 69 % of the cases. Clinicians should be aware that a more effective agent (TMP-SMX) should be given as first line therapy or reintroduced systematically when clinically permitted.

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ACTINOMYCES AND NOCARDIA INFECTIONS IN CHRONIC GRANULOMATOUS DISEASE

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Objective: We presented in the retrospective review of medical records, the etiology, presentation, clinical characterístics the infections detected, predisposing condition and outcome of nocardiosis and actinomycosis involved in a group of pediatric patients diagnosed with CGD.

Material and methods: The material for investigations was collected from scrapings, crusts, pus from subcutaneous abscesses or exudation from sinus tracts, surgical debridement and biopsy specimens. The microbiological diagnosis was determined by biochemical tests, histology, microscopy, and culture of clinical samples.

Results: The medical records of 12 diagnosed CGD patients with suspected nocardiosis or *actinomycosis were reviewed. One patient was diagnosed with actinomycosis and one* patient with nocardiosis.

Patients consisted of 7 males and 5 females with ranging ages of 3 to 18 years. Nocardiosis and actinomycosis isolated in the two patients were confirmed by histology and culture methods. Neutrophil oxidative burst were absent (NBT=0) in both patients. The most common manifestations of CGD due to fungal infections, actinomycosis, and nocardiosis were osteomyelitis (42.8%), pulmonary infections (28.6%), lymphadenopathy (14.3%) and skin involvement (14.3%) during their illness.

Conclusion: Nocardiosis and Actinomycosis in children indicate the need for evaluation for an underlying immunological deficiency. Early diagnosis remains critical for decreased morbidity and occasional mortality. Physicians caring for patients with CGD should maintain a high index of suspicion for nocardiosis and actinomycosis especially if work up for TB and fungal infections are negative.

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VARICELLA ZOSTER INFECTION IN A BOY TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTING WITH SUBMANDIBULAIRY GLAND SWELLING AND SEPTIC SHOCK

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Varicella Zoster Virus infection (VZV) is a potential life-threatening complication in immunosuppressed hosts with often an atypical presentation.

We present a 7 years old boy treated for acute lymphoblastic leukemia with a rather peculiar presentation of VZV infection.

He presented with acute bilateral submandibular salivary gland swelling. Three days later he was admitted with high fever and septic shock. At this time he had several small macular leasions. After 2 days he developed a generalized maculopapular rash, with crusted papules but no vesicles, typical for varicella primo infection. Blood tests showed a severe neutropenia and lymfopenia as well as hypogammaglobulinemia. There were signs of hepatitis with elevated levels of LDH, AST, ALT, gamma GT and ferritin. A PCR swap of his tear-film was positive for VZV. Central nervous system liquid was negative by PCR for VZV. All bacterial cultures remained negative. IgM en IgG for Varicella are being determined.

At diagnosis IgG for VZV was positive . Notably, the patients sibling had developed VZV 3 weeks earlier. Treatment with aciclovir was initiated promptly when the skin leasions appeared leading to a fast improvement of the clinical signs.

Conclusion: VZV reactivation and reinfection is a potential life threatening event in immunocompromised children. Treatment with aciclovir needs to be initiated as soon as possible. This patient had an atypical presentation with salivary gland swelling and septicemia as presenting symptoms, making the diagnosis difficult.

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EXPERT OPINION REGARDING IMMUNE RECOVERY AND INFECTION PROPHYLAXIS FOLLOWING STEM CELL TRANSPLANTATION (SCT) -- SURVEY AMONG EBMT-WPIE AND WPPD MEMBERS

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Background: ´Recovery of immunity´ after SCT remains poorly defined. In clinical practice, physicians are left with many uncertainties, such as when to stop infection prophylaxis and when to allow different outdoor activities. It is unclear how decisions on these issues are affected by the actual immune status.

Methods: Through an internet survey amongst pediatric SCT units in Europe, we are collecting expert opinion. The survey consists of 5 actual cases covering the whole spectrum of SCT and showing data on immune recovery during the first year after SCT. 377 transplant physicians have been invited.

Preliminary results: Until now, 90 physicians (24%) have started and 35 (9%) have completed the survey. Prophylaxis was either started early after SCT or not started at all. There is little agreement on when to supply IVIG. In general, prophylaxis is stopped towards the end of the first year. The diversity in policy increases progressively in difficult cases, especially regarding stopping anti-fungal prophylaxis. A majority will allow various outdoor activities, mostly in week 26 or week 52 post SCT; being generally later in severely immunocompromised cases. There is least agreement on outdoor play. Most physicians disallow travel abroad in all but an uneventful course post SCT.

Conclusions: There are profound dissimilarities in certain areas of preventive measures following SCT, presumably because of differences in interpretation as to when immunity has recovered. This indicates a need for further supplementary guidelines.

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LUNG BIOPSIES IN CHILDREN WITH CHRONIC GRANULOMATOUS DISEASE ASSESSED FOR HAEMATOPOIETIC STEM CELL TRANSPLANT

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Background & aims: Chronic Granulomatous Disease (CGD) is a rare primary immunodeficiency predisposing to infection, inflammation and chronic lung disease with abnormalities on high resolution computerised chest tomography (HRCT). Haematopoietic stem cell transplant (HSCT) is curative, however, pre-existing infection is associated with poorer outcome. Identifying pre-existing infection is important but can be difficult.

This study reviewed diagnostic yield of open lung biopsy in these patients.

Methods: A retrospective review of children with CGD evaluated for HSCT between 01/01/2006 - 31/12/2010. Case notes and electronic records were reviewed. Chest radiographs (CXR) and HRCT image abnormalities were documented. Histological and microbiological results from biopsies and following management were recorded.

Results: 20 children (19 male) underwent assessment, median age 7.4 years (range 0.3 - 17.5 years). 9 (45%) CXR and 10 (50%) HRCT were abnormal. 5 (25%) had open lung biopsy, all had imaging abnormalities.

Microscopy demonstrated granulomatous inflammation in 4 and inflammatory pneumonitis in 1. Burkholderia cepacia was cultured in one case. No fungi were identified.

2 were treated for fungal infection despite biopsy results. One who didn't undergo biopsy had fungal infection identified from broncho-alveolar lavage. One child with abnormal imaging but no biopsy went on to develop disseminated fungal infection post HSCT.

Conclusions: Open lung biopsy has a role in children with abnormal imaging about to undergo HSCT for CGD. Careful liaison between disciplines is necessary to ensure maximum information is extracted from biopsy material. Results should be interpreted in the context of clinical and other investigation findings.

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PULMONARY AND ABDOMINAL TUBERCULOSIS IN ADOLESCENT WITH HIV-HBV COINFECTION

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Diagnosis and treatment of tuberculosis in patients with HIV-HBV coinfection is a challenge for the physician, particularly choice and timing of HAART because of the risk of Immune reconstitution inflammatory syndrome. A 17 years old black female, was admitted 5 days after arrival in Italy with cough, fever and deterioration of general conditions. She underwent laboratory studies, abdominal ultrasound, CT - scan, MRI and laparoscopy with omental biopsy. Laboratory studies showed a Leucopenia with WBC at 2780/mm3 (N 38.8%, L 51.8%), HIV-RNA 5.339.330 copies/ml, CD4 = 87 cells/ul (8 %), HbeAg pos, HbeAb neg, HbsAg pos, HBV-DNA 528.000.000 UI/ml. Abdominal and pelvic MRI showed peritoneum thikening, tubercolosis nodules in liver, on both glutei, right ovarian turbercolosis abscess and groin bilateral linfoadenopathy. On pulmonary CT scan there were thikening of the lingula, with wide-spread and pre tracheal linfoadenopathy. Culture on omental biopsy, and urine were positive for Mycobacterium tubercolosis. Test of drug resistance for HIV did not show resistance. Standard TB regimen was started (INH+RIF+ETB+PZA). Eight weeks later the patient was in stable clinical condition, without side effects to TB therapy, so HAART regimen was started with efavirenz+emcitrabine+tenofovir. After 6 months of TB therapy and 4 months of HAART : HIV-RNA 540 copies/ml, CD4 260 cells/ul (16%) HBV-DNA: 102.080.000 UI/ml, improvement of tubercular lesions on imaging. Tuberculosis can be associated with HIV in patient coming from high endemic areas. In TB infection HAART must be delayed to avoid IRIS. The choice of antiretroviral drugs should considered the presence of coinfection HIV-HBV.

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INTERFERON A TREATMENT OF MOLLUSCUM CONTAGIOSUM IN TWO BOYS WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Molluscum contagiosum is due to pox virus; this cutaneous infection is frequent and usually benign and not extensive in children in good health.

In the case of immunodeficient patients incidence is higher, and infection may be more severe. Recently in our unit, two 6 and 10 years old boys developed aggressive molluscum contagiosum during their chemotherapy for acute lymphoblastic leukaemia. They were in maintenance phase and received maximal tolerated doses of oral purinethol and methotrexate. These two children presented widely disseminated and very inflammatory skin and mucous membranes infection particularly of the anogenital region. Molluscum contagiosum was considered too extensive to benefit from conventional local therapies such as curettage or cryotherapy. Decision was taken not to stop maintenance treatment during several weeks and both patients were treated with systemic Interferon α (3 million units subcutaneously three times a week). This treatment enable considerable improvement of molluscum contagiosum in a short time. Subcutaneous interferon α was well tolerated without adverse effect; duration of interferon therapy was respectively 7 and 4 weeks. Later there was no recurrence despite continuating oral chemotherapy. These boys are still in complete remission.

Interferon α treatment seems to be a well tolerated alternative treatment for aggressive molluscum contagiosum infection in immunodeficient children.

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RISK FACTORS FOR STAPHYLOCOCCUS AUREUS INFECTIONS IN SMALL BOWEL TRANSPLANT RECIPIENTS

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Background: Data is lacking on risk factors for *S. aureus* (SA) infections in small bowel transplant (SBT) recipients.

Methods: SBT recipients with SA infections (22 cases) were retrospectively identified and compared to age, gender and transplant-type matched (1:2) non-SA infected recipient (44) controls. Wilcoxon rank-sum, chi-square or Fisher's exact tests and regression analysis were performed.

Results: The baseline characteristics are presented below:

Variables	Cases (N=22)	Controls (N=44)	p-value
Male(%)	63.64	52.27	0.38
Age,median	2.1	2.1	0.9
Tacrolimus(%)	100	100	
MMF(%)	0.00	15.91	0.09
CMV sero-mismatch	36.36	13.64	0.05

[Table 1]

There was a difference with regard to CMV sero-status (p=0.05). 36.36% infections were caused by MRSA. The sites of infections and time to infection are described below:

Sites	Number of infections	Mean time to infection (days)	Standard deviation	p-value
Surgical site	6	40.33	30.71	0.02
Blood/catheter	9	139.44	133.58	
Lung/pleura	7	248.66	89.71	

[Table 2]

By univariate analysis, cases were more likely to have CMV sero-mismatch (OR=4.0[1.03,15.6];p=0.046), lower tacrolimus level (0.84[0.69,1.03];p=0.09) and mycophenolate mofetil (0.1[0.001,0.94];p=0.043) compared with controls. By multivariate analysis, CMV sero-mismatch increased the odds of SA infection by 4 times (p=0.046), adjusting for matched criteria.

Conclusion: CMV sero-mismatch was an independent risk factor associated with SA infections after SBT.

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INFLUENZA-ASSOCIATED MORBIDITY IN CHILDREN WITH CANCER: EXPERIENCE AT THE UNIVERSITY CHILDREN'S HOSPITAL MÜNSTER

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Background: Influenza is an important cause of respiratory tract infections. Little data exist on its impact on immunocompromised children with cancer and/or HSCT.

Methods: Cases of laboratory-documented influenza infection in patients receiving care at the Department of Pediatric Hematology/Oncology between September 2005 and March 2010 were identified by review of laboratory and medical records.

Results: 26 patients (m, 18; f, 8) had 29 episodes of influenza, of which 3 were nosocomially acquired. The median age at diagnosis was 8.5 years (range, 2 - 18). There were 15 episodes of seasonal influenza A, 7 of new influenza A (H1N1; all in 2009), and 7 of influenza B infection. The majority of pts (n=23) had haematological malignancies or bone marrow failure; 6 of the pts were post allogeneic HSCT and received immunosuppressive therapy. The most frequent symptoms were cough (n=29), fever (n=27), malaise (n=15), and vomiting and diarrhea (n=6). Eleven of the 29 episodes (38%; two ICU admissions) resulted in hospital admission (median length of stay: 6 days; range: 1 - 43). In 11 of 23 episodes in pts receiving antineoplastic chemotherapy, anticancer treatment was delayed for a median of seven days (range, 4 - 38).Twelve of 29 influenza-episodes were treated with antiviral agents. Outcome was ultimately favourable in 27 episodes but two pts died from respiratory causes in association with influenza (influenza B; oseltamivir resistant new influenza; 6.8%).

Conclusions: Influenza in children with cancer and/or HSCT may cause significant morbidity resulting in excess hospitalization, delays in anticancer treatment, and infectious mortality.

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SIGNIFICANT CLINICAL PARAMETERS TO DETECT BACTEREMIA IN THE SETTING OF FEVER WITH OR WITHOUT NEUTROPENIA AMONG PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS

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Background and aims: Bloodstream infections are major concern in hematology-oncology patients. Our aim was to identify clinical predictors for bacteremia in febrile children with cancer.

Methods: As a part of a study to evaluate the role of 16SrRNA to detect bacterial pathogens in blood cultures (BC), (9/2004-11/2005) clinical parameters were prospectively collected including demographic, clinical, CVC status, previous bacteremia, and neutropenia.

Results: BC were positive in 21/115episodes (18.3%), 3/11 (27.3%) in infants < 1 y, 4/24 (1-5 y) and 14/80 (17.7%) in children age 5-18 y. 24.2% with tunneled catheters vs. 9.1% with Portcath, (P= 0.046). Predictors of bacteremia included ≥2 previous episodes of bacteremia vs. 0-1 previous episodes (5/11 vs. 16/104 respectively, p=0.028), shivering in 8/ 17 (47.1%), slightly higher T^0 , ($39.2C^0$ ± 0.7, vs. 38.9 C^0± 0.7, CVC duration (7.1± 7.8 vs. 4.2± 5.6 months, p, 0.05). Bacteremia was comparably common in neutropenic and non neutropenic patients (8/46 vs. 13/69 P=0.1). There were 10/51 (19.6%) with hematological malignancies, 5/54, (9.3%) solid tumors and 13/55 (23.6%) following BMT. A simple regression model may predict bacteremia in 85.7% of cases using few significant variables: previous bacteremia, Chills, and Hickman/Broviac. P value OR, CI 95 were respectively: (0.023, 5.7, 1.26-25.4), (0.003, 6.25, 1.8-21.1) and (0.05, 3.1, 1.0-9.6).

Conclusions: Previous bacteremia, chills and Hickman/Broviac are significant predictors of bacteremia in our hematology oncology patients. Simple risk factor may detect the existence of bacteremia in over 80 % of episodes, interestingly not including neutropenia. Rapid laboratory tests to detect bacteremia are warranted.

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THE A/H1N1 VIRUS FLU TO HIV POSITIVE PATIENTS CLINICAL AND THERAPEUTIC ASPECTS

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Introduction: The AH1N1 flu virus infection was firstly identified in April of 2009, in Mexico. The following evolution was fast and global. The specter of clinical manifestations is not entirely known.

Methods: We present 4 AH1N1 flu patients (3 HIV+ and a child born from an HIV+ mother).

Results: Only one in patients has evolved to cardiac-respiratory complications (severe cardiac-respiratory insufficiency, miocarditis and right pneumonia with Acinetobacter).The first patient, who had the most severe complications, has presented a level of the oxygen saturation 76%. There oxygen could only be administered by mask. In this case, we've administered the following treatment: Oseltamivir 150 mg/day, Zanamivir, antibiotherapy with Meropenem, anti-fungal IV and treatment for sustaining the heart. The evolution of the respiratory phenomenon has been slow. The oxygen saturation was maintained between 67-75% (while on oxygen) for 5 days. We mention that this patient hasn't received an AH1N1 flu vaccine. The convalescence was long and the signs of cardiac-respiratory insufficiency were maintained for a long period of time after being discharged from the hospital. The second HIV+ patient has presented a medium form of the flu. He had received the AH1N1 flu vaccine a month before being admitted to the hospital.

Conclusions: The severe forms of the AH1N1 flu have been identified in people who haven't received the vaccine and in those with immune-depression. The specific treatment has been constantly updated. A thing to consider is that the first patient was given a double dose of Oseltamivir.

P492

CLINICALLY EVOLVING ASPECTS OF MDR TUBERCULOSIS TO HIV PATIENTS

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Introduction: The opportunistic infections to HIV patients who have been on HAART therapy for a long time constitutes a priority and an open problem for clinicians especially in the case of MDR TB.

Methods: We present the evolution of MDR TB to 2 HIV positive youngsters who have been on ARV therapy for a long time.

Results: A 22 years old patient, who has been for 20 years in the evidence of the Regional Center in Constanta, gets transferred from the Pneumo-Phthisiology Hospital for the sudden appearance of some generalized tonoclonic convulsions and fever. From the patient's abundant medical history we should consider the following: pulmonary TB as a child, TB Pericarditis as a teenager and presently, secondary pulmonary TB MDR (Rifampicina, streptomicina).After 24 hours from being admitted to the hospital a PL analysis is done - the meningococcus is present on the smear (700 elements). The antibiotic therapy is started against the meningococcus. The tuberculostatic treatment is being taken into consideration and the phthisiologists along with the MDR Committee decide the introduction of two medicines: cycloserine and capreomycin in the tuberculostatic treatment.The evolution of the meningococcus meningitis was a favorable one, after 7 days no more germs appeared on the smear (54 elements). The evolution of the respiratory manifestations was not favorable and the patient died within 12 days from admission.

Conclusions: The evolution of opportunistic infections in incompliant patients with a low immunological status is, most of the times, fatal, despite all the doctor's efforts.

P493

INFECTIONS IN PATIENTS WITH ATAXIA TELANGIECTASIA - WHEN IS IMMUNOGLOBULIN REPLACEMENT THERAPY INDICATED?

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Background: Ataxia telangiectasia (AT) is a rare primary immunodeficiency characterized by progressive neurological dysfunction, oculocutaneous telangiectasia, recurrent sinopulmonary infections and radiation hypersensitivity.

Aims: To review the infections, characterize the immunodeficiency and analyse criteria for immunoglobulin (Ig)G replacement therapy in AT patients.

Methods: Retrospective review of infectious history, immunological evaluation and IgG replacement therapy was conducted on five AT patients (mean age: 12,2 ± 4,4 years) with follow-up ≥ 6 years.

Results: Recurrent respiratory infections occurred in 4 patients, 3 with frequent hospitalizations. Three had recurrent diarrhea (Giardiasis and Salmonellosis). Septic arthritis was registered in one case and sepsis in another. Uncomplicated varicella and H1N1 infections occurred in 2 cases. No patient had opportunistic infections or a complication of live viral vaccines.

The most common humoral abnormalities were Ig deficiencies: IgA (4/5), IgE (3/5) and IgG2 (2/5). One patient presented IgG deficiency and reduced antibody responses to vaccines. Four patients had T and B lymphopenia with normal numbers of NK cells. CD4 lymphopenia was present in all with high numbers of gamma/delta and memory T- cells (CD4/CD45RO+).

Intravenous or subcutaneous IgG replacement therapy was given to 3 patients: 2 for frequent and serious infections with subsequent clinical improvement; the third for hypogammaglobulinemia.

Conclusions: Respiratory and gastrointestinal infections were the most prevalent. Two patients presented systemic bacterial infections and improved with IgG replacement therapy. More data is necessary to establish guidelines for IgG administration in this group of patients.

P494

REFRACTORY COLD ABSCESSES AT THE SITE OF VACCINATION AS A SOLE MANIFESTATION OF CGD

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Case Report: The patient is an 8 year old girl who developed a large abscess at her thigh just at the site of childhood vaccinations when she was 2 years of age. The large 4×5-sized abscess contained voluminous yellow-greenish pus which led to persistent drainage. Many topical and systemic antibiotics were used without any benefit. Gram stain and smear always showed a mixture of microbial agents for instance staphylococcus. The abscess had 2 to 4 stoma apart from each other and sometimes locolation of pus posed the need to incision and drainage of mutiple sites. Once acid fast bacilli were grown and anti tubercolosis medications were prescribed and used for at least 9 months without any significant relief. Because of refractoriness of abscesses , phagocyte defect were sugessted and an immunological consultation performed when she was 6 years of age. Immunoglobulines were within normal limits. Nitro Blue Tetrazolium (NBT) and Di Hydro Rhodamine test (DHR) was performed and showed a significant defect of respiratory burst and the patient regarded as " Chronic Granulomatous Disease". Long term therapeutic doses of Trimetoprim-Sulfisoxazole followed by continous prophylaxis, resulted to some relief. Introduction of Gamma- interferon as an every-other-day schedule were terminally led to closure of abscess stoma and terminated the discharge. Multiple scars of previously draining abscesses are visible at her thigh. There was no other site of local or systemic infection and the general status remained good during and after Gamma- interferon therapy

P495

SPLENIC ABSCESSES AND INFLUENZA A (H1N1) INFECTION IN AN IMMUNOCOMPROMISED CHILD

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Introduction: Splenic abscesses, when isolated, are a rare clinical entity with nonspecific signs and symptoms, therefore remaining a substantial diagnostic challenge. Although multiple infectious agents have been involved, there is no report so far to an association with Influenza A (H1N1) infection.

Case report: The authors present a 9 year-old boy with DiGeorge Syndrome (del.22q11.2), with persistent lymphopenia (B and T cells), and Evans Syndrome dependent on systemic corticoids. He was admitted for prolonged fever and flu like symptoms, after a 5 day treatment with oseltamivir. H1N1 virus was confirmed. Persistent hypoxia, progressive weakness, anorexia and abdominal pain in the upper left quadrant were subsequently detected. Clinical examination revealed a palpable splenomegaly. Laboratory findings included leukocytosis, neutrophilia, aggravated anaemia and high c reactive protein. Urinalysis and chest radiograph were normal. An oseltamivir-resistant H1N1 strain (H275Y mutation) was confirmed by molecular analysis. Abdominal ultrasound revealed multiple hypoechoic liquefied lesions suggesting splenic abscesses, confirmed by CT scan. History of trauma was denied. Echocardiography excluded endocarditis. Large spectrum antibiotics were initiated with clinical and analytical improvement. Blood cultures were negative. Splenectomy was not considered due to its high risk. Serial ultrasound examinations were done to assess the evolution of abscesses, which resolved after 16 weeks of conservative treatment.

Discussion: In spite of the rarity of splenic abscesses, immunosuppressed patients are among the most susceptible to develop this complication, as in the case presented. However, the relevance of this presentation lies in the association with H1N1 infection and its possible role in the etiopathogenesis.

P496

MANIFESTATIONS OF CUTANEOUS LEISHMANIASIS OCCURRING DURING INFLIXIMAB THERAPY FOR CROHN'S DISEASE

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Background and aims: The use of infliximab in the management of inflammatory bowel disease is associated with an increased risk of intracellular infections due to inhibition of TNF-α. We describe the first case of localised cutaneous leishmaniasis (LCL) developing during infliximab treatment of Crohn's disease and illustrate the diagnostic difficulty in differentiating between these two diseases.

Methods: A 14 year-old male adolescent with refractory Crohn's disease established on infliximab for 6 months, presented with a 3-month history of 4 painless nodules on the right leg. Repeated cultures from the nodules were negative. No pathogens were visualised or isolated from an excision biopsy of one of the lesions which showed non-caseating granulomata. With a presumed diagnosis of cutaneous Crohn's disease, he was treated with topical tacrolimus and maintained on infliximab. Since no improvement was noted within 2 months, he was transited to topical steroid therapy, with subsequent evident growth of the lesions. By seven months from presentation, the lesions had coalesced into a wet ulcer. Cytology of the ulcer smears revealed multiple *Leishmania* amastigotes.

Results: Following treatment with liposomal amphotericin B the ulcer healed slowly with complete epithelialisation within 5 weeks. Despite subsequent continuation of infliximab the ulcer healed completely with scarring within 3 months.

Conclusion: In Malta children on infliximab are at a higher risk of developing *Leishmania infantum* infections. Both LCL and cutaneous Crohn's disease have a similar clinical and histological appearance. When amastigotes are not visualised *Leishmania* PCR would differentiate between LCL and cutaneous Crohn's disease.

P497

VISCERAL LEISHMANIASIS IN A CHILD INFECTED WITH THE HUMAN IMMUNODEFICIENCY VIRUS

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Introduction/aim: We report the case of a boy who fled from Chechnya to Belgium. He was diagnosed with a human immune deficiency virus (HIV)/Visceral Leishmaniasis (VL) co-infection. In both countries, the prevalence of HIV-infected children is low and VL is not endemic.

Case: A six-year old boy originating from Chechnya, fled with his family to Belgium. He presented at the Emergency Department with dyspnoea, irresponsiveness, severe anemia and leucopenia. A bone marrow aspiration confirmed the diagnosis of VL and serology was positive for HIV. He was treated with liposomal amphotericin B for the VL and with highly active anti-retroviral therapy for HIV. Multiple other infections were also diagnosed. Despite initial improvement, the boy became progressive and irreversible respiratory insufficient and died.

Discussion: The presentation of VL varies from an acute febrile illness to a progressive disease. Clinical manifestations of HIV/VL co-infected patients may be influenced by the CD4+ count. The parasite can be found on culture of blood smears, buffy coats, bone marrow and splenic aspirates. Leishmania PCR assays of bone marrow and peripheral blood smears were proven to be very reliable for the diagnosis in co-infected patients. Lipid formulations of amphotericin B are the preferred drugs to treat VL.

Conclusion: HIV/VL co-infected patients show lower cure rates, higher drug toxicity, higher relapse rates and higher mortality rates than other patients infected with VL. Caring for refugee children carrying diseases with which we have no experience in our sheltered life is a real challenge.

P498

POTENTIAL IMPACT OF A RISK-STRATIFICATION APPROACH ON INTRAVENOUS ANTIBIOTIC USE IN PAEDIATRIC FEBRILE NEUTROPENIA

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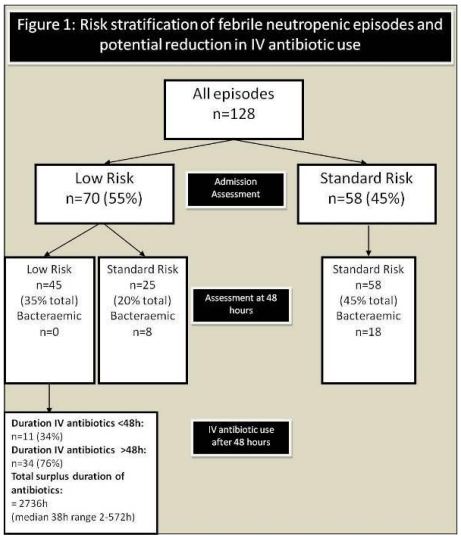
Background and aims: There is currently no validated risk-stratification algorithm for paediatric febrile neutropenia. Few studies apply risk-stratification criteria developed in one population to another. This study applies risk-stratification criteria developed by Dommett et al[1] in London to a Glasgow population to determine whether patients with bacteraemia were successfully identified as 'standard-risk', and to assess potential impact of a 'step-down' change from intravenous to oral antibiotics in low-risk episodes after 48 hours.
Methods: Data were collected retrospectively on all episodes of febrile neutropenia managed in a tertiary paediatric haemato-oncology unit, April-October 2009. Risk-stratification criteria based on Dommett et al were applied. For low-risk episodes duration of intravenous antibiotics >48 hours was calculated.
Results: 128 episodes in 66 patients were included for analysis and categorised according to risk (Figure 1). All episodes associated with bacteraemia (n=26) were categorised as standard risk at 48 hours. The mean duration of intravenous antibiotics in low-risk episodes beyond 48 hours was 77.66 [95% CI 38.81 - 116.51] hours/episode.



[Figure 1]

Conclusions: Dommet et al's risk-stratification criteria appear reliable in predicting bacteraemia in a different UK population. A step-down approach could potentially significantly reduce intravenous antibiotic duration in low-risk episodes.

1.Dommett et al. Successful introduction and audit of a step-down oral antibiotic strategy for low-risk paediatric febrile neutropenia in a UK, multicentre shared-care setting. European Journal of Cancer 45(2009):2843-49

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CUTANEOUS MANIFESTATIONS MAY BE A CLUE TO PRIMARY IMMUNODEFICIENCY DISORDERS

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Early diagnosis Primary immunodeficiencies are important as it could be life-saving. The mucocutaneous manifestations might be the first sign of these disorders; therefore a dermatologist may be the first one who faces the patient. The aim of this study was to find the frequency and clinical features of mucocutaneous manifestations of some PIDS which were: chronic granulomatous disease (CGD), leukocyte adhesion deficiency syndrome (LADS), Wiskott-Aldrich syndrome (WAS), hyper IgE syndrome (HIES) and severe combined immunodeficiency (SCID). This study was conducted on 46 patients including children and adults with one of the mentioned diagnosis. Diagnosis of PID was based on the criteria of international union of immunological societies PIDs classification committee. Through this study, demographic data and the mucocutaneous manifestations of the patients were registered by a dermatologist in a special questionnaire. In a time period of 12 months among 46 patients with different kinds of PIDs (20 cases of CGD, 10 cases of LADS, 6 cases of WAS, 6 cases of HIES syndrome and 4 cases of SCID), skin diseases and mucocutaneous alterations were recorded. In 74% of our cases, the mucocutaneous manifestations were the first signs of the diseases that from the most to the least frequency were as follows: Superficial and deep bacterial skin infections, ulcerative stomatitis and periodontitis, mycobacterial skin infection due to BCG vaccination and eczematous dermatitis. This study shows that dermatologists should be aware of the mucocutaneous manifestations of PIDS that could be a clue to early diagnosis of these diseases.

P500

MOLECULAR BASED DIAGNOSIS OF BACTEREMIA IN THE SETTING OF FEVER WITH OR WITHOUT NEUTROPENIA AMONG PEDIATRIC HEMATOLOGY - ONCOLOGY PATIENTS

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Background and aims: Bloodstream infections are major concern in hematology-oncology patients. Our aim was to assess the efficacy of the 16S rRNA polymerase chain reaction (PCR) in identifying bacteria in blood samples as compared with standard blood cultures during febrile episodes of patients treated in the department of hematology -oncology.

Methods: Prospective study (Sep 2004 - Nov 2005). Three ml of blood were inoculated into pediatric blood culture bottle that were processed using the automated continuous-monitoring blood culture system according to standard microbiological protocols.16SrRNA gene was PCR amplified from direct blood sample. Sequence identity was determined by Blast analysis software.

Results: 148 paired samples of standard blood culture and PCR were evaluated in 115 new onset febrile episodes. For some patients more than one set was available from peripheral and central line lumens. In 26/148 (17.6%) a single pathogen was isolated; including Klebsiella, S. pneumoniae, Enterococcus, Non tuberculous mycobacteria, Coagulase negative Staphylococcus, and Pseudomonas. PCR detected correctly 12/26 isolates. In two negative blood cultures PCR detected Fusobacterium nucleatum and Roseateles aquatilis. PCR sensitivity, specificity, positive and negative predictive value were 46%, 98%, 86% and 89% respectively, as compared to standard blood culture. 13 negative PCR with standard blood cultures reviled gram negative and positive pathogens.

Discussion: 16SrRNA PCR performed on fresh blood samples has high specificity (98%) and negative predictive value. Positive yield is still lower than satisfactory. Fastidious or slow growing organisms may be better detected by molecular methods. Improvement of PCR technology on fresh blood samples is warranted.

P501

EPIDEMIOLOGY AND RISK FACTORS FOR CENTRAL VENOUS CATHETER INFECTION IN CHILDREN WITH CANCER

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Background: Permanent central venous catheters are essential in pediatric oncology patients. One common complication is catheter-related infection. The aim of this study was to analyze the episodes of catheter-related infections in children with cancer and to determine possible risk factors for this infection.

Methods: Retrospective study evaluating demographic, clinical and surgical characteristics of 70 children with cancer and 80 central catheters from 2003 to 2009 at a pediatric oncology service in a tertiary hospital in Madrid.

Results: Thirty five episodes of catheter-related infection occurred in 27 patients during the study period. Rate of infection was 0.39 episodes/1000 catheter-days. Median number of days before infection was 144 (1-1228). Most frequent microorganisms isolated were coagulase negative *Staphylococcus* (43%), *S. aureus* (11%), *P. aeruginosa* (11%), *E. coli* (9%) and *Candida parapsilosis* (9%). The risk of infection was higher in patients with leukemia (p=0.046), bone marrow transplant (BMT) (p=0.054) and in those with a subclavian catheter (p=0.021). Previous colonization of the catheter (p=0.019) and having neutropenia at the time of catheter placement (p=0.054) also increased the rate of infection. Fifteen catheters (43%) had to be removed for persistent infection. Antibiotic lock-therapy was used in 14 episodes and in 4 cases (28%) the catheter was preserved.

Conclusions: Having neutropenia at the time of catheter placement and subclavian vein catheterization may increase the rate of catheter-related infections in children with cancer. This rate may be higher in children with leukemia and those who underwent a BMT. Larger, prospective studies are needed to confirm these results.

P502

FATAL OUTCOME OF INFLUENZA A VIRUS INFECTION IN A CHILD UNDERGOING BONE MARROW TRANSPLANTATION; A COMPREHENSIVE CASE REPORT

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Immunocompromized children are at risk for a complicated course following influenzavirus infection. In children receiving Bone Marrow Transplantation (BMT), pulmonary complications are frequently reported and cause significant mortality. However, we do not understand the underlying pathophysiology.A 5-year-old boy with high-risk acute lymphoblastic leukemia contracted infection with Pandemic influenza A (H1N1) virus during myeloablative conditioning for BMT. He received oseltamivir 75 mg bd, which was continued because persisting viral excretion. After switch to zanamivir (iv) because of oseltamivir resistance, patient recovered and was discharged. Three weeks after discharge, he presented again with respiratory complaints with influenzavirus still detectable. Zanamivir was re-initiated, however zanamivir resistance was discovered and triple therapy with oseltamivir, zanamivir and ribavirin was initiated [1]. The boy was admitted to ICU with respiratory insufficiency. Influenzavirus, cytomegalovirus and rhinovirus were repeatedly detected in respiratory samples. Lung biopsy revealed signs of chronic viral pneumonia, however, negative for cytomegalovirus and influenzavirus replication by immunohistochemistry. The patient died because of respiratory failure in spite of long-term antiviral treatment Cytokine analysis in plasma and bronchoalveolar lavage showed a specific significant increase in IL-8 levels prior to death indicating an extensive chemotactic response to mobilise neutrophils. The pathophysiological events leading to a fatal outcome in our patient may be explained by an inefficient immune response instead of ongoing viral replication. To prevent chronic pulmonary damage due to respiratory viral infections in immunocompromized children, anti-viral therapy alone may not be sufficient. We hypothesize that interferon alpha might be of value if administrated early during infection.

P503

SEPTIC SHOCK AND SOFT TISSUE LESIONS IN *PSEUDOMONAS AERUGINOSA* BACTERAEMIA IN PAEDIATRIC HAEMATO-/ONCOLOGIC PATIENTS - A RETROSPECTIVE ANALYSIS

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Background and aims: *Pseudomonas aeruginosa* (*Pa*) causes difficult-to-treat nosocomial infections in neutropenic patients including sepsis and soft tissue defects (ecthyma gangraenosum, necrotising fasciitis, perityphlitic abscess). We describe a single center experience of *Pa* infections, complicated by soft tissue lesions in paediatric haemato-/oncologic patients.

Methods: At the Division of Paediatric Haematology/Oncology of the Medical University of Graz, Austria, we retrospectively analysed blood cultrure (BC) results from the years 1999 through 2010. Frequency and clinical course of *Pa* bacteraeimas were analyzed.

Results: From 1999 through 2010 a total of 3376 blood cultures (BC) were drawn. In 190/3376 (5,6%) BC a pathogen was isolated. In 18/190 (9,4%) BC *Pa* was detected. 17/18 patients with *Pa* bacteriaemia developed septic shock. Five out of 18 (27,8%) patients had septic shock combined with soft tissue complications (2x ecthyma gangraenosum, 1x necrotizing fasciitis, 1x *perityphlitic abscess* , 1x inflamed hemorrhoids), of whom 4 patients required surgical interventions (1x incision and drainage combined with temporary colostomy, 1x vacuum assisted closure dressing, 1x appendectomy, 1x incision,)

Conclusions: *Pa*-associated bacteraemias are life-threatening complications in immunocompromised patients. Soft tissue lesions are dreaded complications. In addition to antibiotic therapy and G-CSF-application, surgical intervention is frequently required in complicated courses.

P504

THE SPECTRUM OF PARVOVIRUS B19 INFECTION AT A PEDIATRIC HEMATO-ONCOLOGIC WARD - A 20-YEAR LONGITUDINAL OBSERVATIONAL STUDY

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During the last 2 decades, 35 of 1059 consecutive children with various hemato-oncologic diseases were diagnosed for PVB19 infection by polymerase chain reaction (PCR) and/or detection of PVB19 specific antibodies. The clinical spectrum of PVB19 infection included 11 immunocompromised patients under chemotherapy for different malignancies presenting with prolonged pancytopenia (n=7), pure red cell aplasia (n=2), rash (n=2), or hemophagocytosis (n=1), and 7 patients with stem cell transplantation complicated by poor graft function and delayed hematologic recovery (n=6) or myocarditis (n=1). In 5 additional patients, PVB19 was discovered as possible causative agent of severe aplastic anemia (n=3) or myelodysplastic syndrome (n=2), and in 12 children with hemolytic anemia, PVB19 caused transient aplastic crisis. In conclusion, children with hemato-oncologic diseases and PVB19 infection present with different, frequently non-specific symptoms, sometimes mimicking relapse of the malignancy or drug induced myelodepression. Physicians should be aware of this complication and screening of blood and tissues for PVB19 by PCR is recommended in immunocompromised children.

P505

ACTIVE SURVEILLANCE CULTURES IN PAEDIATRIC HAEMATO-/ONCOLOGIC PATIENTS

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Background and aims: Active surveillance cultures (ASC) in critically ill patients are used to predict possible causative pathogens of subsequent blood stream infections (BSI). Feasibility is under discussion. Paediatric data are scarce.
Methods: At the Division of Paediatric Haematology and Oncology of the Medical University Graz, ASC are routinely taken before and during prolonged episodes of neutropenia. In febrile patients, blood cultures are drawn before initiation of empiric antimicrobial therapy. In a retrospective analysis of the years 1999 through 2010, we compared isolates causing bacteraemia with the results of ASC obtained in the respective patients within 4 weeks prior BSI. Coagulase-negative Staphylococci were considered as contamination unless they were isolated in at least 2 blood cultures within the same episode.
Results: Out of 3376 blood cultures drawn during the analysed period, an organism was isolated in 190 (5.6%). These isolates were assigned to 84 BSI episodes in 69 patients. In 37 episodes, no ASC had been performed within 4 weeks prior to BSI. In 32 (68.1%) of the remaining 47 episodes the causative agent had been isolated by ASC. Details see table 1.

84 BSI episodes in 69 patients

underlying diseases
- haematological malignancies (n=40)
- non malignant haematological diseases (n=6)
- solid tumors (n=23)

10 episodes after
- allogeneic (n=11)
- autologous (n=6) stem cell transplantation

age at BSI episode
- 0.4 – 28.8 (median 7.1) years

Isolates

	BSI	congruence of ASC prior to BSI		
		pos. (%)	neg.	missing
Staphylococcus aureus	5	1 (50)	1	3
other gram-positive cocci	28	9 (64)	5	14
gram-positive rods	9	0 (0)	5	4
Pseudomonas aeruginosa	16	8 (100)	0	8
Eenterobacteriaceae	21	12 (86)	2	7
yeasts	3	2 (67)	1	0
others	2	0 (0)	1	1
total	84	32 (68)	15	37

Table 1. Characteristics of patients and episodes of blood stream infections (BSI), congruence of blood and active surveillance cultures (ASC)

[Table 1]

Conclusions: By means of ASC the causative agent of a subsequent BSI had been isolated in advance in two thirds. Therefore, ASC might assist in the choice of the empiric antimicrobial treatment in febrile paediatric haemato-/oncological patients.

P506

A DIAGNOSTIC DEFICIENCY

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Background and aims: Mean age of presentation for sporadic X-linked agammaglobulinaemia is 35 months (2 months-11 years). We review a late presentation in a 13 year old boy extensively investigated for tuberculosis (TB).

Methods: Retrospective case-note review.

Results: The boy presented in 2010 with a right basal pneumonia. Persistent chest x-ray changes and cough prompted further investigation. CT chest showed bronchiectasis. Immunological investigations identified reduction of all immunoglobulin subclasses and absent B cells. Molecular genetics revealed deletion in btk gene, confirming the diagnosis of X-linked agammaglobulinaemia.

He was born in Pakistan, moving to Scotland in 2004. He received routine immunisations including BCG. There was no significant family history.

He had been reviewed by multiple paediatric specialists over several years.

He had spastic diplegia with periventricular leucomalacia.

From 2005-2007 he had persistent diarrhoea, ear discharge and poor weight gain. Full blood count, inflammatory markers and biochemistry were normal. A low IgA level of 0.1g/l (part of Coeliac Disease serological screen) was felt not to be significant.

From 2005 he developed recurrent cough and fever. He was assessed for TB in 2006 and again in 2008 following a right lobar pneumonia with associated *Streptococcus pneumoniae* bacteraemia. There was no history of TB contact or recent travel. On each occasion right-sided chest x-ray changes were noted but all TB investigations negative.

Conclusions: Primary immunodeficiency should be considered in the differential diagnosis of children presenting with recurrent respiratory and gastro-intestinal symptoms, even in older children with risk factors for alternative explanations of their symptoms.

P507

TWO CASES OF CEREBRAL ASPERGILLOSIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA, SUCCESSFULLY TREATED WITH VORICONAZOLE

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Background: Invasive aspergillosis predominantly occurs in immunocompromised patients and is often difficult to treat. Mortality approaches 100% if the central nervous system is affected. Vorizonazole is one of the few available antifungal drugs active against *Aspergillus* spp. with a sufficiently high CNS tissue penetration.

Methods: We retrospectively report 2 cases of children undergoing induction chemotherapy for acute lymphoblastic leukaemia (ALL) who developed cerebral aspergillosis.

Results: The first case is a 3 year-old boy treated for ALL. Two days after discharge he was readmitted to the ICU because of status epilepticus. CT scan showed two cerebral lesions, the biopsy revealed a suspected *Aspergillus* infection. CT thorax showed multiple lesions. Serum galactomannan was negative, as were haemocultures and fungi cultures on BAL. Voriconazole IV was started at 14mg/kg/d. Patient recovered and follow-up imaging showed complete resolution of cerebral lesions and significant reduction in lung lesions.

The second case is a 7 year-old boy who developed convulsions a month after the start of induction chemotherapy for ALL. An NMR showed multiple cerebral lesions. CT thorax showed one and later multiple lesions in the lungs. Voriconazole IV was started at 14mg/kg/d. BAL, performed under a 2-day voriconazole stop, only showed hyphae, culture was negative. Serum and BAL galactomannan were negative. A subsequent brain biopsy revealed an *Aspergillus fumigatus* infection. Patient recovered and follow-up imaging showed a discrete reduction in cerebral lesions and sequellae lesions in the lungs.

Conclusions: Two children undergoing induction chemotherapy for leukaemia who developed cerebral aspergillosis recovered under voriconazole.

P508

PREVALENCE OF STRONGYLOIDES STERCORALIS IN FOREIGN-BORN CHILDREN

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Background and objective: Foreign-born children are often diagnosed with intestinal parasites.We evaluated the prevalence of *Strongyloïdes stercoralis* (SS) infection in these children.

Methods: Prospective study at Immigrant Health Clinic, CHU Sainte-Justine, a paediatric tertiary care center in Montreal, Canada (2009/11-2010/06). We collected demographic information, growth parameters and laboratory screening tests including SS serology and stool exams.

Results: 236 immigrant children (46.6% male, mean age of 6.8 years [0.2-18.7]) were evaluated 12.7 months (median period) after arrival. Regions of origin were: Americas (52.5%; mainly Haiti 83.9%), Africa (19.1%), East Asia/Western Pacific (14.0%), Mediterranean/Middle East (9.8%), and Southeast Asia (4.7%). Height, weight and head circumference < 5thpercentile were observed in 14.2%, 14.9% and 28.6% of patients, respectively; anemia, iron deficiency and eosinophilia (≥400 cells/mm^3) in 32.8%, 52.6% and 16.2%. Fifty-seven of 193 children (29.5%) had pathogenic intestinal parasites. Prevalence of SS was 7.7%: serologies were positive in 13 patients, doubtful in 4; stools were positive in 4 cases (1 with negative serology). The 18 children positive for SS emigrated from Haiti (88.2%), Africa (5.9%) and Asia (5.9%). Fourteen of these (82.3%) had eosinophilia (mean: 1458.8±1066.6/mm^3). Immigration from Haiti was identified as a significant risk factor (OR: 11.657; CI: 2.598-52.292), however, eosinophilia was not (OR: 2.302; CI: 0.696-7.610).

Conclusion: We found a significant prevalence of *Strongyloides stercoralis*. Screening for this infection should be performed in all children from Haiti and should be considered in immigrant children with eosinophilia.

P509

MULTI-NATIONAL COLLABORATION TO ASSIST PAEDIATRIC INFECTIOUS DISEASE SURVEILLANCE - INTERNATIONAL NETWORK OF PAEDIATRIC SURVEILLANCE UNITS

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Background: The International Network of Paediatric Surveillance Units (INoPSU) started as the European paediatric surveillance network comprising UK, Netherlands, Germany and Switzerland. Launched in 1998, INoPSU comprised 10 nations including Australia, Canada, New Zealand, and Ireland. INoPSU enables communication among existing national paediatric surveillance units (PSUs) and researchers, and facilitates international studies using similar surveillance methodology to study rare paediatric conditions, including infectious diseases.

Aims: To review the impact of INoPSU demonstrating its potential for multi-national surveillance of rare paediatric infectious diseases.

Methods: Asses output of INoPSU to consider impact on policy and international collaboration.

Results: The PSUs have facilitated surveillance of over 200 rare paediatric conditions including 70 infectious/communicable diseases. PSUs have collaborated by sharing protocols and data collection tools to study HIV (3PSUs); pertussis (6PSUs) acute flaccid paralysis (4PSUs) and haemolytic uraemic syndrome (7PSUs). These international studies have led to recommendations on screening; vaccine introduction and assessment of vaccine effectiveness. PSUs have also performed enhanced surveillance in response to the H1N1 pandemic (3PSUs). Data are widely disseminated through joint papers, presentations at national paediatric scientific meetings and international conference such as ESPID and ESPR.

Conclusions: INoPSU has provided unique and timely data to support policy and clinical practice. It has been a blueprint for the development of similar networks in other areas of medicine. Such active surveillance systems can be responsive to emerging infectious disease threats and supplement existing national monitoring systems. However, the lack of funding at a national and international level needs to be addressed.

P510

MEDICAL CONDITIONS IN IMMIGRANT CHILDREN IN GENEVA, SWITZERLAND

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Background: Because of poor medical follow-up in their own country, high exposure to infectious diseases, confrontation with war, violence, and exile, refugee children are at higher risk of physical illness and psychological difficulties.

We analyzed the medical conditions of immigrant children in Geneva.

Materials and methods: We retrospectively collected data from recently immigrated children who were followed in our hospital for general pediatric care. Past medical history, physical examination, tuberculin test (Mantoux test, which was followed by chest X-ray and interferon gamma essay if >10mm), and parasites screening in stool samples were reviewed.

Results: 94 paediatric patients aged 6 months to 16 years old (median 7 years) were evaluated between January 2009 and May 2010. Most were from Eastern Europe and Africa.

14 patients (15 %) had a positive Mantoux test. Amongst those, 4 were diagnosed with latent tuberculosis and 1 with active tuberculosis. The most frequent other infectious diseases were cutaneous infections (tinea, pediculosis, impetigo, and scabies) in 9.6 % of patients and digestive parasitosis in 8.5% of patients (mainly Giardia Lamblia). The main non infectious medical conditions were dental cavities, and psychological difficulties (eating, sleeping and anxious disorders) in respectively 42 % and 28 % of the patients.

Conclusion: The general physical health condition of refugee children in Switzerland seems acceptable. However, tuberculosis remains highly prevalent in this population. Detection of intestinal parasitosis, dental cavities, and psychological difficulties should be improved.

P511

TAILORING TST AND/OR IGRA FOR MIGRANT SCREENING

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Background and aims: Rates of positive tuberculin skin tesat (TST) reactions are poorly correlated to the incidence of active tuberculosis (TB) in various migrant groups.

Method: We performed interferon-gamma release assays (IGRAs) in 181 adolescents, referred because of a positive (≥10 mm) TST.

Results: The IGRA was positive in 54/91 children (59%) from high-incidence (>100/100.000) countries, in 11/52 (21%) from countries with an intermediate (20-99) incidence, 6/26 (29%) from Eastern Europe/former USSR, and in 1/12 from low-incidence (< 20/100.000) countries. IGRAs were also performed in 7 African children with TST reactions of 6-9 mm, and 4 were positive.

Conclusions: When used for screening of migrant children from countries that practice regular TST sreening and BCG revaccination of negative children, such as many in Eastern Europe, the specificity of the TST is unacceptably low, even if the cut-off level were to be increased to 15 mm. If risk factors for MTB infection are present, an IGRA should be used instead.

A TST may be used for screening of migrants with risk factors from areas with a relatively low prevalence of MTB infection and low background TST reactivity, such as Iraq, if an IGRA is used to support a diagnosis of MTB infection.

In high prevalence groups such as migrants from sub-Saharan Africa, a TST cut-off level of 5 or 6 mm may be considered in order to increase sensitivity, and the negative predictive value of an IGRA test may be too low.

P512

USE OF INTERFERON-GAMMA RELEASE ASSAYS IN THE CONTACT TRACING OF IMMUNODEFICIENT CHILDREN EXPOSED TO A PATIENT WITH PULMONARY TUBERCULOSIS

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Background: Interferon-gamma release assays (IGRAs) have high specificity and sensitivity for the diagnosis of active and latent tuberculosis (TB) infection; however their role as a screening tool in children with immunodeficiency disorders is still unclear.

Objective: To evaluate IGRAs performance in the contact tracing of immunodeficient children.

Methods: Children of a Hematology/Oncology ward who shared the same airspace for more than eight hours with a contagious TB case underwent serial QuantiFERON®-TB Gold test in tube (QFT-GIT) and T-SPOT testing. The association between total lymphocyte count and IGRA results was evaluated using multivariable models.

Results: Eighteen children were evaluated; after the first testing, 67% and 83% resulted negative to T-SPOT and QFT-GIT, respectively, and two children (11.1%) were positive to T-SPOT. Indeterminate results (17%) were equal in both tests and one T-SPOT failed. In the second testing, two months later, no positivity to IGRAs was detected; 88% resulted negative to T-Spot, 65% to QFT-GIT. Indeterminate results were more frequent with QFT-GIT (35%) than with T-Spot (12%). In the multivariable analysis, a statistically significant association of lymphocyte count < 500 cells/mm^3 ($p < 0.00005$) and low age ($p=0.03$) with indeterminate results for QFT-GIT test but not for T-SPOT ($p=0.10$ and $p= 0.88$, respectively) was found. No case of TB disease was diagnosed after one year of follow-up. Isoniazid chemoprophylaxis was indicated to all children, independently of IGRAs results.

Conclusions: T-SPOT provided more determinate results and was less influenced by low age and lymphocytopaenia than QFT-GIT in our sample of immunodeficient children.

P513

QUANTIFERON®-TB GOLD IN-TUBE PERFORMANCE FOR TUBERCULOSIS DIAGNOSIS IN 0-5 YEARS OF AGE CHILDREN

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Background and aims: Interferon-Gamma-Release Assays (IGRAs) are increasingly used for the diagnosis of tuberculosis (TB). Unknown performance in infants and controversial rate of indeterminate results in < 5 years children limit their pediatric usage.

Methods: Immunocompetent children (n=82, 0.10 to 5.6 years of-aged; median: 1.8) referred for suspected TB or TB contact and sequentially evaluated for QuantiFERON®-TB Gold In-Tube (QF-TB-IT) reactivity were included for QF-TB-IT performance evaluation.

Results: BCG vaccination rate at birth was high (91%). Fifteen children were diagnosed as active TB disease; 10 had latent TB: recent TB contact and positive Tuberculin-Skin Test (TST); 16 were healthy contacts: recent TB contact and negative TST; the 41 remaining children, with TB excluded, were used as controls. The rate of QF-TB-IT indeterminate was 5% in active TB, latent TB and healthy contact children (0% in < 2 years; n=23) while 22% in controls with irrelevant diseases. QF-TB-IT sensitivity and specificity, as determined by positivity in active TB and negativity in controls were 86% and 100% respectively (67% and 100% in < 2 years). Four out of nine children with latent TB had QF-TB-IT positivity (2/4 were < 2 years). Finally, concordance between TST and QF-TB-IT results was high only when considering TST negativity < 10mm and positivity >15mm induration diameter respectively.

Conclusions: QF-TB-IT sensitivity and specificity were high and the rate of indeterminate results was low in < 0-5 years children with TB or TB contact. QF-TB-IT appears therefore a promising tool for TB diagnosis in young immunocompetent children.

P514

POPULATION DIFFERENCES IN IMMUNE RESPONSES FOLLOWING BCG VACCINATION IN DIFFERENTAFRICAN SETTINGS

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Background and aims: BCG protects against severe childhood cases of tuberculous meningitis and miliary TB but confers variable protection against pulmonary TB later in life, particularly in TB endemic areas. Earlier studies attempting to study mechanisms behind this discrepancy have shown that *Mycobacterium tuberculosis* (*M.tb*) PPD stimulated IFN-γ concentrations were much higher in UK BCG vaccinated infants compared to age-matched Malawian infants given the BCG vaccine. We have now tested another group of infants and their mothers using identical laboratory protocols in another TB endemic country, The Gambia.

Methods: Three-month-old infants vaccinated with BCG in the first week of life and their mothers were recruited into the study. Venous blood samples were taken from infant-mother pairs for the detection of IFN-γ production by ELISA following diluted whole blood assay stimulation with an array of tuberculous antigens over 6 days.

Results: 93% of Gambian infants (28 of 30) made a positive IFN-γ response (>62pg/ml) to *M.tb* PPD stimulation, comparable to previously studied UK infants (93% vs. 100%), and higher than the proportion of responders previously detected in Malawi (93% vs. 53%). However, the median IFN-γ response from Gambian infants was lower than median IFN-γ responses from UK infants (310pg/ml vs. 1,779pg/ml; p=< 0.0001). The median IFN-γ responses in Gambian and Malawian infants were comparable (310pg/ml vs. 289pg/ml; p=0.7036).

Conclusions: The study findings indicate quantitative differences in cytokine secretion in different African settings in response to *M.tb* PPD antigen stimulation. The underlying mechanisms influencing cytokine secretion post-vaccination warrant further investigation.

P515

PRIMER OCULAR TUBERCULOSIS PRESENTED WITH UVEITIS IN CHILDREN

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Background and aims: Uveitis associated with rheumatic diseases is more common in children. In the developing world, infectious uveitis occurs in greater frequency, attributing from 11.9% to 50% of cases to infection.

Methods: Herein, we report two cases of primary ocular tuberculosis when they were under the corticosteroid and azathioprine treatment for sight-threatening uveitis. First case had granulomatous uveitis, but it was non-granulomatous inflammation at the time of diagnosis and the second one was devaloped non-granulomatous inflammation. The positive tests results of purified protein derivative and QuantiFERON-TB® Gold In-tube test (QFT-GIT) and with the clinical response to anti-tuberculosis treatment were convincing for the diagnosis of ocular tuberculosis. In these cases, chest x-ray and computed thorax tomography did not show any evidence of active or healed/primary or reactivated disease in the study period.

Results: During the anti-tuberculosis therapy, uveitis was subsided and, complete remission was achieved in six month.

Conclusions: Up to now it has been reported very few cases of uveitis presented with primary ocular tuberculosis. Tuberculosis should be considered in the differential diagnosis when the uveitis worsens despite immunosuppressive therapy for those living in high-risk regions.

P516

IDENTIFICATION OF SERUM BIOMARKERS OF PAEDIATRIC TUBERCULOSIS USING SELDI

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Background: Improved diagnosis of tuberculosis (TB) is essential for reducing the incidence of disease in sub-Saharan Africa. Currently half of all cases of infectious TB are undiagnosed. This proportion is higher in children, as clinical features overlap those of many chronic infections and microbiological confirmation is complicated by paucibacillary load. The development of a rapid, sensitive and affordable serological diagnostic test for TB in children is urgently needed. Surface-Enhanced Laser Desorption Ionisation (SELDI) technology has been widely employed to identify serum based biomarkers in infectious diseases.

Methods: Serum samples (n=1000) were collected from children and adults (HIV-positive and HIV-negative) with active TB (culture confirmed), latent TB (IGRA+ and TST+) and controls (other infections and inflammatory conditions). Patients were recruited from two regions of sub-Saharan Africa with differing patterns of HIV, TB and malarial infection to ensure that the biomarker candidates would not be population specific. Serum proteomic profiles were obtained by SELDI using cation capture (CM10; pH 4.0 and 6.0), anion capture (Q10; pH 7.5 and 9.5) and immobilized metal affinity (IMAC30; Cu) ProteinChip™ arrays.

Results: SELDI analysis generated over 6000 serum protein profiles. Specific proteins were identified as statistically significant ($P < 0.001$) in distinguishing children with active TB from those with latent TB infection regardless of HIV status. Several of these potential biomarkers were observed in both children and adults.

Conclusions: A series of serum proteins have been found that will potentially enhance the diagnosis of TB in children. These are currently being identified at the molecular level.

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MOLECULAR FINGERPRINTING OF THE MYCOBACTERIUM ABSCESSUS COMPLEX

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Background and aims: Mycobacterium abscessus complex is associated with lung disease in Cystic Fibrosis (CF) patients. It comprises three species, *M. abscessus* (sensu stricto), *massiliense* and *bolletii*. Little is known about whether certain strains are associated with lung disease. This study begins to address this issue through the molecular fingerprinting of 52 *M. abscessus* complex isolates from respiratory samples from children with CF and non-CF lung disease.

Methods: Isolates were typed using a novel in-house VNTR (Variable Number Tandem Repeat) and a commercial repetitive-PCR based system (Diversilab,Biomerieux). Analysis of the DNA fingerprints was performed with the Diversilab software.

Results: Both methods were reproducible and could differentiate strains between and within the three members of the complex. Several clusters were observed using the Diversilab method that were broadly supported by the VNTR method. There were two *M. abscessus* clusters that contained only isolates from CF patients from whom *M. abscessus* complex had been isolated on multiple occasions. These two *M. abscessus* clusters did not contain any isolates from patients (CF and non-CF) from whom *M. abscessus* complex was isolated on just a single occasion.

Conclusions: Both VNTR and Diversilab typing methods can be used to differentiate between members of the *M. abscessus* complex.The data suggests that patients from whom *M. abscessus* was isolated on multiple occasions were colonised with strains from two distinct but related genetic clusters. Further work will establish if each of these clusters represents a single strain and future studies would seek to link these strains with clinical outcomes.

P518

CHLAMYDIA PNEUMONIAE, AND MYCOPLASMA PNEUMONIAE. ARE THEY RELATED TO ACUTE EXACERBATIONS IN CHILDHOOD ASTHMA?

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Background and aims: *Mycoplasma pneumonia* and *Chlamydia pneumoniae* are frequent causative agent of acute respiratory diseases and have been recognized as a possible infectious triggerings of asthma. In the present study we investigated the frequency of these agents and their relationship with asthma attacks.

Methods: A prospective study, performed in the emergency department, of the Teaching National University, and the Children and Adolescent Institute, from January 2007 to January 2010. Eighty one patients were included in the study, of which 55 had asthma. Patients were divided into three groups: group one consisted of 26 children with asthma attacks , group two 29 children with stable asthma, and as a control group 26 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: Mean age was 10,9 ± 2.5 group 1, 10,1 ± 2,9 group 2 and 10,9 ± 1,9 group 3, p = 0.4

There were 40 female *M. pneumonia* specific IgM antibody.

was observed: in the asthma attack group 5/26 19,2 %, in group 1, 2/29 3,4% group 2 and the control group 0/26 (p=0,01). Regarding Chlamidia IgM we found in 7/26 26,9 % in group 1, 2/29 6,9% in the stable asthma group, and 0/26 in the control (p = 0,005). No significant difference was found between the stable asthma group and the control group. (p > 0.05)

Conclusions: *M. pneumoniae* and C. *pneumoniae* may play a role in development of severe asthma in childhood.

P519

MYCOBACTERIUM LENTIFLAVUM: AN EMERGING PATHOGEN IN NON TUBERCULOUS MYCOBACTERIAL LYMPHADENITIS

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Background and aims: Lymphadenitis is the most common manifestation of nontuberculous mycobacterial (NTM) infection, but *M.lentiflavum* is considered a rare pathogen. Prompted by an increased in the number of M .lentiflav*um* cervicofacial adenitis in our area, we investigated the frequency and clinical characteristics of this mycobacteria.

Methods: Retrospective review of patients less than 14 years with culture-confirmed NTM lymphadenitis treated at three hospitals from the same area over the period 2000-2010. Clinical data, antimicrobial resistant pattern, treatment and outcome were recorded from children with *M. lentiflavum* infection.

Results: Twenty-eight cultured-confirmed NTM lymphadenitis were identified: 11 caused by *M.avium* (39.2%),13 by *M.lentiflavum* (46,4%) and 1 by both. Eleven out of 14 *M.lentiflavum* cases were diagnosed in the last five years. Median age was 22 months. Submandibular nodes were the most affected (10 cases) and spontaneous drainage was observed in 58%. Tuberculin skin test gave an induration between 5 and 10 mm in 6 children. Drug-susceptibility tests performed in 10 cases showed complete susceptibility to clarithromycin and cycloserine, 90% rifampin resistance, and full resistance to other antimycobacterial drugs. All but one child required surgery (10 complete excision, 3 drainage) and 11 were additionally treated with different drug combinations. Three presented transient facial paralysis after surgery. Eleven patients healed and three had persistent adenopathy.

Conclusions: This is the largest case report series of *M.lentiflavum* lymphadenitis in children. *M.lentiflavum* is an emerging pathogen in NTM cervicofacial lymphadenitis in Spain. Treatment is often difficult due to the spontaneous drainage and antimycobacterial high resistance rates.

P520

EXTRAPULMONARY TUBERCULOSIS. REVIEW OF EIGHT YEARS OF TUBERCULOUS MENINGITIS

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Background: Tuberculous meningitis (TM) is an uncommon pathology in developed countries. The aim of this review is to increase awareness of this potentially fatal disease in Europe.

Methods: Retrospective analysis of children diagnosed with TM over the last eight years.

Results: A total of 5 patients suffered from TM. Previous tuberculosis contact was found only in a four-month old infant who has been receiving INH chemoprophylaxis since birth; the other children had no apparent risk factors. One patient each were from Romania and Bolivia, whereas three children were of Spanish origin. Subsequently the index case was identified in three children. BCG was not given to any patient. 2/5 patients presented with acute hydrocephalus and pulmonary involvement was detected in 3/5. Mantoux test was only positive in one infant (>10mm). Microbiological diagnosis was established in four cases; three children had *M.tuberculosis* detected by Lowenstein culture (CSF n=2 and gastric washing n=1, sensitive to INH/RIF)) whereas one patient had a positive PCR result in CSF(sensitive to RIF). Standard four drugs treatment was used in all patients with adjuvant corticoid therapy in 4/5 children. A ventricular-peritoneal shunt was placed in two cases. One patient died two suffered from severe neurological complications, all three presented with advanced stage disease at time of diagnosis.

Conclusions: TM continues to occur in our population. High level of suspicion is necessary to early diagnose this disease in order to prevent devastating sequel.

P521

PLEURO-PERICARDIAL EFFUSION (PPE) IN A 12-YEAR OLD PATIENT WITH PULMONARY TUBERCULOSIS (TBC) - THE ROLE OF CORTICOSTEROID THERAPY

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Background: Tuberculous PPE is rare in developed countries whilst being an important complication in developing countries. Treatment consists of quadruple tuberculosis therapy with or without adjunctive corticosteroids.

Case presentation: A 12-year-old girl born in Senegal and resident in Spain since 2007 was hospitalized for chest pain, recurrent fever, weight lost, productive cough and hemoptysis. Physical examination revealed hypoventilation, soft cardiac sounds, no rubbing, hepatomegaly and presence of the BCG-scare. ECG showed low voltage and diffuse alterations of repolarization. Blood results revealed a normal WBC with raised platelets (616.000cells/mm3), CRP 36mg/L and ESR 28mm/h, Mantoux 16mm/48h, HIV negative. Chest X-ray demonstrated bilateral pleural effusion and a thoracic ultrasound confirmed 5cm pleural effusion. Echocardiography revealed 3cm pericardial effusion with marked fibrosis whilst bilateral ventricular functions were preserved. Pleural fluid: 2400cells/mm3 (90% mononuclear cells), high protein (43,4g/L), smear for acid-fast bacilli and cultures were negative. TBC-index case was her brother. Excellent clinical response was achieved within 1-week using quadruple anti-tuberculosis therapy (RHZE) and adjunctive oral prednisolone (1mg/kg/day). 2 weeks after discharge she returned with reappearance of symptoms and PPE due to poor adherence to corticosteroid therapy. Therapy was reinitiated with completely recovery of the patient.

Commentary: The role of adjuvant steroid therapy in non-HIV patients suffering from tuberculous PPE is not clearly proven. However our experience is in line with published guidelines recommending adjuvant anti-inflammatory/immunomodulatory therapy, which might reduce the need for surgical intervention (pericardectomy or pericardiocentesis) in the future and prevents the important complication of constrictive pericarditis.

Strang; Lancet(1988)

Evans; RespMed(2008)

P522

IMPACT OF SPUTUM POSITIVE TUBERCULOSIS ON PEDIATRIC TUBERCULOSIS DURING ART ERA ATTENDING KANOMBE MILITARY HOSPITAL BETWEEN JANUARY 2009-JUNE 2010

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Introduction: TB infection has markedly increased in the HIV era becoming the most common opportunistic infection. With ART the TB burden is expected to reduce.

Methods: A retrospective cohort study utilizing chart review of patients on TB treatment at Kanombe Military Hospital in Kigali, Rwanda from January 2009 to June 2010 was done. We abstracted demographic data, sputum microscopy results, HIV serostatus and analysed using STATA version 10.

Results: Of 452 TB cases reviewed, male: female ratio was 2:1, median age 29 years (range: 0.125 to 99 years) and pediatric TB 19.5% (88/452) with median age of 5.25 years (IQR: 1.2-12.5 years). Pediatric HIV/TB coinfection was 13/88 (14.8%).Incidence of positive PTB was 138/452 (30.5%) with HIV coinfection 30.9 %(44/138). The burden of smear positive PTB was 108/266 (40.6%) and 30/186 (16.1%) in 2009 and 2010 respectively with OR: 0.28(CI: 0.2-0.4), p value of < 0.001 while the HIV incidence was 98/266 (36.8%) in 2009, 54/186 (29%) in 2010.Risk factors for sputum smear positive TB were >18-25 years, >25-35years OR: 2.3 (CI: 1.32-4.0), OR: 1.7 (CI: 1.0-2.9) with p-values of 0.003 and 0.035 respectively.

Conclusion: Pediatric TB continues to be high against a background of high burden of positive PTB/HIV coinfection. However evidence from this data indicates that with excellent national ART programs TB can be reduced over time. Therefore there is need for strengthening ART programs as prevention strategy of TB as well as prospective studies to assess the impact of ART on TB in resource limited settings.

P523

A DRAMATIC DECREASE IN CHILDHOOD TUBERCULOUS MENINGITIS IN QUEEN SIRIKIT NATIONAL INSTITUE OF CHILD HEALTH, BANGKOK, THAILAND

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Background: Tuberculous meningitis (TBM) is a severe and life-threatening form of tuberculosis (TB). Thailand is in the top 18th of the world high-burden countries of TB.

Methods: Thirty patients (age 11 months to 14 years) with TBM, who were admitted to Queen Sirikit National Institute of Child Health (QSNICH), Bangkok, Thailand, during the period 2003-2009, were retrospectively studied for clinical and laboratory characteristics.

Results: Ninety-six percent of the patients had a positive history of BCG vaccination. Forty, 27, and 33% of the patients were in stage I, II, and III, of TBM, respectively. On admission, fever, weakness, neck stiffness, headache, vomiting, and seizures were present in 83, 62, 53, 43, and 40% of patients, respectively. Positive tuberculin skin test was demonstrated in 70% of the studied patients. The results of this study agreed with typical CSF findings (leukocytes >5 cells/mm^3, protein >100 mg/dl, and CSF glucose < 50% of plasma glucose, were present in 91, 69, and 78% of patients, respectively). Six- and 9-month anti-tuberculous drug regimens were used for 28 and 39% of patients, respectively. Sixty-seven percent of the patients underwent a combination-regimen of 4 anti-tuberculous drugs (isoniazid, rifampicin, pyrazinamide, and streptomycin), 90% were administered steroids, while 30% received ventriculo-peritoneal shunt. The case fatality rate was 10%; all fatal cases had hyponatremia. Fifty percent had neurological sequelae.

Conclusion: Only 30 patients of TBM were admitted in QSNICH (the largest tertiary care pediatric hospital of Thailand) during 7-year-period, which clearly shows a dramatic decrease in childhood TBM cases in Thailand.

P524

A RARE CASE OF OSTEOMIELYTIS BY BCG

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Background and aim: The main agent of osteomyelitis is *Staphylococcus aureus*. *Mycobacterium*, *Streptococcus*, *Salmonella* are more rare agents. Our aim is to describe a case of osteomyelitis caused by a rare etiologic agent.

Methods: Clinical record analysis.

Results: Two-year-old boy with history of Bacille Calmette-Guérin (BCG) adenitis and ganglion excision at five month old, who started limping with pain and swelling of the right hallux with progressive worsening. Radiograph showed lytic lesions in the proximal phalanx of right hallux; scintigraphy revealed hyperfixation and magnetic resonance showed hypersignal at the phalanx without bone destruction. Analytically without leukocytosis, normal C-reactive protein and sedimentation velocity of 17mm/hr. Histopathology of bone biopsy showed granulomatous inflammation with epithelioid cells/histiocytes and giant cells of Langhans. PCR for Mycobacteria was negative; sarcoidosis and autoimmune disease were excluded.

Two months later the boy presented with inflammatory signs of the left foot and 3rd finger of the right hand. The new biopsy was positive for methicillin-resistant *Staphylococcus aureus* (MRSA), as well as in his mother nasopharyngeal exudate. He began treatment with cotrimoxazole and riphampicin. After three weeks *Mycobacterium bovis* was also isolated, which lead to substitution of therapy to isoniazid, riphampicin, ethambutol and linezolid.

Immunodeficiency investigation was negative.

Conclusions: Osteitis after BCG vaccination is rare. However, in BCG vaccinated children with osteomyelitis and no contact with tuberculosis the hypothesis of BCG osteitis should be considered. Although co-isolated MRSA could be secondary to colonization, it should be considered in the osteomyelitis approach due to its increasing incidence in the community.

P525

OSTEOARTICULAR LESIONS CAUSED BY *MYCOBACTERIA* IN CHILDREN

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Background and aims: Osteoarticular infection by *Mycobacteria* is rare in children; its indolent course often leads to misdiagnostic. The possible etiologic agents are *M. tuberculosis*, *M. bovis* and *M. avium*. Our aim is to describe three cases of osteoarticular infection.

Methods: Clinical records analysis.

Results: Boy, 12-month-old, with swelling of right wrist with five months of evolution. Radiograph showed lytic lesion of right radius. Histopathology of bone biopsy revealed chronic necrotizing granulomatous inflammation (CNGI); *Mycobacterium avium* was identified by PCR.

Boy, 11-month-old, with swelling of right elbow with two months of evolution. Radiograph showed lytic lesion of right humerus and surrounding soft tissue swelling. Magnetic Resonance Imaging (MRI) evoked a metastatic lesion. Histopathology revealed CNGI; *Mycobacterium tuberculosis complex* was identified by PCR.

Boy, 14-year-old, with left hip pain with one year of evolution, followed by evening fever, anorexia and weight loss. MRI and Computer Tomography confirmed an aggressive lesion of hip joint, previously suspected by radiograph. PCR and culture of joint fluid and of bone biopsy were positive for *Mycobacterium tuberculosis*.

The first case was treated with riphampicin, azithromycin and ethambutol and the others with isoniazid, riphampicin, pyrazinamide and ethambutol. Clinical and radiological evolution was favorable in all cases. Immunodeficiency investigation revealed deficit of CD4 cells in case 2 (HIV negative).

Conclusions: Diagnosis of osteoarticular tuberculosis requires high index of suspicion because its manifestations are insidious and nonspecific. Only a timely diagnosis can avoid functional sequelae. After diagnosing bone tuberculosis in a child it is important to exclude an immunodeficiency.

P526

INITIAL THREE-DRUG THERAPY IN PEDIATRIC TUBERCULOSIS: AN EXCEPTION TO THE RULE?

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Background and aims: Initial four-drug therapy in pediatric tuberculosis (TB), is recommended in Spain, where the overall isoniazide (INH) resistance rate is higher than 4%. However, this recommendation is inferred from adult guidelines since drug-resistance data in children are scarce. Our aims were to document the prevalence of pediatric drug-resistant TB over the last five years (January´05 to June´10), and to analyze risk factors associated with this resistance.

Methods: A multicenter, retrospective study was performed in 21 hospitals from Madrid area. Medical records of children younger than 18 years diagnosed with TB were reviewed. A multivariate logistic regression was performed in order to identify independent risk factors for TB-resistance.

Results: Among 396 children (148 boys) diagnosed with TB (83.8% pulmonary), 74.5% were born to immigrant parents, and 25.5% to native parents. *Mycobacterium tuberculosis* was cultured in 200 children (50.5%) and susceptibility testing was performed in 93% of isolates: 13.9% were drug-resistant, 9.6% INH-resistant and 3.2% multidrug-resistant. INH-resistance was more common in children born to immigrant parents (12% vs. 0%) (p=0.024). In children born to native parents (including those whose susceptibility was inferred from the adult source isolate), only 2 INH-resistant strains were found (3.7%), one of them from an immigrant baby-sitter.

Conclusions: Initial four-drug therapy is recommended for children in our area, where INH-resistant TB far exceeds 4%. However, selected children born to native parents and without known close contact to immigrant population could be initially treated with the standard three-drug combination.

P527

OSTEOMYELITIS DUE TO NON-TUBERCULOUS MYCOBACTERIA, A CHALLENGING DIFFERENTIAL DIAGNOSIS OF NON-BACTERIAL OSTEOMYELITIS

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Introduction: Primary osteomyelitis in children may be challenging, both with respect to diagnosis and treatment. This is particularly true, if histology is not unambiguous or if culture does not retrieve the causative organism. We report here on a 6 year-old boy with an inconspicuous medical history, who developed primary osteomyelitis due to *Mycobacterium xenopi*.

Case report: A boy presented with a 4-week history of pain in the right foot. X-ray, MRI and bone scan revealed a lytic lesion in the right calcaneus. Physical examination was unremarkable except for discrete inflammation below the right ankle. A biopsy showed disorganized accumulation of neutrophils. Initial cultures were negative, and a positive PCR for *M. xenopi* was regarded as resulting from contamination. Accordingly, non-bacterial osteomyelitis (NBO) diagnosed and anti-inflammatory therapy was initiated. However, a follow-up MRI after 4 weeks showed progressive affection of soft tissue. A subsequent biopsy revealed granulomatous inflammation and PCR and finally culture retrieved *Mycobacterium xenopi* . In full accordance with atypical mycobacterial disease, a TB skin test was positive, whereas the interferon release assay was negative. Antibiotic therapy with rifampicin, ethambutol and clarithromycin was initiated.

Discussion: *M. xenopi* is an exceedingly rare cause of osteomyelitis in children, despite its ubiquitous presence in the environment, especially in water. Chronic granulomatous disease, Mendelian susceptibility to mycobacterial disease and defects in NFkappaB signaling need to be excluded as underlying diseases.

Conclusion: Environmental mycobacteria are potential causes of osteomyelitis and need to be considered if the diagnosis of non-bacterial osteomyelitis is made.

P528

OSTEOMYELITIS DUE TO NON-TUBERCULOUS MYCOBACTERIA, A CHALLENGING DIFFERENTIAL DIAGNOSIS OF NON-BACTERIAL OSTEOMYELITIS

K. Schuster[1], H. Löffler[2], M. Hufnagel[1], T. Wiech[3], A. Serr[4], P. Henneke[2]

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Conclusion: Environmental mycobacteria are potential causes of osteomyelitis and need to be considered if the diagnosis of non-bacterial osteomyelitis is made.

P529

CLINICAL PROFILE AND FACTORS RELATED TO AGE DISTRIBUTION, DIAGNOSIS AND OUTCOME IN CHILDREN WITH ABDOMINAL TUBERCULOSIS

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Aims and methods: A retrospective study was conducted in children suffering from abdominal tuberculosis (TB) from 2007 to 2009and their clinical and laboratory features were analysed.

Results: Out of 285 children with TB, 32 (11.2%) had abdominal tuberculosis. Male: Female ratio was 2.1:1.7. The most common clinical and laboratory features were fever 24(75%), pain in abdomen 17(53%), loss of weight 15(46%), raised ESR 14(43%), loss of appetite 13(40%), raised liver enzymes 12(37%), anemia 10(31%), malnourished 9(28%), ascitis 9(28%), abdominal distension 7(21%), hepatomegaly 7(21%), constipation 3(9%) and diarrhea 2(6%). TB Contact was present in 10(31%) and 7(21%) had tuberculosis in the past. Extra-abdominal TB was found in 17(53%) patients. Lymph node TB (17 patients, 54%) was found to be the commonest, followed by intestinal (10 patients, 32%) and peritoneal TB (4 patients, 13%). Among the clinical features, fever was seen most commonly with lymph node TB (45%), while pain in abdomen was seen most with intestinal type of TB (25%). Abdominal distension (9%) was seen more with peritoneal type. Eighteen (56%) patients had recovered, 7(21%) failed first line therapy and had to be started on second line drugs.

Conclusion: Abdominal TB is seen in 11% of children affected with TB of which over 50% will have extra-abdominal manifestations. Lymph node TB is the most common type of abdominal TB, followed by intestinal and peritoneal type. Fever is seen mostly in lymph node type, pain in abdomen in intestinal type and abdominal distension in peritoneal type.

P530

RISK FACTORS FOR PREVALENT TUBERCULOSIS INFECTION AMONG CHILDREN IN GREENLAND

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Objectives: It is unknown why tuberculosis infection remains a significant problem in Arctic communities. In the 1990ies the TB incidence in Greenland doubled and TB control efforts were re-enforced, however the effect is not yet visible. This study examines risk factors for Mycobacterium tuberculosis infection (MTI) among Greenlandic children in order to characterize the children most at risk of infection during the current epidemic.

Material and methods: Between 2005 and 2007, a survey was undertaken among 1,797 Greenlandic school children using questionnaire and registry data analysed by prevalence odds ratios (OR) and 95% confidence intervals. MTI was defined as a dual-positive interferon gamma release assay and tuberculin skin test.

Findings: The overall MTI prevalence was 8.4% (152/1797). Among children with known TB contact (10%), 26.6% were infected compared with 6.4% of children without TB contact. Overall MTI increased with Inuit ethnicity ($OR_{\text{inuit vs non-Inuit}}$ = 4.22(1.55-11.5)) and narrow age gap to closest older sibling ($OR_{\text{< 1yr vs ≥1 yr}}$=2.48(1.33-4.63). Self-reported TB contact modified the profile to include household crowding and mother's education. Notably, siblings of an older MTI-positive sibling were more than 14-fold more likely of being MTI-positive ($OR_{\text{infected older sibling vs non-infected}}$ = 14.2 (5.75-35.0)).

Conclusion: Ethnicity, sibship relations, domestic crowding, and maternal level of education are factors associated with TB infection among Greenlandic children. The strong clustering of MTI by household suggests family sources of exposure are important. The study findings could aid target operational TB-control efforts towards the most vulnerable groups of children in Greenland.

P531

IMPACT OF GEN-PROBE'S AMPLIFIED MYCOBACTERIUM TUBERCULOSIS DIRECT TEST ON TUBERCULOSIS DIAGNOSIS IN CHILDREN

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Background and aims: The aim of the study was to evaluate the performance of Gen-Probe Amplified Mycobacterium tuberculosis Direct Test (AMTD, Gen-Probe, San Diego, California) for the diagnosis of tuberculosis in children, compared to conventional culture and clinical diagnosis.

Methods: We retrospectively studied 81 children (48 males; mean age 7 years; range 1-16 years) evaluated for possible active TB over a 2-year period. Respiratory samples (n=64/95;67%) examined included gastric aspirates (n=30), induced sputa (n=30), bronchial aspirates and bronho-alveolar lavages (n=4). Non-respiratory samples (n=31/95; 33%) included lymph nodes (n=20), and other sterile fluids (n=11). Specimens were examined using AFB microscopy, Gen-Probe and bacterial culture using BACTEC™ MGIT™ 960 (Becton Dickinson, USA) and Löwenstein-Jensen (LJ) media.

Results: The clinical diagnosis of TB was made in 34/81 (42%) children (29/34 with pulmonary disease). Direct smear was positive for AFB in 2/34 (6%) children; Mycobacterium tuberculosis (MTB) was recovered by culture from 13/34 (38%) and AMTD was positive in 20/34 (59%). Based on clinical diagnosis, the sensitivity, specificity, PPV and NPV of the AMTD test vs. culture were 59%, 96%, 91%, and 76% vs. 38%, 100%, 100% and 69%, respectively. For pulmonary vs. extra-pulmonary disease the performance of AMTD compared to culture was: 100%, 87%, 67%, 100% vs. 75%, 96%, 75%, and 96%, respectively.

Conclusions: Nucleic acid amplification tests are more sensitive and very specific methods for the (rapid) detection of MTB compared to culture in children with TB. The Gen-Probe technique increases TB detection in children by about 50% compared to culture.

P532

TRENDS IN THE EPIDEMIOLOGY OF CHILDHOOD TUBERCULOSIS IN GREECE DURING THE LAST DECADE AND THE EFFECT OF IMMIGRATION

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Background and aims: Tuberculosis (TB) remains a major public health threat even in developed countries since immigration from highly endemic areas seems to globally affect the disease profile. Our aim was to evaluate the epidemiological and clinical features of childhood TB in the greater Athens area during the last decade.

Methods: We retrospectively reviewed the medical records of patients < 14 years of age treated for active TB between January 2000 and December 2009 at our pediatric TB clinic, which is referral center for childhood tuberculosis. Data concerning demographic and clinical characteristics were analyzed.

Results: A total of 321 children (median age 5.57 years, 157 males) with active TB were identified. About one third originated from highly endemic areas. Twenty three children (7%) had extra-pulmonary TB and 61% of them originated from TB endemic areas. Bacteriological confirmation was achieved in 40% of patients from whom specimens were obtained and 1/26 (3.8%) strains were multi-drug resistant. Most cases with drug-resistant Mycobacterium tuberculosis infection were noted among immigrant children. The average annual TB incidence was estimated at 5.37/100,000 for children < 14 years of age in the greater Athens area. Time trend analysis revealed a significant decrease in the annual number of cases among children of low endemicity origin (p=0.019).

Conclusions: In our settings, active TB is decreasing among children of Greek origin and the disease epidemiology as well as drug-resistance is influenced by the increasing influx of immigrants from areas where the disease is highly prevalent.

P533

COMPARISON OF QUANTIFERON-TB GOLD TEST WITH TUBERCULIN SKIN TEST IN CHILDREN WHO HAD NO CONTACT WITH ACTIVE TUBERCULOSIS CASE

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Objective: In this study, we aimed to compare the diagnosis of latent tuberculosis infection (LTBI) in the children with BCG vaccine by using in vitro quantiferon-tb gold test (QFT-G) based on interferon-γ (IFN-γ) or in vivo tuberculin skin test (TST).

Methods: We enrolled 81 children for this study from 2008 through 2011 at Dr. Sami Ulus Hospital. Subjects were selected for inclusion in the study, who have positive TST result without a known history of TB contact. Patients were seperated to groups according to their ages, the reason of TST application, number of BCG vaccination scar and diameter of TST induration. Posteroanterior, lateral chest graphies and if necessary computerized tomography were performed. QFT-G test were administered to all patients.

Results: The study population consist of 48 boy (59.3%) and 33 girl (40.7%) with mean age 94.8± 51.9 months (ranged from 6 month to 193 month). Among them, 65 (%85.2) had a TST induration 15-19 mm, 16 (%14.8) had ≥ 20 mm TST induration. Of these, only 12 (%14.8) were QFT-G positive, and treatment was performed to these patients. In three years follow-up period, any TB case was identified in this study whom treatment was not performed.

Conclusion: We suggested that, in countries which BCG vaccination routinely recommended, confirmation of positive TST results with tests based on IFN-γ could reduce false positive results and prevents unnecessary treatment and adverse reactions especially for low risk population. We believe that IFN-γ based tests will be routinely used in the diagnosis of TB infection.

P534

PAEDIATRIC TUBERCULOSIS AT A RESEARCH HOSPITAL IN ISTANBUL, TURKEY: A RETROSPECTIVE STUDY

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Background: Tuberculosis (TB) still remains a growing public health problem globally. Pediatric tuberculosis cases constitude 10% of total burden in Turkey.

Objective: To determine the clinical features and diagnostic tests including radiological findings of pediatric TB cases in our hospital.

Methods: We conducted a retrospective chart review of children with TB during a five-year period at Bakırkoy Maternity and Children's Research hospital, Istanbul, Turkey.

Results: A total of 277 patients (64.2% hospitalised) were included. Mean age was 7.8 years (2 months to 19 years). 64.4% patients had a history of contact with a person with TB. Pulmonary TB was the most common diagnosis (74.7%), while extapulmonary TB cases included lymphadenitis (9.7%), peritonitis (2.5%), meningitis (2.1%), renal TB (0.7), bone TB (0.4), pericarditis (0.4%), and uveitis (0.4%). Thirty eight patients (14%) presented with recurrent pneumonia. The common clinical features were: cough (68%), long standing fever (42%) and weight loss (25.5%). Up to 40% of patients had a normal physical examination on admission. Radiologic findings of the chest revealed 29 independent events: Infiltrates (67.8%), lymphadenitis (52.4%), pleural effusion (16.8%), cavitations (6.2%). Tuberculin skin test was positive in 51.3% of cases. *Mycobacterium tuberculosis* could be identified in only 16.6% of cases. In addition 22 patients were diagnosed by histopathological findings.

Conclusion: TB continues to be an important cause of morbidity in children in our region. Signs and symptoms are nonspesific and microbiologically confirmed ratio is low. Positive history of contact with an adult that had TB is important in diagnosis.

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QUANTIFERON - TB GOLD TEST AS A DIAGNOSTIC TOOL IN CHILDREN WITH LATENT TUBERCULOSIS INFECTION AND TUBERCULOSIS

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Background: Few data are available evaluating interferon gamma release assays (IGRAs) in children with tuberculosis (TB). Currently, neither tuberculin skin test (TST) nor IGRAs can be accepted as gold standard for the diagnosis of TB.

Objective: To compare the results of Quantiferon -TB Gold and TST in children with a diagnosis of latent TB infection and active TB.

Methods: We conducted a retrospective study of 103 children referred to a tertiary care hospital in Istanbul. Patients were evaluated in three categories including TB diagnosed clinically or with microbiological and histopathological confirmation (n=32), latent tuberculosis infection with isolated TST positivity (n=59), and healthy normal clinical findings, negative TST, no history of contact with TB (n = 10) . TST and Quantiferon -TB Gold test were compared in all three groups.

Results: Among 34 patients diagnosed as TB, both tests were positive in 8, TST positive in 12, Quantiferon TB Gold test positive in 16, both tests negative in 10 patients. Three out of seven children with culture-confirmed tuberculosis disease had positive Quantiferon -TB Gold test (42%) while TST positivity was 28%. Among 59 children diagnosed as latent TB infection, 41 tested negative by Quantiferon TB Gold test and 90% of these children were at low risk (no history of contact with TB).

Conclusions: Children with a positive TST or Quantiferon TB Gold test are more likely to have latent TB infection or TB. Quantiferon -TB Gold test seems to be a better alternative than TST to detect latent TB infection.

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SYSTEMS BIOLOGY OF CEREBRAL GRANULOMA FORMATION CAUSED BY *MYCOBACTERIUM TUBERCULOSIS*

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Background and aims: Tuberculous meningitis (TBM) is the most severe extra-pulmonary manifestation of tuberculosis (TB). To study cerebral granuloma formation, an *in silico* model was developed based on an existing computer model for pulmonary TB.

Methods: In addition to immune cells already captured in the lung mode (macrophages, T helper cells, cytotoxic T cells and regulatory T cells), we added into the model the dynamics of meningeal macrophages and ramified/activated microglia (tissue macrophages of the central nervous system). The model also accounts for cytokines (TNF-α, IFN-γ) and chemokines (CCL2, CCL5 and CXCL9/10/11). Finally, intra- and extracellular bacteria are tracked along with development of caseation. We performed *in silico* knock-out experiments regarding IFN-γ and TNF-α.

Results: We identified parameter values from literature estimates when available, and used a sensitivity/uncertainty analysis to determine what mechanisms result in formation of stable granuloma in which bacterial numbers remained constant over time (containment). By simulating a TNF-α knock-out, we observed that infection in the brain is no longer contained and that bacteria break through the meninges resulting in meningitis. *In silico* knock-out of IFN-γ resulted in even higher bacterial numbers than the TNF-α knock-out.

Conclusions: These insights are important first steps toward elucidating the dynamics of cerebral granuloma formation in TBM. In the future we will extend our model based on data obtained from human post mortem studies and data from animal models.

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HOMOCYSTEINE LEVEL IN CHILDREN WITH CEREBEROVASCULAR STROKE

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Background: Cerebrovascular stroke is an important cause of morbidity and mortality in children. Recent epidemiologic data suggest that 3200 cases of stroke occur per year in the population aged between. Although outcome for stroke in children is significantly better than in adults, 20% die and 50% to 80% are left with significant disability. Moderately elevated homocysteine status is considered an independent risk factor for occlusive arterial disease in the peripheral arteries and cerebral vessels

Aim: To evaluate the role of homocysteine as a risk factor of cerebrovascular stroke in children.

Methods: 52 children with stroke (65.4% ischemic and 34.6% hemorrhagic) 34 males and 18 females, aged 30 days to 18 years also 20 healthy children as control group. All cases were evaluated by Pediatric National Institute of health stroke Scale .Evaluation of plasma levels of homocysteine, random blood glucose, serum sodium and potassium were done

Results: The annual frequency rate of stroke was 0.3%. The mean±SD of serum sodium and potassium and blood glucose were significantly higher in ischemic compared to hemorrhagic and control groups. The mean±SD of homocysteine in children with ischemic and hemorrhagic strokes were more than control group .The odds ratio of homocysteine for ischemic and hemorrhagic stroke were (3.3, CI 2.38-26.9) and (1.9, CI 2.3-46.8) respectively. The mean±SD of homocysteine was significantly higher in children with hospital stay more than 2 weeks, in children with PedNIHSS ^{3} 12 and in non survivors.

Conclusion: Hyperhomocysteinemia is significant risk factor of stroke in children.

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TRANSIENT AND CHRONIC NEUTROPENIA IN CHILDREN WITH FEBRILE ILLNESS: CLINICAL COURSE AND OUTCOME

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Background and aim: The aim of the study was to examine the role of infections in acquired neutropenias in childhood and to assess their clinical course, complications and outcome.

Method: All children admitted to two pediatric wards with febrile neutropenia during a four-year period were prospectively investigated for underlying infections with inflammatory indices, cultures of body fluids and serological tests.

Results: 161 previously healthy children, aged mean±SD 3.02(±3.86) years (range:0.1-14), were identified with febrile neutropenia/leukopenia during the study period. An infectious agent was identified in 90/161 cases (55.9%) (viral infection: n=62, bacterial: n=19, parasitic: n=9).

130/161(80.7%) patients had transient neutropenia (TN) (118 patients recovered within 60 days and 12 in 60-180 days), while in 31 patients neutropenia persisted for ≥180 days. From them 7 cases had antineutrophil antibodies and 4 had malignancy. In all age-groups (0-2 y, 2.1-5 y, >5 y), TN was predominantly associated with viral infections of short duration (< 1 mo) and of mild/moderate severity. Two years after diagnosis 143/157 children (91.1%) were available for follow-up examination. Of these, 26/143 (18.2%) remained neutropenic while 117/143 (81.8%) had recovered completely. The latter patients had a remarkably benign course despite markedly reduced granulocyte counts.

Conclusion: Febrile neutropenia during childhood is usually transient, often following viral and common bacterial infections, does not present serious complications and in the majority of cases it resolves spontaneously. However, in a significant percentage of patients, neutropenia is discovered during the course of an infection, on a ground of a preceding chronic neutropenic status.

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ORBITAL AND PERIORBITAL CELLULITIS AFFECTING CHILDREN IN THE POST- HIB VACCINATION ERA

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Objectives: Routine immunization against Hib was introduced in the UK in 1992. We reviewed the clinical features, management, complications and follow up of the condition in the post-immunization era.

Methods and setting: Retrospective review of medical notes of 50 children admitted with diagnosis of orbital or periorbital cellulitis to Paediatric Department of a District General Hospital in England, 2000 - 2010. Each case recorded: age, gender, month of admission, days of illness before admission, clinical features, immunisation, temperature, WCC, CRP, microbiology studies, radiology findings, antibiotics, complications, duration of hospital stay and follow up.

Results: Forty five patients had preseptal cellulitis. Nine (18%) were aged less than 1 year and 27 (54%) were aged 1-7. 27 (54%) were female. 23 (46%) admissions were between December & February. 22 (44%) had ENT symptoms and five patients had signs of orbital cellulitis. 80% (40) of patients were apyrexial, 13 (26%) had CRP >60 and 6 had WCC of >20. 43 (86%) had blood cultures, with one positive growth of Micrococcus. Eye swabs were performed in 12 patients and 3 had positive growth of Staphylococcus aureus. Most patients were seen by ophthalmologists and had radiology studies, all received antibiotics. Surgery was required for six patients and three of whom had preseptal cellulitis.

Conclusions: In the post Hib-vaccination era bacteraemia and sepsis are now rarely seen in acute orbital infections. Upper respiratory tract infection and conjunctivitis remain important predisposing factors. Significant complications still occur when preseptal cellulitis is present.

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INFECTIOUS MONONUCLEOSIS IN CHILDREN INFECTIOUS DISEASES CLINIC OF CONSTANTA

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Introduction: Infectious mononucleosis is characterized by fatigue, malaise, fever, red or white tonsillitis, sore throat and generalized lymphadenopathy. Epstein Barr virus is involved in 90% of cases of infectious mononucleosis.

Material and method: Retrospective study about 76 childrens with mononucleoz-lyke syndrome hospitalized in Children Infectious Diseases Clinic of Constanta over a period of 6 years. Diagnosis was established on clinical and paraclinical data, and etiologic diagnosis was based on presence of heterophile antibodies (Paul Bunnell reaction) and other antibody (IgM VCA- EBV; IgM and IgG CMV) detected by ELISA.

Results: Over a period of 6 years (January 2005-December 2010) were hospitalized in Children Infectious Diseases Clinic of Constanta a number of 76 children with mononucleoz-lyke syndrome. From the total of the patients with mononucleoz-lyke syndrome 37 were boys, and 65 patients were from urban area. The most affected group of age was 5-10 years with 45 cases. Number of cases registered by year increased from less than 10 per years 2005 and 2006 to 30 in year 2010. 8 were infectious mononucleosis caused by CMV (4 cases - IgM CMV positive and other 4 cases IgM + IgG positive). 50 cases were infectious mononucleosis with Epstein Barr virus (21 cases - Paul Bunnell reaction positive, and 29 cases with IgM anti VCA - EBV positive). In 18 cases etiology remain unknown.

Conclusions: We noticed increased number of infectious mononucleosis cases with Epstein Barr virus and CMV in children with age between 1-4 years over the last 3 years.

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VARICELLA ZOSTER VIRUS ENCEPHALITIS ASSOCIATED WITH STEVENS-JOHNSON SYNDROME IN AN IMMUNOCOMPETENT CHILD

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Background: VZV encephalitis is rarely seen in immunocompetent patients. The Stevens-Johnson syndrome (SJS) is a multimorphous rash, induced by drugs or viral infections. Despite its increased incidence in childhood, the varicella zoster virus (VZV) was the etiological agent for SJS in only a small number of cases.

Case report: An 11 year old female was admitted in June 2010, on the 10th day of chickenpox, with headache, lethargy and 2 convulsive episodes. The clinical exam, EEG modifications (delta and theta waves) and MRI head test (millimetric demyelinating lesions on the temporal and bilateral corticosubcortical lobes) lead to the diagnosis of VZV encephalitis. The lumbar puncture showed no modifications. The treatment given was antiretroviral (Acyclovir), corticopulstherapy and anticonvulsive (Carbamazepine). On the 17th day of chickenpox and 7th day of Carbamazepine, the patient developed a maculo-papular and vesiculo-bullous rash, and hemorrhagic crusts on the lips, diagnosed as SJS. The evolution was favorable following corticotherapy, the substitution of the antiepileptic and local treatment. The neurological status improved and the mucocutaneous syndrome subsided after 21 days. During the 6 months after the hospital discharge, no more convulsions were observed and the repeat MRI was normal.

Conclusions: This case portrays the rare association of 2 childhood entities. It is difficult to establish the trigger factor for the SJS: the VZV, the Carbamazepine or both. A more in depth study is required to explore the relationship between the VZV and the SJS.

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INTRAVENOUS IMMUNOGLOBULIN AS A TREATMENT OPTION IN SEVERE KIKUCHI-FUJIMOTO DISEASE

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Introduction: Kikuchi-Fujimoto disease (KFD) is characterized by lymphadenopathies associated to systemic symptoms, and characteristic pathological findings of unknown etiology. Usually a benign condition, it may however have severe forms, for which the best management is not established.

Case Report: A previously healthy 13 year-old boy was referred to our Unit with one-month lasting intermittent fever and anorexia. In the last days, prostration and transient generalized exantema involving the face appeared. Submandibular lymphadenopathy (1 cm) and a tender hepatomegaly were present.

Laboratorial parameters: pancytopenia (hemoglobin 7,7g/dL, leucocytes 1120/mm^3, platelets 73000/mm^3), ESR 63mm/h, CPR 7,28mg/dl, LDH 719U/L, ferritin 12.000. Triglycerides and fibrinogen levels were normal. No auto antibodies were found.Thoracic CT scan showed slight pericardial and bilateral pleural effusion.He had started large-spectrum antibiotics and B-anfotericin. At day four of admission, the fever became higher (>40ºC), associated with generalized lymphadenopathy, exacerbation of the exantema and severe prostration. Intravenous immunoglobulin (IVIG), 1g/Kg/day in 2 consecutive days was administered with prompt clinical improvement.Blood and urine cultures were negative. Bone biopsy and myelogram were normal. The lymph node biopsy made the diagnosis of KFD. He was discharged at day-eleven. Laboratory parameters normalized and the child remained well at 9-month follow-up.

Comments: The patient presented with a lupus-like severe form of KFD. IVIG was started considering an autoimmune disease, and willing to avoid steroids before the biopsies. Though steroids are usually recommended for KFD, they were not used as IVIG 2g/Kg proved to be promptly and long lasting effective.

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LYME BORRELIOSIS IN CHILDREN

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Background and aims: Lyme borreliosis is a multi-systemic disease caused by *Borrelia burgdorferi*. A complete presentation of the disease on child is an extremely unusual observation, in which a skin lesion follows a tick bite, the lesion itself is followed by heart and nervous system involvement, and later on by arthritis; late involvement of the eye, nervous system, joints and skin may also occur. Information on the relative frequency of individual clinical manifestations of Lyme borreliosis is limited; however, the skin is most frequently involved and skin manifestations frequently represent clues for the diagnosis. The only sign that enables a reliable clinical diagnosis of Lyme borreliosis is a typical erythema migrans. Laboratory confirmation of a borrelial infection is needed for all manifestations of Lyme borreliosis, with the exception of typical skin lesions.

Methods: We did a retrospective study of hospitalized cases with borreliosis in children on National Institute of Infectious Diseases "Prof. Dr. Matei Bals " in the period 2005 - 2010, which we followed the clinical manifestation.

Results: During this period in pediatric wards of our institute were hospitalized a total of 36 cases in children borreliosis. We observed that clinical manifestations of the child are polymorphic: most have clinical picture of erythema migrans, the rest involving various clinical forms (arthritis, optic neuritis, diplopia, facial paresis, hemiparesis, polyradiculonevritis).

Conclusions: Lyme borreliosis in children is a multisystem disease with a polymorphous clinical manifestations that can be dressed in various clinical forms.

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BCG SCAR REACTIVATION IN KAWASAKI DISEASE

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BCG scar reactivation is rare but specific sign of Kawasaki disease and, especially important for diagnosis of inkomplet Kawasaki disease in infants. Two infants with BCG scar reactivation due to Kawasaki disease are reported. An eleven month-old boy with a history of recurrent fever for one month and erythema around the BCG scar for two days. Last fever period was unknown. Physical examination was revealed fever (38.3 C axillary), generalized maculopapulary erythema and, BCG reactivation. Anemia, elevated erythrocyte sedimentation rate, procalsitonin, and liver enzymes, piyüri were detected. Because of he was immunocompotent BCG reactivation was considered in favor of the Kawasaki disease and, IGIV (2 gr/kg/dose) and acetyl salisylic acid were ordered. In follow up all five criteria of Kawasaki disease was developed. A six month-old girl was admitted with fever for five days, diarrhea and vomiting for three days. Fever (39 C axillary), bulbar conjunctivitis, bright red lips, hypertrophic tongue papillae, reactivation of BCG scar, anemia, raised white blood cell count, erythrocyte sedimentation rate, procalsitonin, C reactive protein and, liver enzymes, hypoalbuminemia, were detected. IGIV and acetyl salisylic acid were ordered with diagnosis of the incomplet Kawasaki disease and fever was subsided within eight hours and the erythema around the BCG site disappeared.

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SEPTICAEMIA IN EXTREMELY PRETERM INFANTS < 28 WEEKS OF GESTATIONAL AGE IN A NEONATAL INTENSIVE CARE UNIT

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Background, aims: Septicaemia is a significant cause of morbidity and mortality in preterm infants. We investigated the incidence of septicaemia in preterm infants during an 8 year period in the NICU.

Material, methods: Population based of this retrospective study of 138 infants born before 28 weeks of gestational age (GA) and hospitalized in NICU in Lund during 2002-2009. Criteria for septicaemia were positive blood cultures or U-Arabinitol quota>5. Diagnosis was clinical compatible with laboratory findings of infection (C-reactive protein>8mg/l; total WBC >15000 or < 5000, platelet count < 100000u/L). Septicaemia onset was registered as early (< 72 hours of life) or late (> 72 hours).

Results: Out of 138 infants 31.1% (95% CI 24.1-39.2%) were identified as cases of septicaemia. Median of GA and birth weight (BW) was 25weeks+4days and 735g respectively.Of 43 septicaemia 11,6% (95% CI 5.9-23.7%) were early septicaemia (1 Candida, 2 coagulase negative staphylococcus (CoNS) ,2 other), 76.7%(95% CI 62.8-86.3%) were late septicaemia (22 CoNS, 4 staphylococcus aureus,7other) and 11.6%(95% CI 5.9-23.7%) were affected by both early (5 Candida) and late (5 CoNS) septicaemia. Laboratory findings of infection were most often an increase of CRP 93% (95% CI 82.4-96.6%), followed thrombocytopenia 60.5% (95% CI 46.0-73.2%). The most frequent clinical signs were cardiopulmonary instability (apnea 48.8%/95% CI 35.1-62.8%/, bradycardia 41.9%/95% CI 28.8-56.2%/),abdominal distention 39.5% (95% CI 26.8-53.9%), respiratory distress (RD) 20.9% (95% CI 12.0-34.6).

Conclusions: The incidence of septicaemia was 31.1% (95% CI 24.1-39.2%). Late septicaemia was more frequent and the most frequently identified bacteria were CoNS.

Causes of septicaemia	No.of early septicaemia	% (n=10)	95%-CI	No.of late septicaemia	% (n=38)	95%-CI	Total	% (n=43)	95%-CI
CoNS	2	20	9,6-47,1	22	58	42,7-71,6	24	56	41,6-69,1
Cand+CoNS	5 candida	50	26,6-73,4	5 CoNS*	13	6,6-26,4	5	12	5,9-23,7
Staphylococcus aureus	0	0		4	10,5	5,1-23,1	4	9	4,6-20,7
CoNS+Candida	0	0		3**	8	3,9-19,6	3	7	3,4-17,6
Candida albicans	1	10	7,0-35,2	2	5	2,8-15,9	3	7	3,4-17,6
Other	1Klebs.p1 E.coli	20	9,6-47,1	1Enterob. 1Enteroc.	5	2,8-15,9	4	9	4,6-20,7
* Five infants were affected by bhot early and late septicaemia **Three infants were affected by CoNS and Candida simultaneously									

[Incidense of early and late septicaemia]

Clinical sings and symptoms of septicaemia	Number of infants	% (n=43)	95%-CI
Apnea	21	49	35,1-62,8
Bradycardia	18	42	28,8-56,2
Abdominal Distention	17	39,5	26,8-54,0
Respiratory Distress	9	21	12,0-34,6
Hyporeactivity	6	14	7,3-26,5
Vomiting	3	7	3,4-17,6

[Clinical sings and symptoms of septicaemia]

Laboratory findings	Number of infants	% (n=43)	95%-CI
CRP>8	40	93	82,4-96,6
Thrombocytopenia	26	60	46,0-73,2
Leukopenia	3	7	3,4-17,6
Leukocytosis	3	7	3,4-17,6

[Labaratory findings of septicaemia]

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GENDER AND GESTATIONAL AGE INFLUENCE SUPPRESSOR T CELL COUNTS IN NEONATES

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Introduction: Generally, the immune system is a remarkable defense mechanism; it acts in a wide range of clinical conditions. The maternal-fetal immunologic relationship is unique. Not only must the fetus be protected against a variety of patentally pathogenic organisms, but the mother must also protect the fetus from rejection as foreign tissue. The problems of immunologic adaption during the transitional period from intra- to extrauterine life are responsible for the physiologic immaturity of the immune function in newborn infants.

Material and methods: Peripheral blood mononuclear cells were obtained from peripheral blood samples of 44 term and preterm infants after obtaining informed consent. Cells were prepared by ammonium chloride mediated lysis, incubated with the respective antibodies and analyzed by flow cytometry according to standard procedures.

Results: Suppressor T cells (CD8+) and naive suppressor T cells (CD8+CD45RA+) were significantly lower in preterm infants **(p< 0.01).** Comparing males with females CD8+ as well as CD8+CD45RA+ cells were significantly lower in males **(p< 0.01).** Relating

T cell counts in males and females to the respective gestational ages CD8+ and CD8+CD45RA+ cell counts were higher in term females compared to preterm females or term/preterm males (**p< 0.01**).

Conclusions: Our data suggest that T lymphocyte surface antigen expression is influenced by gender as well as by gestational age. Since septicaemia is more common not only in very low birth weight infants but also in male neonates (Fanaroff et al, 1998) we propose that lower suppressor T cells might contribute to this phenomenon.

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A QUALITATIVE ASSESSMENT OF FACTORS INFLUENCING CHILDHOOD VACCINE PROVIDERS' INTENTION TO RECOMMEND ROUTINE IMMUNIZATION IN THE NETHERLANDS

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Background and aims: Childhood vaccine providers (CVP) are well-positioned to address uncertainties and possible misconceptions about vaccines among parents, but must be motivated and acquire the knowledge and possibilities to do so. Our aim was to examine factors related to CVPs' intention to recommend vaccines of the Dutch national immunization program (NIP) to parents.

Methods: We performed four focus group discussions with nurses and physicians, working with children of 0-4 years old, in different regions of the Netherlands. One focus group included anthroposophical CVPs only. For the design of our focus groups, elements from the Theory of Planned Behavior were used. Thematic analysis was used to structure and analyze the dataset.

Results: Four main themes were identified:

1. CVPs' perceived responsibility in relation to recommending vaccines.

2. CVPs' attitude towards the NIP: CVPs were positive about the current program.

3. Organizational factors associated with recommending vaccines such as limited time and inadequate information supply.

4. The relationship between parents and CVPs: trust and the possibility to communicate were important.

Conclusions: Our qualitative assessment provides a comprehensive overview of CVPs' beliefs associated with the intention to recommend vaccines to parents. CVPs were motivated to support the NIP, however, their intentions had limits; their willingness and capabilities were affected by practical issues, information supply and knowledge, attitudes towards vaccines and by the group of parents they were confronted with. The present study provides relevant recommendations for future communication and organization of the NIP that might also be useful for other countries.

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THE EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE (ETS) ON PNEUMONIA RISK IN CHILDREN UNDER 7YEARS IN NORTHERN NIGERIA

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Background: The numerous effects of ETS on the non-smoking public have being evidenced through decades of research. This does not only affect adults but children. ETS effects on children have shown to be grave as it worsens asthma conditions, increases pneumonia cases and causes Sudden Infant Death Syndrome (SIDS). This study considers pneumonia risk on children under age 7 in Northern Nigeria exposed to ETS.

Methods: Most residents in all 44 Local Government Areas (LGAs) in Kano State of Northern Nigeria took part in a population-based large-scale cross-sectional survey in Kano state from 2007-2010. Demographic information coupled with socioeconomic status, smoking status and house environment of each household member, was collected from participants. General records were takent.

Results: Out of a total of 528, 800 people resident in 102,334 homes identified in the survey areas and visible/present, 52,888 (10%) were children aged 7 years and below. While the prevalence of ETS exposure on children was 81%, the prevalence of reported pneumonia cases was 3.5%. Multiple logistic regression analysis showed that exposure to ETS was independently associated with reports of pneumonia cases (adjusted odds ratio 1.55, 95% CI 1.25 to 1.92). The prevalence of tobacco smoking was higher among men than women (63.5% vs 44.1%). It is estimated that 32.7% of childhood pneumonia in the northern region of Nigeria is attributable to ETS.

Conclusions: Attention should be given to reduction to children's exposure to ETS not only in Nigeria but in all affected areas mostly all parts of the world.

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THE MANAGEMENT OF THE OTITIS MEDIA WITH EFFUSION IN THE ENT CLINIC TIMISOARA

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Otitis media with effusion (OME) is a pathologic condition of the middle ear in which an effusion is present behind an intact eardrum without signs of acute inflamation.

The authors made a retrospective study on 134 children diagnosed with OME between 2004-2009 in the ENT Clinic Timisoara. In order to establish a diagnosis and a therapeutic conduct, children have been examined by otomicroscopy, audiometry and tympanometry with the testing of the acoustic reflex. When necessary, allergy tests have been added. A study protocol included that all patients benefit fron the treatment according to the aetiology. 74 patients (55.22%) were cured after 21 days following a drug treatment with nasal decongestants and antiinflamatory therapy. For 26 children (19.4%) adenoidectomy was performed due to the fact that repeted episodes of acute otitis media (AOM) and OME were asociated with chronic adenoiditis. For 18 patients (13.43%) antiallergic treatment was prescribed due to the rhinosinusal allergy association. Aditionally, 7 (5%) of these patients were the subjects of adenoidectomy and ventilation tube insertion. Ventilation tube insertion as stand alone treatment was performed on 16 patients (11.94%). However, in spite of the treatment, 10 patients presented refractory OME: 7 patients with medical treatment, 2 patients with grommet insertion and 1 patient with adenoidectomy.

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MICROBIOLOGY OF THE TONSILS IN PFAPA (PERIODIC FEVER, APHTOUS STOMATITIS, PHARYNGITIS AND ADENITIS) SYNDROME

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Background: The etiology of PFAPA -syndrome (Periodic Fever, Aphtous stomatitis, Pharyngitis and Adenitis) is unknown but the symptoms disappear after tonsillectomy. We wanted to investigate the microbiology of the tonsils removed from children with PFAPA -syndrome and to compare it with controls.

Methods: Thirty one consecutive children sent for tonsillectomy because of PFAPA were recruited. Twenty four children coming to tonsillectomy mainly due to a clinical suspicion of obstructive sleep apnea, served as controls. The removed tonsils were cultured for bacteria, mycobacteria, yeasts and viruses. Polymerase chain reaction -analyses were performed to find bacteria, mycobacteria and 15 viruses. Biofilms were visualized with scanning electron microscope and categorized as present or lacking. All analyses were done blinded for the indication for tonsillectomy.

Results: Biofilm was present in 55% of PFAPA tonsils but only in 21% of the controls (P=0.01, difference 34%, 95% CI 8-54%). *Candida albicans* was found in 16% of the cases but in none of the controls (P=0.04, difference 16%, CI 4-33%). *Staphylococcus aureus, Varizella zoster* -virus and actinomyces-like organisms were significantly more commonly found among control tonsils than in the cases. There were no other significant differences between the groups.

	PFAPA, N=31	Controls, N=24	P, Difference (95 CI)
Actinomyces-like organisms	5 (16 %)	10 (42 %)	0.04, -26 % (-47 - 0 %)
Biofilm	17 (55 %)	5 (24 %)	0.01, 34 % (8-54 %)
Candida albicans	5 (16 %)	0	0.04, 16 % (0-33 %)
Hemofilus influenzae	12 (39%)	9 (38 %)	NS
Fucobacteria/Prevotella	10 (32 %)	3 (13 %)	NS
Pneumococci	7 (23 %)	1 (4 %)	NS
Streptococcus, group A	1 (3 %)	2 (8 %)	NS
Staphylococcus aureus	3 (10 %)	9 (38 %)	0.01, -28 % (-49 - -6%)
Mycobacteria	1 (3 %)	0	NS

[Table 1. Microbiology of PFAPA and control tonsils]

Virus	PFAPA, N=31	Controls, N=24	P, Difference (95CI)
Adeno	14 (47 %)	7 (29 %)	NS
Cytomegalo	0	0	NS
Entero	4 (13 %)	5 (21 %)	NS
Ebstein Barr -virus	8 (27 %)	9 (38 %)	NS
Influenzaviruses	0	1 (4 %)	NS
HHV6	16 (53 %)	14 (58 %)	NS
Herpes simplex 1 or 2	0	2 (8 %)	NS
Varicella zoster	0	5 (21 %)	0.009, -21% (-41 - -5%)
Parainfluenza, RSV, metapneumo, papilloma	0	0	

[Table 2. Viruses in PFAPA and control tonsils]

Conclusion: There were more often *Candida albicans* and biofilm formation in tonsils removed from children with PFAPA as compared to controls. These and other differences that we found may not reflect the microbiological etiology of the syndrome but more the differences in the immunological features between PFAPA syndrome and other conditions leading to tonsillectomy.

P551

RECURRENT INFANT SEPSIS - CAUSED BY ANTIBODY MEDIATED COMPLEMENT FACTOR H (CFH) DEFICIENCY

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Background: Sepsis within the first months is associated with perinatal risk factors, immature immune systems and loss of maternal protection. Recurrent sepsis necessitates further evaluation for underlying predisposition. We present a novel causal mechanism for recurrent sepsis.

A boy was born to consanguineous parents of Pakistani origin. Ten days later, he developed sepsis and multi-organ failure requiring intensive care. He had 3 further episodes of life-threatening sepsis by 4 months, each with: anaemia and schistocytosis, thrombocytopaenia, renal impairment with low C3/C4 proteins and coagulopathy.

Methods: The clinical and laboratory features suggested abnormal control of complement activation. Therefore, the complement pathway was investigated with measurement of alternative and classical pathway regulation.

Results: The patient had low serum CFH levels. CFH antibodies were identified at high titres, which subsequently became undetectable. His mother did not possess CFH antibodies. CFH functional assays revealed poor CFH activity. Genotyping of mother and child identified no CFH loci mutations. The diagnosis was transient autoantibody mediated CFH deficiency resulting in shock, multi-organ failure and features of atypical haemolytic uraemic syndrome.

Conclusion: CFH is a key regulator of the alternative pathway. It is postulated that in this patient CFH autoantibodies arose in utero or postnatally with resultant susceptibility to infection, defective CFH mediated control of complement activation and severe shock with multi-organ failure. The autoantibodies resulted in low serum CFH levels, impaired alternative pathway activity with persistent C3/C4 consumption. This is the first report of sepsis due to transient CFH autoantibody production with such early disease onset.

P552

BILIARY LITHIASIS IN CHILDREN

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Background and aims: Until recently, biliary lithiasis was considered infrequent in childhood. Their etiology is often unknown. Biliary lithiasis in children differs from that in adults and there is very little scientific evidence on the most suitable therapeutic procedures.

Methods: We studied biliary lithiasis pattern in children. The diagnosis was based on abdominal ultrasonography, computed tomography and ERCP in some cases. In all cases we made the differential diagnosis of acute viral hepatitis.

Results: We have reported 12 cases of pediatric cholelithiasis in our hospital between 2006 and 2010. All cases are female, from 13 to 16 years of age. All children were hospitalized with suspected acute viral hepatitis. The most frequent symptom was nonspecific abdominal pain (8 patients) followed by nausea, vomiting and jaundice; moderately elevated transaminases were observed in all cases and direct bilirubin increases were noticed in 5 cases. We found risk factors in 8 of these cases, the most frequent risk factors were obesity, excessive diet and familial hyperlipidemia. Five children required surgery, two children required ERCP for common bile duct lithiasis, and one case was solved by eliminating spontaneous common bile duct stone. Medical treatment with ursodeoxycholic acid was indicated in oligosymptomatic lithiasis with transparent, soft, cholesterol-rich stones and in patients with a high surgical risk.

Conclusions: The prevalence of biliary lithiasis in children is low, however, be taken into consideration in this risk factors such as obesity.

P553

CASE REPORT: A CASE OF RECURRENT KAWASAKI DISEASE ASSOCIATED WITH CARDIAC SEQUELAE IN A CAUCASIAN CHILD

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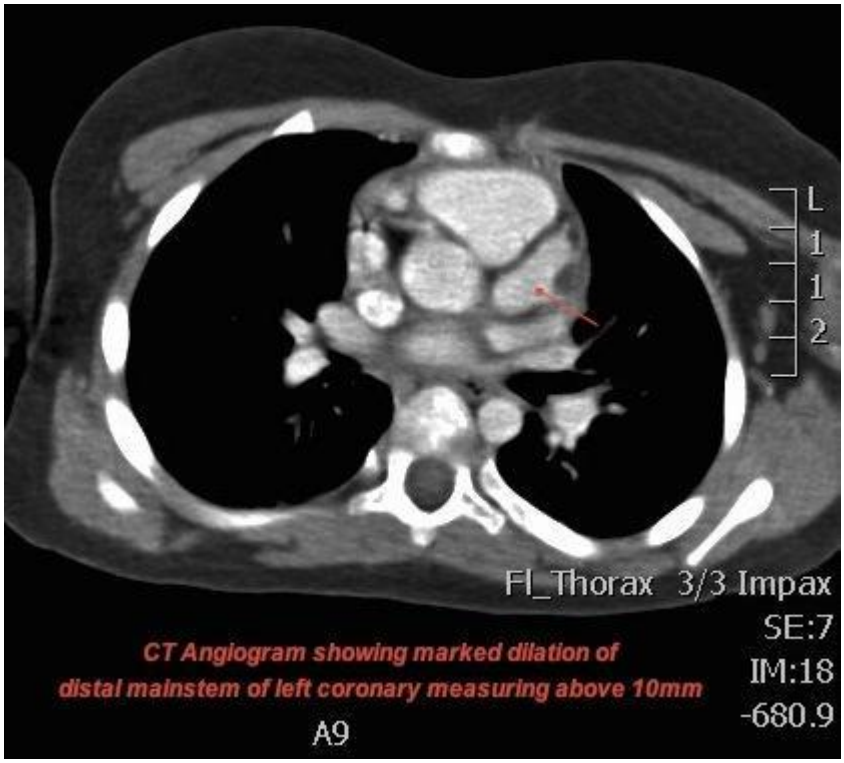
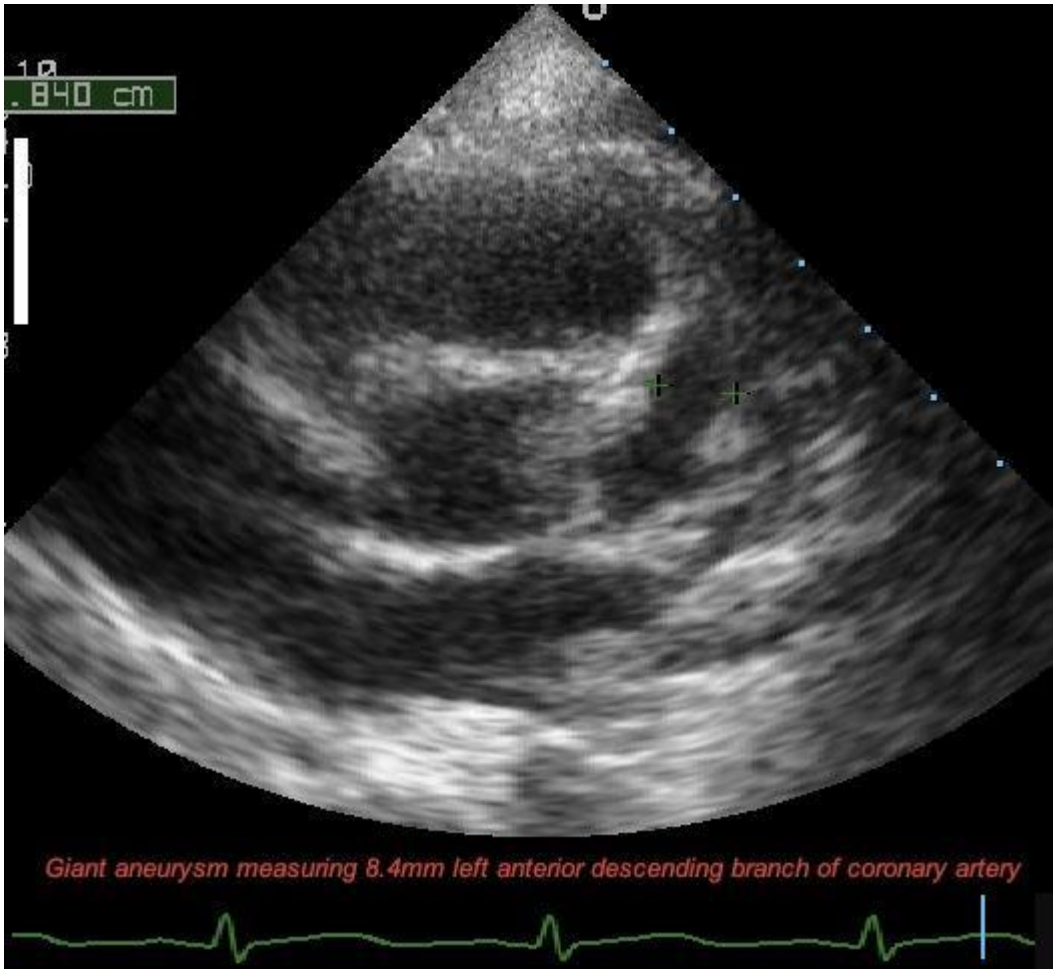
Aims: Present the first European case of a Caucasian boy with three episodes of Kawasaki disease(KD) with giant coronary aneurysms.
Background: Recurrent KD is well described in Asian cohorts. Data from Japan shows that cardiac sequelae are more common with recurrences. These have not been well studied in Western populations due to lower incidence.
Methods: Casenote review of episodes and cardiac follow-up by echocardiography and CT-angiography.
Results: Initial episode presented as complete KD with no cardiac complications. The second episode was less severe but still met all criteria and was complicated by aneurysms in left anterior descending artery(LAD) measuring 6.5mm and 8mm, which partially resolved on follow-up. During third episode he met less than 4 criteria for KD and developed a giant coronary aneurysm measuring 8.4mm in LAD. CT angiogram at one month showed marked dilation of main stem left coronary(>10mm).



[Echocardiograph-Day 12 of illness]



[CT Angiogram-4 weeks of illness]

Conclusions: Early recognition is crucial in recurrent cases as episodes are often atypical, hence more difficult to diagnose, but present greater risk of cardiac complications.

Accurate surveillance on incidence, complications and mortality of Kawasaki disease and recurrence in Europe is needed. Although guidelines have been proposed for management, there is no consensus between centers in Europe and clear recommendations for recognition and management of incomplete/atypical cases are lacking. Education for clinicians and parents to have a high index of suspicion in children with a previous history is needed.

DAY OF ILLNESS	4	5	7	10	13	14
WBC	10.0	9.4	14.5	15.4	11.6	11.6
Neutrophils	6.6	6.8	11.2	11.3	5.1	5.3
Platelets	258	309	408	590	845	870
CRP	191	174	331	241	43	25
ESR	100				95	130
ALT	639	702	350	146	60	
ALP	240	396	427	324	219	
Bilirubin	29	37	25	12		

TREATMENT	*CO-AMOXICLAV*	*CO-AMOXICLAV*	*CEFTRIAXONE*	*CEFTRIAXONE IMMUNOGLOBULIN ASPIRIN*	*ASPIRIN*	*ASPIRIN*

[Trend of inflammatory markers - third presentation]

P554

TREATMENT WITH NATALIZUMAB DURING PREGNANCY FOR MULTIPLE SCLEROSIS - EFFECT ON THE INFANTILE IMMUNE SYSTEM

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Backround and aims: Multiple sclerosis (MS) is a common neurologic disorder especially affecting young women. Modern therapies with immune-modulation with IFNbeta and a4integrin-receptor-antagonists (Natalizumab) have lead to benefits in the course of the disease and to an increase of the overall survival and the rate of pregnancies in patients with MS. IgG4-antibodies such as Natalizumab are passing the placenta-barrier. Effects on the infantile immune system and a possible enhanced risk for infections in the newborns have not been investigated yet.

Methods: Basic immunological testing has been performed in a 14 day old newborn (38th week of gestation), whose mother was treated with Natalizumab until the 34th week of pregnancy and a newborn-control-person. Additionally, the chemotaxis of granulocytes and T lymphocytes of these patients was assessed.

Results: The distribution of the lymphocyte subpopulations was normal in the Natalizumab exposed newborn. In the chemotaxis assay the basal but not the stimulated rate of migrating granulocytes was adequate. Moreover, the CXCL-12 induced chemotaxis of T lymphocytes was reduced.

Conclusions: We demonstrate for the first time functional immunological data of a newborn whose mother has been treated with Natalizumab until the 34th week of pregnancy. A significant reduction in chemotaxis of granulocytes and T cells could be demonstrated. More newborns have to be investigated to validate our findings and estimate the risk of infections due to a possible granulocyte and T cell disfunction.

P555

THE MANCHESTER TRIAGE SYSTEM UNDERESTIMATES THE URGENCY OF FEBRILE CHILDREN WITH COMORBIDITY

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Background: The Manchester Triage system (MTS) is a 5-level triage system used at emergency departments (EDs) to prioritise patients. Our aim was to compare the validity of the MTS in febrile paediatric patients with and without comorbidity.

Methods: Prospective observational study among febrile children (0-16 years) who visited the ED of a university-affiliated hospital in the Netherlands (2008-2009). Comorbidity was defined as neutropenia including malignancies, immune deficiencies, short bowel syndrome, kidney failure, cystic fibrosis, bronchopulmonary dysplasia, hemodynamic relevant congenital heart diseases, and psychomotor retardation. We used hospitalisation and presence of serious bacterial infections (SBIs) as markers for severity of illness. The MTS was validated by an independent reference standard which levels were based on abnormal vital signs (urgency 1), potentially life-threatening conditions (urgency 2) and a combination of resource use, hospitalisation, and follow-up for the three lowest levels (urgencies 3, 4 and 5).

Results: Among 1,897 eligible patients, 19% had comorbidity. Febrile children with comorbidity were hospitalised more often (OR3.2, 95%CI 2.0-4.0) and had an increased risk for SBI (OR1.6, 95%CI 1.2-2.1). The sensitivity of the MTS in children with comorbidity was 54% (95%CI 41-67%) and in children without comorbidity 80% (95%CI 72-86%). The specificity was 73% in both groups. Subgroup analysis of neutropenia/immune deficiencies, other comorbidities versus no comorbidity showed no differences.

Conclusion: Febrile children with comorbidity were more severely ill than children without comorbidity. The real urgency of febrile children with comorbidity is underestimated by the MTS. Modifications of the MTS for febrile children with comorbidity are needed.

P556

THE ELEVATION OF SUBCLASSES ANTIBODY IN THE PATIENTS UNDERGOING ADENOTONSILLECTOMY

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Background: Adenoid and tonsils are involved in both local immunity and immune surveillance for the development of immune defense mechanisms. Several studies have found decreased immunoglobulin levels after adenotonsillectomy while others have not found changes. The effects of adenotonsillectomy on the humeral immunity of children have not been investigated extensively.

Aim: To observe the change in humeral immunity before and after operation in children undergoing adenotonsillectomy.

Methods: Eighty five of the children underwent adenotonsillectomy. The level of IgG, IgM ,IgA were measured for humeral immunity in blood samples taken from these patients 24 hours before operation and also 8 weeks after the operation.

Results: The study comprised 85 patients (46 girls and 39 boys), aged from 2 to 14 years (mean age 5.5 year).There was no statistically significant difference between age groups and sex of patients. Eight weeks after the operation, the serum level of IgA decreased to preoperative value($p < 0.01$).In addition, there were an increase of the serum level of IgM and a decrease in IgG level, which was not statistically significant, compared to preoperative measures.

Conclusion: The results of this study point to the fact that the immune system maintains its normal status several weeks after adenotonsillectomy.

P557

ASSOCIATION BETWEEN SODIUM SERUM WITH CLINICAL SPECTRUM OF DENGUE IN CHILDREN

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Background and aim: Dengue virus infection is an endemic disease in tropical and subtropical countries. Dengue viral infection has a broad clinical spectrum, from mild to severe disease such as dengue shock syndrome (SSD). The most important thing that differentiates dengue fever (DF) and dengue hemorrhagic fever (DHF) is plasma leakage. Some molecules will decrease because of plasma leakage including sodium, who has a moderate size. The purpose of this study is to evaluate the association between serum sodium with dengue clinical manifestation in children.

Methods: The study was conducted during February to May 2010 with crosssectional method. Inclusion criteria are children under 14 years old who came to Hasan Sadikin Hospital and fulfill the dengue criteria by WHO. Statistical analysis using rank Spearman and Curve of Receiver Operating Characteristic (ROC).

Result: During the study there were 96 patients, 49 (51,1%) males and 47 (48,9%) females. The youngest was 4 months old. Most of the patients were 5-9 years old and had good nutritional status (56.3%). Sodium serum in DF are between 121-141 mEq/L, DHF are between 119-137 mEq/L and in SSD are between 116-138 mEq/L. The relationship between sodium serum and clinical manifestation of dengue were significant (p=0.01). The cut-off point which can be used to predict DHF/SSD are ≤ 130 mEq/L with sensitivity of 63,08% , specificity of 67,74%, and accuration 64,58%.

Conclusion: There were a significance between the lowest sodium serum and clinical manifestation of dengue in children.

P558

CAPILLARY REFILL AND BLOOD LACTATE LEVEL AS SHOCK RECOVERY PREDICTOR IN DENGUE SHOCK SYNDROME

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Background and aims: Dengue shock syndrome (DSS) characterized by increase of capillary permeability that cause plasma leakage. Standardized DSS fluid resuscitation using isotonic crystalloid often cause fluid overload and reperfusion injury. The new inovation in fluid resuscitation for shock patients is using small volume hypertonic sodium lactate. The study on fluid resuscitation using hypertonic sodium lactate in children with DSS had never been performed previously. This study aimed to find the shock recovery difference between children with DSS using hypertonic sodium lactate and Ringer lactate (RL).

Method: The study method was single blind randomized controlled trial. There were 62 children aged 2─14 years met the inclusion criteria, between June 2008─June 2010, four subjects were dropped out and 58 subjects were participated. Group I (30 subjects) received hypertonic sodium lactate (5 mL/BW/15 minutes) and group II (28 subjects) received RL (20 mL/BW/15 minutes). The subjects were observed for pulse pressure, fluid balance, capillary refill time and blood lactate examination. Statistical analysis using t-test, Mann-Whitney test, Friedman test, and chi square.

Results: The result showed that fluid resuscitation using hypertonic sodium lactate was faster in shock recovery than RL ($p< 0.05$). The significant difference of capillary refill time recovery start at 30 minutes, first, and second hour of observation ($p< 0.05$). The significant difference decrease in blood lactate level showed at twelfth hour of observation ($p< 0,05$).

Conclusion: This study concluded that small volume fluid resuscitation on DSS children using hypertonic sodium lactate has faster shock recovery compared to RL.

P559

CHEST RADIOLOGICAL IMAGE OF PNEUMONIA AND ASSOCIATED FACTORS

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Aim: To assess which clinical factor could correlate with the radiological image at the time of admission.

Material and method: It was conducted a retrospective study. Eligible subjects were children aged less than 10 years old. The diagnosis of pneumonia was based on clinical and radiological features. The following fields were recorded and analyzed: gender, age, fever, malaise, days of disease, toxic appearance, month, presence of pneumococcal antigen in urine (PnAg) and IgM antibodies for Mycoplasma. Radiological images were divided in consolidations and in diffuse images. For the analysis of our data was used logistic regression analysis. In multivariable model were introduced factors which were statistically significant at level of 20% in invariable analysis.

Results: We recorded 184 cases of pneumonia (94 females and 92 males) within three years. 136 cases had consolidation on their chest radiography and 50 cases had diffuse radiological image. In invariable analysis statistically significant at the level of 20% were the age (p=0.016) and the days of disease before the diagnosis (p=0.144). In multivariable analysis the only factor which was correlated with the chest radiological image was the age (p=0.021).

Conclusion: The radiological image at the time of admission was only correlated with the age. Our study cannot support the correlation of the radiological image with other factors like the cause or the toxic appearance.

P560

ROTAVIRUS RNA DETECTED IN SERUM IN HOSPITALIZED CHILDREN SUFFERING FROM ACUTE ROTAVIRUS-INDUCED GASTROENTERITIS USING REAL-TIME RT-PCR

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Aims: Rotaviruses primarily infect intestinal epithelial cells. Recent findings, however, demonstrate spread of rotaviruses systemically. This prospective observational study was conducted during a 12-month period to evaluate rotavirus RNA in serum of hospitalized children with acute rotavirus gastroenteritis (RV GE).

Methods: Four study hospitals in different Swedish geographical regions participated. A subset (n=207) of all hospitalized children (n=604) with a laboratory-confirmed RV GE were enrolled. Serum samples were collected shortly after hospital admission. Rotavirus RNA was manually extracted and quantification of the rotavirus *NSP3* gene was performed using real-time RT-PCR at the Swedish Institute for Infectious Disease Control.

Results: The median age of the children was 15 months. Viral RNA was detected in 194/207 (93.7%) serum samples. The Geometric Mean Concentration (GMC) was 2048 (95% CI; 1625 LL; 2581 UL) genome equivalents/mL in the study cohort with limited variation between study hospitals.

Center	Number of children tested (n)	Number of children with RV RNA in serum (n)	Percentage of tested children with RV RNA in serum (%)	Geometric Mean Concentration (genome equivalents/mL)	95% CI	
					Lower Limit (LL)	Upper Limit (UL)
1	44	42	95.5	3359	1868	6043
2	22	20	90.9	1409	903	2195
3	104	99	95.2	1790	1279	2504
4	37	33	89.2	2051	1267	3319
Total	**207**	**194**	**93.7**	**2048**	**1625**	**2581**

[RV RNA in serum of children with RVGE]

Conclusions: This observational study indicates that the presence of rotavirus RNA in serum is common in children with acute RV GE. Further studies should elucidate the importance of this finding in relation to disease severity.

P561

GENETIC PROTHROMBOTIC FACTORS IN CHILDREN WITH OTOGENIC LATERAL SINUS THROMBOSIS. FOUR CASE REPORTS

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Objectives: Lateral sinus thrombosis (LST) is an uncommon but life-threatening complication of both acute and chronic otitis media. There is some evidence that acquired or hereditary prothrombotic disorders are risk factors for LST. The aim of this work is to evaluate the role of thrombotic screening, anticoagulant therapy or prophilaxis in patients with acute or chronic otitis media and LST.

Methods: The files of four children hospitalized at Pediatric Hospital Bambino Gesù of Rome because of acute or chronic otitis media complicated by mastoiditis and LST were reviewed. All children underwent laboratory work up for hypercoagulability including the following tests: PT, PTT, fibrinogen, platelet levels, measurement of APC resistance, protein C, protein S, antithrombin III, polymerase chain reaction-based analysis for the factor V Leiden, C667T MTHFR and prothrombin gene G20210A mutations and assays for lupus anticoagulants, anti-cardiolipin/antiphospholipid antibodies and homocysteine.

Results: We described cases of four children with otitis media complicated LST. All the children showed heterozygosity for MTHFR mutation and a child presented also heterozygosity for factor V Leiden mutation. They have been treated successful with anticoagulant therapy without sequences.

Conclusions: Children with acute or chronic otitis media may have a prothrombotic tendency because of inflammatory state. Patients with a family and/or personal history of thrombosis and/or thrombophilic conditions need anticoagulant prophilaxis also in absence of clear signs of LST. We suggest that use of LMWH at the dosage of 100 UI/Kg twice daily is a successful therapeutic approach.

P562

INTESTINAL PARASITOSIS IN COLOMBIAN CHILDREN. PREVALENCE AND ASSESSMENT STUDY OF THE RE-INFECTION RATE AT 3 AND 6 MONTHS POST-TREATMENT

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Background: Intestinal parasitosis represents a public health problem in developing countries. Its prevalence is originated on sanitary services lacking and poor hygienic habits. This project assessed the prevalence of intestinal parasitosis in scholar's children in Quibdó Colombia, and determines the re-infection rate 3 and 6 months after treatment.

Methods: Transversal study performed in four public schools. Randomized sample was used to choose schools, grades and children. Stool samples were taken at the beginning, 3 and 6 months later.

Results: 155 children were studied. The prevalence of intestinal parasitosis was 89%. (81% helminthes, 63% protozoan). The most frequent helminthes was T. trichiuris (66%), followed by A. lumbricoides (58%)*, Uncinarias* 10% and *S. stercoralis 3%. Between protozoans the most frequent was E. coli 44%, followed by E. histolytica/dispar 25% y G. lambia* with 17%. Reinfection rate at 3 months was 58% for protozoans and 48% for helminthes. At 6 months an increase of 40% more for protozoan and 8% for Helminthes. Protozoan infection wasn't associated with socio-demographic factors. Helminthes infection was associated with the conditions of not having a latrine in their homes, p=0.02 OR 2.09 (IC95% 1.25-3.50) and having an earth floor p=0,05 OR 1,76 (IC95% 1,05-2,96).

Conclusions: There is a really high prevalence of intestinal parasitosis in scholar's children of Quibdó. Reinfección rate at 3 months was around 50% and at 6 month close to 100%, what suggests that deparasiting every 12 months has a little value for school going children when hygienic habits and their homes sanitary conditions aren't intervened.

P563

VISCERAL LEISHMANIASIS - DO NOT FORGET!

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Background: Visceral leishmaniasis, classically known as *Kala-azar*, is characterized by systemic infection of the liver, spleen and bone marrow caused by the protozoan *Leishmania donovani* and transmitted by the infected sandfly *Phlebotomus argentipes*. Although uncommon in Portugal, this disease is endemic in many countries, such as those of the Mediterranean Basin, and in these countries it mainly affects children.

Case report: We present the case of an 8-month-old boy, previously healthy, who lives near Douro river, with a history of 12 days of recurrent high fever, anorexia and weakness. On physical examination, he was pale and cachectic, had a cardiac murmur and abdominal distention. Laboratory examination revealed normocytic-normochromic anemia (Hb 7 g/dL), thrombocytopenia (20 000/mm3 platelets) and elevated hepatic transaminase (AST 1083 U/L) and LDH (5790 U/L) levels. Coagulation studies showed raised prothrombin and activated partial thromboplastin times. Abdominal ultrasound showed marked enlargement of the spleen (11cm) and liver (12cm). Bone-marrow aspiration revealed Leishman-Donovan bodies. Serological antibodies against *Leishmania* were detected using an enzyme-linked immunosorbent assay (ELISA). The patient was treated with Amphotericin B lipid complex, 3 mg/kg/day, on days 1-5 and again on day 7 and 14. This treatment was effective - blood counts returned to normal and hepatosplenomegaly disappeared.

Conclusion: Visceral leishmaniasis is a progressive disease, with mortality rate ranging from 75-95% if untreated. Several therapies have been used, with Amphotericin B lipid complex being the most effective drug, although its high cost often precludes its use.

P564

PREVALENCE OF PEDICULOSIS CAPITIS AMONG STUDENTS OF PRIMARY AND SECONDARY SCHOOLS IN HAMADAN PROVINCE, IRAN

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Background and aims: Pediculosis is an infestation of lice-blood-feeding ectoparasitic insects of the order Phthiraptera. The condition can occur in almost any species of warm-blooded animal (i.e., mammals and birds), including humans. The aim of this study was to determine the prevalence of pediculosis capitis and epidemiological factors associated with head lice infections in Iranian students of primary and secondary schools in Hamadan province.

Methods: A total of 103885 students (52955 boys and 50930 girls) were selected from urban and rural schools in 8 cities of Hamadan province (west of Iran), and screened for head lice between October and December 2008. The diagnosis of head lice infestation was confirmed by clinical inspection of scalp and hair for the presence of adult lice nymphal stage, or eggs (nit) by line-toothed head lice comb. All children and their family who infested with lice were treated with 1% Permethrin shampoo.

Results: The overall prevalence of head lice infestation was 0.62% (645 students). There was a significant relationship between head louse infestation and sex ($P < 0.0001$); and the prevalence of infestation was significantly higher in girls (1.2%) than in boys (0.07%). The infestation rate was greater among pupils who were living in urban areas (1.65%) compared with rural areas (0.44%).

Conclusions: Pediculosis capitis, or head lice infestation, occurs most commonly in children, but also affects adults. Education campaigns by health care officials, physicians and teachers are expected to be helpful for head lice control.

P565

NO EVIDENCE OF CARDIOTOXICITY OF QUININE AND ARTHEMETER/LUMEFANTRINE USED SEQUENTIALLY IN SEVERE FALCIPARUM MALARIA

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Due to the increasing resistance of *P. Falciparum,* Artemether-Lumefantrine (AL) becomes worldwide one of major treatment of malaria. Potential cardiotoxicity of halofantrin and quinine are known. AL alone does not cause clinically relevant QTc prolongation despite its structure related to quinine and halofantrine in experimental and field studies, But we have few data on the potential cardiotoxic consequences of sequential AL treatment with quinine. However, in endemic areas, the possibility to switch intravenous quinine to an oral treatment is very often requested to obtain a complete cure of severe falciparum malaria

Methods and results: QTc was measured in 24 hospitalized children receiving AL for falciparum malaria in Mayotte Island before and after treatment. In 14 patients with severe falciparum attack, oral AL was given. In 10 others, cerebral malaria symptoms required parenteral quinine. Intravenous treatment with quinine was given for 2 or 3 days and switched for oral AL after clinical amelioration. No patient had increase of QTc interval > 40 ms. Only 4/14 children treated with AL alone had slight QTc prolongation between 20 & 40 ms and 2 /10 treated with AL following intravenous quinine.

Conclusion: No important ECG changes suggesting clinically relevant cardiotoxic interactions were found when AL is given after parenteral quinine in this small sample of children treated for severe malaria.

P566

A TROPICAL PARASITOSIS COMING TO EUROPE

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Case report: A firm, aching and itchy nodule appeared on the scalp of a two-years-old boy coming from Ecuador. A strong digital pressure on the nodule revealed a maggot, which has been brought to our observation.

The boy physical examination showed a singular 10-mm nodular red lesion, centrally ulcerated, located on the vertex of the head, of parenchymal consistency, firm and surrounded by an erythemato-edematous halo. Squeezing of the wound showed no other larvae. Laboratory findings revealed only a slight increase in eosinophil percentage (6,7%). The lesion progressively healed and patient fully recovered within one week.

The larva was yellow-brownish in colour and 10 mm in diameter, classified as Dermatobia hominis.

Discussion: The term “myiasis” refers to the infestation of live human and animals with dipterous larvae which feed on the host's tissue. The life cycle consists of the adult Dermatobia hominis depositing eggs on various bloodsucking flies. These eggs will then rapidly hatch and penetrate the host skin to the subdermal cavity. When mature, the larva will emerge from the skin, drop to the soil, and pupate.

In Europe, diagnosis is easily overlooked because of its rarity, but should be considered in patients coming from endemic areas and presenting a non-follicular furuncular swelling on exposed skin.

Treatment consists of removal by expression. Antibiotic treatment is often recommended. Surgical extraction can be required.

[Image 1]

P567

PARASITIC INFECTION AND GROWTH PATTERN OF FINGER- SUCKING SCHOOL AGE CHILDREN IN ABEOKUTA, NIGERIA

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Background: Finger sucking is a common habit among many children and has been considered more as a social problem for school age children but may be the source of infections and growth retardation.

Materials and methods: The prevalence of parasites utilizing the faecal-oral route of transmission and growth pattern was studied in primary school children with finger sucking(FS) habit and compared with non finger sucking(NFS) children. Growth pattern of enrolled children was measured using weight and height for age and growth percentile calculated.

Results: Infection with one or more faecal-orally transmissible parasites was recorded in 80% of the school children with infections being significantly higher among the FS children. The prevalence of parasites recorded were *Entamoeba, histolytica* (44%), *Ascaris lumbricoides* (30%), *Enterobius vermicularis* (23%), *Trichuris trichiura* (19%) and *Giardia duodenalis* (17%). The level of personal hygiene was generally poor with about 85% of the children lacking the proper hand wash practice after defecation. The type of toilet facility available to the children also affected the infection pattern with finger-sucking children using pit latrines recording the highest prevalence. Finger sucking habit in children may have contributed to parasitic infection and invariably to their growth pattern as the proportion of children under the 50th growth percentile were significantly high among infected finger sucking children.

Conclusion: There is the need to educate mothers and children on the medical risks involved in the finger sucking habit especially for those living in or traveling to areas where there is a high level of faecal contamination.

P568

LYMPHOTOXIN-ALPHA GENE POLYMORPHISM IS NOT ASSOCIATED WITH SUSCEPTIBILITY TO KALA-AZAR IN IRANIAN PATIENTS

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Background and aims: Leishmania species are kinetoplastid protozoa and obligatory intracellular parasites that are responsible for a diverse collection of clinical manifestations ranging in severity from spontaneously healing skin ulcers to fatal visceral leishmaniasis. Lymphotoxin-alpha is a cytokine which has important roles in immunity against Leishmania infection. As the cytokine production is under the genetic control, we decided to investigate the association between this cytokines gene polymorphisms and susceptibility to leishmaniasis in Iranian pediatrics patients.

Methods: Our study groups consisted of one hundred and twenty pediatric patients involved with visceral leishmaniasis, sixty healthy individuals, from the same area as patients, and ninety healthy individuals with positive leishmanin skin test but without any history of leishmaniasis. LT-alpha (position +252 A/G) polymorphism was determined on genomic DNA extracted from blood samples obtained from study groups using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Genotypic and allelic frequencies were estimated by counting method. Associations were analyzed using Chi-square test with the level of significance set at < 0.05.

Results: It was not found any significant differences in allele and genotype frequencies of LT-alpha (+252 A/G) polymorphisms among the patient and the two control groups.

Conclusions: Our analysis did not reveal a significant difference between the frequencies of LT-alpha (+252 A/G) genotypes and alleles among the patient and the two control groups. Analysis of polymorphism in other positions of these two cytokine genes is recommended.

P569

EFFICACY OF 1% PERMETHRIN SHAMPOO FOR TREATMENT OF PEDICULOSIS CAPITIS

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Background and aims: Pediculosis capitis, or head lice infestation (pediculosis capitis) is a common problem worldwide. Although, multiple therapies exist for the treatment of this condition, including topical pediculicides and oral medications; in the present study, we investigated the efficacy of 1% Permethrin shampoo in treatment of pediculosis capitis.

Methods: This study was carried out in 8 cities of Hamadan province (west of Iran), involving 2861 school children and their family who infested with Pediculus humanus capitis during a survey conducted between October 2008 and September 2010. Infested case was defined as a person with observable crawling lice (adults or nymphs) or a person with nits on the hair shaft. All children and their family who infested with lice were treated with 1% Permethrin shampoo, and all of them were reexamined 14 days after treatment.

Results: The overall prevalence of head lice resistance to Permethrin was 1.89%. At 2 weeks after the primary treatment, the success rate of treatment was 98.11%.

Conclusions: Pediculosis capitis, or head lice infestation, occurs most commonly in children, but also affects adults. If left untreated the condition can become intensely irritating and skin infections may occur if the bites are scratched. Resistance of head lice to Permethrin induces difficult therapeutic problems. In these cases we had better use other pediculicides.

P570

GIARDIASIS IN CHILDREN: NEW METHODS FOR DIAGNOSIS AND TREATMENTS IN THERAPEUTIC FAILURE

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Background: Giardia lamblia (GI) pathogenesis and drugs sensibility are scarcely known. Therapeutic failures have been reported for all used treatments.

Methods: Retrospective study (1997-2010) of GI infestation among internationally-adopted-children and immigrants: Epidemiology, symptoms, co-infestations, GI-copro-antigen+ (ELISA) usefulness, therapeutic-failure rate and used treatments.

Results: We revised 351 clinical reports with GI positive isolation in children from 30 countries; 87% at first stools triple series isolation (99% after three series). Stool GI antigen analyzed samples (n=58) didn't improve sensitivity nor specificity related to usual methods (S=45.3%). Co-infestation found in 156 patients (44.4%), quarter of them for pathogenic parasites. Half of children are asymptomatic, displaying diarrhea (32%), failure to thrive (49%), anemia (29%), and iron deficiency (44%). The 84.4% of symptomatic children healed after stool became negative. The standard Metronidazole cycle wasn't effective in 82 patients (23.3%) (Significantly more frequent in symptomatic children or children from Latin-America) despite good adherence, requiring 2-3 Metronidazole cycles(n=44) or: Mebendazole(n=9), Albendazole(n=3), Tiabendazole(n=3), Tinidazole(n=2), Furazolidone(n=3), Quinacrine(n=18). Quinacrine achieved full eradication; even other treatments had failed before. Unlike previously reported, we haven't found increasing failures related with anemia, iron deficiency, failure to thrive, neither in children with GI in their family, nor adopted versus immigrants.

Conclusions: Antigen detection doesn't seem to improve microscopic examination efficiency.

No relationship between therapeutic failures to anemia, iron deficiency, failure to thrive, GI cases in the family, or adopted versus immigrants.

Quinacrine stands out as a rescue treatment for giardiasis failing to other treatments and it saves antiparasitic-high-spectrum, as Albendazol, for systemic diseases.

P571

CONTROL OF NEGLECTED TROPICAL DISEASES

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The Millennium Development Goals (MDGs) recognise the role of improved health as a key contributor to poverty reduction. MDGs focussing on child health (MDG4) and maternal health (MDG5) have specific targets but they are far from being achieved. MDG 6 specifies HIV/AIDS and “other diseases”. The latter term is a catch all that makes priority setting by policy makers difficult.. The creation of the Global Fund and the inclusion of TB provided additional support to countries for implementation of control programme for the big three diseases. However, there remains a group of diseases that have been largely ignored until recently. These diseases have been termed the Neglected Tropical Diseases (NTDs) and represent the most prevalent infections of poor people. More than one BILLION people are infected and some 2 BILLION at risk. Many helminth diseases can be eliminated. The NTDs have been categorised in two categories “tool ready” and “tool deficient” a useful concept emphasising that wide scale implementation is possible but research is necessary to improve the tools available. Significant progress has been made against the targets set by World Health Assembly Resolutions for control or elimination of NTDs. The NTDs are characterised by generous donations of drugs, NGDO support for implementation, operational research to improve progress to endpoints, strong monitoring and evaluation, robust surveillance and strong partnerships. The talk will review progress on policy, implementation and the science of NTDs and focus on NTDs in the context of child health and the Millennium Development Goals.

P572

INVESTIGATION OF INTERLEUKIN-18 GENE POLYMORPHISMS IN VISCERAL LEISHMANIASIS

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Background and aims: Interleukin-18 (IL-18) is a pleiotropic cytokine that is involved in regulation of both the innate and acquired immune response. The most prominent biologic property of IL-18 is its ability to induce the production of IFN-gamma in presence of IL-12. Then it seems that IL-18 has a crucial role in immunity against Leishmania infection. Since the expression of IL-18 can be affected by polymorphisms in its gene, we decided to find whether IL-18 gene polymorphisms can affect the outcome of Leishmania infection in Iranian pediatrics patients.

Methods: The study groups included 120 pediatric patients involved with visceral leishmaniasis and 150 healthy individuals, from the same area as the patients. Six IL-18 polymorphisms at positions -656, -607, -137, +113, +127 and codon 35/3 were determined using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Genotypic and allelic frequencies were estimated by counting method.

Results: It was not found any significant differences in alleles and genotype frequencies of IL-18 (G -656 T), (C -607 A), (G -137 C), (T +113 G), (C +127 T) and (codon A 35/3 C) polymorphisms among the patient and the control group.

Conclusions: Our analysis did not showed any significant difference between the frequencies of IL-18 polymorphisms at positions -656, -607, -137, +113, +127 and codon 35/3 genotypes and alleles among the patients and the controls. It might be the result of our limited number of controls, so we suggest this study be continued on larger population of the controls.

P573

CLINICAL FEATURES OF VISCERAL LEISHMANISIS IN PAEDIATRICS

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Kala-azar (visceral leishmaniasis [VL]) is endemic in southern Iran. We retrospectively evaluated 367 infants and children suffering from VL at hospitals affiliated to the Shiraz University of Medical Sciences in Fars Province, southwest Iran). Seasonal variations were observed with more cases presenting in late winter, spring and fewer in summer. The predominant clinical features in these patients were chronic fever, pallor, weight loss, abdominal distention and hepatosplenomegaly. Lymphadenopathy was less common.

P574

CLINICAL FEATURES OF VISCERAL LEISHMANISIS IN PAEDIATRICS

M.A. Moslehi

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Kala-azar (visceral leishmaniasis [VL]) is endemic in southern Iran. We retrospectively evaluated 367 infants and children suffering from VL at hospitals affiliated to the Shiraz University of Medical Sciences in Fars Province, southwest Iran). Seasonal variations were observed with more cases presenting in late winter, spring and fewer in summer. The predominant clinical features in these patients were chronic fever, pallor, weight loss, abdominal distention and hepatosplenomegaly. Lymphadenopathy was less common.

P575

INTERLEUKIN-1BETA GENE POLYMORPHISM AND SUSCEPTIBILITY TO KALA-AZAR

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Background and aims: Protozoan parasites of the genus Leishmania causing a wide spectrum of diseases collectively termed leishmaniasis that varies in their clinical manifestations. Whereas cutaneous leishmaniasis, an infection characterized by ulcerative lesion of the skin, is generally a self-healing disease, visceral leishmaniasis (kala-azar), represents the most severe clinical manifestation of Leishmania infection. Interleukin-1beta is a cytokine which has important roles in immunity against Leishmania infection. As the cytokine productions are under the genetic control, we tried to find any probable relationship between this cytokine gene polymorphism and susceptibility to leishmaniasis in Iranian pediatrics patients.

Methods: Our study groups consisted of one hundred and twenty pediatric patients involved with visceral leishmaniasis, sixty healthy individuals, from the same area as patients, and ninety healthy individuals with positive leishmanin skin test but without any history of leishmaniasis. IL-1beta (position +3953 C/T) polymorphism was determined on genomic DNA of the study groups using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Genotypic and allelic frequencies were estimated by counting method.

Results: It was not found any significant differences in allele and genotype frequencies of IL-1beta (+3953 C/T) polymorphism among the patient and the two control groups.

Conclusions: As data showed there is no statistical significant difference between the frequencies of IL-1beta (+3953 C/T) genotype and allele. It might be the result of our limited number of controls, so we suggest this study be continued on larger population of the controls. Also, analysis of polymorphism in other positions of this cytokine gene is recommended.

P576

AN OUTBREAK OF WATERBORNE HUMAN CRYPTOSPORIDIOSIS IN ÖSTERSUND, SWEDEN, A PEDIATRIC PERSPECTIVE

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Background and aim: In November-December 2010 an outbreak of gastroenteritis occurred in the city of Östersund, Sweden. The water supply system proved to be infected with Cryptosporidium Hominis Subtype IbA10G2. About 59.000 inhabitants were exposed to the water, about 12.000 under the age of 18.

The aim of this study is to describe incidence and morbidity in children (< 18 years).

Method: The inhabitants of Östersund were invited to answer an internet questionnaire, based on symptoms and open questions. Not every illness reported can certainly be related to a cryptosporidiosis diagnosis.

Results: Symptoms were reported in 10.705 persons, out of which 1.536 children < 18 years.

In children, reported symptoms of illness were; 86% diarrhoea, 82 % abdominal discomfort/pain, 41 % fever, 25 % headache, 23 % vomiting.

3 children, diagnosed with Cryptosporidium infection, had severe symptoms and were admitted to the Department of Pediatrics, Östersund Hospital.

A girl, 13 years old, who had undergone a heart transplantation with consequent drug-induced immunosuppression.

A boy, 17 years old with bloody diarrhoea, who has recently got a diagnosis of Inflammatory Bowel Disesase (IBD).

A boy, 16 years old, with severe diarrhoea. He is now under investigation for IBD.

Conclusions: Using an internet questionnaire we could estimate the incidence of cryptosporidiosis in a waterborne outbreak of Cryptosporidiosis.

Out of about 1500 reported children with symptoms only three children were admitted to a pediatric department. These three children have underlying diseases and have suffered from long lasting symptoms of Cryptosporidiosis.

P577

BURDEN OF INPATIENT PNEUMONIA, SEPTICEMIA, MENINGITIS AND ACUTE OTITIS MEDIA IN MALAYSIA

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Background and aims: *Streptococcus pneumoniae* is a leading cause of pneumonia, septicemia, meningitis and Acute Otitis Media(AOM) in children and the elderly. There is limited data on disease burden in Southeast Asia. This study estimates the burden of inpatient pneumonia, septicemia, meningitis and AOM in Malaysia.

Methods: Retrospective medical review of inpatients with pneumonia, septicemia, meningitis and AOM was conducted at four hospitals in Malaysia from January-08 to December-09. The catchment population is imputed based on each hospital's location including total local population of hospitals' area plus 30% of state population.

Results: A total of 6,164 patients were admitted during the study period. Of these, 5551 pneumonia(Lab Confirmed cases [LC]: 267), 290 septicemia(LC:111), 77 meningitis(LC:1) and 246 AOM(LC:30) cases were identified. Incidence (per 100,000 population) of pneumonia is projected at 138.6, with peak at 1088.3(age over 65), followed by 259.1(age 0-4). Incidence of septicemia is projected at 7.3, with peak at 47.4(age over 65), followed by 7.1(age 0-4). Incidence of meningitis is projected at 1.9, with peak at 10.8(age over 65), followed by 2.8(age 0-4). Incidence of inpatient AOM is projected at 6.0, with peak at 18.8(age over 65) followed by 11.1(age 0-4).

Conclusions: Despite the conservative assumptions in this study, the burden of inpatient pneumonia, septicemia, meningitis and AOM is high in Malaysia especially in children and the elderly. This can potentially be reduced by preventative measures such as vaccination.

P578

INCREASING INCIDENCE OF PNEUMOCOCCUS SEROTYPE 19A AND EMERGENCE OF ST695 VACCINE-ESCAPE RECOMBINANTS IN LIGURIA, ITALY, 7 YEARS AFTER PCV7 IMPLEMENTATION

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Background and aims: The aim of the study is to describe the serotype distribution of non- and invasive isolates over time after implementation of PCV7 in Liguria, Italy, an Italian administrative region with long-lasting high coverage, an unusual occurrence in Europe.

Methods: Since May 2003, a large-scale programme of vaccination against pneumococcus was started in Liguria, Italy. All newborns were invited to receive PCV7 according to 3-5-11 month schedule. Beginning 2005, mixed active-passive laboratory surveillance system for detection and characterization of non- and invasive strains in children and adults was implemented, supporting the universal vaccination program. Pneumococcal detection, serotype determination and molecular characterization were performed using real-time-PCR, Quellung reaction, primer-specific PCR and MLST.

Results and conclusions: PCV7 uptake began to increase after May 2003, reaching a coverage of >80% and >90% in every district since 2004 and 2007, respectively. During surveillance period, 194 strains were collected and characterized: an increase of non-PCV7 serotype illness was has been observed, reaching 89.9%, 92.3%, 64.3% and 77.7% in 0-5 and 6-17 year children and 18-64 and >64 year adults, respectively. In particular, the proportions of IPD and non-IPD cases due to serotype 19A increased from 7 and 13%, respectively, for the period 2006 to 2008 to 11 and 19%, respectively, for the period 2009 to 2010. Two serotype 19A (ST695) vaccine escape recombinant strains attributable to capsular switching events were detected. PCV13 would offer a significant added benefit covering 48.6%, 69.2%, 57.1% and 66.6% of pneumococcal illness in the above mentioned age groups.

P579

PNEUMOCOCCAL CARRIAGE IN LIGURIA, ITALY, 7 YEARS AFTER PCV7 IMPLEMENTATION: ALMOST COMPLETE REPLACEMENT OF VACCINE SEROTYPES

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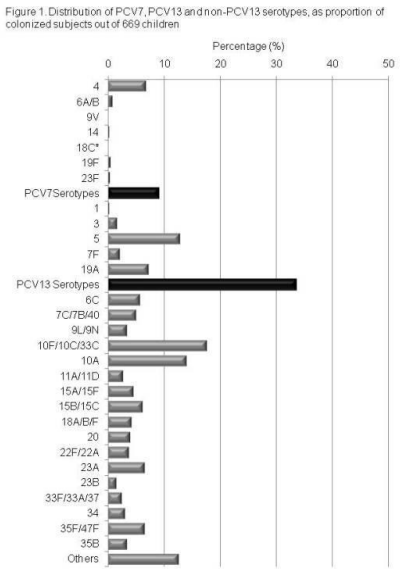
Background and aims: Since May 2003, a large-scale programme of vaccination against pneumococcus was started in Liguria, Italy. All newborns have been invited to receive PCV7 according to 3-5-11 month schedule. PCV7 uptake reached coverage of >80% and >90% in every districts since 2004 and 2007, respectively, determining an epidemiological picture infrequent in Europe. As part of the surveillance of PCV7 introduction, a cross-sectional study was performed in the autumn 2010 to determine the prevalence of carriage, the risk factors for and serotype distribution of pneumococcal carriage in 0-5 year population.

Methods: Broth enrichment, real-time PCR, conventional multiplex PCR and MLST approaches were used for pneumococcus detection, serotyping and characterization, as recently recommended by CDC. Nasopharyngeal specimens and standardized questionnaires were obtained from 669 children, that were enrolled using cluster sampling.

Results and conclusions: The overall carriage rate was 43.5% and carriage varied significantly across age groups with 22%, 48.6% and 60% of 0-12, 13-24 and 25-59 month children carrying Streptococcus pn, respectively. Distribution of PCV7, PCV13 and non-PCV13 serotypes, as proportion of colonized subjects out of 669 children is reported in figure 1. PCV7 serotypes (9.1%) were almost completely replaced; now-available PCV13 serotypes cover 33.6% of total serotypes. Among predictors of carriage, “age”, “number of brothers or sisters” “group child care” played a significant role.



[Figure1]

P580

SEROTYPE DISTRUBUTION OF *STREPTOCOCCUS PNEUMONIAE* IN BACTERIAL MENINGITIS: TURKISH NATIONAL BACTERIAL MENINGITIS SURVEILLANCE: 2006-2009

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Streptoccoccus pneumoniae is one of the most common cause of bacterial meningitis. Herein we invastigated serotype distrubution of S. pneumoniae causing bacterial meningitis by real time and conventional multiplex PCR metot in Turkey between 2006 to 2009. A total of 1510 cerebrospinal fluid (CSF) samples obtained from 35 different medical center arroud the country. Among them 131 patients revealed *S. pneumoniae.* and in 23 patients C_t for *S. pneumoniae* lyt A gene were ≥35. Serotype distrubution of S. pneumoniae were as following: **nontypeable** in 40 patients, **Serotype 1:** in 13 patients, **Serotype 23F:** in 7 patients, **Serotype 6A/B:** in 13 patients, **Serotype 18:** in 5 patients, **Serotype 19F:** in 12 patients, **Serotype 15A:** in 1 patient, **Serotype 14:** in 5 patients, **Serotype 23A:** in 1 patient, **Serotype 4:** in 2 patients, **Serotype 34:** in 1 patient, **Serotype 19A:** in 5 patient, **Serotype 9V:** in 2 patients, **Serotype 17F:** in 2 patients, **Serotype 12F:** in 2 patients, **Serotype 15B/C:** in 2 patients, **Serotype 23B:** in 1 patients, **Serotype 8:** in 1 patients, **Serotype 5:** in 8 patients, **Serotype 9N/L:** in 2 patients, **Serotype 21:** in 1patients, **Serotype 13:** in 1 patients, **Serotype 35B:** in 1 patients, **Serotype 3:** in 1 patients, **Serotype 9V/A: in** 1 patients, and **Serotype 35F:** in 1 patients. The most common cause of bacterial meningitis in Turkey was *S. pneumoniae* and serotype coverage of pneumococcal conjugate vaccine 7, 10 and 13- valent were 35%, 51% and 56%, respectively.

P581

SERO-EPIDEMIOLOGY IN EU AND US PLASMA DONATIONS AND PROTECTIVE PNEUMOCOCCAL CAPSULAR ANTIBODY (PNPSAB) CONTENTS IN PLASMA POOLS AND THERAPEUTIC IVIGS

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Background and aims: A number of S.pneumoniae serotypes are responsible for invasive pneumonia. Although protective antibody contents in intravenous immunoglobulin are ill defined, estimating them is crucial to treating immunodeficient patients. IVIGs are produced from large pools of plasma (>10,000 donations) and contain a wide range of PnPsAb. Standardised serotype-specific ELISAs selectively measure PnPsAb after pre-incubation with the common cell wall polysaccharide (CWPS) with or without 22F. Under these conditions, WHO13 recommends thresholds of 0.35 and 0.2 µg /ml respectively in vaccinated paediatric patients. We have aimed to quantify 16 major PnPsAbs in different IVIG preparations and to evaluate their epidemiology in donations collected in Belgium, the Netherlands, France, and the US.

Methods: Multigams® produced from Belgian plasma were compared with IVIG concentrates from four manufacturers. PnPsAbs were determined by a ICH-Q2(R1) validated HTQ process (WHO13). Calibration was done with 89-SF (FDA).

Results: All the PnPsAb contents appeared remarkably stable in Multigam® batches produced over the 2002-2008 period. For a dose of 400 mg IVIG, the major PnPSAb titres were between 219 µg and 109 µg (5-fold enrichment as compared to plasma pools). Although a comparable distribution was found in all IVIG concentrates and plasma pools from different origins, qualitative differences were observed according to the product and plasma origin. In pools from healthy human donors, PnPsAb against some serotypes failed to reach the putatively protective titre of 1.3 µg/ml recommended by Sorensen et al (1998).

Conclusion: IVIGs meet most of the requirements of WHO13 for PnPsAb contents and constitute a powerful tool for anti-infective immunoprophylaxis.

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PNEUMOCOCCAL CARRIAGE AMONG MOTHERS AND CHILDREN OF THE PANARE AMERINDIANS FROM VENEZUELA

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Background and aims: In North America, the Amerindians have been identified as a population with increased risk of pneumococcal colonization and pneumococcal invasive disease. However, little information is available from South American natives. In the present study we evaluated the nasopharyngeal carriage and serotype distribution of Streptococcus pneumoniae in mothers and children of the Panare people from Venezuela.

Methods: In May 2008, in 8 distinct geographically isolated communities, 148 nasopharyngeal samples were obtained from 64 healthy mothers and 84 healthy Panare children under 5 years of age. S. pneumoniae was isolated and identified by standard techniques. Strains were typified by multiplex PCR and resistance patterns were determined by the disk diffusion method.

Results: A total of 65 strains were isolated and 11% of the mothers and 69% of the children carried S. pneumoniae. Serotypes 6B (48%), 33F (21,5%), 6A (6%) including 1 strain identified as 6C, 19A (3,1%) and 23F (1,5%) were the most predominant strains. All strains were sensitive to penicillin and 13,7% were resistant to macrolides.

Conclusions: The high colonization rates in the Panare people suggest that the children are at increased risk of pneumococcal invasive disease and could benefit from vaccination. Four conjugate vaccine serotypes (6B, 6A, 19A and 23F) were present in the population at the moment of sampling. A relatively low theoretical coverage of 58 % for the 13 valent conjugate vaccine was calculated. Resistance to antibiotics is (still) not a problem in this Amerindian population.

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P584

STUDY OF NASOPHARYNGEAL CARRIAGE OF *STREPTOCOCCUS PNEUMONIAE* IN HEALTHY CHILDREN AGED LESS THAN TWO YEARS IN THE MARRAKECH REGION

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The healthy carrier of *Streptococcus pneumoniae* has been very little researched at the national level.

Objectives: This study had for aim to determine the prevalence and risk factors of pneumococcal nasopharyngeal carriage in children less than two years of age in the Marrakech region, and to assess the antibiotic susceptibility of the isolates and the serotypes present prior to the introduction of the conjugate pneumococcal vaccine.

Material and methods: From 2008 to 2009, 660 nasopharyngeal samples were collected on children under two years of age during scheduled visits to dispensaries for routine immunization in the Marrakech region.

Results: *Streptococcus pneumoniae* carriage was found in 45.8 % of children. Of the 660 samples, 301 strains were isolated. The percentage of pneumococcal strains with reduced susceptibility to penicillin (PRSP) was 34,7 %. Among these strains, 87.1% were high-level resistance and 12.9% were low-level resistance. Several risk factors for pneumococcal carriage were identified. The most frequent serotypes were 19 F, 6, 14, 23, 18 and 9. The study of the vaccine serotype distribution showed that the theorical vaccinal coverage of the seven valent vaccines was at 57, 33 % for all the isolates.

Conclusion: These data shows the frequency and the risk factors on nasopharyngeal carriage, and report the status of penicillin resistance of strains carrying children less than two years of age. The fluctuation of circulating serotypes at national level underlines the importance of epidemiological surveillance carried out before the introduction of the heptavalent vaccine in our country.

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PEDIATRIC PARAPNEUMONIC EMPYEMA EPIDEMIOLOGY IN SOUTHERN SPAIN (2005-2009)

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Objetive: To describe pediatric parapneumonic empyema(PPE) epidemiology in the previous years to the introduction of the new generation of conjugate pneumococcal vaccines (10 and 13-valent).

Methods: All patients < 14 years old admitted to a tertiary pediatric hospital with a diagnosis of PPE were prospectively enrolled from January 2005 through December 2009.

Patients: Overall 219 patients had PPE. Incidence rates for PEE remained stable during the study period with a non statistically significant increase in 2009 (p=0.08 for comparison with 2005). There was a significant higher frequency of PPE cases in the last quarter of 2009 compared to historical data for the same term in previous four years (p=0.001),coincidental with increasing circulation of 2009 pandemic influenza A (H1N1) in our population. Median age and duration of symptoms prior to admission were 44 months (intercuartilic range 32-70 m) and 4 days (intercuartilic range 3-6 days), respectively. Nearly a third (30%) of patients were admitted to ICU. There were no fatalities. A microorganism was isolated from blood and/or pleural fluid cultures in 21% PPE cases. Pneumococci were detected in 72% of culture-positive and 79% culture-negative samples. Serotypes were determined for 104 PPE cases; serotype 1 was the most prevalent serotype identified (42%) followed by serotypes 7F (20%), 3 (16%), 19A (8%) y 5 (7%).

Conclusion: Pneumococcal serotype 1 remained the most common cause of PPE cases over the last 5 year period. Continued enhaced surveillance is essential to monitor impact of new generation of pneumococcal conjugate vaccines in PPE epidemiology.

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IMPACT OF SEVEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON THE INCIDENCE AND SEROTYPE DISTRIBUTION OF INVASIVE PNEUMOCOCCAL DISEASE IN THE NETHERLANDS

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Background: In the Netherlands, the 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in the national immunization program for infants at age 2, 3, 4 and 11 months born after 1st April 2006. The impact of vaccination on the incidence and serotype distribution of invasive pneumococcal disease (IPD) in all age categories was determined.

Methods: CSF isolates from patients with pneumococcal meningitis nationwide and pneumococcal blood isolates from nine sentinel laboratories - representing 25% of the Dutch population - were serotyped. Age- and serotype-specific incidences in June 2006-December 2010 were compared with incidences before introduction of vaccination (June 2004-June 2006).

Results: The incidence of pneumococcal meningitis caused by PCV-7 vaccine-type pneumococci in 0-5 years-old children declined by 78% from 5.0 per 100,000 in 2004-2006 to 1.1 per 100,000 in 2006-2010. Non-PCV7 vaccine type meningitis increased with 44% from 1.9 to 2.8 per 100,000, giving a net reduction of pneumococcal meningitis by 43%. Similar results were seen for non-meningitis IPD. In older (not-vaccinated) patients the incidence of meningitis and other IPD caused by vaccine types decreased with ±35% while non-vaccine type IPD increased with 15%, giving a net reduction of 6%. Serotypes that had increased in the post-vaccination period were 1, 19A and 22F.

Conclusion: After 4.5 years PCV-7 vaccination (coverage>95%), a substantial reduction of vaccine-type IPD was observed in vaccinated cohorts and other age categories. However, the number of non-PCV-7 IPD cases partly neutralized vaccine benefits. Serotype 19A is increasing also in the Netherlands and serotype 1 has become more evident.

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CROSS-SECTIONAL POPULATION-BASED STUDY TO EVALUATE THE SEROPREVALENCE OF 13 SEROTYPE SPECIFIC IGG ANTIBODIES AGAINST *STREPTOCOCCUS PNEUMONIAE*

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Background and aims: In 2006 the 7-valent pneumococcal vaccine was introduced in the Dutch National Immunization Program. We assessed the seroprevalence of IgG antibodies against 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) in the general population in the Netherlands before introduction of the vaccine, to establish baseline IgG concentrations against these serotypes.

Methods: A serum bank consisting of 7904 sera from individuals aged 0-79 years was used. The 13 serotype specific IgG concentrations were assessed simultaneously using a fluorescent bead-based multiplex immuno assay (MIA).

Results: Overall, the geometric mean IgG concentrations (GMCs) against the 13 serotypes increased with age up to 5 years and remained at a plateau thereafter. Individuals appeared to have antibodies against an increasing number of different serotypes with increasing age. The lowest GMCs were found for antibodies directed against serotype 4 and 5, and the highest against serotypes 14 and 19F. There was no uniform relationship between the occurrence of serotypes causing invasive pneumococcal disease (IPD) and the GMCs.

Conclusions: This study provides an overview of the seroprevalence of IgG against 13 pneumococcal serotypes in a cross-section of the Dutch population. The results of this study showed there was no uniform relationship between IPD incidence and GMCs. The GMCs are likely dependent on the immunogenicity of the polysaccharides and on the frequency and duration of pneumococcal exposure, which in turn depends on the frequency of circulation of the pneumococcal serotypes.

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RAPID PNEUMOCOCCAL SEROTYPE DETERMINATION IN CHILDHOOD PARAPNEUMONIC EMPYEMA

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Background and aims: The rate of complicated pneumonia defined as forms with parapneumonic effusion, empyema, or necrotizing pneumonia have increased these last few years. In our university pediatric tertiary care center, the incidence of parapneumonic empyema (PE) increased from 3.6 to 10.3/1000 admissions between 2007 and 2009, particularly during the H1N1v pandemic. The knowledge of the pneumococcal serotypes involved in PE is of importance with the generalization of PCV13 immunization.

Methods: We developed a one-step multiplex polymerase chain reaction for identifying all pneumococcal serotypes covered by the 13-valent conjugate vaccine.

Results: Over 2 years January 2009 to januray 2011, we identified serotypes 19A (n = 6), 1 (n = 5), 3 (n = 2) and 7F/A (n = 3), both in culture-positive (n= 10) and culture-negative (n=6) pleural fluid from 16 children with empyema. In one patient with sterile pleural fluid, pneumolysine PCR was positive for *wzg* gene (formerly *cps*2A) common to all capsular serotypes but the strain was non typable.

Conclusion: Our rapid and simple one-step multiplex PCR approach may be a useful and less costly alternative to conventional serotyping, notably for monitoring changes in the distribution of PCV-13 serotypes in children with empyema but also to identify a pneumococcal infection in a culture negative pleural fluid.

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COMPARING HEALTH OUTCOMES AND COSTS OF GENERAL VACCINATION WITH PNEUMOCOCCAL CONJUGATE VACCINES IN SWEDEN - A MARKOV MODEL

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Background: Two new pneumococcal conjugate vaccines are licensed to immunise infants and young children against pneumococcal disease.

Objectives: The objective of this study was to estimate the expected health benefits, costs and incremental cost-effectiveness of routine vaccination with the 10-valent pneumococcal non-typeable haemophilus influenzae protein-D conjugate vaccine (PHiD-CV) compared with the 13-valent pneumococcal conjugate vaccine (PCV13) in Sweden.

Methods: A Markov cohort model was used to estimate the impact of vaccination at vaccine steady-state, taking a societal perspective and using 2+1 vaccination schedule. Price parity is assumed between the vaccines. Outcomes were measured by reduction in disease burden, costs, quality-adjusted life-years and incremental cost-effectiveness ratio.

Results: The results predict that PCV13 would prevent 3 additional cases of IPD and 34 additional cases of pneumonia, whereas PHiD-CV would avoid 3 additional cases of mastoiditis, 1,010 tube insertions and 10,420 cases of ambulatory AOM compared to PCV13. By combining morbidity and mortality benefits of all clinical outcomes PHiD-CV would generate 45.3 additional QALYs compared to PCV13 and generate a saving of an estimated 62 million SEK.

Conclusion: The present study predicts lower costs and better health outcome (QALYs) gained by introducing PHiD-CV compared to PCV13 in routine vaccination. Our results indicate that PHiD-CV may be cost-effective compared to PCV13 in Sweden.

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IMPROVED DIAGNOSIS OF CHILDHOOD PNEUMOCOCCAL PNEUMONIA

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Background: Studies underline the importance of combining new laboratory markers to improve the diagnosis of Childhood Pneumococcal Pneumonia (CPP), because traditional markers are insufficiently sensitive and specific.

Methods: Children aged ≤16 years with clinical and radiological pneumonia were enrolled in a multicentric prospective cohort-study. C-reactive-protein (CRP), Procalcitonin (PCT) and serum pneumococcal PCR (SP-PCR) were used as possible biological markers of CPP. Viral determination was also performed by multiplex-PCR in nasal swabs. An imbedded Case Control study allowed comparisons of pneumonia cases with healthy children for combined biological markers. Multivariate analyses were performed.

Results: 142 pneumonia cases and 96 healthy controls were analyzed: SP-PCR was positive in 31% of pneumonia cases and in 22% of controls (p=0.122). Among the SP-PCR positive children, increased PCT (>2 ng/ml) and CRP (>40mg/l) were found in 51.2% and 63.6% of pneumonia cases, respectively, but in none of the control cases (p< 0.0001). In pneumonia cases virus positivity was strongly associated with low CRP (OR=0.22; p=0.002) and PCT (OR=0.37; p=0.016), even after multivariate analysis with possible confounders (age, pneumococcal-vaccination, antibiotic treatment and SP-PCR). A CPP variable, defined as "*positive SP-PCR and CRP>40mg/l"*, was strongly correlated with pneumonia cases compared to controls (p< 0.001), and with usual signs of pneumococcal pneumonia: positive blood and pleural cultures, leukocytosis, lobar consolidation (p< 0.05).

Conclusion: In the absence of gold standards defining pneumococcal pneumonia, SP-PCR positivity associated with elevated CRP>40mg/l (or PCT>2ng/ml) and nasal virus negativity, seem to be excellent surrogate markers to delineate CPP more precisely.

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EXPECTED IMPACT OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN INVASIVE BACTERIAL INFECTION RATE IN THE PEDIATRIC EMERGENCY DEPARTMENT

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Objective: To study the impact we can expect from the introduction of the 13-valent pneumococcal conjugate vaccine (PCV-13) in the spectrum of invasive bacterial infections (IBI) in the Pediatric Emergency Department (PED)

Methods: Retrospective study of children under 14 years diagnosed with an IBI (bacterial culture/protein chain reaction in blood or cerebrospinal fluid - CSF) in a PED of a tertiary hospital between January 2008 and December 2010.

Results: Among 180,202 episodes, an IBI was diagnosed in 88 patients (36, 40.9%, under 1 year).

The most frequent diagnoses were: sepsis with/without meningitis 28 (31.4%), bacteraemia 21 (23.6%), pneumonia 13 (14.6%), meningitis 9 (10.1%). The most commonly isolated bacteria were *S. pneumoniae* 33 (37.5%), *N. meningitidis* 21 (23.9%), *E. Coli* 9 (10.2%).

The bacterium was isolated from blood in 77 patients (27 pneumococcus, 18 meningococcus), from CSF in 3 (pneumococcus), and from both fluids in 8 (3 pneumococcus, 3 meningococcus, 2 Group B *Streptococcus*).

29 isolated pneumococcus were serotyped. The distribution of the serotypes related to the different PCV was: 5 were included in the PCV-7 (17.2% CI 95% 7.1-35.0), 15 in the PCV-10 (51.7%, 95% CI 34.4- 68.6) and 25 in the PCV-13 (86.2% CI 95% 68.8-95.1).

None of the patients died. Two patients with invasive pneumococcal infection had sequels.

Conclusions: In the era of 7-valent PCV, pneumococcus is the leading cause of IBI in PED. The introduction of 13-valent PCV may lead to a very significant decrease of IBI rate and meningococcus may become the leading cause of IBI.

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EMERGING NONVACCINE SEROTYPES IN INVASIVE PNEUMOCOCCAL DISEASE IN A PEDIATRIC POPULATION OF A TERTIARY CARE HOSPITAL IN MADRID (SPAIN)

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Background: To describe the epidemiology and microbiological characteristics of emerging nonvaccine serotypes (NVS) of invasive pneumococcal disease (IPD) in children from a tertiary care hospital in Madrid (Spain).

Methods: Retrospective (1998-2004) and prospective (2005-2009) study of NVS in children with IPD. The study was divided into three periods: P1 (1998-2001) in which PCV7 had not been commercialized; P2 (2002-2005) with 40% vaccine coverage; and P3 (2006-2009) when the vaccine was added to the Childhood Immunization Schedule in Madrid.

Results: We analyzed 155 isolates of *S. pneumoniae* (SP) producing IPD. An increase in the incidence in P1 from 11.43 cases/100,000 pediatric emergencies, to P3 28.4 cases (250% increase). The most relevant NVS were: 19A (P1 =2%, P3 =23.5%, p =0.001), 1 (11% vs 22%), 7F, 5, 3 15C, 35B and 38. Serotypes 1, 3, 5 and 15C produced respiratory symptoms and no cases of meningitis, with serotype 1 being the most frequently implicated in pleural empyema (33% of empyema). Serotype 19A produced respiratory infections as well as bacteremia and meningitis, and was the most implicated in meningitis (25%). NVS were less resistant to penicillin than VS (19% vs 68%, p = 0.001) with the exception of 19A (52% resistant). Vaccination with PCV10 and PCV13 would achieve a 55% and 78% coverage, respectively, of isolates during P3.

Conclusions: After the introduction of PCV7, there was an increase of NVS. Epidemiological and clinical characteristics are different from the VS, presenting lower rates of resistance, with the exception of serotype 19A.

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THE DYNAMICS OF SERUM LEVELS OF ANTIPNEUMOCOCCAL ANTIBODIES IN CHILDREN WITH NEPHROTIC SYNDROME AFTER IMMUNIZATION OF PNEUMOCOCCAL POLYSACCHARIDE VACCINE

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Patients with nephrotic syndrome have a high risk of development of heavy pneumococcal infections which can be prevented by means of vaccination. Estimation of adequacy of the immune answer can be spent by means of dynamics definition of serum levels of antipneumococcal antibodies.

To investigate the dynamics of antibodies levels (class IgG and subclass IgG2) in whey of blood after immunization of PPV.

11 patients with nephrotic syndrome were vaccinated with Pnevmo-23. They included: hereditary nephrite (n=3), steroid sensitive NS (n=3), steroid resistant NS (n=5). All patients were examined the levels of antipneumococcal antibodies before and after vaccination. Statistical processing of results spent by means of package SPSS16.0. The data was presented in a kind of median (25 %-75 % disorder). The levels of antibodies compared with the test of Vilkokson, statistically significant distinctions were at $p < 0,05$.

The maintenance of general IgG to antipneumococcal antibodies after vaccination has increased in 4,1 times (from 25,0 to 103,6 mg/l; p=0,003), and the maintenance of subclass IgG2 - in 3 times (from 13,3 to 39,9 mg/l; p=0,01). At 9 of 11 vaccinated the increase of antibodies was adequate (has grown in ≥2 times). Two patients with steroid resistant NS, connected with a mutation of a gene NPHS2, hadn´t change at the levels of antibodies after immunization.

The majority of patients with NS adequately react to vaccination, that can testify to the effective immune answer. At the same time for patients with NPHS2 mutation this kind of immunization will be less effective.

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DISTRIBUTION BY AGE OF SEROTYPES ISOLATED FROM PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASES IN 2009-2010 IN MADRID, SPAIN

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Background and aims: Serotype distribution is related to age. In 2006, Madrid (6 million inhabitants) included the heptavalent pneumococcal conjugate vaccine (PCV7) in the vaccination calendar. This study analyses per-age distribution of serotypes causing invasive pneumococcal disease (IPD) in hospitalized children in Madrid in 2009-2010.

Methods: A prospective, laboratory-confirmed (culture and/or PCR) IPD surveillance was performed in May09-April10 in all hospitals with Pediatric department (28 centres). All isolates (for serotyping) and culture-negative pleural/cerebrospinal fluids were sent for PCR analysis.

Results: 169 IPDs were identified. The Table shows per-age [in months, n (%)] serotype distribution.

Serotype	≤12 m	>12 - ≤24 m	>24 - ≤59	>59 m
1	3 (8.6)	2 (6.3)	25 (39.7)	24 (61.5)
3	2 (5.7)	4 (12.5)	5 (7.9)	0 (0.0)
5	1 (2.9)	0 (0.0)	1 (1.6)	2 (5.1)
6A	0 (0.0)	1 (3.1)	0 (0.0)	0 (0.0)
7F	4 (11.4)	1 (3.1)	6 (9.5)	0 (0.0)
19A	13 (37.1)	14 (43.8)	17 (27.0)	4 (10.3)
PCV7 serotypes	1 (2.9)	0 (0.0)	1 (1.6)	4 (10.3)
Other serotypes	11 (31.4)	10 (31.3)	8 (12.7)	5 (12.8)
TOTAL	**35 (100)**	**32 (100)**	**63 (100)**	**39 (100)**

[Per-age serotype distribution]

Calculated coverages by the new 13-valent pneumococcal conjugate vaccine (PCV13) were: 68.6% (**≤**12m), 68.7% (>12-**≤**24m), 87.3% (>25-**≤**59m) and 87.2% (>59m).

Conclusions: In children < 59m, serotype 19A (33.8%) was the most prevalent followed by serotype 1 (23.1%). Both serotypes accounted for 60.4% of all pediatric IPDs in 2009-2010 in Madrid, showing the added value of PCV13.

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PREVENTION AND TREATMENT OF RESPIRATORY INFECTIONS AT PRESCHOOL CHILDREN: PRELIMINARY RESULTS OF THE 2ND HELLENIC NATIONWIDE PNEUMOCOCCUS RESISTANCE STUDY

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Background and aims: Respiratory tract infections (RTI) cause significant morbidity in young children. This study aimed to identify and evaluate preventive and therapeutic measures of RTI at preschool children.

Patients-methods: This study constitutes a part of a nation-wide study of nasopharyngeal carriage of *Streptococcus pneumoniae*. Questionnaires were answered by the parents of children attending day-care centers 1-2 days before the sampling of nasopharyngeal swabs and provided demographic data, data on antibiotic consumption, history of RTI and vaccination coverage.

Results: From February-April 2010 questionnaires were collected from 1258 healthy children (median age 5 years, range 2-7 y, 51.2% boys). Within the last year RTI was reported in the majority (86.4%) of children. Overall, 672 (53.4%) children received at least one antibiotic course in the 3-month period preceding sampling. The reason for antibiotic prescription was upper RTI (13.3.%), lower RTI (7.1%), otitis (15.8%), pharyngitis (6.9%), while 2.5% reported H1N1 as cause of antibiotic prescription. The distribution of antibiotic use was: penicillin (0.6%), amoxicillin (5.3%), amoxicillin/clavulanic (26.2%), second-generation cephalosporins (26.4%) and macrolides (24.1%); treatment duration ranged 2-16 days. Antibiotics were prescribed after visiting a doctor (92.1%) or after his advice through telephone (6.2%). The population coverage with at least one dose of heptavalent pneumococcal vaccine was 91.6% (73.7% received >=2 doses, 26.3% 1 dose) and 33.7% was vaccinated against influenza.

Conclusions: High antibiotic consumption was noted among preschool children compared to their episodes of RTI. There is a predilection for using antibiotics covering a broader spectrum of organisms than the usual causative agents of RTI.

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CLINICAL EVALUATION OF A RAPID IMMUNOCHROMATOGRAPHIC KIT FOR DETECTING *STREPTOCOCCUS PNEUMONIAE* ANTIGEN IN NASOPHARYNGEAL SECRETION SAMPLES FROM PATIENTS WITH PNEUMONIA

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Introduction: *Streptococcus pneumoniae* is one of the major pathogens in pediatric lower respiratory tract infection. Identification of the causative pathogen as early as possible and selection of a suitable antibacterial drug are thus desirable to stop the progression of pneumonia. In this study, we evaluate the immunochromatographic kit "RAPIRUN® S. pneumoniae", which specifically detect C-polysaccharide, a common antigen of *S. pneumoniae.* The sensitivity of this kit is approximately 1.3×10^4 colony forming unit/mL, and it does not cross over to *Streptococcus mitis.*

Methods: A total of 105 nasopharyngeal secretion samples were obtained from pediatric patients with pneumonia or acute bronchitis. We evaluated the clinical performance of "RAPIRUN® S. pneumoniae", urinary antigen detection kit "Binax NOWâ *Streptococcus pneumoniae"*, real-time PCR, and conventional bacterial culture. Informed consent was obtained from the patients or their parents/guardians if the patients were under age.

Results: The sensitivity and specificity of "RAPIRUN® S. pneumoniae" were 62.5 % (20/32) and 100% (26/26) in patients with lower respiratory tract infection, respectively, based on the results of bacterial culture. On the other hand, the sensitivity and specificity of "Binax NOWâ *Streptococcus pneumoniae"* were 53.1 % (17/32) and 96.2% (25/26) in the same patients, respectively, based on the bacterial cultures.

Conclusions: Since "RAPIRUN® S. pneumoniae" evaluates nasopharyngeal secretion samples from local sites of infection, and is more sensitive detection method of S. pneumoniae antigen than urinary antigen detection, it is suggested that this kit will significantly contribute to the rapid and noninvasive diagnosis of pneumococcal infection in children.

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DEVELOPMENT OF A RAPID METHOD FOR IDENTIFICATION AND QUANTITATION OF PNEUMOCOCCAL CAPSULAR POLYSACCHARIDES

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Background and aims: During the development and release of a pneumococcal vaccines, it is essential to identify and estimate the concentration of capsular polysaccharides at various stages. The conventional methods employed for this purpose e.g. colorimetric assays, rate nephelometry, ELISAs etc., have limitations of lack of sensitivity/specificity and/or are time consuming. We developed a highly sensitive and rapid bead based assay for simultaneous identification and quantitation of pneumococcal polysaccharides(PnPS) at various stages of vaccine development viz., polysaccharide production, purification, conjugation and final vaccine formulation.

Methods: A competitive inhibition assay was performed using Luminex microspheres coupled to various target polysaccharides. The PnPS of various serotypes were coupled with polystyrene microspheres by standardized methods. The standard and unknown samples were incubated with defined specific antibody dilutions followed by incubation with PnPS-Beads and conjugated secondary antibody. The reaction was estimated using BioPlex 200 system. The assay was evaluated for various validation parameters as per ICH guidelines.

Results: The 3 hour assay was found to be highly specific and sensitive. Assay could detect upto 15 ng/ml of various PnPS with a spiking recovery of 80-120%. Assay was highly repeatable with an Inter- and Intra-assay percent CV within + 20%. The assay was applicable for multivalent sample analyses.

Conclusions: The x-MAP technology based assay can be highly useful tool with multiplexing possibilities for pneumococcal vaccine development and characterization. The assay is being explored for clinical diagnosis of pneumococcal infections also. The authors would thank PATH, USA and its consultants for providing all the technical inputs.

P600

RECURRENT PNEUMOCOCCAL MENINGITIS DESPITE VACCINATION WITH THREE DIFFERENT PNEUMOCOCCAL VACCINES AND PENICILLIN PROPHYLAXIS

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We report a nine-year-old girl suffering from six episodes of meningitis within the last three years. Five were caused by different serotypes (ST) of penicillin susceptible *Streptococcus pneumoniae* (SP).

SP serotype-6A and ST-35B were identified in CSF cultures from episode 1 and 2, when the child had not received pneumococcal vaccination yet. Immunodeficiency was excluded. MRT of the scull revealed a temporo-mesial meningocele as potential entry for pathogens. Exploration of rhinobasis using intrathecal fluorescein revealed a bony defect and surgical occlusion was done. 7-valent pneumococcal conjugate vaccine (PCV-7) and 23-valent polysaccharide vaccine (PPV-23) were applied. However, a third episode due to SP ST-23A occurred, but a repeated intrathecal fluorescein test did not reveal further CSF leakage at the rhinobasis. Therefore 13-valent PCV and long term penicillin prophylaxis were given. However three further meningitis episodes occurred (n° 4: ST-28F; n° 5: ST-35F; n° 6: unknown). Exploration of the right otobasis revealed an extended defect by the meningocele of the posterior wall of the auditive tube, which was closed with bone grafts.

Neither penicillin prophylaxis nor PPV-23, PCV-7 and PCV-13 vaccination could prevent recurrence of meningitis. 5 of 6 episodes were caused by penicillin susceptible SP with ST not covered and potentially selected by PCV vaccination. This report confirms the persisting risk of invasive pneumococcal disease due to nasopharyngeal colonization with non-vaccine susceptible SP ST and the future need for pneumococcal vaccines with extended serotype coverage.

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INVASIVE PNEUMOCOCCAL DISEASE BEFORE AND AFTER INTRODUCTION OF GENERAL PNEUMOCOCCAL VACCINATION OF CHILDREN < 5 YEARS IN STOCKHOLM COUNTY 2005-2010

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Aim: Conjugated pneumococcal vaccines have been associated with a decrease in invasive pneumococcal disease (IPD) and serotype replacement in many countries. Here we investigated the effects of the 7-valent vaccine (PCV7) in Stockholm, Sweden with nearly 100% vaccine coverage, >80% day care attendance and low antibiotic consumption as compared to most countries.

Methods: PCV7 was introduced in the child vaccination program with three doses at 3, 5 and 12 months of age the 1st of October 2007 in Stockholm. IPD is notifiable by law and clinical isolates were collected and serotyped. We compared the incidences and bacterial serotypes for children below five years, two years before and after vaccine introduction, excluding the introductory year (Oct. 1st 2005 - Sept. 30st 2007 and Oct. 1st 2008- Sept. 30st 2010).

Results: Preliminary results show a decreased incidence of vaccine types (VT) IPD in children < 2 years (25.4 to 10.5/100 000; RR 0.41 CI 0.19-0.85) and in children 2-< 5 years (4.0 to 1.2/100 000; RR 0.3 CI 0,03-1,70), whereas non-VT IPD remained stable in children < 2 years but increased in children aged 2-< 5 years (RR 8.2).

Conclusions: Introduction of PCV7 was associated with a 59% decreased risk of IPD caused by vaccine serotypes in children < 2 years of age. Serotype replacement was seen only in the age group 2-< 5 years, a group with lower vaccine coverage (since no catch-up vaccination was performed) and higher day care attendance, as compared to children below 2 years of age.

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THE IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINE - 7 ON PNEUMOCOCCAL DISEASE BURDEN IN KUWAIT: NEW SEROTYPES AND ANTIMICROBIAL RESISTANCE CHALLENGE

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Background and aims: Lack of surveillance data on pneumococcal disease burden is a problem worldwide. This study was carried out to evaluate the impact of the pneumococcal conjugate vaccine-7, introduced in Kuwait in 2006, on the burden of invasive and non-invasive pneumococcal disease in children less than 5 and adults above 50 years, and to determine their serotype distribution as well as the antimicrobial resistance pattern.

Methods: Isolates from invasive and non-invasive pneumococcal disease in children less than 5 years and adults above 50 years from January 2006 till December 2010 were included. The serotype distribution was done by Quelling reaction using set of specific rabbit pneumococcal antisera (Statens Serum Institute, Copenhagen, Denmark) and the anti-microbial susceptibility pattern was determined using Etest.

Results: Out of a total of 327 pneumococcal isolates 125 were invasive (Blood, CSF) and 206 were non-invasive (sputum). Seventy-two percent of the isolates from children less than 5 years and 30% from elderly above 50 were invasive isolates. The overall percentage of antimicrobial resistance was 3% and 0.5% in invasive and non-invasive isolates, respectively. Percentage coverage by the 13-valent conjugate vaccine in children less than 5 years was 66% for invasive and non-invasive isolates, while in elderly above 50 years was 73% and 52% compared to less than 40% coverage by the 7-valent conjugate vaccine for all the isolates in both the age groups..

Conclusion: Four years following the use of the 7-valent conjugate pneumococcal vaccine in Kuwait, the need for broader vaccine cover is highly recommended.

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FALL OR SPRING FOR PNEUMOCOCCUS? CHANGES IN INVASIVE PNEUMOCOCCAL DISEASE IN SPANISH CHILDREN

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Background: Epidemiology of invasive pneumococcal disease (IPD) has changed since routine introduction of 7-valent pneumococcal conjugate vaccine (PCV7) in childhood vaccination calendar. Data from Spain and other countries where PCV7 is not routinely included remain controversial.

Methods: A retrospective-prospective study was performed in a single tertiary care pediatric hospital in Barcelona (Spain), in which data from all children aged < 16 years with culture-proven IPD were compared in two different periods, before and after PCV7 introduction (prevaccine period, January 2000-December 2002; vaccine period, January 2007-December 2009).

Results: Twenty-seven and 84 cases of IPD were studied in the first and second period, respectively. The IPD rate increased from 19.65 to 50.84 episodes per 100,000 children-year between the two periods ($p < 0.05$). A dramatic decrease in PCV7 serotypes was observed (from 68.2% to 10.8%), and a consequent increase in non-PCV7 serotypes (from 31.8% to 89.2%) ($p < 0.05$). Penicillin susceptibility rose in the second period from 58.3% to 83.9% ($p < 0.05$). In the prevaccine period, bacteremia without focus and meningitis were the most common clinical forms of IPD (55.5%), whereas respiratory forms increased to 69% in the vaccine period ($p < 0.05$), with pneumococcal empyema being the most frequent clinical presentation (39.3%).

Conclusions: Our study found statistically significant variations in IPD presentation in our area between the prevaccine and vaccine eras, including a higher incidence and predominance of non-PCV7 serotypes in the vaccine period, increased susceptibility to penicillin, and more cases of respiratory disease. These changes are likely associated with the introduction of PCV7, among other factors.

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PROSPECTIVE, MULTINATIONAL ACTIVE HOSPITAL-BASED EPIDEMIOLOGIC SURVEILLANCE FOR IPD AND PNEUMONIA BURDEN AMONG CHILDREN IN BANGALORE SOUTH ZONE, BANGALORE, INDIA

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Background and aims: Pneumococcus is a leading cause of childhood morbidity and mortality. Invasive pneumococcal disease (IPD) data in India are scarce. This study estimated IPD in the targeted population.

Methods: Prospective, hospital-based surveillance conducted from 27/2/2009 -26/2/2010. Children 28d to ≤36m with temperature/temperature history ≥39.0°C (within 24h) or clinical suspicion of IPD or >36m to < 60m with suspected IPD, residing in surveillance area were eligible. Blood cultures were obtained from all enrolled children, cerebrospinal fluid (CSF) in suspected meningitis, and chest radiographs (CXRs) in suspected pneumonia. IPD was confirmed by pneumococcus-positive blood and/or CSF cultures.

Results: 5,249 children from estimated study population of 112,483 were enrolled.Mean age = 19.8m, (66.5% = 28d to < 24m).17 children with IPD were confirmed (12[70.6%] pneumonia, 3[17.6%] meningitis, 2[11.8%] bacteraemia). Overall, estimated IPD incidence was 15.11/100,000 (28d—60m). Highest IPD incidence occurred in 6m to < 12m age group: 46.01/100,000.Pneumococcal serotypes: 6A (n=5; 29.4%); 5 (n=3;17.6%); 1 (n=2;11.8%), 14 (n=2;11.8%), and 9V, 19F, 3, 18C and 19A each one. 7-, 10-, and 13-valent pneumococcal vaccine serotype coverage was 29.4%, 58.8%, and 100%, respectively.Four of 16(25.0%) isolates were resistant to trimethoprim/sulfamethoxazole, 3(18.8%) to erythromycin, and 1(5.9%) to ceftriaxone. 6A, 14, 1 and 19A showed antibiotic resistance. 6A isolates showed resistance to trimethoprim/sulfamethoxazole, ceftriaxone, and erythromycin.Clinical pneumonia incidence among children aged 28d to < 6m and 28d to < 24m: 2,107.87/100,000 and 3,452.04/100,000, respectively. Incidence of CXR-confirmed pneumonia: 983.26/100,000 (28d—60m).

Conclusions: IPD and pneumonia are important causes of morbidity in children of Bangalore South Zone.

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LOW IMPACT OF THE 7-VALENT CONJUGATE VACCINE AGAINST NON-SUSCEPTIBILITY TO PENICILLIN NASOPHARYNGEAL PNEUMOCOCCI IN CHILDREN IN GREECE

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Background and aims: To evaluate the current trends in non-susceptibility to common antimicrobials and serotype distribution among nasopharyngeal pneumococcal isolates in childen through a 6-year period after the introduction of the 7-valent conjugate vaccine (PCV7) in Greece.

Methods: A total of 513 consecutive pneumococci isolated from children with no history of infection attended as outpatients in two major pediatric hospitals in central Greece between 2005 and 2010 were collected.

Results: The resistance to penicillin, cefotaxime, erythromycin and trimethoprim/sulfamethoxazole among pharyngeal isolates in 2005 and 2010 was as follows: penicillin 42.3% vs 41.1%, cefotaxime 0.0% vs 2.2%, erythromycin vs 40.8 and 31.1%, trimethoprim/sulfamethoxazole 43.0 vs 40.0%, respectively. The intermediate susceptibility to penicillin increased from 31.0 in 2005 to 38.9 in 2010, whereas penicillin-resistance declined from 11.3% in 2005 to 2.2% in 2010. PCV7, 10-valent conjugate vaccine and 13-valent conjugate vaccine (PCV13) serotypes represented the 11.1%, 14.4% and 38.9% of nasopharyngeal isolates in 2010, respectively. The proportions of four prevalent PCV7 serotypes in 2005 significantly decreased in 2010: serotype 19F; 23.2% vs 8.9%, serotype 6B 13.4% vs 1.1%, serotype 14 9.9% vs 1.1%, 23F 5.2% vs 0.0, respectively. Non-PCV7 serotype 19A was significantly increased throughout the surveillance period; 2.1% in 2005 vs 13.3% in 2010.

Conclusions: Our data show no significant changes in proportion of non-susceptible pneumococcal carriage strains to most antimicrobials tested between 2005 and 2010. The PCV13 coverage in pneumococcal nasopharyngeal isolates, just before its introduction in our country, seems to be moderate.

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COMPARATIVE IN VITRO ACTIVITIES OF TEN B-LACTAMS ANTIMICROBIAL AGENTS AGAINST PNEUMOCOCCAL RESPIRATORY ISOLATES

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Background and aims: Increase resistance to penicillin in Streptococcus pneumoniae has become common in Greece. Therefore, we evaluated the in vitro activity of ten b-lactams antimicrobials against 138 respiratory pneumococcal isolates to determine drugs that can be used alternatively for oral or parenteral therapy in these infections.

Methods: Pneumococci obtained from middle ear fluid (124 strains) or bronchial aspirates (14 strains) from children with acute otitis media or pneumonia, respectively. The above isolates included 42 susceptible and 96 non-susceptible to penicillin strains (28 resistance and 68 intermediate). All isolates were tested for in vitro susceptibility to ten b-lactams by the Etest, following the CLSI latest guidelines.

Results: Among 96 non-susceptible to penicillin strains, a total of two isolates (2.1%) showed reduced susceptibility to cefepime (MICs for 90% of isolates tested [MIC90] equal to 1 μg/ml), six isolates (6.2%) showed reduced susceptibility to amoxicillin, [MIC90=2 μg/ml], 24 (25.0%) to meropenem [MIC90=0.50 μg/ml], 66 (68,7%) to imipenem [MIC90=0.50 μg/ml], 58 (60.4%) to cefprozil [MIC90=16 μg/ml], 80 (83.3%) to cefuroxime [MIC90=8 μg/ml], 84 (87.5%) to lorarcabef [MIC90= ≥256 μg/ml], and 90 (93.7%) strains to cefaclor [MIC90=≥256 μg/ml]. Cefotaxime was found active against all non-susceptible to penicillin isolates [MIC90= 1 μg/ml]. All b-lactams were uniformly susceptible to penicillin-susceptible strains.

Conclusions: Our data showed the wide variability in activity against S. pneumoniae that newer b-lactams antimicrobial agents may possess. Among the oral b-lactams, only amoxicillin appear to possess excellent in vitro susceptibility, and among the parenteral ones cefotaxime seems to be the most active.

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PNEUMOCOCCAL SEROTYPES IN COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN VACCINATED WITH PCV-7

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Aim: In countries with high vaccine coverage with PCV7, infections due to non-vaccine serotypes increase progressively, but little is known in community acquired pneumonia (CAP) in immunized children.

Methods and results: Among 76 children fully vaccinated with 7-valent conjugate vaccine and hospitalized from 2006 to 2009 for community-acquired pneumonia, ten (13.1%) had confirmed pneumococcal infections (4 pts with CAP and 6 patients with CAP & empyema). All *S. pneumoniae* isolated blood culture were non-vaccine serotypes : 19A (3 pts), 1 & 7F (2 pts each), 5 (1 pt) and 2 patients with positive Binax® test in pleural fluid. Other causes of CAP were *Mycoplasma pneumonia* (MP) in 10.5% and viruses in 26.3%. Two identical studies were performed in the same unit before introduction of PCV7 in France, in 1992-96 and 1996-99. During the first period, 8/71 (11.2%) children with CAP had positive blood culture for *S pneumoniae* and 10 /88 patients (11.4%) during the second period. The other causes of CAP in these two studies were respectively 11.3% and 21.1% for MP and 42% and 25.1% for viruses. Non-vaccine serotypes isolated in children CAP were non-vaccine were relatively rare : 13.1% for serotype 1 and 1% for each serotypes 7F, 5 and 19A as reported by national French survey in 1996, before vaccine introduction.

Conclusion: These data show that vaccine-type pneumococci are not rare in children immunized with PCV7. The new PCV13 vaccine will be usefull, but the bacteriological survey of CAP in children either immunized or not remains necessary.

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CLONAL EXPANSION OF *S. PNEUMONIAE* SEROTYPE 19A IN ADULTS AS IN CHILDREN IN PARIS AREA ASSESSED BY THE DIVERSILAB®SYSTEM

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Background: To search a clonal expansion of *Streptococcus pneumoniae* serotype 19A in invasive diseases in adults and children between 2007 and 2009.

Methods: We analyzed 110 *S. pneumoniae* strains, collected from Paris area by the members of the ORP Ile de France and isolated from adults (n= 66) and children (n=34) invasive infections, together with 15 reference strains previously characterized by MLSTyping and 10 from various other serotypes. For all strains, capsular typing was performed by PCR. Each isolate was analyzed using the semi-automated rep-PCR Diversilab® system. The relatedness was determined by cluster analysis and guidelines provided by the manufacturer.

Results: The *Streptococcus pneumoniae* serotype 19A were responsible of respectively 11% and 18% of invasive in adults and children in 2007 and 15% and 19% in 2009. The 110 strains grouped into 4 main Clusters: Cluster I including 74 strains (3 CSF, 1 joint fluid, 5 pleural fluid , 63 blood samples), Cluster II including 13 strains (2 pleural fluid, 11 blood samples), Cluster III including 1 strain from CSF, Cluster IV including 7 strains (3 pleural fluids, 4 blood samples). The 15 other strains exhibited various profiles. Comparing with *S. pneumoniae* 19A belonging tio known clonal complec (CC), most of them belonged to CC276.

Conclusion: These results suggest that the Diversilab® method is correlated with the CC analysis. We identify a clonal expansion of *S. pneumoniae* serotype 19A strains in the Paris area in children as in adults.

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PNEUMOCOCCAL INFECIONS CAUSE PROLONGED STAY AT THE PICU: EXPERIENCE OF 20 YEARS

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Introduction: Invasive pneumococcal infections such as septicaemia, pneumonia, and meningitis lead to life threatening infections. Permanent complications of infection include brain damage and deafness. Pneumococcal infection is spread from one person to another by coughing, sneezing or close face-to-face contact.

Objective: We present our experience about patients with pneumococcal infection compared to other bacterial infection during the last 20 years in our PICU.

Setting: 12 bed interdisciplinary PICU, University hospital.

Patients: 315 patients with severe bacterial infections were enroled prospectively from 1990 to 2010. Patients were cohorted in groups of 3 years, pneumococcal or other infection, and location of infection. Time of ventilation, PICU and physiological scoring were monitored.

Results: 27 out of 315 patients showed pneumococcal positive bacterial cultures. Out of 103 patients with diagnose of bacterial meningitis 15 were tested positive for pneumococcus. Out of 139 patients with bacterial pneumonia 10 patients were tested positive for pneumococcus. Out of 73 patients with septic shock 2 patients were tested positive for pneumococcus. Physiological scoring systems did not differ between these subgroups, time on ventilation was highest in subgroup of pneumococcal positive septic shock (10 days vs 0.6 to 2.8 days). The most significant difference resulted in prolonged ICU treatments of pneumococcal positive patients (meningitis 16 vs 10 days, pneumonia 22 vs 12 days, and septic shock 17 vs 9 days, respectively).

Conclusion: Pneumococcal infections cause in prolonged PICU stay, resulting from secondary complications.

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UNUSUAL *S. PNEUMONIAE* INFECTION IN A YOUNG CHILD

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S. pneumoniae is currently the major invasive pathogen of children and older adults. Unusual pneumococcal infections are rare in immunocompetent hosts.

The authors present a case of pneumococcal infection with splenic microabscesses in a child with low IgG4 and discuss its implications.

A previously healthy 20 month-old boy, incompletely vaccinated for *S. pneumoniae*, presented with a 6-day history of fever. On admission he had a toxic-appearance, increased work of breathing and decreased breath sounds to the right. Imaging showed extensive right-sided pneumonia complicated by organized empyema. He was started on IV antibiotics and underwent decortication of the pleural space via VATS.

No agents were identified on cultural exams, and antibiotics were suspended after 21 days, despite maintenance of intermittent fever. 3 days later, persistent fever re-emerged and multisensible *S.pneumoniae* was then identified on blood and bronchoalveolar lavage. An extensive search for other sites of invasive pneumococcal disease excluded endocarditis, meningitis/brain abscess and osteomyelitis; high-resolution US revealed multiple microabscesses of the spleen.

Evaluation for immune function was normal, except for IgG4 = 4 mg/dL and initial low antibody response to pneumococcal conjugated vaccine, which became normal after unconjugated vaccination.

He was successfully treated with antibiotics based upon susceptibility patterns for an additional 4 weeks.

Healthy young children may have very low IgG2/4 concentrations, which partially accounts for their physiologic susceptibility to encapsulated bacteria infection, such as *S.pneumoniae*.

The authors reinforce the importance of pneumococcal vaccination in this age group, whose natural immune responses to polysaccharide pathogens are very weak.

P611

DISTRIBUTION BY CLINICAL PRESENTATION OF SEROTYPES ISOLATED FROM PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASES IN 2009-2010 IN MADRID, SPAIN

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Background and aims: Serotype may be an important determinant forserious infections. In 2006, Madrid (6 million inhabitants) included the heptavalent pneumococcal conjugate vaccine (PCV7) in the vaccination calendar. This study analyses per-clinical presentation distribution of serotypes causing invasive pneumococcal disease (IPD) in hospitalized children in Madrid in 2009-2010.

Methods: A prospective, laboratory-confirmed (culture and/or PCR) IPD surveillance was performed in May09-April10 in all hospitals with Pediatric department (28 centres). All isolates (for serotyping) and culture-negative pleural/cerebrospinal fluids were sent for PCR analysis.

Results: 169 IPDs were identified. Table shows distribution [n (%)] of serotypes by clinical presentation

Serotype	Bacteremic pneumonia (BP)	Parapneumonic pleural effusion (PPE)	Primary bacteremia (PB)	Meningitis (M)	Mastoiditis (MAST)	Other
1	21 (44.7)	28 (41.8)	1 (6.3)	2 (11.1)	0 (0.0)	2 (16.7)
3	2 (4.3)	7 (10.4)	1 (6.3)	0 (0.0)	0 (0.0)	1 (8.3)
5	2 (4.3)	1 (1.5)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)
6A	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
7F	8 (17.0)	0 (0.0)	1 (6.3)	1 (5.6)	0 (0.0)	1 (8.3)
19A	10 (21.3)	15 (22.4)	10 (62.5)	4 (22.2)	7 (77.8)	2 (16.7)
PCV7 serotypes	0 (0.0)	4 (6.0)	1 (6.3)	1 (5.6)	0 (0.0)	0 (0.0)
Other serotypes	4 (8.5)	12 (17.9)	2 (12.5)	9 (50.0)	2 (22.2)	5 (41.7)
TOTAL	**47 (100)**	**67 (100)**	**16 (100)**	**18 (100)**	**9 (100)**	**12 (100)**

[Per clinical presentation serotype distribution]

Calculated coverages by the new 13-valent pneumococcal conjugate vaccine (PCV13) were: 91.5% (BP), 82.1% (PPE), 87.5% (PB), 50% (M), and 77.8% (MAST).

Conclusions: Serotype 1 (followed by 19A) was the most prevalent in respiratory infections (BP and PPE) while serotype 19A was the most prevalent in non-respiratory infections, causing approx. 75% MAST.

P612

THE HERACLES STUDY (2007-2010): A PROSPECTIVE HOSPITAL-BASED SURVEILLANCE OF SEROTYPES CAUSING PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASE IN MADRID, SPAIN

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Background and aims: In 2006, Madrid (6 million inhabitants) included the heptavalent pneumococcal conjugate vaccine (PCV7) in childhood vaccination calendar. This study identifies changes over time of serotypes causing invasive pneumococcal disease (IPD) in hospitalized children in Madrid in 2007-2010.

Methods: A prospective, laboratory-confirmed (culture and/or PCR) IPD surveillance was performed in all hospitals with Pediatric department: 1st period (20 centres; May07-April08), 2nd period (+2 centres, May08-April09) and 3rd period (+6 new centres; May09-April10). All isolates (for serotyping) and culture-negative pleural/cerebrospinal fluids were sent for PCR analysis.

Results: 499 IPDs were identified. The Table shows serotype distribution by study period [n (%)].

Serotype	1st period [n (%)]	2nd period [n (%)]	3rd period [n (%)]
1	36 (22.1)	50 (29.9)	54 (32.0)
3	5 (3.1)	8 (4.8)	11 (6.5)
5	34 (20.9)	17 (10.2)	4 (2.4)
6A	4 (2.5)	0 (0.0)	1 (0.6)
7F	14 (8.6)	14 (8.4)	11 (6.5)
19A	23 (14.1)	39 (23.4)	48 (28.4)
PCV7	9 (5.5)	6 (3.6)	6 (3.6)
Other	38 (23.3)	33 (19.8)	34 (20.1)
Total	**163 (100)**	**167 (100)**	**169 (100)**

[Per-period serotype distribution]

Calculated coverages by the new 13-valent pneumococcal conjugate vaccine (PCV13) were: 76.7% (1st period), 80.2% (2nd period) and 79.9% (3rd period).

Conclusions: The increase in IPDs by serotypes 1 and 19A (both accounting for 60.4% of IPDs in 2009-2010) shows the added value of the new PCV13.

P613

INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN YOUNGER THAN 15 YEARS OLD IN THE REGION OF CASTILLA Y LEON (SPAIN), 2007-2010

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Background and aims: In Castilla y Leon (Spain) the pneumococcal conjugate vaccine (PCV) is not included in the Public Health Childhood Vaccination Program but it is recommended by pediatricians. The aim of this study is to describe the epidemiological characteristics of invasive pneumococcal disease (IPD) in children younger than 15 years old during 2007-2010.

Methods: Since 2007, IPD is a mandatory notifiable disease in Castilla y Leon, a standard case definition is provided. Clinical, epidemiological and microbiological data are collected by mean of a structured questionnaire in every case. Annual incidence rates per 100.000 persons and case-fatality rates were calculated.

Results: We indentified 84 cases of IPD. Annual incidence rate of IPD was 7.05 per 100.000 children younger than 15 years old. Rates were higher (26.67) in children younger than 1 year old. Bacteremic pneumonia (33.3%), meningitis (22.6%) and septicaemia (17.9%) were the most frequent diagnoses. Case-fatality rate was 4.8% for global IPD and 15.8% for meningitis. Long-term effects were reported in 10.7% of the cases. Serotypes were isolated in 86.9%. Serotypes 7F (28.8%), 19A (19.2%) and 1 (15.1%) were the most frequent ones. New 13-valent pneumococcal conjugate vaccine (PCV13) would provide 76.7% coverage of serotypes in this serie.

Conclusions: The incidence and epidemiologic characteristics reported are similar to those in other developed countries after licensure of the PCV7. This study shows a high burden disease related with PCV13. By this, the study provides an important baseline data to make public health decision and to assess epidemiology of IPD.

P614

STUDY-PRESENTATION:NATIONWIDE SURVEILLANCE-STUDY ON PARAPNEUMONIC EMPYEMA IN CHILDREN IN GERMANY

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Introduction: An increase in the incidence of pediatric parapneumonic empyema (PPE), mainly caused by *Streptococcus pneumoniae* and *Staphylococcus aureus* has been observed in several countries. In Germany a general childhood pneumococcal conjugated vaccination (pcv) has been introduced in July 2006 and a vaccination coverage of ~80% has been reached. The objective of the present study is to identify incidence, etiology, complications and influence of pneumococcal vaccination on pathogens of PPE in Germany.

Methods: Between 10/2010-and 9/2012 surveillance of children with PPE will be conducted in all 472 German paediatric hospitals using the German Surveillance Unit for Rare Diseases in Childhood (ESPED). Inclusion criteria are *diagnosis of pneumonia accompanied by pleural effusion persisting for ≥7 days or necessitating pleural drainage in children* ≤17 years. Additional pathogen detection from pleural fluid by broad-spectrum 16S-rDNA-PCR and pneumococcal serotyping is offered. Clinical and epidemiological data are evaluated via questionnaires.

First Results: Between 10-12/2010, 28 cases (15 males) aged 4.9 (Median, IQR: 3.2-9.3) years were documented, hospitalized for a median of 15.5 (9.3-19.8) days. Thirteen patients (36%) needed intensive care, two of them mechanical ventilation. Isolated pathogens were *Streptococcus pneumoniae* (n=5/6) and *Haemophilus influenzae* (n=1/6). In 6 patients (21%) possible predisposing factors were present and 12 (35%) had received pcv.

Discussion: The current study will systematically identify the age-adjusted incidence, the spectrum of bacterial pathogens, the influence of currently used pneumococcal vaccines and the current practice of therapeutic management of PPE in German hospitals.

P615

SEROTYPE DISTRUBUTION OF *S. PNEUMONIAE* AMONG CHILDREN WITH CHRONIC LUNG DISEASES ADMITTED TO HOSPITAL WITH PNEUMONIAE

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S. pneumoniae is the most common cause of bacterial pneumoniae in all age groups. In this study we retrospectively investigated respiratory cultures of children with chronic lung diseases who admitted to hospital with pneumoniae. Respiratory cultures that yielded growth of *S. pneumoniae* were selected and serotype determination of those isolates done by conventional multiplex PCR. A total of 61 children (31 female, 30 male) with a median age of 107 $\pm$ 60 months (range: 2 to 284 months) were enrolled. Underlying chronic lung diseases among those children were bronchiectesia in 13 (28%), asthma in 9 (20%), cystic fibrosis in 9 (20%), Kartagener syndrome in 6 (13%) and others in 24 (19%). Respiratory culture samples were obtained from sputum in 41 (67%) patients, broncho-alveolar lavage in 4 (7%) patients, endotracheal aspiration fluid in 14 (23%) patients and nasopharyngeal aspiration in 2 (3%) patients. Serotype 19F (n=15,), 23F (n=9,), 6 (n=8), 17F (n=3), 25F (n=3) were the most prevelant serotypes. Other isolated serotypes were serotype 14 (n=2), 18 (n= 2), 20 (n=2), 7F (n=2), 9A(n=2), and serotypes 22F, 23A, 3, 34, 4, 7C, 9V, and 5B (n=1, for all). In 4 patients serotype of *S. pneumoniae* were not determined. Serotype covarage of 7-, 10- and 13-valent conjugate vaccines was 57%, 61% and 62%, respectively. *S. pneumoniae* is one of the most common cause of respiratory illness among patients with chronic lung diseases and five serotypes account for most cases.

P616

SEROTYPE DISTRIBUTION AND ANTIMICROBIAL SUSCEPTIBILITIES OF *S. PNEUMONIAE* FOLLOWING INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINES IN GREECE

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Background and aims: The aims were to describe the serotypes and antimicrobial susceptibilities of *S. pneumoniae* isolates causing invasive pneumococcal disease (IPD) or acute otitis media (AOM) in children ≤14 y.o. following the introduction of pneumococcal conjugate vaccines in the National Immunization Programme of Greece.

Methods: A prospective nationwide study was conducted between September 2008 and November 2010 in 10 pediatric hospitals. Serotyping was performed by latex agglutination and quellung reaction using anti-sera (SSI, Copenhagen, Denmark). Susceptibilities to penicillin were determined by E-test and interpreted by the CLSI criteria.

Results: Among 229 isolates collected (120 boys, 109 girls, 80.3% ≤5 y.o., IPD: 99, AOM: 130) the commonest serotypes for IPD were 7F (23.2%), 19A (20.2%), 1 (11.1%) and 3 (8.1%) and for AOM 19A (29.2%), 19F (16.1%), 3 (12.3%) and 6A (10,0%). For children ≤2 y.o with IPD, the anticipated coverage for PCV7, PCV10 and PCV13 is 12.2%, 34.1% and 73.17% respectively whereas for AOM is 17.4%, 26.1% and 78.3%. In children 2-5 y.o the coverage is 2.9%, 40% and 68.6% for IPD and 25.6%, 30.8% and 82.0% for AOM. High resistance to penicillin was exhibited by 5.1% of IPD isolates and 15.4% of AOM. The most prevalent resistant serotypes were 19A and 19F.

Conclusions: After wide use of PCV7, the frequency of PCV7 serotypes causing IPD and AOM is low. The majority of pneumococcal infections in children ≤2 and 2-5 y.o. are caused by the 6 additional serotypes included in the 13-valent vaccine.

P617

PNEUMOCOCCAL INFECTIONS IN CENTRAL GREECE: EARLY AND LATE POST-HEPTAVALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7) PERIOD

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Background and aims: In Greece, PCV7 was introduced in October 2004. Surveillances at a regional level as well as those at a national level are valuable, in order to monitor the impact of pneumococcal conjugate vaccines and serve as a guide for empirical treatment.

Methods: The medical records of children 0-15 y.o. examined at the outpatient clinics or admitted to the pediatric wards of the University General Hospital of Larissa and the General Hospital of Volos, Central Greece, with pneumococcal infections from January 2005 to February 2011 were reviewed.

Results: The cases of invasive pneumococcal disease (IPD), acute otitis media (AOM) with otorrhea, and conjunctivitis, as well as the rate of penicillin-nonsusceptible (Pen-NS) isolates appear in the following table:

Infection	2005-2007 (n=49)	2008-2/2011 (n=72)	P
	Pen-NS/total isolates (%)	Pen-NS/total isolates (%)	
IPD	8/18 (44.4)	2/11 (18.2)	0.234
AOM with otorrhea	9/19 (47.4)	16/34 (47.1)	0.999
Conjunctivitis	5/12 (41.7)	7/27 (25.9)	0.455

[Rate of penicillin-nonsusceptible isolates]

A 38.9% reduction in the IPD cases was noted during the late post-PCV7 period (2008-2/2011) compared to those in the early period (2005-2007). Serotype 19A cases were observed only during the late period. During that period, serotyped Pen-NS isolates belonged to serotypes 19F (n=9), 19A (n=6), 6A (n=2), nontypeable (n=2), and 14 (n=1).

Conclusions: In Central Greece during the late post-PCV7 period, a trend towards a reduction in cases of IPD was noted. AOM due to Pen-NS *Streptococcus pneumoniae* remains common.

P618

ETIOLOGY OF MIDDLE EAR FLUID OF INFANTS WITH ACUTE OTITIS MEDIA (AOM) IN GERMANY, 2ND STUDY YEAR

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Background and aims: In December 2009, the pneumococcal conjugate vaccine PCV13 was introduced in Germany, where a general recommendation for pneumococcal conjugate vaccination was issued in 2006. In this poster, we analyzed the pathogens recovered from children suffering from severe AOM with efflux in the most recent study period from Oct. 2009 to Oct 2010.

Methods: Swabs were taken from the middle ear fluid of children with spontaneous draining AOM regardless of their immunization state. Serotyping of *Streptococcus pneumoniae* isolates was performed using the Neufeld-Quellung reaction. *Streptococcus pyogenes* isolates were *emm*-typed by sequencing of the *emm*-gene. *Haemophilus influenzae* was typed using type-specific antisera.

Results: From Oct. 2009 to Oct 2010, 310 children with severe AOM were documented, in comparison with the period Oct. 2008 - Oct 2009 considerably less patients (459). Following pathogens were identified from 120 of these patients: *S. pneumoniae* (35, 29.2%), *S. pyogenes* (35, 29.2%), *S. aureus* (32, 26.7%), *H. influenzae* (16, 13.3%) and *M. catarrhalis* (2, 1.7%). Unchanged to the previous study period, serotypes 3 (9, 25.7%), 19A (7, 20.0%) and 19F (4, 11.4%) were most prevalent. Coverage of the respective conjugate vaccines was as follows: PCV7: 11.4%, PCV10: 22.0%, PCV13: 68.6%. The vaccination rate increased from 71.9% (year 1) to 84.5% (year 2).

Conclusions: While the pathogens recovered were almost unchanged, considerably less children with severe AOM were documented in the second study year. A possible effect of the pneumococcal conjugate vaccination has to be carefully studied in the coming years.

P619

NASOPHARYNGEAL CARRIAGE ISOLATES (NCI) FROM INFANTS WITH ACUTE OTITIS MEDIA (AOM) IN GERMANY

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Background and aims: A general recommendation for pneumococcal conjugate vaccination was issued in Germany in 2006. In this presentation, we analyzed the NCI recovered from children suffering from severe AOM in the most recent study period from Oct. 2009 to Oct. 2010.

Methods: Nasopharyngeal swabs were taken from children with spontaneous draining AOM regardless of their immunization state. *Streptococcus pneumoniae* isolates were serotyped using the Neufeld-Quellung reaction. *Streptococcus pyogenes* isolates were *emm*-typed and *Haemophilus influenzae* isolates were typed using type-specific antisera.

Results: Nasopharyngeal swabs were obtained from 294 of 310 patients with AOM, with 243 swabs being positive for *S.pneumoniae*, *S. pyogenes*, *H. influenzae and/*or *M. catarrhalis*. The highest carriage rate was found for *S. pneumoniae* (57.8%), followed by *H. influenzae* (36.1%), *M. catarrhalis* (33.0%) and *S. pyogenes* (11.9%). All *S.pneumoniae* NCI revealed the same serotype as the corresponding isolate recovered from the middle-ear fluid (mef). Also both, the carriage and the mef *S. pyogenes* isolates showed the same *emm*-type. Almost all *H. influenzae* isolates were non-typable, not differing between NCI and mef-isolates. The most prevalent *S. pneumonia* serotypes were serotype 3 (20.0%), 19A (10.0%), 19F (6.5%), 11A (5.3%) and 35F (5.3%). Coverage of pneumococcal conjugate vaccines was as follows: PCV7, 10.6%; PCV10, 15.9%; PCV13, 48.2%.

Conclusions: Nasopharyngeal swabs were obtained from 94.8% of patients suffering from severe AOM, with *S. pneumoniae* being the most common pathogen recovered. Pneumococcal NCI had the same serotype as the mef-isolates. Most prevalent serotypes were serotypes 3 and 19A, both covered by PCV13.

P620

SEROTYPE DISTRIBUTION AND SENSIVITY TO PENICILLIN OF *STREPTOCOCCUS PNEUMONIAE* ISOLATES THAT CAUSE INVASIVE DISEASE AMONG BRAZIL CHILDREN

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In Brazil the 10-valent pneumococcal conjugate vaccine(PCV 10) was introduced in to de National Immunization Program in April 2010. We conducted a study to identify the most common pneumococcal serotypes in children with invasive disease, correlate isolated serotypes with those included in conjugate vaccines, and ascertain the sensivity to penicillin

Methods: From January 2003 to July 2010, a retrospective study of children with a diagnosis of invasive disease for *Streptococcus pneumoniae* was conducted at the University Hospital of São Paulo. Criteria for inclusion were: age greater than 29 day and less than 15 years, with isolation of pneumococcus from a normally sterile site.

Results: The study included 198 children. Of these, 142cases of pneumonia, 29 bacteremia , 20 meningitis, 3 cellulitis, 3 pyoarthritis and 1 pericarditis.The most common serotypes were: for pneumonia 14(42,3%), 5(13,8%), 1(13%), 6B(6,5%) and 19A(4,1%); for bacteremia were 14(34,5%), 6B(24,1%), 12F(6,9%), 19F(6,9%) and 18C(6,9%); for meningitis were 14(29,4%), 18C(11,8%), 10A(11,8%) and 19F(11,8%). The coverage rates of PCV10 and PCV13 in meningeal disease was 64,7% and 76,5% respectively. For non-meningeal disease was 84,4% and 93,8%. The sensitivity to penicillin in meningeal disease were: sensitive(MIC< 0,06µg/mL) in 13 cases (65%) and resistant(MIC≥0,12µg/mL) in 7 cases (35%). For non-meningeal disease were: sensitive(MIC< 0,06µg/mL) in 170 cases(95%), intermediate resistant(MIC=4µg/mL) in 9 cases(5%).

Conclusions: Our results confirm a significant potential impact of PCV 10 for non-meningeal disease but no for meningeal disease. The susceptibility testing results show that penicillin is still the treatment of choice for non-meningeal pneumococcal disease.

P621

ANALYSIS OF INVASIVE PNEUMONIA CAUSING STRAINS OF STREPTOCOCCUS PNEUMONIAE: SEROTYPES AND ANTIMICROBIAL SUSCEPTIBILITY

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In Brazil the 10-valent conjugate vaccine was introduced in to de National Immunization Program in April 2010. We conducted a study to identify the most common pneumococcal serotypes in children hospitalized with invasive pneumonia, correlate isolated serotypes with those included in conjugate vaccines, and ascertain the sensivity of the isolated pneumococcal strains to penicillin and other antibiotics.

Methods: From January 2003 to Jully 2010, a restrospective study of hospitalized children with a diagnosis of *Streptococcus pneumoniae* pneumonia was conducted at the University Hospital of São Paulo. Criteria for inclusion were: age greater than 29 day and less than 15 years, radiological and clinical diagnosis of pneumonia, and isolation of Streptococcus pneumoniae in blood cultures and/or pleural effusion.

Results: The study included 142 children. The most common serotypes isolated were 14(42,3%), 5(13,8%), 1(13%), 6B(6,5%), 19A(4,1%) and 3(3,3%). The proportion of identified serotypes contained in the heptavalent, 10-valent and 13-valent conjugate vaccines was 59,3%, 87,8% and 97,6% respectively. Pneumococcal strains were sensitive to penicillin (MIC≤2µg/mL) in 133 cases (93,7%) and intermediate resistance (MIC=4µg/mL) 9 cases (6,3%). No strains were penicillin-resistant (MIC≥8µg/mL) according to CLSI-2008 standards. Tested isolates were highly sensitive to vancomycin, rifampicin, ceftriaxone, clindamycin, erythromycin and chloramphenicol.

serotype	N isolates	%
14	52	42,3
5	17	13,8
1	16	13
6B	8	6,5
19A	5	4,1
3	4	3,3
4	4	3,3
6A	3	2,4
18C	3	2,4

[Serotype of S.pneumoniae in invasive pneumonia]

serotype	median age (months)
14	21
5	42
1	67,5
6B	18
19A	33
3	14
4	26

[Serotypes of S.pneumoniae and median age]

Conclusions: Our results confirm a significant potential impact of conjugate vaccines, mainly 10-valent and 13-valent, on invasive pneumonia. Furthermore, susceptibility testing results show that penicillin is still the treatment of choice for invasive pneumonia in our setting.

P622

SCREENING OF MYOCARDITIS WITH CARDIAC TROPONIN-I IN HOSPITALIZED CHILDREN FOR RESPIRATORY VIRAL INFECTION

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Aim: Myocarditis is an uncommon, potentially life-threatening disease that presents with a wide range of symptoms in children and adults. Viral infection is the most common cause of myocarditis. The diagnosis is usually made based on clinical presentation and noninvasive imaging findings.

The incidence of myocarditis in children is uncertain because patients with minor symptoms can remain undiagnosed. The aim of this study is screening all children who are hospitalized for an acute respiratory infection with troponin-I (TnI) that would reveal myocarditis cases and performed a prospective screening study.

Methods: Troponin-I(TnI) measurement was performed in all children that hospitalized for acute respiratory infection , If TnI value was above the normal limit (0.06 microg/L), electrocardiogram (ECG) and echocardiography were performed. TnI measurements were repeated at next 24 hours .CXR was performed in all cases.

Results: 56 children (between 5 to 36 months) with acute respiratory infection were screened during the autumn and winter 2010. TnI was above the normal range (0.06 microg/L) in 3 children without any signs of myocarditis in ECG or echocardiography.

Conclusion: The incidence of myocarditis during viral infections is low and a routine TnI screening for asymptomatic myocarditis is not useful, but myocarditis should be considered in any case of acute respiratory infection especially in younger age.

P623

RESPIRATORY VIRUSES ARE FREQUENTLY ASSOCIATED WITH SEVERE PNEUMONIA IN CHILDREN IN KARACHI, PAKISTAN

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Objective: Pneumonia remains the leading cause of child mortality in Pakistan. Role of respiratory viruses in causing severe pneumonia in Pakistan remains largely unknown. Our study aims to determine the prevalence of respiratory viruses (Respiratory Syncytial Virus (RSV), Influenza A virus and Human Metapneumovirus (HMPV)) in children aged 2 - 23 months who were hospitalized with severe pneumonia at a public sector hospital in Karachi during this winter season.

Methods: Prospective surveillance is in progress at a public tertiary care hospital in the metropolitan city of Karachi. Children admitted with tachypnea and chest indrawing (WHO definition of severe pneumonia) were recruited and throat swabs were obtained to detect respiratory viruses using real time RT-PCR. Chest x-rays were also obtained and independently interpreted by two radiologists to diagnose radiologic pneumonia.

Results: Seventy one children with severe pneumonia were identified during the three winter months *(1st November 2010 to 31st January 2011)*, out of which 64 (90%) children were recruited after parental consent. Atleast one respiratory virus was detected in 23 (36%) children. HMPV was found in 11 (17%) subjects, RSV in 8 (12%) subjects, and Influenza A in 6 (9%). Co-infection was found in two children with Influenza A and RSV. Out of the four radiological proven pneumonia cases, one had influenza A.

Conclusion: HMPV, RSV, Influenza A are common causes of pneumonia in hospitalized children in Karachi during the winter season. Knowledge of the viral etiology of pediatric pneumonia can help in recommending appropriate preventive strategies like influenza vaccination.

P624

COMMUNITY-ACQUIRED *MYCOPLASMA PNEUMONIAE* LOW RESPIRATORY TRACT INFECTIONS MOTIVATING HOSPITALIZATION IN CHILDREN

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Backgroud and aims: *Mycoplasma pneumoniae* (Mp) pneumonia occur worldwide with higher incidence between 5 and 15 years old, and has insidious onset. Severe pneumonia occurs in less than 10% of cases. The aim of this study was the revision of epidemiological and clinical data of Mp pneumonia in hospitalized children.

Methods: A retrospective study was conducted by reviewing the clinical records of hospitalized patients with pneumonia and Mp DNA detection by polymerase chain reaction in upper respiratory tract specimens, in a level 2 hospital paediatric service from August 2006 to July 2010.

Results: There were 35 cases. The age ranged from 6 to 156 months with half cases occurring under 5 years old. The admissions occurred mainly in summer and there were no cases in 2008 and 2009. The most common clinical manifestations were cough (100%), fever (88,6%) and dyspnoea (51,4%). At admission, 57,1% children had respiratory distress, with hipoxemia being the main hospitalization's reason. The most frequent auscultatory finding was bilateral crackles. There were no characteristic radiological patterns, with bilateral alveolar changes present in half cases. Supplementary oxygen were needed in 45,7%, fluidoterapy in 5,7%, and systemic corticosteroids in 42,8%. Macrolide was started at admission in 82,9% patients. Average hospitalization time was 6,9 days. There was one re-infection.

Conclusions: Mp infections have a large range of clinical manifestation with pneumonia being an example. This study shows a high incidence of infection in young children as the possibility of re-infections. This etiologic agent needs to be considered in pre-school children.

P625

SUBGROUP CHARACTERISTICS OF RESPIRATORY SYNCYTIAL VIRUS DURING 2009/2010 SEASON IN LATVIA

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Background and aims: The aim of this work was to detect circulation patterns and clinical characteristics of respiratory syncytial virus (RSV) subgroups, A and B, in a tertiary children's hospital in Latvia.

Methods: Nasopharyngeal aspirates (NPA) were collected from children hospitalized with lower respiratory tract infections between April 2009 and June 2010. Viral RNA was extracted from the NPAs and cDNA was synthesized by standard methods. For screening PCR, intercistronic M-P gene locus was amplified, regardless of the genotype. RSV-positive samples were subtyped by amplification of specific G gene fragments. Genotypes were detected by sequencing of randomly selected full-length G gene amplicons.

Respiratory Distress Assessment Instrument was used for clinical assessment. Comparison of means was done using t-test and correlations were performed using Spearman's correlation.

Results: During the observation period, 70 samples were collected. In 26 (37%) samples RSV specific RNA was detected. 18 (69%) group A and 8 (31%) group B isolates were distinguished. Genotype distribution analysis revealed at least two different RSV-A and two RSV-B strains co-circulating.

Patients with RSV-A infection were more likely to be previously hospitalized ($p=0.021$), meet systemic inflammatory response syndrome criteria ($p=0.019$), and receive antibacterial treatment ($p=0.048$). No significant differences were found in the clinical severity or respiratory distress between the two groups.

Conclusions: This is the first study to analyze RSV genetic variability in Latvia. Both RSV subgroups with several genotypes within them were co-circulating during 2009/10 season in our hospital. Some clinical differences were found between the both subgroups.

P626

USEFULNESS OF BIOMARKERS TO RESTRICT ANTIBIOTIC PRESCRIBING FOR LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN

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Background and aims: The identification of lower respiratory tract infections (LRTI) in need of antibiotic treatment (AB) remains challenging. This study investigated procalcitonin (PCT) and c-reactive protein (CRP) as predictive biomarkers of bacterial infection not in need of antibiotic treatment.

Methods: Data were obtained from a randomized controlled trial (ProPAED) comparing pediatric febrile LRTI treated with AB either according to international guidelines or to PCT cut offs accepted for AB of LRTI in adults. Of 337 children enrolled in the original trial, all previously healthy children with complete diagnostic and outcome data were analyzed. Test performance parameters of PCT and CRP in predicting outcome with restricted AB were calculated.

Results: 125 patients were eligible for analysis of PCT and CRP dependent treatment outcome. The PCT and CRP values were higher in patients with community acquired pneumonia as compared to those with other LRTI ($p < 0.05$). PCT (cut-off 0.25mg/dl) combined with CRP (cut-off 40mg/dl) showed a sensitivity of 81% (CI 95 67-96) and a negative predictive value of 88% (CI 95 77.3-97.7)) to rule out non-favorable outcome of children with LRTI without AB.

Conclusion: The combination of low PCT and CRP values may predict favorable outcome of restricted AB for LRTI in children. Larger prospective intervention studies with higher PCT cut offs are needed to further crystallize outcome driven paediatric cut offs for biomarker guided AB of LRTI in children.

P627

RESPIRATORY TRACT ILLNESSES DURING THE FIRST YEAR OF LIFE: EFFECT OF DOG CONTACTS

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Background and aims: Respiratory infectious symptoms and diseases are frequent during early childhood. Our goal was to investigate the effect of dog contacts on the frequency of respiratory symptoms and infections during the first year of life.

Methods: In birth cohort study, 397 children were followed from the pregnancy onward. The frequency of respiratory symptoms and infections together with information about dog contacts during the first year of life were reported by weekly diaries.

Results: Children having dog at home were healthier than children with no such animal contact (adjusted odds ratio [aOR], 1.34; 95% confidence interval [95% CI], 1.11-1.60). Furthermore, they had less frequently otitis (aOR, 0.58; 95% CI, 0.39-0.85) and tended to need fewer courses of antibiotics (aOR, 0.74; 95% CI, 0.54-1.03) than children without such contact. The highest protective association between dog ownership and the shown health parameters was detected among children who had dog inside at home less than six hours daily compared with the other dog owner groups: no dog or dogs mainly outdoors and dogs more than 6 hours inside the home daily.

Conclusion: These results suggest that dog contacts may have a protective effect on the respiratory tract infections during the first year of life and may have a role in the development of immune maturation possibly leading to better resistance to infectious respiratory illnesses during childhood.

P628

SEVERITY OF INFLUENZA IN HOSPITALISED CHILDREN: COMPARISON WITH OTHER RESPIRATORY PATHOGENS

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Background: We compared the clinical presentations in children (£15 years) hospitalised with influenza or other respiratory viral infections (RVIs) in a tertiary paediatric hospital and the likelihood of having an invasive procedure (eg. lumber puncture: LP) on admission.

Methods: A retrospective medical record review was undertaken of all children admitted to the Children's Hospital at Westmead, Sydney, Australia with laboratory confirmed influenza or other RVIs (except respiratory syncytial virus) in 2007.

Results: Of 253 children hospitalised, 131 (51.7%) had laboratory confirmed influenza and 122 (48.2%) had other RVIs (eg. Para-influenza, Adenovirus). Compared to those with other RVIs, children with influenza were more likely to have high temperature of ³39°C (OR: 2.1, p=0.01), lethargy (OR: 1.8, p=0.007), poor feeding (OR: 1.7, p=0.01) and petechiae/rash (OR: 3.4, p=0.003). There were more young infants (aged £3 months) in the influenza group compared to the other RVIs (19.0% vs 7.3%, p=0.004). 26 (19.8%) children with influenza had LP compared to 8 (6.5%) in other RVIs (OR: 3.4, p=0.002); however, none had a positive result.

Conclusions: Children hospitalised with influenza appear significantly more unwell than those with other RVIs. They often look septic on presentation and are more likely to have an LP. Sensitive and non-invasive diagnostic tests are available for early diagnosis of influenza (eg. rapid antigen tests). Influenza positive cases are also unlikely to have meningitis and an early diagnosis may prevent expensive and invasive procures like LPs in young children with influenza.

P629

LENGTH OF HOSPITAL STAY FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) IN PROPHYLAXED VERSUS NON-PROPHYLAXED PREMATURE INFANTS

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Background and objective: RSV is the most prevalent cause for lower respiratory tract infection (LRTI) hospitalizations in infants under 2 years of age. Palivizumab for RSV prophylaxis helps reduce the risk of severe RSV disease that requires hospitalization in high-risk infants. The objective was to determine the difference in hospital length of stay (LOS) among premature infants who received and did not receive RSV prophylaxis.

Methods: Premature infants (< 37 weeks of gestational age) hospitalized within the first year of life for a LRTI were extracted from the I3 Medical Claims database (2000-2008). Prophylaxed infants were defined as having at least 1 dose of palivizumab prior to hospitalization. Multivariate regression determined the difference in hospital LOS, while adjusting for confounders including birth gestational age, birth weight, age at admission and medical comorbidities.

Results: The database identified1728 premature infants that were hospitalized due to RSV-confirmed LRTI. 36 (2.1%) had received palivizumab. Univariate analysis showed palivizumab-prophylaxed infants had more comorbidities (p=0.038), and were born at an earlier gestational age (p=0.005). The multivariate model revealed that prophylaxed infants had, on average,1.4 fewer days LOS in hospital for severe RSV (p-value=0.032).

Conclusions: These data suggest that compared to premature infants not receiving at least 1 dose of palivizumab, there is an independent association between prophylaxed infants and a decreased LOS for a severe RSV hospitalization. Reasons for this finding, validation of these results in other country databases, as well as an assessment of the impact of full palivizumab adherence and LOS, warrant further research.

P630

PREDICTORS OF HOSPITAL LENGTH OF STAY (LOS) IN INFANTS HOSPITALIZED FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN THE RUSSIAN FEDERATION

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Background and aim: Identification of variables that predict duration of RSV-associated hospitalization may be useful in the identification of preventive and therapeutic strategies. The objective of this analysis was to identify predictors of hospital LOS in infants hospitalized for RSV in the Russia Federation during the 2008-09 RSV season.

Methods: Infants ≤ 2 years hospitalized due to a LRTI with confirmed RSV were included, for which data on co-morbidities, complications and resource use was collected. Differences of LOS were compared using t-tests and chi-square tests for continuous and categorical variables, respectively. Statistical significance was set at 0.05. Multivariate linear regression analysis was conducted for LOS including potential predictors such as ICU admission, oxygen supplementation, time from symptom onset to hospitalization, age at admission, prematurity, complications and co-morbidities.

Results: 197 infants were hospitalized due to RSV. Of those, 16 (8%) were admitted to ICU and had LOS increased by 2.3 days (p=0.001) compared to those without ICU admission. In 23 infants (12%) who needed oxygen supplementation, LOS was increased by 2.2 days (p=0.010). 47 infants (24%) with complications had an increased LOS of 1.6 days (p=0.037). 76 infants (39%) with co-morbidities had 1.5 days longer LOS compared to those without co-morbidities (p=0.028). Public insurance coverage increased the LOS by 2 days compared to those receiving private insurance or family paid insurance (p=0.002).

Conclusions: This study suggests that ICU admission, receipt of oxygen supplementation as well as complications, co-morbidities and public insurance may lead to an increase in the length of stay.

P631

ELEVATED RISK OF ASTHMA AFTER HOSPITALIZATION FOR SEVERE RESPIRATORY SYNCYTIAL VIRUS INFECTION IN INFANCY: A SYSTEMATIC REVIEW AND EVIDENCE SYNTHESIS

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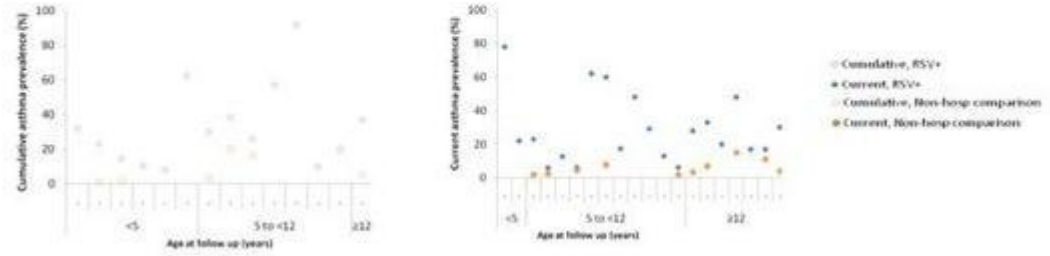
Background and aim: Respiratory syncytial virus (RSV), the most common cause of severe bronchiolitis among children, is associated with substantial morbidity and mortality worldwide. Whether individuals hospitalized for RSV during infancy are at increased risk of asthma is unclear. This study aimed to characterize the risk of asthma after RSV-related hospitalization during infancy.

Methods: A systematic search was conducted in MEDLINE, EMBASE, and the Cochrane databases (through July 2010). Review of reference lists identified additional studies. Data were extracted by two reviewers from all studies according to three age categories (< 5, 5-11, and ≥12 years of age (y)), clinically relevant for asthma management. Asthma was classified according to the definitions in the original articles.

Results: The search identified 2,544 articles; 28 focused on RSV hospitalization during infancy and asthma. Estimates of current (typically, within 1y) and cumulative (period) asthma prevalence are presented in Figure 1. Attributable fractions of asthma (measured cumulatively) due to RSV were 13% and 22% among those < 5y, 11% to 27% among those 5 to 11y, and 32% among those ≥12y, from studies comparing asthma prevalence among those hospitalized, to those who were not (Figure 1). Trends were consistent for current asthma prevalence.

Figure 1 Prevalence (%) of (*A*) cumulative and (*B*) current asthma, among those previously hospitalized for RSV, and non-hospitalized comparisons, by age



[Figure 1]

Conclusions: Prevalence estimates vary widely. Nevertheless, the data suggest a link between severe RSV infection requiring hospitalization in infancy and asthma in childhood.

P632

DRIVERS OF THE FINANCIAL AND HEALTH-RELATED QUALITY-OF-LIFE IMPACTS OF HOSPITALIZATION FOR RESPIRATORY SYNCYTIAL VIRUS INFECTION IN INFANCY

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Objective: Hospitalization for respiratory syncytial virus (RSV) in infancy is associated with substantial direct medical costs. As less is known about the parental health-related quality-of-life (HRQoL) and non-medical (financial) impact, a survey was developed. This study explored that survey's validity for estimating the financial and HRQoL burden of a child's RSV-related hospitalization.

Methods: Six parents of children < 3 years hospitalized for RSV at the Alberta Children's Hospital within the preceding year completed the survey. It included questions (over the hospitalization) on: hospital or travel time; extra expenses, paid help, and home care required; missed work and lost productivity; and HRQoL impact. Qualitative cognitive debriefing interviews were conducted to assess the interpretation and comprehensiveness of survey items.

Results: Participant feedback, which was judged to reach information saturation, indicated the survey had face and content validity for measuring the financial and HRQoL burden of RSV-related hospitalization. Parents were uncertain how to value the impact of hospitalization on work, if on parental leave. An interesting finding was the large financial and HRQoL impact both days to weeks before, and months after, hospitalization, including substantial negative impacts on workplace functioning; parental anxiety and HRQoL; and increased medical (ambulance, Emergency room, physician/nurse) resource use.

Conclusions: Cognitive debriefing exercises, one step in survey validation, identified modifications to maximize survey validity. In addition to the hospitalization event, events before and after admission also drove the financial and HRQoL burden. Parental costs and HRQoL impacts should be included when assessing the economic burden of RSV-related hospitalization.

P633

ACUTE BRONCHIOLITIS - THERAPEUTIC EVALUATION

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Background and aims: Viral bronchiolitis is a frequent cause of hospitalization in young children. In spite of its high prevalence, to date there is no effective unanimously accepted therapy for it. We aimed to study the efficacy of nebulized epinephrine therapy and inhaled corticosteroids therapy in children with acute bronchiolitis.

Methods: The study included children aged 6-24 months, hospitalized with the diagnosis of moderate/severe acute bronchiolitis. The inclusion criteria were wheezing, first bronchial obstructive episode, no previous therapy at home (except for antithermics), absence of a chronic disease (cystic fibrosis, congenital heart disease, brochopulmonary dysplasia, immunodeficiency), O2 saturation < 90%. Two study groups were formed and compared. The first group consisted of 25 subjects who received 1:1000 aerosol epinephrine 0,5mg/kg every 8 hours. The second group, including 26 subjects, received inhaled corticosteroids 0,5mg every 8 hours. Oxygen was administered to the subjects of both groups.

Results: The subjects were evaluated by the measurement of a clinical score that included the following parameters: respiratory effort, respiratory rate, O2 saturation assessed by pulse-oximetry. Both nebulized epinephrine therapy and inhaled corticosteroids therapy had favorable effects, without significant differences being found between the two groups. There were no factors predicting a favorable response to either of the drugs administered in aerosols.

Conclusions: Moderate/severe acute bronchiolitis had a favorable evolution under treatment with both nebulized epinephrine plus oxygen-therapy, and inhaled corticosteroids plus oxygen-therapy, without significant differences between the two types of therapy.

P634

THE BURDEN OF INFECTIONS BY PARAINFLUENZA VIRUS IN HOSPITALIZED CHILDREN IN SPAIN. A FORGOTTEN AGENT?

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Background: The specific role of parainfluenza viruses (PIVs) in hospitalized children has been insufficiently investigated.

Objective: We have designed a prospective study to describing the clinical impact of the different PIV types detected in hospitalized children with respiratory tract infections.

Patients & methods: From September 2008 to August 2010 a prospective study was conducted in children younger than 14, admitted with respiratory infection to the Pediatrics Department of the Severo Ochoa Hospital, in Madrid (Spain). Specimens of nasopharyngeal aspirate (NPA) were taken for virologic study with polymerase chain reaction. Clinical and epidemiological features of different types of PIV have been compared both between them, and with respiratory syncytial virus (RSV) infections.

Results: Positive viruses were detected in a total of 740 NPA samples (80.8% of the 916 tested). PIVs were detected in 82 patients,11.8% of positive cases, 8.9% of the whole analyzed group. PIV type 1 was detected in 12 cases (14.6%), PIV type 2 in 8 cases (9.8%), PIV type 3 in 47 cases (57.3%) and PIV type 4 in 15 cases (18.3%). PIV1 & 2 were more frequently associated with diagnosis of larygitis and pneumonia and PIV 3 & 4 were associated mainly with asthma crisis and bronchiolitis (p= 0.05).Patients with RSV infection suffered hypoxia more frequently (73% vs 50%, p=0.01). Bronchiolitis was more frequent in RSV group (58% vs 28%, p=0.001).

Conclusions: PIV infections have a significant proportion of viral respiratory detections in hospitalized children. There are clinical differences between PIV and RSV infections.

P635

RETROPHARYMGEAL AND PARAPHARYNGEAL ABSCESS: EXPERIENCE IN A TERTIARY-CARE CENTER IN THE SOUTH OF SPAIN DURING 2000-2009 PERIOD

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Introduction: Retropharyngeal and parapharyngeal abscess are rare but

associated with significant morbidity and potential mortality. This study reviews our experience in the diagnosis and management of retro and parapharyngeal abscesses and compares children treated conservatively with those undergoing surgical intervention.

Methods: Retrospective analysis of children diagnosed with retro and

parapharyngeal abscess from 2000 to 2009 in our tertiary-care centre.

Results: Thirty-one children were identified. There were 17 retropharyngeal

abscess and 11 parapharyngeal abscess ; 3 children suffered from both

conditions. Mean annual frequency increased significantly from 1.4 cases/year

during 2000-2004 to 4.8 cases/year during 2005-2009 (p= 0.006). Median age

was 3 years (range 1-10). A total of 18 (58%) children had received preadmission

oral antibiotics (beta-lactamics in 84%). Clinical findings at presentation were: fever (93%), cervical lymphadenopathy (93%), neck pain (90%), torticollis (74%), odinophagia (64%), trismus (32%), drooling (22%) and stridor (6%). Thirteen (42%) children underwent surgical intervention, of those microbiological culture was positive in 8 children; *S.pyogenes* being the most commonly isolated organism (n=4). All the patients received parenteral antibiotic therapy. There were no significant differences in the length of hospital stay, complication or recurrence rates between children treated conservatively compared to those undergoing surgical intervention.

Conclusion: Retro- and parapharyngeal abscesses were increasingly observed

during the second part of study period. The majority of children (58%) were treated conservatively with excellent clinical response. Indication for surgical

intervention should be made based on the clinical presentation and response to

antibiotic therapy.

P636

HOSPITALIZED CHILDHOOD COMMUNITY ACQUIRED PNEUMONIA (CAP) IN BELGIUM: PNEUMOCOCCAL ETIOLOGY AND SEROTYPE DISTRIBUTION BASED ON CULTURE AND SEROTYPE SPECIFIC SEROLOGY

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Aim: To evaluate pneumococcal etiology and serotype (ST) distribution in hospitalized children with community acquired pneumonia (CAP).

Methods: Children < 15y with X-ray confirmed CAP were included. Pneumococcal etiology was evaluated by culture with serotyping on blood (BC) and pleural fluid (PF) samples, and by IgA&IgG serotype specific serology (SSS) against the serotypes 1, 5, 6B, 7, 9N+V, 14, 19A, 19F, 23F. Seroconversion criteria: >3-fold rise in Ab-concentrations for IgG or ≥2-fold rise for IgA, with an Ab-concentration ≥600 pg in the convalescent sample. In case seroconversion criteria were met for ≥2 serotypes, the serotype with the highest Ab-concentration was retained.

Results: 561 eligible patients were included, median age: 3.6 years. 80% had lobar pneumonia, though 18% with pleural effusion. PF-culture was positive in 12/49 cases (24%), with S. pneumoniae isolated in 7.

From BC S. pneumoniae was isolated in 45 of 538 cases (8.4%). ST 1 was most prevalent and was identified in 53% of cases. ST 5, ST 3 and ST 19A were identified in 21%, 8%, and 8% respectively.

In 86 of 149 (58%) culture-negative cases, seroconversion was detected. IgA&IgG-SSS identified serotypes 1, 7, 19A and 5 as most prevalent.

None of the identified serotypes are included in the PCV7 currently used in Belgium.

Conclusions: The use of SSS may substantially increase the diagnostic yield in childhood-CAP. However, SSS results must be interpreted with caution as SSS-criteria need further validation

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RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION REQUIRING HOSPITALIZATION IN LATE PRETERM INFANTS

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Background and aims: RSV infections are a common cause of hospitalization in the first two years of life. Preterm infants are at higher risk for severe disease. Palivizumab prophylaxis is given routinely in our hospital in infants < 29 WGA and < 12 months and 29-32 WGA and < 6 months.
Methods: Retrospective review of patients ≤24 months, hospitalized for community-acquired RSV infection in the last 5 seasons. Diagnosis was made by antigen detection in nasopharyngeal aspirates. The outcomes measured were hospital stay and PICU admission.
Results: We included 1057 episodes. Median postnatal age was 3 months (range 0.2-24) and mean hospital stay 7.6±5.7 days. By gestational age, differences in patient age, hospital stay and PICU admission were were observed (Table). PICU admission was required in 177 (16.7%) patients, mainly infants < 3 months (20.8% vs. 12.8% in > 3 months, p< 0.01). Mean hospital stay was significantly longer in patients who had required intensive care (11.97 vs. 6.71 days, p< 0.01).

Gestational age (weeks)	<29	29^0-32^0	32^1-35^0	35^1-36^6	≥37	p
Number of patients (%)	34 (3.2)	27 (2.6)	78 (7.4)	80 (7.6)	838 (79.3)	-
Mean age (months)	10.66	7.93	6.16	4.39	5.04	<0.01
Mean hospital stay (days)	9.76	8.00	10.77	8.80	7.08	<0.01
PICU admission (%)	5 (14.7)	6 (22.2)	16 (20.5)	24 (30)	126 (15)	0.01
PICU admission in patients without comorbidities (%)	3 (11.1)	5 (20.8)	13 (20.6)	22 (28.9)	110 (14.3)	<0.05

[Outcome of patients according to gestational age]

Conclusions: RSV associated morbidity is higher in infants under 3 months and born prematurely. Late preterm infants (>32 WGA) have a significant incidence of severe infections.

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RESULTS OF A NATIONAL STUDY FOR THE TREATMENT OPTIONS AND COST OF ACUTE OTITIS MEDIA (TR-AOM STUDY PART II)

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Aims: Acute otitis media(AOM) is one of the most frequent diagnosis in children and also most common reason for prescribing antibiotics. The aims of this prospective study were to evaluate treatment options and to estimate potential cost of AOM in Turkey.

Methods: This is a web-based cross-sectional survey of a national convenient sample (633 pediatricians, family physicians, ENT) about antibiotic therapy or watch-see protocol, antibiotic choice and duration, decongestant and analgesic uses.

Results: 77.5% of pediatricians, 71.5% of FP&GPs, 83.6% of ENTs have indicated they are using direct antibiotic therapy when they diagnose AOM. 31.1% of participants describes “viruses” for the main cause of AOM, besides 62.1% still continue to use antibiotics. 55-60.7% of participants prefer to add paracetamol and 5-8.6% (especially from watch and see group) prefer to use combined antipyretics. 63-78% of all participants have been prefer to use oral decongestants(3-5 days). First line choice of antibiotics is amoxicillin-clavulanate and second was cefdinir. If there is unresponsiveness to first drug, all specialties prefer to use a parenteral 3rd generation cephalosporin. Calculated mean cost per case of AOM was 28±4$(14.5-118$). In our country estimated incidence of AOM was 24.000-33.000 cases per 100.000 children under 5 years (1.820.000-2.100.000cases/per year). Estimated total cost of AOM is 61,152,000$ (not including complications).

Conclusion: Regarding to our results, total cost of AOM is very high for in our country and guidelines for antibiotic policy need to be revised. Vaccine seems to be hope for the prevention of AOM and further studies about the effectiveness of new vaccines needed.

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PREMORBID LUNG FUNCTION AND RHINOVIRUS-ASSOCIATED WHEEZE IN PREMATURELY BORN INFANTS

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Background and aim: Increased resistance of the respiratory system in the neonatal period may predispose term born infants to rhinovirus (RV) associated wheeze. The aim of this study was to determine whether prematurely born infants were predisposed to RV-associated wheeze by abnormal premorbid lung function.

Methods: One hundred and fifty three infants born at a median gestational age of 34 (range 23-35) weeks had their lung function (functional residual capacity and compliance [Crs] and resistance [Rrs] of the respiratory system) measured at 36 weeks postmenstrual age. The infants were then prospectively followed from neonatal/maternity unit discharge until they were one year corrected age. Nasopharyngeal aspirates (NPAs) were obtained whenever the infants had a lower respiratory tract infection (LRTI), regardless of whether this was in the community or in hospital. NPAs were tested for rhinovirus, RSV A and B, influenza A and B, parainfluenza 1, 2 and 3 and human metapneumovirus by real time reverse transcriptase polymerase chain reaction and adenovirus by real time polymerase chain reaction.

Results: Thirty two infants developed RV LRTIs, 21 of whom had wheeze; 74 infants did not develop a LRTI. Infants who wheezed with the RV LRTI compared to those who did not develop a LRTI had a higher median Rrs (77 versus 69 $cmH_20/L/s$) ($p=0.026$) and lower Crs (1.2 versus 1.6 $ml/cmH_20/kg$) ($p=0.012$); there were no significant differences between the groups in the FRC results.

Conclusion: Prematurely born infants who have RV-associated wheeze in infancy do have reduced premorbid lung function.

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RESPIRATORY SYNCYTIAL AND INFLUENZA VIRUS ASSOCIATED HOSPITALIZATIONS IN INFANTS AGED BELOW 12 MONTHS

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Background and aims: Acute respiratory illnesses cause significant morbidity in infants. Aim of this study was to compare the severity of Respiratory Syncytial virus (RSV) to Influenza virus associated respiratory tract infections requiring hospitalization and to analyse white blood cell counts during the course of disease.

Methods: The retrospective cohort study included all infants aged below 12 months, who were hospitalized due to either proven RSV or Influenza virus infection at the Department of Pediatrics of the Medical University of Graz. Study period was from October 2005 to May 2009 and was extended for Influenza virus cases due to a generally low number.

Results: Of 318 infants included, 275 (86 %) were tested RSV positive, 37 showed an Influenza virus infection (12 %) and 6 infants were positive for both viruses. Infants with RSV associated hospitalizations were of significantly younger age and showed a longer length of stay. Severity of respiratory tract infection measured by LRI-score also differed significantly among the two viruses with RSV being more severe (mean 2,9 vs. 1,6; $p < 0,001$). Concerning laboratory data lymphocytes and eosinophil counts were higher, while neutrophils and monocyte counts were lower in RSV compared to Influenza infection.

Conclusion: Infants with RSV infection were of significantly younger age and exhibited a more severe course of disease compared to infants with Influenza virus infection. CRP values showed an increase and decrease during the course of disease of both viruses, and lymphocyte and eosinophil counts were higher in infants with RSV infection.

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LIMITED IMPACT OF THE 7-VALENT PNEUMOCOCCAL VACCINE ON PAEDIATRIC EMPYEMA IN THE NORTH OF ENGLAND

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Background: The incidence of paediatric empyema has increased substantially in the UK since 1995. Paediatric empyema in the UK is predominantly a pneumococcal disease and a 7-valent pneumococcal conjugate vaccine (PCV-7) was introduced into the UK routine immunisation schedule in September 2006. A recent report has suggested a significant reduction on the incidence of empyema following introduction of the vaccine[1]. The objective of this study was to investigate the impact of the pneumococcal conjugate vaccination programme on the incidence of paediatric empyema in our region.

Methods: An interrupted time-series analysis was performed using clinical data from empyema admissions for children aged up to 14 years in Northern England from May 1995 to April 2010. Seasonality was accounted for by including monthly temperature measurements within the regression models.

Results: A total of 298 patients were included in the study. The incidence of empyema increased from a mean monthly rate of 1.1 cases per million children in 1996 to 5.2 per million in 2009. No significant impact was observed on the number of cases following the introduction of the PCV-7 vaccine (regression co-efficient 0.096, 95 % CI -0.038 - 0.23, p = 0.16).

Conclusions: The PCV-7 vaccine had no impact on the incidence of paediatric empyema in Northern England. These findings do not confirm a recent report of a decline in the incidence of paediatric empyema following the introduction of this vaccine.

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IMPACT OF THE 13-VALENT PNEUMOCOCCAL VACCINE ON THE INCIDENCE OF PAEDIATRIC EMPYEMA IN THE NORTH OF ENGLAND

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Background: The incidence of paediatric empyema has increased substantially in the UK since 1995. Paediatric empyema in the UK is predominantly a pneumococcal disease and a 13-valent pneumococcal conjugate vaccine (PCV-13) replaced the seven-valent vaccine in the UK routine immunisation schedule in April 2010. The 13 valent vaccine includes antigen for serotype 1, which has been the commonest cause of paediatric empyema in the UK. The objective of this study was to investigate the impact of the introduction of PCV-13 on the incidence of paediatric empyema.

Methods: A preliminary interrupted time-series analysis was performed using clinical data from empyema admissions for children aged up to 14 years in Northern England from May 1995 to November 2010. Seasonality was accounted for by including monthly temperature measurements within the regression models. Terms for the seven-valent vaccine were also included.

Results: A total of 313 patients were included in the study. The incidence of empyema increased from a mean monthly rate of 1.1 cases per million children in 1996 to 5.2 per million in 2009 and fell in 2010 to 3.2 per million. Introduction of the PCV-13 vaccine was associated with a significant reduction in the number of monthly cases of paediatric empyema (regression co-efficient -0.26, 95% CI -0.42 ─ -0.10, p=0.002).

Conclusions: We have documented a recent reduction in the incidence of paediatric empyema in the North of England, but it would be premature to conclude a causal relationship with introduction of the PCV-13 vaccine.

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PROCALCITONIN (PCT) MEASUREMENT FOR GUIDING DECISIONS ON ANTIBIOTIC TREATMENT OF PEDIATRIC COMMUNITY ACQUIRED PNEUMONIA OF CHILDREN

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Background and aims: In adults with lower respiratory tract infections, PCT guided therapy has been demonstrated a useful mean to reduce antibiotic prescriptions with a clinical outcome not inferior to standard therapy. This study was planned to evaluate the possible use of an algorithm based on a PCT cut-off value to guide the management of CAP cases in children.

Methods: In this prospective, single center, two-year, randomized study, 319 otherwise healthy children hospitalized for moderate to severe CAP were randomized to receive antibiotics based on a PCT algorithm (PCT group; n=160) or according to national guidelines (control group; n=159). Children in PCT group did not receive antibiotics if their PCT level at admission was ≤0.25 ng/mL and those receiving antibiotics were treated until PCT level reached values < 0.25 ng/mL.

Results: Antibiotic prescription rate (85.8% vs 100%; $p< 0.05$) and antibiotic exposure (mean days ± SD, 5.37 ± 5.16 vs 10.96 ± 3.49; $p< 0.0001$) were significantly lower in PCT group than in control group. No significant difference in duration of symptoms and clinical outcome was observed between the groups. Incidence of probably antibiotic-related adverse events was registered significantly less frequently among PCT group than in control group (3.9% vs 25.2%; $p< 0.001$).

Conclusions: In children hospitalized for moderate to severe CAP the algorithm based on PCT level of 0.25 ng/mL was non inferior to evidence-based guidelines for pediatric CAP therapy in terms of clinical outcome and was more effective in reducing antibiotic exposure and associated adverse events.

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HOW RHINOVIRUS AFFECTS PEDIATRIC PATIENTS IN A INTENSIVE CARE UNIT?

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Background: Rhinovirus is a major cause of banal cold in general population, although some cases may conduce to respiratory failure and intensive care admission.

Aims: To describe Rhinovirus clinical manifestations and outcome in a Pediatric Intensive Care Unit (PICU).

Methods: Prospective, observational study of patients lower than 18 years admitted at PICU during 2010. Diagnosis was made by a Real-Time PCR technique (RealAccurate Respiratory RT PCR kit, Pathofinder, laboratories, Netherlands).

Results: There were recruited 63 cases (male 71,4%), mean age was 11,3 months (DS ± 3,4). Forty-two were diagnosed between October-December. Mean Pediatric Risk Mortality was 4(DS ± 3,4). All patients presented respiratory failure with bronchoespasm in 44 (69,8%), and 35 (55,5%) had fever. Viral coinfection was found in 13(20,6%). X- Ray showed atelectasy image in 36 cases (57,2%).Fifty-one (81%) required respiratory support: 48(94%) non invasive ventilation, 25(49%) conventional ventilation and High frequency oscillatory ventilation 7(13,7%). Duration of respiratory support was 63,7(DS ± 46), 159(DS ± 95,9) and 84(DS ± 57) hours, respectively. A FiO_2 requirement > 0.5 was needed in 29 cases (46%) and corticotherapy was used in 41 (65%). Eight patients presented acute respiratory distress syndrome (ARDS) (12,6%). Mean PICU length of stay was 9(DS ± 8,5days). There wasn't any exitus.

Conclusions: Rhinovirus may contribute to severe respiratory failure. It seems to follow a homogeneous pattern: high incidence in autumn months, predilection for younger children, clinical data of severe bronchoespasm and hypoxemia, and possible progress to SDRA. Corticotherapy seems to be recommended for its treatment.

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HOSPITAL STAY DUE TO PNEUMONIA AND ASSOCIATED FACTORS

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Aim: To examine the significance of simple clinical and laboratory data in predicting hospital stay due to pneumonia.

Material and method: A longitudinal study carried out. Eligible subjects were children less than 10 years old. The diagnosis of pneumonia was based on clinical and radiological features. The following fields were analyzed: gender, age, fever, toxic appearance, radiological image at admission, duration of hospital stay, presence of pneumococcal antigen in urine (PnAg) and IgM antibodies for Mycoplasma. Hospital stay was categorized in two variables, short (< =5 days) and long (>5 days). The predictive variables for the score were selected initially using invariable logistic regression model. At the end a multivariable logistic regression model was performed as to reveal the independent variables.

Results: We recorded 184 cases of pneumonia (94 females and 92 males) within three years. 64 cases stayed in hospital for less than 5 days and 122 cases for over for 5 days. In invariable analysis statistical significant factors associated with long hospital stay were the radiological image at admission (p=0.003) and the presence of urine PnAg (p=0.02). In multivariable analysis radiological image and the presence of urine PnAg retained their significance (p=0.004 and p=0.034 respectively).

Conclusion: Evidence from our study supports that the radiological image at admission and the evidence of pneumococceal infection, through the presence of urine PnAg, were revealed as independent factors for longer hospital stay. Moreover, based on our model, the radiological image was still significant indifferently from the evidence of cause of pneumonia.

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BORDETELLA PERTUSSIS HOSPITALIZATIONS IN CHILDREN

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Background: In populations with high rates of vaccination against *Bordetella pertussis* an increase of whooping cough (WC) in infants has been noticed.

Aims: To assess the burden of hospitalizations due to *B. pertussis* in a tertiary teaching Hospital in Madrid during 2006-2010. Clinical course in hospitalized children was also evaluated.

Methods: Retrospective review of the clinical records. *Bordetella pertussis* infection was diagnosed by a real-time PCR assay. Demographic, clinical data and complications were collected and analyzed.

Results: Ninety nine patients were identified. Median age was 3 months (range 9 days-17.6 years) and 66% of them were < 1 year. Fifty six percent of children were hospitalized (mean age 2.5±3.5 months). More than a half (51.4%) of admitted children were < 1 year. The average stay in hospital was 8.4± 6.2 days.

Eleven children (9.1%) required admission to PICU (mean of age 3.1±5.8 months) because of: acute respiratory failure, 4 cases; apnea and/or hypoxemia, 4 cases; toxic appearance, 1 case; pulmonary hemorrhage and shock, 1 case; age, 1 case. Four patients died, because of pulmonary hypertension and respiratory failure. Five (72%) of patients admitted to PICU had prominent leukocytosis (mean 42533 ± 13616 leukocytes/mm^3). WBC count in hospitalized children was 23289 ± 22989 leukocytes/mm^3.

Conclusions: WC is still a relevant cause of hospitalizations and morbimortality in infants. Implementation of new vaccinations policies is necessary to avoid these infections.

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BACTERIAL AETIOLOGY OF RECURRENT, TREATMENT-FAILURE AND UNRESOLVED ACUTE OTITIS MEDIA (AOM) IN SPANISH CHILDREN AS CHARACTERISED BY CULTURE AND PCR

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Background and aims: *Streptococcus pneumoniae* (Spn) and *Haemophilus influenzae* (Hi) cause a high childhood AOM burden. Traditionally, middle ear fluid (MEF) is cultured to identify bacterial pathogens, but PCR may increase sensitivity. This Spanish study characterised bacterial AOM pathogens using culture and PCR.

Methods: Children aged ≥3-< 36 months visiting paediatricians for recurrent or unresolved AOM or treatment-failure were enrolled between June 2008 and March 2010. MEF samples were collected by tympanocentesis or sampling spontaneous otorrhoea and cultured to determine bacterial aetiology; culture-negative samples were further analysed for Spn and Hi using PCR.

Results: 105 children were included; 79 unilateral and 26 bilateral infections yielded 131 samples. 46 children had recurrent AOM, 35 treatment-failures and 24 unresolved AOM. 72% of children had received ≥1 dose of pneumococcal conjugate vaccine. Bacteria were cultured from 92/131 (70%) samples, most commonly Hi (54 samples) and Spn (25 samples), including 1 Spn+Hi sample, 1 Spn+Hi+*M. catarrhalis* and 1 Hi+*M. catarrhalis*. All Hi samples were non-typeable (NTHi). No association was detected between bacterial pathogen and case-type. Aetiology did not appear to differ by sampling method. PCR on culture-negative samples additionally identified 20 Hi and 20 Spn, which included 12 Spn+Hi co-infections. Combining culture and PCR results, Hi and Spn may be implicated in 70% and 43% of clinically problematic bacterial AOM episodes, respectively.

Conclusions: NTHi was the predominant bacterial pathogen in recurrent, treatment-failure and unresolved AOM. Culture and PCR combined could detect more Spn/Hi samples, including more Spn+Hi co-infections, confirming the high sensitivity of PCR.

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ETIOLOGICAL STRUCTURE OF CHILDREN' ACUTE VIRUS RESPIRATORY INFECTION

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Background: Acute respiratory infection (ARI) is the most common cause of children's hospitalization in Minsk, and viral etiologies play an important role. In hospitals the most common investigational method for suspected viral ARIs is immunofluorescence (IF) test of nasal swabs (NS) specimens. However, sensitivity and specificity of this method are from 10 to 30% which is not so high.

Methods: Samples of nasal swabs (NS) from 298 children hospitalized at Children Infection Diseases Hospital were studied for the detection of influenza virus A and B, parainfluenza 1-4 types, respiratory syncytial (RSV), adenovirus, rhinovirus, human coronavirus (HCoV), bocavirus (HBoV), metapneumovirus (HMPV) by multiplex PCR assay. Nasal swabs were taken in first day at the hospital.

Results: One or more respiratory viruses were detected in 180 of 298 (61%) cases. Monoinfection was diagnosed in 91, 1% cases and at 16 (8, 9%) patients were proved mixinfection. The most often etiological agents of ARVI were Rhinovirus (25, 5%), Parainfluenza virus 1-4 types (23, 9%) and RSV (20%). Influenza virus was detected in 6, 7%, adenovirus - 7, 2%, HCoV - 0, 6%, HBOV - 6, 1%, HMPV - 1, 1%. Among mixinfection were HBoV+Rhino (8 cases), HboV+HMPV (2), HBoV+Adeno (1), HBoV+Parainfluenza (2), Parainfluenza+RSV (1), Influenza A (H1N1)+RSV (1), Parainfluenza 2+3 types (1).

Conclusions: During this study it was determined that noninfluenza viruses (Rhinovirus, Parainfluenza virus, RSV) are the main etiological agents of ARVI in hospitalized children. This investigation allowed to recognize the role of HBoV and HMPV in structure of ARVI in Belarus.

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RELATIVE BURDEN OF RESPIRATORY SYNCYTIAL VIRUS ASSOCIATED COMMUNITY-ACQUIRED PNEUMONIA (RSV-CAAP) IN CHILDREN BORN 30-35 WEEKS GESTATIONAL AGE

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Background: Respiratory syncytial virus (RSV) is frequently associated with community-acquired alveolar pneumonia (CAAP). In Israel, RSV-monoclonal immunoglobulin (RSV-Ig) is reimbursed for infants born < 30 weeks of gestational age (GA). This prospective study compared hospitalization and pediatric intensive care unit (PICU) admission for RSV-CAAP in children born at 30-35w GA (30-35wGA) vs. those born at term (≥36wGA).

Methods: Nasopharyngeal wash specimens obtained prospectively over a 9-year period (2001-2010) from children < 5 years old hospitalized with radiologically-diagnosed CAAP, were tested for RSV (RT-PCR or immunofluorescence and culture). Soroka is the only hospital in southern Israel, providing services to all children of the region. During the study period, 130,164 and 2,859 ≥36wGA and 30-35wGA births occurred respectively (data provided by the Dept. of Neonatology). Relative risks (RR) and 95% CI were calculated comparing incidence in patients 30-35wGA vs. those ≥36wGA.

Results: CAAP hospitalization incidence (per 1000) were 26.3 and 136.1 in ≥36wGA and 30-35wGA, respectively (RR: 5.2; 95% CI 4.7-5.7). The respective PICU admission rates were 0.7 and 10.7 (RR: 16.1; 10.6-24.3). Relative risk and 95% CI specific for RSV-CAAP hospitalizations and PICU admission rates were RR: 6.6; 5.2-8.3 and RR: 32.1; 14.9-69.0. The observed high risk for 30-35wGA children was still present when each ethnic group was analyzed separately.

Conclusions: Children < 5y born 30-35wGA are at a markedly increased risk for hospitalization and PICU admission compared to those born ≥36wGA. The risk may be reduced by extending RSV-Ig reimbursement to this population.

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NEBULIZED 3% HYPERTONIC SALINE AND NORMAL SALINE IN THE TREATMENT OF CHILDREN WITH ACUTE VIRAL BRONCHIOLITIS: IS THERE ANY DIFFERENCE?

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Background and aims: Viral bronchiolitis is an extremely common disease in children less than 2 years of age. We determined the efficacy of nebulized 3% hypertonic saline solution in the treatment of children hospitalized with mild to moderate viral bronchiolitis in the emergency department (ED) and in children who admitted in pediatric ward.

Methods: In a randomized controlled trial, 60 children aged 2-24 months with mild to moderate bronchiolitis received inhalation of 0.15mg/kg salbutamol dissolved in either 3cc of 0.9% normal saline (control group, n=30), or 3cc of 3% hypertonic saline (treatment group, n=30). Three doses of each drug were given at 20 minute intervals. Respiratory rate, RDAI score and clinical score were evaluated before initiation of treatment protocol and 10 minutes after administration of the last dose to assess the response to therapy. In hospitalized patients this therapy was repeated 3 times every hospitalization day until discharge.

Results: In ED, both treatments caused significant improvement in mean symptoms score and oxygenation. There were no significant difference between two groups regarding discharge rate from ED after 4 hours (40% vs 36.7%), admission rates (60% vs 63.31%), the time of remission of cough, wheezing and pulmonary physical signs (P value>0.05). Mean length of hospital stay was 3.88±1.77 and 4.63±1.97 in treatment group and control group, respectively (P value>0.05).

Conclusions: There was no difference between nebulized hypertonic saline and normal saline in the treatment of children with acute bronchiolitis in the ED and in hospitalized children with bronchiolitis.

P652

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

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Background and aims: Influenza and respiratory syncytial viruses (RSV) are two important players in the etiology of children's respiratory infections. It is generally assumed that the clinical features of these viral infections are largely different. We compared the clinical presentation and the course of illness in young children with influenza A or RSV infection.

Methods: This study was conducted as part of a randomized controlled trial of oseltamivir treatment of influenza in children aged 1-3 years. The children were routinely examined within 24 hours of symptom onset and during a follow-up visit 5-8 days later. During each visit, nasal swabs were obtained for virological analyses. Detailed data on the symptoms of the children were derived from daily symptom diaries filled out by the parents.

Results: This analysis consisted of 50 children with influenza A and 46 children with RSV infection. At presentation, cough was more frequent in children with RSV (96% vs. 74%; p=0.008). During the follow-up, acute otitis media developed more frequently in RSV-infected children (65% vs. 30%; p=0.001). The duration of rhinitis was longer in children with influenza A (13.3 vs. 11.3 days, p=0.046). No differences were observed in the prevalence or duration of any other symptoms, the use of relief medications, or absenteeism between the groups.

Conclusions: Acute otitis media develops significantly more frequently in young children with RSV than in those with influenza A infection. Otherwise, the clinical features of these viral illnesses are quite comparable in this age group.

P653

EFFECT OF INHALED HYPERTONIC SALINE SOLUTION TO TREAT INFANTS HOSPITALIZED WITH VIRAL BRONCHIOLITIS

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Background and aims: At present there is only symptomatic treatment available for acute viral bronchiolitis. However none of these treatments are evidence-based. Recent trials show a reduction in hospital stay after inhalation of 3% hypertonic saline solution.This randomised double-blind, placebo-controlled, interventional multicenter trial, performed at 12 peripheral and academic Dutch hospitals, compares nebulization with hypertonic saline, either a 3% or 6%, with 0.9% isotonic saline.The primary end point is the time to discharge, aiming to achieve a 25% reduction in hospital stay.

Methods: Children younger than two years with clinical diagnosis of viral bronchiolitis, not responding to a single inhalation with Salbutamol 2.5 mg may be included after obtaining informed parental consent. Trial medication will be nebulized three times daily until discharge criteria are met.

Results: The analysis was performed on the data of 119 patients, all included in the season 2009-2010. Patient characteristics and the number of exclusions didn't differ significantly. The duration of hospital stay, need for tube feeding and supplemental oxygen shows no significant difference, but there is a trend that 3% seems to be more effective than the other two concentrations.

Conclusions: Preliminary analysis showed no significant reduction in hospital stay but a trend that 3% hypertonic saline is the most effective regarding reduction in duration of hospital stay, need for supplemental oxygen and tube feeding. The use of 6% hypertonic saline solution seems to be safe but has no additional benefit even compared with 0.9%. More research will be necessary to clear up this trend.

On behalf on the Trial Research Group: A.A.P.Vaessen-Verberne, J.Wesseling, A.L.M.Boehmer, R.vanGent, H.J.L.Brackel, C.C.J.M.Smeets, R.deMoor, P.P.Rosias, R.P.Droog, S.Potgieter, M.D.Ottink, J.J.E.Hendriks, D.Logtens-Stevens

P654

HIGH CONCENTRATIONS OF AMNIOTIC FLUID PRO-INFLAMMATORY CYTOKINES IN HEALTHY NEONATES ARE ASSOCIATED WITH LOW RISK OF RSV BRONCHIOLITIS

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Background and aims: The burden of respiratory syncytial virus (RSV) bronchiolitis in individual children and their families, the medical system, and society is considerable. Mechanisms underlying RSV bronchiolitis in healthy term infants are largely unknown. We aimed to determine whether high amniotic fluid interleukin-8 (IL-8) and tumor necrosis factor-α (TNF-α) protect against RSV bronchiolitis in healthy term infants.

Methods: Prospective birth cohort study of healthy term newborns, born after uncomplicated pregnancy of ≥37 weeks. Of 882 eligible newborns, 292 (33%) were enrolled. Amniotic fluid was collected during labour. In case of medical attention for respiratory symptoms during the first year of life, a nose-throat swab was taken to establish the presence of respiratory viruses by PCR.

Results: Physician-attended RSV infection was observed in 27 (9.3%) of 292 children at median age 6 months. Amniotic fluid concentrations of IL-8 were higher in children without physician-attended RSV infection than in children with physician-attended RSV infection (11.1 vs 5.5 ng/mL, *P*=.002). Similarly, in children without physician-attended RSV the proportion of detectable amniotic fluid TNF-α was higher (159/265 (60%) vs 8/27 (30%), *P*=.002). Among children with physician-attended RSV infection, amniotic fluid IL-8 was inversely correlated to the number of wheezing days during the first year of life (ρ=-0.38, *P*=.048).

Conclusions: High concentrations of amniotic fluid IL-8 and TNF-α are associated with low risk of RSV bronchiolitis in healthy infants. We hypothesize that direct exposure of fetal lungs to pro-inflammatory signals induces local protection against viral infection during infancy.

P655

ACTINOMYCOSIS, A CAUSE OF RECURRENT AND CHRONIC AIRWAY INFECTIONS IN CHILDREN

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Background: The anaerobe microbe Actinomyces, though part of the normal oral and GI-flora, can cause serious airway infections. We present 4 cases of pulmonary actinomycosis.

Methods: Review of cases.

Results: 4 boys; aged 8m, 1y, 5y and 8.5y, with persistent respiratory symptoms are presented. The 8m-old boy presented with persistent wheezing over the left lung since 2m due to an obstructive granuloma in the left main stem bronchus. The 2nd had recurrent pneumonia and atelectasis in the left lower lobe (LLL) with signs of acute and chronic infection on chest CT-scan. The 3rd had chronic atelectasis of the LLL following inhalation of a corpus alienum. The latter had chronic cough with spontaneous expectoration of white amorphous material, and a tracheal bronchus was found on bronchoscopy. In all cases, bronchoscopy revealed viscous white mucus in the affected area. Actinomyces was cultured from broncho-alveolar lavage (twice A. odontolyticus; once A. meyeri and once A. gerensceriae). In the youngest patient co-infection with M. avium-intracellulare was demonstrated.3/4 patients were successfully treated with penicillin for 6 months. The patient with proven co-infection was treated with a combination of rifampicin and clarithromycin during 9 months. 2 patients recovered completely. The second and third patient recovered clinically with radiological sequellae (bronchiectasis).

Discussion and conclusion: Actinomyces should be considered in recurrent or chronic pulmonary infections in children, especially in the presence of possible predisposing factors such as anatomical airway anomalies, chronic corpus alienum or localized mucosal tissue damage.The treatment of choice is long term penicillin.

P656

INDETIFICATION OF RELATION BETWEEN RSV INFECTION, NEOPTERINE LEVEL AND WHEEZING

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The target of our research was the evaluation of the role of the marker of macrophage activation - neopterine in children with recurrent wheezing developed during onset of RSV infection. In the study 52 children of age from 1 to 12 months having RS-virus infection were included. Two groups were determined as controls - group of healthy children and children with wheezing of non RSV etiology. Determination of neopterine was performed by enzyme immunoassay method (ELISA). During the RS-virus induced acute respiratory infection the rate of neopterine in the blood serum was significantly decreased in the group of patients with recurrent wheezing in comparison with the I group (first episode of wheezing). At the same time the significant difference between the group with wheezing of non - RSV etiology and the control group was not observed. Decreasing of neopterin was significant in the II and III groups.

P657

INCIDENCE AND MANAGEMENT OF ACUTE RESPIRATORY TRACT INFECTIONS IN PRESCHOOL POPULATION OF GEORGIA

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Aim and methods: To assess the frequency of ARI in preschool children population, identification of risk factors and main principles of treatment. The cross sectional study was conducted using the special questionnaires for parents of 3-6 years children and in all regions of Georgia. At all 1448 parents and caregivers were interviewed.

Results: 2,3 % of children have 7-8 episodes of ARI per year, 19,9 % have 3-5, 53,4 % 1-2 episodes per year and in 24,2% ARI are very rare. The incidence of ARI is higher in urban population, then in rural area and in mountain regions (p< 0, 001). The main symptoms for admission to health care facilities were cough (82, 8 %) and fever (75, 9%). Study revealed the risk factors for ARI: male sex, living in urban area, attendance of day care centers, exposure to passive smocking, big number of family members significantly increase risk of ARI. There was no correlation between the type of feeding in infancy and frequency of ARI infection in 3-6 years old children. In 47 % of ARI cases antibiotics were used from those in 32 # parents started antibiotics by self.

Conclusion: Male sexes, urban regions, attendance of day care center, passive smoking are the significant risk factors for development of ARI in children aged 3-6 years. Primary health care providers still prescribe unnecessary and excessive antibiotics. The incidence of ARI may be reduced substantially through public health measures.

P658

PRESCHOOL ASTHMA AFTER BRONCHIOLITIS IN INFANCY

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Background: The outcome after bronchiolitis depends on disease definition, age of included patients and presence of risk factors.

Objective: To evaluate the outcome at preschool age in children, who were hospitalized for bronchiolitis in early infancy, with special focus on the role of early-life risk factors.

Subjects and methods: Out of 205 infants hospitalized for bronchiolitis at < 6 months of age, 127 (62%) attended the study visit at the mean age of 6.5 years, and the parents of additional 39 children were interviewed by phone. Thus, follow-up data collected by identical structured questionnaires with a focus on parent-reported cough and wheezing episodes and doctor-diagnosed asthma were available from 166 (81%) children. Data on viral etiology of bronchiolitis, studied on admission by antigen detection or polymerase chain reaction, were available in all cases.

Results: Current asthma was present in 21 (12.7%) children. The figure was 8.2% in the 110 former RSV bronchiolitis patients vs. 27.3% in the former non-RSV patients (p=0.015). The number of children with asthma ever in life, defined by the use of inhaled corticosteroids, was 45 (27%). The presence of atopic dermatitis in infancy, the history of asthma in mothers and the development of allergic rhinitis were significant risk factors for asthma. Atopic dermatitis, non-RSV bronchiolitis and asthma in mothers were independently significant early-life risk factor in adjusted analyses.

Conclusion: The risk of asthma after hospitalization for RSV bronchiolitis at < 6 months of age does not substantially differ from asthma risk in non-selected child population.

P659

SURVEILLANCE OF VIRAL RESPIRATORY INFECTIONS IN THE EMERGENCY DEPARTMENT USING MICROARRAYS

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Introduction: Impact of viral coinfections and recently discovered viruses on epidemiology of respiratory infections (RI) is still unclear.

Aim: To study the viruses that are involved in the etiology of RI we used microarrays that allow simultaneous detection of many viruses.

Methods: Rhinopharyngeal washes were taken from children (1 month-14 years) who presented in the emergency department from 1/2009 - 12/2010 with RI and treated as outpatients. Laboratory investigation was done for 17 viruses using a microarray platform.

Results: Out of 200 children, upper (URI) and lower (LRI) respiratory infections were diagnosed in 104 and 96 respectively. Viral coinfections were found in 20% of children. The most frequent combinations in URI were the PIV3 -Rhinovirus(9%), PIV- RSV(3%) and in LRI RSV-INFL(8%) and RSVA-RSVB(5%). PIV in URI and RSV in LRI were the prevalent viruses found in coinfections. The most common causes of single infection in URI were PIV3(22.7%), HRSVB(9%), Rhinovirus(9%), Enterovirus(7.5%), Infl(3%), Bocavirus(3%), Adenovirus(3%), HMPV(1.5%) and in children with LRI were RSVB(14.5%), Rhinovirus(11.2%), PIV3(11.2%), PIV4(11.2%), Influenza(8%), HRSVA(5%) and HMPV(3.2%). Respiratory distress was associated with Rhinovirus infection (P = 0.006), while no statistically significant relationship with severity was observed regarding viral coinfections (P = 0.667).

Conclusions: Viral coinfections and recently discovered viruses are involved in significant percentage of outpatient RI. Nevertheless, they are not associated with more serious clinical presentation as happens with rhinovirus infection that is related with respiratory distress. Viral microarrays method can probably help to reduce unnecessary hospitalizations and use of antibiotics in outpatient settings.

P660

EFFECTIVENESS OF HYPERTONIC SALINE SOLUTION IN MANAGEMENT OF ACUTE BRONCHIOLITIS IN INFANTS

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Background and aims: Acute bronchiolitis is a leading cause of hospitalization of young children. It is associated with bacterial colonization in 40-50% of cases. Repeated episodes of bronchiolitis with wheezing may be considered as risk factor for asthma.

The treatment of acute bronchiolitis with routine use of bronchodilatators and corticosteroids is a controversial issue. Recent trials have revealed effectiveness of nebulized hypertonic saline.

The purpose of the study was to assess the effectiveness of administration of hypertonic saline, corticosteroids, bronchodilatators and antibiotics in management of acute bronchiolitis.

Methods: A retrospective study of medical records was carried out with 65 infants, diagnosed with acute bronchiolitis, aged 6-12 months. The data was statistically analyzed in the program packet _SPSS 16.0. Infants were assigned into 4 groups by type of treatment:

I group: hypertonic and isotonic saline

II group: hypertonic and isotonic saline with bronchodilatators and corticosteroids

I I I group: isotonic saline with bronchodilatators and corticosteroids

IV group: isotonic saline and antibiotics

The wheezing was present in 64, 7% of cases (in 42 patients).

Results show that type of treatment plays important role in improvement of clinical condition of patients ($p < 0.001$). This result was evident on second day in the group treated by hypertonic saline.

The difference in the length of hospital stay was significant between I-IV groups ($p < 0.05$)

Conclusions: The effectiveness of nebulized hypertonic saline in acute bronchiolitis is statistically significant, in comparison with treatment by bronchodilatators, corticosteroids and antibiotics. Routine administration of the latter is not recommended.

P661

INFLUENZA A (H1N1) 2009: VIRAL LOAD CORRELATES WITH EPIDEMIOLOGYCAL CHARACTERISTICS AND COULD BE USED AS A RISK-MARKER OF SEVERITY[

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Aims: To describe the influenza A (H1N1) 2009 viral-load in admitted paediatric patients and its relation with epidemiological and clinical characteristics.

Methods: Patients admitted with (H1N1) 2009 infection (confirmed by positive RT Real-Time PCR for both matrix protein 2 (M2) and pandemic H1 genes in nasopharyngeal specimens) were prospectively included from July to November of 2009. Viral-load was determined through cycle-threshold (Ct) values of M2 gene corrected according to the Ct value of internal control (human-myostatine-gene). Poor quality samples (internal control Ct > 27), were excluded.

Results: Seventy patients were included. Viral-load was in relation with the time from onset of fever to the moment of collecting the nasal aspirate (Spearman rho=-0.4; p< 0.05) and with age (Spearman rho=0.4; p< 0.05). Children with encephalopathy and those with immunosuppressive-chemotherapy had higher viral loads. Having more than 35,000 copies/mL at any time of disease was associated with requiring for mechanical ventilation (invasive or non-invasive) with a relative risk (RR)=13.1 (95%CI:1.6-106). Patients who exceeded that viral-load after four days of symptoms had an increased risk of requiring mechanical ventilation (Fisher p< 0.02, RR=4.3 (95%CI:1.2-14.9) when comparing to those that exceeded that viral-load and were still within the first three days of symptoms.

Conclusions: (H1N1) 2009 viral-load was in relation with age, comorbidity, and the time from the onset of symptoms to the collection of the sample. Patients with high viral loads had an increased risk of needing for mechanical ventilation, especially if they had those viral-loads after four days of symptoms.

P662

BURDEN OF RSV DISEASE FOLLOWING A PALIVIZUMAB IMMUNISATION PROGRAMME. OUR LADY´S CHILDREN'S HOSPITAL, DUBLIN, 2004/05 TO 2009/10 SEASONS

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Background: Respiratory Syncytial Virus (RSV) infection occurs primarily during winter months in temperate climates, and is the leading cause of bronchiolitis and pneumonia in the paediatric population. In 2005, Palivizumab RSV prophylaxis was introduced in Our Lady´s Children´s Hospital for infants at high risk of complicated infection.

Objective: To determine the continuing burden of RSV infection in our hospital following introduction of a prevention programme.

Methods: Health care records of all RSV-positive patients were reviewed at the end of each season. Information recorded included: number of patients with documented RSV infection each month (community or hospital acquired); patient demographics; risk factors for RSV; co-morbidities; length of hospital stay; number requiring ICU admission and mechanical ventilation.

Results: Over the 6-year period, 805 RSV-positive cases were identified. Peak incidence occurred between November and January each year. 491 (61%) cases occurred in infants without known risk factors. 102 (12.6%) required ICU admission and 79 (9.8%) mechanical ventilation, respectively. 47 (5.8%) cases were hospital-acquired. 25 (3.1%) of infections occurred in infants receiving Palivizumab.

Conclusions: The time of onset, duration and severity of RSV infection varied from year to year. This study demonstrates the variance and severity of RSV seasons and informs the selection process for Palvizumab prophylaxis. Hospital acquired RSV infections highlights scope for further improvements in infection control. Despite targeting high risk groups for prophylaxis, significant morbidity associated with RSV infection occurs. The majority of morbidity occurs in previously well infants. The need for a safe, effective vaccine remains.

P663

INCIDENCE OF ACUTE OTITIS MEDIA IN EUROPEAN CHILDREN UNDER 5 YEARS: RESULTS OF A PROSPECTIVE OBSERVATIONAL COHORT STUDY

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Background and aims: Acute otitis media (AOM) is one of the most frequent paediatric infections. We previously reported high incidences of AOM with large variations across five European countries in a retrospective study.[1] This prospective, observational cohort study was conducted to generate precise incidence estimates of AOM.

Methods: 5882 healthy children ≤5 years of age were randomly selected from 73 convenient medical practices in Germany, Italy, Spain, Sweden and the UK. Of these, 5764 children were followed prospectively for 12 months and episodes of AOM leading to physicians visits were recorded. The incidence of AOM was estimated, applying uniform case definitions.

Results: 1113 children experienced 1419 AOM episodes. The overall incidence of any AOM episode was 256/1000 person-years (95% CI: 243-270) ranging from 195 (171-222) in Italy to 328 (296-364) in Spain. AOM incidence was higher in 0-2-year olds than 3-5-year olds (299 [279-319] *vs* 212 [195-230]). Except for Italy, this trend was observed across all countries, being most pronounced in Sweden (344 [298-394] *vs* 174 [141-212]). 7.1% (101) of episodes were associated with perforation of the tympanic membrane, 4 episodes were associated with other complications.

Conclusions: In agreement with our previously reported retrospective study[1], these results confirm the high incidence of AOM in European children, although this is lower than reported in Finnish and US studies (700-1200/1000 person-years). Variations between countries may indicate possible differences in diagnostic and reporting procedures, as well as primary healthcare organisation and social structure.

1. Liese. WSPID 2009, Buenos Aires, Argentina

P664

PNEUMONIA WITH PLEURAL EFFUSION: EVOLUTION OVER THE LAST 6 YEARS

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Background and aims: Pleural effusion is an important complication of children´s pneumonia. The aim of our study was to describe the clinical and therapeutic characteristics of children with pleural effusion.

Methods: Retrospective study of children diagnosed with pneumonia with pleural effusion admitted to our hospital between 2005-2010. We reviewed clinical charts and collected demographic, clinical and therapeutic variables.

Results: We evaluated 120 children. There was a decrease in the prevalence of pleural effusion in recent years: 70 (59.3%) 2005-2007 vs 48 (40.7%) 2008-2010.

Median age on admission was 48 months (24-72). Median duration of admission was 10.5 (7-17) days, and was shorter for the 38 (32%) children taking antibiotics at presentation (10.3 vs 13.5 days p=0.041) and longer for children under 36 months (13.8 vs 11 p=0.048), without a significant difference between study periods (11.4 vs 13.8 p=0.10).

Fifty (57.3%) patients received only antibiotics, with a significant decrease between the two periods (36 (52,2%) in 2005-2007 vs 14 (29,2%) in 2008-2010 p=0,011).

In 40 (34.2%) patients a video-assisted thoracoscopic surgery (VATS) was performed, with no differences between type of effusion: unloculated 16 (51,6%) vs loculated 15 (48.4%); but a trend towards more VATS in the second period: 19 (27.5%) vs 21 (43.8%); p=0.053.

Conclusions: In our study we observed a decrease in the prevalence of pleural effusion in recent years. Hospital admission was longer in younger children and shorter in children taking antibiotics at presentation, thus, early treatment of pneumonia may improve the outcome of developed pleural effusion.

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RESPIRATORY INFECTIONS IN CHILDREN WITH PRIMARY IMMUNODEFICIENCY DISEASES (PID)

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Introduction: The limited capacity of antibacterial defense causes the pulmonary diseases involving children with primary immunodeficiency diseases to have a particular evolution depending on the PID type.

Objectives: This study proposes an evaluation of pulmonary disease relating with PID on which the infection has grafted.

Methods: A retrospective study has been done between 2001-2010, involving all the 122 cases with PID. Every case was investigated based on the age, number and placement of respiratory infections, etiology, treatment response and their evolution.

Results: The PID types were: selective IgA deficit (76 cases), variable PID (19), hypogammaglobulinemia with hyper-IgM (3), mixed PID (3), cellular PID (6), neutrophyle anomalies (5) and the rest of 9 cases included C3 , Nk deficite and Job syndrome. In 86% of cases, the PID diagnostic was determined in the first 3 years of life. In the first 5 years of evolution, upper respiratory tract infections were dominating (69%), from which, 25% associated at least one pneumonia episode. After 5 years of evolution, 3% of children suffered from chronic respiratory insufficiency determined by pulmonary fibrosys, from which 2 patients have died. 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.

P666

RESPIRATORY INFECTIONS IN CHILDREN WITH PRIMARY IMMUNODEFICIENCY DISEASES (PID)

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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.

P667

NASOPHARYNGEAL BIOFILM PRODUCING RESPIRATORY PATHOGENS IN CHILDREN WITH RECURRENT ACUTE OTITIS MEDIA

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Backgrounds and aims: Differences in nasopharyngeal (NP) bacterial flora in children with nonsevere recurrent acute otitis media (RAOM) and chronic otitis media with effusion have been described. Recently bacterial biofilms, highly resistant to antibiotics, been suggested to play a role in recurrences of upper respiratory infections. Most of the studies rely on biofilm detection from specimens obtained during surgery. We assessed the nasopharyngeal carriage rate of respiratory pathogens and the presence of nasopharyngeal biofilm producing bacteria (BPB) in children with RAOM.

Methods: Nasopharyngeal swabs were obtained from 113 children (aged 10 months to 5 years), including 55 children with RAOM (≥ 3 episodes in 6 months, with or without othorrea), and 58 healthy controls. Nasopharyngeal colonization by respiratory pathogens was assessed by means of semiquantitative analysis, and the presence of BPB by means of spectrophotometric analysis.

Results: The nasopharyngeal carrier rates of respiratory pathogens and the presence of of BPB were significantly higher in children with RAOM (41.4% and 29.3%) compared to controls (14.8% and 10.9%) (p=0.01). Among children carrying BPB, H. influenzae was detected in 52.0%, S. pneumoniae in 26.1% and M. catharralis in 8.7% of cases.

Conclusions: Our results confirm the role of biofilm and of H.influenzae in recurrent middle ear infections in children, and suggest to take it into account in management of otitis-prone children. As nasopharyngeal swab could underestimate the presence of biofilm producing bacteria, these results need to be compared to those obtained on bioptic assays in children scheduled for surgery.

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THE CAUSES OF LONG LASTING CAUGHT IN CHILDREN

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Background: Pertussis is preventable in early childhood, but later it can be a problem, needing changes in vaccinations schedule.

Aim and methods: To evaluate the causes of persistent cough (lasting > 2 weeks) in children sent for consultation to the Outpatient Department of Children Infectious diseases of Kaunas 2nd Clinical hospital during January-March, 2009. Serological ELIZA test was used for confirmation of the diagnosis of pertussis.

Results: 112 patients with persistent cough were sent for consultation because of suspicion of pertussis in 46% of cases, M.pneumoniae infection - 11%, TB infection - 5%, with diagnosis of bronchitis - 22%, long-lasting caught - 10%, other causes - 6%. Consulted patients were mostly teenagers (girls - 64%). Age distribution: children until 9y old -13 %; 10-12y 22 %; 13-15y 37%;15-17y 28%. At the time of consultation most of children had no fever - 68%, subfebral fever had 30% of children. The cough usually lasted for 3-4 weeks - 77% (2 weeks - 16%, 3 weeks - 50%, 4 weeks 27%, more than 4 weeks 7%). 87% of patients previously got antibacterial treatment. The diagnosis of pertussis was confirmed in 87% of cases - all children were older than 10y old.

Conclusions: Pertussis was more often cause (87%) of long-lasting cough

as suspected (46%). All children with confirmed pertussis were older than 10y old.

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as suspected (46%). All children with confirmed pertussis were older than 10y old.

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SEVERE ADENOVIRAL INFECTION IN IMMUNOCOMPETENT CHILDREN

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Backgroud and aims: The etiology of community-acquired pneumonia (CAP) differs with age. In children under five years, viral pneumonia is more frequent than bacterial. The clinical course and sequelae of viral pneumonia can be severe, sometimes requiring intensive care.

Methods: We present two cases of severe adenoviral pneumonia in immunocompetent and previously well 14 and 16-month old girls.

Results: Both children initially presented with history of intermittent fever, dry cough, coryza, conjunctivitis, non-pruritic maculo-papular exanthema on trunk and extremities. On initial chest X-ray (CXR) there were bilateral patchy infiltrates with multiple subsegmental atelectatic changes and areas of hyperinflation in the younger patient. The older girl had peribronchial ifiltration in the middle lobe. The initial presentation mimicked clinically Kawasaki disease, except of chest X-ray finding of pneumonia. The younger girl rapidly progressed to respiratory insufficiency and was ventilated for 14 days. The clinical course was complicated by bacterial superinfection. She was dimissed on day 33. In the older girl, the ventilatory support was not necessary. After diagnosis of adenoviral etiology, the older girl was succesfully treated with pulse methylprednisolone therapy, without antibiotics and dimissed on day 14.

Conclusions: Viruses represent clinically important cause of CAP, especially in younger children. The clinical course can mimick other diseases. Thus, it is essential to include the direct viral diagnostics into routine diagnostic protocol of CAP in young children to avoid unnecessary antibiotic or other (immunoglobulin) treatment.

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ACUTE VIRAL BRONCHIOLITIS: FREQUENCY OF CO-INFECTIONS AND THEIR CLINICAL SIGNIFICATION

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Aim: To assess the impact of the virus species and co-infections in children less than 2 years hospitalized for acute viral bronchiolitis (AVB).

Methods: Frozen nasal wash samples from 434 infants with AVB were analyzed by multiplex RT-PCR detecting 15 respiratory viruses (RespiFinder®).

Results: Four hundred thirty one infants (99.3%) carried at least one virus. Respiratory syncitial virus (RSV) was identified in 83.2% infants, rhinovirus (RV) in 21.0%, bocavirus (hBoV) in 16.4% and metapneumovirus (hMPV) in 7.1% infants. Monoinfection was found in 64.3% of the infants and multiple infections in 35.7%. The most frequent associations were: RSV+RV (9.3%), RSV+hBoV (7.4%) and RSV+RV+hBoV (2.6%). RV and hBoV were more frequently involved in any co-infections (respectively 80.2% and 97.2%).

In infants with mono-infection, there was no significant difference in 1) time to recovery, between the three more frequent pathogens (p=0.47) 2) frequency of hypoxemia (pulse oxymetry< 92%) at admission (p=0.65), feeding difficulties (p=0.60) and need for IV fluids (p=0.72) according to the type of the virus involved. Comparison between mono and co-infections did not show any difference on time to recovery (p=0.51), frequency of hypoxemia at admission (p=0.82), feeding difficulties (p=0.16) and need for IV fluids (p=0.62). Finally, time to recovery (p=0.43) frequency of hypoxemia at admission (p=0.46), feeding difficulties (p=0.72) and need for IV fluids (p=1.00) did not differ whether RSV was involved alone or not.

Conclusion: The type and number of viruses involved in our infants hospitalized with AVB was not a prognosis factor of disease severity.

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THE BURDEN OF RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS AMONG INFANTS IN ENGLAND: A RETROSPECTIVE BIRTH COHORT STUDY USING HOSPITAL EPISODE STATISTICS

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Background: Respiratory syncytial virus (RSV) bronchiolitis in infancy may be associated with long-term respiratory morbidity. Severe RSV infection often occurs among high-risk groups such as infants with chronic lung disease, congenital heart disease, immunodeficiency or premature birth. Conflicting evidence suggests many infants with severe bronchiolitis are previously healthy.

Aims: We aimed to describe the clinical burden of RSV bronchiolitis in England, quantifying the long-term impact on respiratory morbidity.

Methods: We developed a retrospective cohort study (n=211772) from birth to age 5 years, using Hospital Episode Statistics. We included all births from 94 NHS hospitals across England during financial year 2003/04. We identified infants with known RSV risk factors based on birth record information and compared bronchiolitis and subsequent respiratory admission rates between risk groups.

Results: 5947 children in our birth cohort (2.8%), were admitted to hospital with a primary diagnosis of bronchiolitis, 36% of these specifying RSV as the cause. Among those identified as healthy at birth the incidence of bronchiolitis admissions was 2.5% (n=4496) compared to 5.1% (n=1451) among high-risk infants. Following a bronchiolitis admission, high-risk infants were more likely than infants with no risk factors to have subsequent hospital admissions with asthma (14.7% versus 11.2%), lower respiratory infections (27.0% versus 10.5%) and wheezing (12.6% versus 7.1%), before age 5 years.

Conclusion: This national, population-based cohort study provides estimates of the burden of RSV-bronchiolitis in England. Subsequent respiratory morbidity following admission with bronchiolitis is greater than previously described, particularly among infants with no risk factors.

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HIGH PREVALENCE OF MERCKEL CELL POLYOMAVIRUS INFECTION IN CHILDREN WITH ASTHMA EXACERBATION ADMITTED TO NRITLD-IRAN

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Background and aims: It has been shown that the respiratory viruses implicated in asthma exacerbations. Data about the involvement of new emerging viruses in asthma exacerbations is quietly limited. The aim of the study was to determine the prevalence of the newly polyomaviruses in Iranian children suffering from asthma exacerbation in a specialty medical centre.

Methods: 50 Respiratory samples were collected from fifty ≤17y/o childhood exacerbated asthma cases admitted to the Masih Daneshvari Hospital, NRITLD, Tehran between October 2007 and September 2008. The presence of human bocavirus genome was reported in our previous study using nested PCR. Influenza A and B viruses, RSV, hMPV, hCoV, PIV1-3, human rhinoviruses, human enteroviruses, Merckel Cell, WU and KI polyomaviruses and human adenoviruses were screened using real-time PCR.

Results: The mean age was 66.74 ± 37.11 months and the gender ratio (male:female) was 2.57. Totally, respiratory viruses were detected in 62% of studied subjects. The MCPyV and WUPyV were detected in 32% and 2% of studied subjects, respectively. No KIPyV was detected. About 44% of MCPyVs were identified co-infected with other viruses such as Rhinovirus, Adenovirus, hBoV and Coronavirus and the most MCPyVs (56%) were detected as monoinfection.

Conclusion: The focus on the new emerging viruses currently implicated in childhood asthma exacerbations. The using of more sensitive methods of virus detection and the identification and characterization of the new emerging viruses in future asthma studies will improve our understanding about viral diversity and the mechanisms of development of asthma exacerbations.

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RADIOGRAPHIC FINDINGS AMONG CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA WITH SOLE OR MULTIPLE ETIOLOGICAL AGENTS

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Background and aims: Attempts have been made to use radiographic findings to distinguish viral from bacterial pneumonia. Those attempts have been hampered by incomplete etiological approaches. We aimed to add evidence on this issue by investigating the etiology of pneumonia cases with conventional and molecular tests in an expanded diagnostic armamentarium.

Methods: A prospective study was conducted in Salvador, Brazil. Children aged< 5 years with fever, respiratory complaints and pulmonary infiltrate or pleural effusion on chest x-ray (CXR) evaluated by the pediatrician on admission were enrolled. Laboratory investigations were done for 18 microbes. CXR was read by a senior pediatric radiologist unaware of clinical/etiological data. Each radiographic change was localized as right and/or left side and upper and/or lower lobe.

Results: Out of 277 patients, pneumonia was confirmed by the radiologist in 206(74.4%) because of alveolar(89.3%), alveolar-interstitial(3.4%), interstitial(2.9%) infiltrate or pleural effusion(12.1%). Radiographic finding was right-sided(51.7%), left-sided(21.0%) or compromised both sides(27.3%). Only one lobe was involved in 65.8%. The lower(55.1%), upper(30.6%) or both lower and upper(14.3%) lobes were compromised. Hyperaeration(6.8%), atelectasis(6.3%), pneumatocele(1.0%) and abscess(0.5%) were reported. Etiology was established in 165(80.1%) cases among which bacterial(20.0%), viral(48.5%) and mixed viral-bacterial(31.5%) infections were detected. Overall, bacterial infection and exclusively viral infections were found in 85(51.5%) and 80(48.5%) cases, respectively. Sole(57%) and multiple(43%) pathogens were identified. None of the radiographic aspects was associated with viral or bacterial infection, irrespective of sole or multiple agents detected.

Conclusions: Our findings suggest that none of the radiographic changes was indicative of the etiology of the pneumonia.

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Conclusions: Our findings suggest that none of the radiographic changes was indicative of the etiology of the pneumonia.

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IMMUNOMODULATORY EFFECT OF AZITHROMYCIN IN CHILDREN WITH MANNOSE BINDING LECTIN (MBL) DEFICIENCY AND RECURRENT RESPIRATORY TRACT INFECTIONS (RTI)

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Background: Azithromycin is known to have immunomodulatory effect in lung diseases possibly by improving macrophage phagocytic functions and expression of the mannose-receptor. MBL-deficiency is associated with an increased risk of encountering infections. Children with MBL-deficiency and recurrent RTI might benefit from adjuvant immunomodulary therapy using azithromycin.

Methods: Ongoing observational study of children with recurrent RTI and MBL-deficiency reviewed in clinic since 08/2008. To determine the influence of azithromycin prophylaxis (10mg/kg/day for 3 days every 2 weeks) analysing number of infections, drug side effects and patients/parents satisfaction post intervention. Indication for prophylaxis was defined as MBL deficiency (defined as < 400ng/ml) plus recurrent RTI +/- microbiological isolate, requiring repetitive antibiotic treatment +/- hospital admission.

Results: 19 patients with MBL deficiency and RTI were seen in outpatient clinic. Of those 9 patients fulfilled inclusion criteria for azithromycin prophylaxis: Median age 5.7 years (range: 2.1-12.1), mean number of 4.5 RTI/year (range: 3-7), mean MBL serum levels 136ng/ml (range: 27-316), normal IgG,A,M levels for age in all and pneumococcal polysaccharide vaccine response in all but 2 patients. One patient each had proven *A. fumigatus* and *S. pneumonia* pneumonia. After initiation of azithromycin prophylaxis and a mean follow-up time of 13.3 months (range: 5-31), mean RTI was 0.44 (range: 0-1) whilst life-quality was improved subjectively in all children. No side effects were observed.

Conclusions: Azithromycin prophylaxis in children with recurrent RTI and MBL-deficiency might be useful in preventing respiratory infections. Randomized prospective studies are needed to clarify our observation.

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CLINICAL AND EPIDEMIOLOGIC CHARACTERISTICS OF CHILDREN HOSPITALIZED WITH INFLUENZA INFECTION. PREPANDEMIC AND PANDEMIC-POSTPANDEMIC SEASON COMPARATIVE STUDY

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Background: We describe clinical and epidemiologic characteristics of children hospitalized during the pandemic and postpandemic season (PPS) and compare with admissions due to influenza in previous years.(PRES)

Methods: Retrospective study from July 2004-June 2009 and a prospective one from July 2009-January 2011 in paediatric wards at Donostia Hospital (assisted population:54119 children< 14 years). All cases of hospitalized children< 14 years with influenza viral infection, confirmed microbiologically, were collected.

Results: 168 children were identified, 122 in period-1 and 46 in period-2. The hospitalization rate (HR) was similar (39 and 38/100.000 inhabitants< 14 years). In children< 6 months the HR was higher in PRES (294 and 115/100.000 inhabitants< 6months). The mean-age of the PPS was higher (4.8/1.8years) being sex distribution homogeneous. During the PPS, cases had a higher percentage of underlying medical conditions: asthma (28.26%/18.03%)(p=0.14); malignancy (17.39%/0%)(p< 0.001); neurological pathology (15%/4%)(p=0.019); and heart disease (8.69%/1.6%)(p=0.048). The most frequent symptoms were in both: coryza (93.47%/77.86%) and fever (86.95/85.24%) The most frequent isolated influenza virus in PRES was AH_3 being the AH_1N_1 the predominant in PPS. No differences were observed regarding the need for oxigenotherapy. The percentage of admissions in PICU was lower in PPS (17.39%/27.05%) but the mean-stay was longer (6.62/3.89), requiring more ventilatory support (50%/9%)(p=0.018). There were no deaths.

Conclusion: The majority of children admitted in PPS had uncomplicated illness despite the frequent presence of underlying conditions and the greater need for ventilatory support. The mean-age was higher in PS and this group had a lower percentage of children< 6 months.

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RSV PROPHYLAXIS IN PREMATURE INFANTS: A COMPARATIVE STUDY FROM THE CARESS REGISTRY

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Background/aims: Infants 33-35 completed weeks gestational age (GA) and those ≤ 32 weeks GA incur similar rates of respiratory syncytial virus hospitalization (RSVH) and morbidities. We examined palivizumab utilization, compliance and outcomes in premature infants within the prospective, Canadian Palivizumab Registry (CARESS).

Methods: . Neonatal and demographic data were collected from infants receiving ≥1 dose of palivizumab during the 2006-2010 RSV seasons with respiratory illness (RI) events captured monthly. Infants´ ≤32 weeks GA (Group 1) was compared to 33-35 weeks GA (Group 2).

Results: 4819 patients were analyzed (Group 1, n=3746, 30.0 ± 3.1 weeks GA; Group 2, n=1073, 34.2±2.0 GA). Groups were similar for proportion Caucasians, mothers' smoking daily and during pregnancy, atopy history and multiples in the family. There were significant differences ($p < 0.005$) in: mean birth weight (g) (1445±606 versus 2142±521), proportion males (54.3% versus 63.1%), number with siblings (54.2% versus 74.6%), siblings in daycare (13.9% versus 35.0%), ≥2 household smokers (9.9% versus 14.0%) and ≥ 5 household individuals (22.7% versus 44.0%). Group 1 had significantly more complicated neonatal courses. Overall infants received 91.9%±30.7% of expected number of injections. Group 1 received more injections (3.9±1.7 versus 3.5±1.6; $p < 0.005$) and had higher compliance rates (92.8% versus 88.9%; $p < 0.005$). Respective RI and RSVH rates (4.5% versus 3.4%; hazard ratio=0.707, p=0.144) and (1.30% versus 1.27%; hazard ratio=0.462, p=0.205) were similar.

Conclusions: Overall compliance with RSV prophylaxis in premature infants is high and despite higher uptake in infants ≤32 weeks GA, group RI and RSVH rates were similar.

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RESPIRATORY SYNCYTIAL VIRUS HOSPITALIZATIONS IN THE CANADIAN REGISTRY FOR SYNAGIS (CARESS)

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Background and aims: Paediatric advisory committee guidelines recommend palivizumab prophylaxis for infants at high risk for respiratory syncytial virus (RSV) infection. However, effectiveness of palivizumab may vary across indications and countries.

Methods: Neonatal and demographic data were collected across 29 Canadian national sites from infants receiving ≥1 dose of palivizumab during the 2005-2010 RSV seasons with respiratory illness (RI) events captured monthly. We determined hospitalization rates for RI (RIH) and RSV-positive infections (RSVH), and compared rates found in this study with other world-wide data from published registries.

Results: The 7699 infants enrolled were premature (≤35 completed weeks gestational age; n=5237), had chronic lung disease/bronchopulmonary dysplasia (n=646), hemodynamically significant congenital heart disease (n=766), or other underlying medical conditions (n=1050). The overall RIH rate was 6.0% with premature infants having a significantly lower rate (4.1%) than the other groups (8.3% -10.3%)(B=-0.904, df=1, p< 0.0005). Details of hospitalizations did not differ between groups, except a lower proportion of infants with chronic lung disease were admitted to the intensive care unit than the other groups (χ^2=8.111, df=3, p=0.044). The overall RSVH rate was 1.47% with no significant differences between groups (χ^2=2.435, df=3, p=0.487).

Conclusions: Rates for RI and RSVH were similar across the groups. Comparisons with other studies indicate that these rates are lower overall (RSVH range 1.3 -5.3%). However, comparisons are difficult to establish as most studies do not account for the varying lengths of observation that arise because infants are enrolled at different time points during the RSV season.

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CLINICAL CHARACTERISTICS OF SWINE FLU (H1N1) COMPARED TO OTHER RESPIRATORY VIRUSES IN THE UNITED KINGDOM

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Background and aims: During winter, paediatricians were concerned that clinical features would not differentiate between H1N1 and other viruses. We investigated whether Health Protection Agency (HPA) H1N1 criteria were accurate in discriminating between different viruses.

Methods: We reviewed the clinical characteristics of children presenting with viral illnesses to the Paediatric Assessment Unit, Heartlands Hospital, Birmingham, UK between 1st November and 1st December 2009. Data was analysed using StatsDirect.

Results: 217 patient notes were reviewed; 25 had positive viral throat swabs for respiratory syncytial virus (RSV), 23 H1N1, 22 human metapneumovirus, 17 rhinovirus, 11 parainfluenza, 6 adenovirus, and 13 multiple viruses. 100 had negative swabs.

Children positive for H1N1 had significantly higher recorded temperatures only when compared to RSV (p=0.02), rhinovirus (p=0.03) and negative swabs (p=0.02). Headache (p< 0.0001) and myalgia (p=0.041) occurred more frequently in H1N1 compared to all other viruses, but arose only in 34% and 17% of H1N1 cases respectively.

12 children required HDU/ITU admission (8 negative, 2 H1N1 (of which one died), 1 RSV, 1 parainfluenza).

Duration of admission did not significantly differ between viruses.

50 children (23%) had underlying disease; 5 of which had H1N1.

9% of all patients received oseltamivir and 32% received antibiotics with no significant difference between viruses.

The HPA criteria sensitivity and specificity for H1N1 were 73.9% and 54% respectively.

Conclusions: Children with viral infections during winter were clinically indistinguishable except for those positive for H1N1 with headache or myalgia. The HPA criteria did not identify or differentiate H1N1 from other viruses.

P681

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME IN CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA

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Background: Pneumonia is one of the common causes of sepsis as well morbidity in children. The early recognition and prompt initiation of therapy are the most important measures in reducing mortality from pneumonia. The Pediatric Sepsis Consensus conference defined sepsis as SIRS in the presence of infection. Evidence of infection includes chest radiograph consistent with pneumonia. The aim of our study was to evaluate occurrence of SIRS and sepsis in children with community acquired pneumonia.

Methods: In retrospective study all children (n=381) with community acquired pneumonia treated in Children's Clinical University Hospital of Latvia in 2010 were included. The evaluation and occurrence of SIRS in children with pneumonia were analyzed.

Results: At the admission to hospital SIRS criteria as heart or respiratory rate were not fixed for 30% (n=113) of patients. From those patients with fixed vital signs (n=268), SIRS was positive in 37% (n=99) cases. Only 15% (n=15) of patients with SIRS had received the antibacterial therapy before hospitalization. During hospitalization children with SIRS had statistically significant higher ($p< 0.001$) CRP levels and leucocytes count compared with those without SIRS (82.33 mg/l and 24.29 mg/l; 20220 mm^3 and 10110 mm^3). For patients with SIRS significantly more clinical investigations were performed, their hospitalization time was significantly longer.

Conclusion: High occurrence of SIRS among children with pneumonia 37% (n=99) demonstrates the necessity for every patient with fever fixed the vital signs. Each patient with SIRS and pneumonia must be evaluated as sepsis patient who requires intensive treatment and close monitoring.

P682

RARE COMPLICATION OF ACUTE BRONCHIOLITIS IN INFANTS: PNEUMATOCELES

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Background: Two infants presented with acute bronchiolitis and proceeding significant pneumatoceles. We present their management, subsequent investigation and progress.

Methods: Case 1:A 9 months old infant was admitted for a moderate acute bronchiolitis. Rapidly unfavourable progressive outcome was a clinical characteristic, with severe acute respiratory insuficiency. Radiological findings was a large hyperlucency in the left superior pulmonary lobe. The patient received i.v.antibiotherapy, oxygen, digoxin. In the tenth day the patient is transferred in surgery department, where a large congenital pulmonary cyst (8/9 cm) was removed.Case 2A 6 months old infant was admitted for a moderate acute bronchiolitis. He was born prematurely, at 28 weeks of gestation and he needed ventilation support for 72 hours after birth. Radiological study identified 2 hyperlucent images (pneumatoceles) in the medium right pulmonary lobe. He left the hospital in the 12th day of life. After 4 days from the discharge he had fever and dyspneea. Repeated pulmonary X-ray revealed extension of pulmonary cysts, observation confirmed also by pulmonary CT. Surgical diagnosis was of adenomatous pulmonary disease.

Results: Pneumatoceles are very rare complication of bronchiolitis. Multiple sources recognize their association with bacterial pneumonia, but none supports a link to bronchiolitis.

Conclusions: A rare complication of an apparently common disease imposes a more complex study for identification of an underlying diseas.

P683

VALUE OF MOLECULAR DIAGNOSTIC TOOLS IN VIRAL RESPIRATORY ILLNESS IN HOSPITALIZED CHILDREN

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Background and aim: With the development of multiplex nucleic acid testing panels, the number of detectable respiratory viruses has expanded. The value of molecular tools for the diagnostic process is not yet well established because of a current lack of relating clinical and epidemiologic data.Here we present potential benefits of molecular diagnostics in the detection and identification of viral causes of respiratory illness in hospitalized children.

Methods: As part of a prospective study into viral respiratory tract infections in hospitalized children, we collected clinical data of all children in whom respiratory samples were taken for detection of 15 respiratory viruses. We further characterized human rhinoviruses (HRVs) by sequencing the VP4/VP2 region of the HRV genome. Molecular diagnostic findings were related to clinical symptoms and patient characteristics.

Results: From September 2009 till January 2011, 1455 respiratory samples were collected from 644 patients with 904 disease episodes. In 916 samples (63.0%), one or more viruses were detected. HRV was the single respiratory virus detected in 446 samples (48.7%), relating to 254 disease episodes. HRV is associated with considerable respiratory symptoms in patients with pulmonary underlying disease. Sequence analysis revealed an upsurge of enterovirus 68 infections (which is identical to HRV87) associated with severe respiratory illness in the absence of other viral or bacterial causes of infection.

Conclusion: Molecular diagnostic tools for the detection and identification of respiratory viruses are helpful in explaining respiratory illness and may give guidance to medical care.

P684

MODULAR NEAR-PATIENT PCR FOR INFLUENZA & RSV PROVIDES RAPID AND ACCURATE RESULTS TO GUIDE MANAGEMENT DECISIONS

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Background and aims: We evaluated a new modular near-patient PCR system in 2 centres between January and March 2011

Methods: 146 children with fever and respiratory symptoms presenting to the emergency service at Coimbra(C) had nasopharyngeal samples and clinical data collected prospectively with consent. 67 samples collected routinely at Bristol(B) during the same period were studied. At each centre, sample sets were analysed using the Verigene modular PCR system for Influenza A(H1, H1 2009,H3),B, RSV A&B & Oseltamivir resistance mutation H275Y. The B set was also analysed using established PCR assays.

Results: By Verigene, in C, 15,0&48/146 were positive for InflA,B,RSV(24A,24B) (4 double positives(dp)) and 87 were negative. The corresponding B results were 27,22&8(5A,3B)/67 (2dp) &12 negative. In C-B 14-25 InflA were H1 2009, 0-1 H3, 1-1 untyped (none H275Y+ in C, 14/25 & 2 indeterminate in B). Results by established assays in B were concordant except the untyped H1 sample which was positive for H1 2009, the indeterminate samples which were H275Y+ & 2 H275Y negatives which were weakly positive. In C, 6/15 InflA+ (1 received Oseltamivir) and 16/48 RSV+ children were admitted.

Conclusions: The Verigene results matched those from established assays closely. The small number of discrepant results generally related to weakly reactive or indeterminate samples. Evident clinical benefit of rapid-near patient testing included RSV bed-management and cohorting decisions and guidance of Oseltamivir use in seriously sick children. The system would also permit tracking of local outbreak epidemiology in centres without ready access to viral PCR testing.

P685

DIAGNOSTIC VALUE OF RESPIRATORY SECRETIONS IN CRITICALLY ILL NEWBORNS OF NEONATAL INTENSIVE CARE UNITS IN EGYPT

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Objective: To evaluate the role of respiratory tract colonization pattern- in predicting pathogens isolated during episodes of neonatal sepsis.

Study design: A prospective study including 50 septic newborns (21 full term & 29 preterm) was carried in the neonatal intensive care units (NICUs) of Cairo University (Kasr el Aini and Abou el Riche Children Hospital) during the period between March 2007 and December 2007. In addition to routine laboratory work up for sepsis, culture was performed on respiratory specimens obtained using either blind (non-bronchoscopic) bronchoalveolar lavage (BAL) or tracheal aspirate (TA).

Results: Comparing blood and respiratory cultures regarding the presence of bacterial growth, there was a statistically significant relation between them; as we retrieved the same organism in almost 30% of cases.

Conclusion: Culture of tracheal secretions could be of use as an indicator of changes taking place in the NICU environment. However, it is recommended only if clinical signs point out pneumonia, associated with variation in amount and character of secretions, even if the chest x-ray shows no abnormality.

P686

THORACIC EMPYEMA IN CHILDREN: CLINICAL PRESENTATION, MICROBIOLOGY ANALYSIS AND THERAPEUTIC OPTIONS

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Background and aims: Empyema is an accumulation of purulent fluid as a complication of pneumonia. An increase of the incidence of empyema in children was reported. *Streptococcus pneumoniae, Staphylococcus and Streptococcus pyogenes* are the most common pathogens. The aims of our study were to present the incidence, clinical presentation, microbiology, and therapeutic options.

Methods: We collected data of children with empyema in our center during 17 years.

Results: Empyema was found in 53 patients. 64% of Jewish origin; 36% of Arabic origin. The median age was 4 years. Forty one cases were diagnosed in the last nine years. Fever, cough and respiratory distress were the most frequent signs. In 29 patients pleural effusion was found at admission. Causative organisms were found in 28 patients, blood (11), pleural fluid (17). *Streptococcus pneumoniae* was the leading pathogen. Most of the S*treptococcus pneumoniae* were sensitive to penicillin. The patients were treated initially by penicillin in 21, cefuroxime 19 and ceftriaxone in 11. The pleural fluid was drained by video assisted thoracoscopy in 32 children. All the children cured.

Conclusions: The incidence of empyema as a complication of community acquired pneumonia had increased in the last decade in our region. Chest ultrasound can be considered as a safety tool for the confirmation of the disease beside laboratory and microbiology exams. Third generation cephalosprins alone or with a combination with clindamycin can be considered as a good empiric treatment. Beside the antibiotic therapy the use of video assisted thoracoscopic excellent outcome can be achieved.

P687

COMPARISON OF NASOPHARYNGEAL MICROBIOTA OF PEDIATRIC PNEUMONIA AND CONTROL PATIENTS BY PYROSEQUENCING

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Background and aims: Lower respiratory tract infections are believed to be seeded from bacteria colonizing the nasopharynx. To test this hypothesis we compared the composition of nasopharyngeal microbiota of children with pneumonia to control patients by a culture-independent approach.

Methods: Nasopharyngeal samples from 50 pneumonia patients and 50 aged-matched control patients without respiratory infections (aged 0.2-5.4 years) were analysed. After DNA extraction, two phylogentically informative fragments of 16S genes were amplified using barcoded primers that allowed later identification of individual samples. The amplicons were sequenced by multiplexed 454 pyrosequencing. High quality sequences were classified using the RDP-Classifier as well as grouped into Operational Taxonomic Groups (OTUs) based on their best BLAST hit.

Results: Twenty seven samples from pneumonia cases and 22 from controls gave adequate PCR product for pyrosequencing analysis generating n=2500 reads per sample on average. RDP classifier detected 41 genera constituting >0.5% of any sample. 80% of sequences belonged to *Streptococcus*, *Haemophilus* and *Moraxella*, which comprised commensal and pathogen species. 119 OTUs were detected. Three OTUs, with 98% identity to *Moraxella catarrhalis*, *Haemophilus influenzae* and *Streptococcus pneumoniae* were more abundant in children with pneumonia (M.c. 10% vs. 6%; H.i. 35% vs. 22%; S.p. 12% vs. 4%). A poorly identified group (family Moraxellaceae, 96% identity with genus *Enhydrobacter*) was more common in healthy children (6% in cases vs. 10% in controls).

Conclusions: Established pneumonia-associated pathogens were found in the nasopharynx microbiota and with higher prevalence in pneumonia than in control patients.

P688

ROLE OF BOCAVIRUS AMONG OTHER RESPIRATORY VIRUSES IN CHILDREN

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Background: Human bocavirus (HBoV), discovered in 2005 in Sweden, is parvovirus which causes respiratory tract diseases mainly in children. The main clinical manifestations of HBoV-infection are involvement of lower respiratory and gastrointestinal tracts.

Objective: The purposes of our research were to determine role of bocavirus in structure of ARVI and the analysis of clinical features of bocavirus infection in the children.

Methods: Virusological examination of nasal swabs by OT PCR method was performed in 298 patients aged < 18 years from October 2009 till November 2010.

Results: In 180 specimens (61%) were determined respiratory viruses. HBoV was detected in 6, 1% of patients with ARI. HBoV formed associations with other respiratory viruses in 7, 2% of cases (rhino-, adeno-, parainfluenza viruses). 98% of patients were children between the ages of one to three years.Among clinical forms of HBoV-infection obstructive bronchitis (50%) and laryngotracheitis (25%) were leading. Complications occurred in 45% of the patients, mainly, otitis media and pneumonia. However, there where no sings of dyspepsia in our patients. However, there where no sings of dyspepsia in our patients. The following changes in blood analysis were determined: leucocytosis (60%), stab neutrophil in (45%). Authentic differences in groups with mono-and mix infections were not established.

Conclusions: More often HBoV combines with other respiratory viruses. It affects predominantly children of the young age (under 3). Clinical manifestations of HBoV-infection in children are characterized by respiratory syndrome with lesion of lower respiratory tract (in 50% cases) with high rate of development of complications (45%).

P689

THE EFFICACY OF ZINC SUPPLEMENTATION IN YOUNG CHILDREN WITH RECURRENT ACUTE LOWER RESPIRATORY INFECTIONS: A RANDOMIZED DOUBLE-BLIND CONTROLLED TRIAL

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Aim: To assess the efficacy of zinc in reducing respiratory morbidity in children aged 6-59 months with recurrent acute lower respiratory Infection (ALRI).

Methods: This randomized double blind controlled trial selected children with recurrent ALRI referred to department of Pediatrics, Jawaharlal Nehru Medical College Hospital. Children were randomly assigned to receive either 10mg zinc gluconate or placebo for 60 days. Demographic and clinical data were collected at baseline and every two weeks during the six month study period.

Results: The final analysis included 96 children allocated equally to the two groups. The incidence of ALRI and severe ALRI were significantly lower in zinc group compared to placebo group (20.8% vs. 45.8% (p=0.009) and 21.7% vs. 58.3% (P< 0.001), respectively).The ALRI free days were higher in the zinc supplemented group (P< 0.001),whereas the duration of ALRI episode; fever and rapid breathing were significantly shorter in zinc group (P< 0.001). The medians of serum zinc concentration were comparable at baseline but increased significantly in the zinc group at two month (P= 0.000). The median recovery time of morbidity was significantly shorter in zinc group compared to placebo group (10 days vs.18days) (P< 0.001).Lower risk (20.8%) of two or more episodes of ALRI was observed in zinc group in comparison to placebo group 45.8% (p= 0.009), with absolute risk reduction (ARR) of 25%.

Conclusions: This trial proved a beneficial effect of the sole zinc supplement resulting in a significant reduction in respiratory morbidly among children less than 5 years with recurrent ALRI.

P690

FACTORS ASSOCIATED WITH ACUTE OTITIS MEDIA (AOM) RISK IN EUROPEAN CHILDREN AGED 0-5 YEARS: A PROSPECTIVE STUDY

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Background and aims: AOM incidence across five European countries was reported previously[1] but evidence from large multi-country prospective studies regarding predisposing factors is limited. This prospective observational cohort study assessed the importance of selected factors in relation to AOM risk.

Materials and methods: 5882 healthy children aged ≤5 years were randomly selected from 73 medical practices in Germany, Italy, Spain, Sweden and the United Kingdom. Of these, 5764 children were followed prospectively for 12 months. Information regarding 25 child and parental characteristics and environmental factors potentially influencing AOM risk was collected upon enrolment. AOM risk related to each factor was analysed both individually (chi-squared test, odds ratio [OR]) and using multiple logistic regression analysis (adjusted OR). Analyses were pooled by country; individual country results were similar.

Results: 1119/5764 children (19.4%) presented with ≥1 of 17 potential factors pre-defined in the case report form, most commonly, ”exposure to cigarette smoke indoors”. 1113/5764 children (19.3%) developed AOM; of these, 21.2% (236) presented with ≥1 of 17 potential factors. By multivariate analysis (of 25 factors), day-care attendance significantly increased AOM risk (OR=2.08 [95%CI 1.48-2.92]), whilst older age at enrolment (OR=0.79 [0.74-0.85]) and breastfeeding (OR=0.57 [0.42-0.79]) were associated with a lower risk. “Exposure to cigarette smoke indoors” was not significantly associated with AOM risk.

Conclusions: Younger age and day-care attendance increased AOM risk; breastfeeding appeared to offer some protection. Promoting increased breastfeeding may reduce AOM burden. Further analyses are underway to determine the interaction of age with other factors.

1. Liese. WSPID2009. Abstract 797.

P691

COMPARISON THE EFFICACY OF ORAL DEXAMETHASONE WITH IM DEXAMETHASONE IN TREATMENT OF CROUP

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Backgrounds: Croup, or acute laryngotracheobronchitis, is the most common cause of upper airway obstruction in children. In this study, the efficacy of intramuscular dexamethasone and oral dexamethasone are compared for treatment of croup.

Methods: This is a double blind randomized trial involving 68 children with group that dived into two groups, the fist group received 0.6 mg/kg intramuscular dexamethasone and the second group received 0.6 mg/kg oral dexamethasone. The clinical score, respiratory rate, heart rate, O2 saturation and clinical response were assessed before and then hourly for four hours after treatment.

Results: The respiratory rate of the second group in the 4^{th} hours was significantly lower than first group. There was no statistical difference among clinical score, respiratory rate in the three first hour, heart rate, O2 saturation and clinical response.

Conclusion: Oral and intramuscular have the same effectiveness for treatment of croup and oral dexamethasone was proposed because this is a non invasive procedure.

P692

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS AMONG PATIENTS HOSPITALIZED WITH ACUTE BRONCHIOLITIS - TWO YEAR STUDY

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Background and aims: Acute bronchiolitis is a viral respiratory tract infection most commonly seen in infants and young children. It causes transient occlusion of small airways of the lungs and is the leading cause of infant death and hospitalization. Epidemiological characteristics of bronchiolitis were recorded among hospitalized in our clinic patients (period 2008-2009) and the data were evaluated.

Methods: From the clinical records, 138 patients with bronchiolitis in that period (92 boys, 46 girls) aged 2 to 24 months, were retrospectively studied. Sex, age, clinical presentation (including respiratory and heart rate), oxygen saturation, the radiological findings of the respiratory complications, the medication treatment and hospitalization length were recorded and the clinical significance of the events was evaluated.

Results: All children in the study (average age : 7.5 months) showed persistent coughing, wheezing / shortness of breath, 37% of them fever. Respiratory rate ≥60 breaths / min, oxygen saturation ≤93%, prolonging the symptoms more than 5 days and corticosteroids entry on regimen (bronchodilators / adrenaline) showed 23.2% of infants aged < 6 months, indicating severe bronchiolitis. Chest x-ray: + (peribronchial infiltrates, pneumonia), otitis media, found in 18 babies 2 -18 months (27.5%) which have received antibiotic p. os / iv, (average length of stay: 6.5 days).

Conclusions:

1. Boys have greater hospitalization frequency in comparison to girls.

2. Patients aged < 6 months are related with more severe infection.

3. Complications in infants with respiratory distress extend the duration of their hospitalization.

P693

INCIDENCE AND CLINICAL DATA OF RSV INFECTION IN CHILDREN: A SINGLE INSTITUTION EXPERIENCE

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Background and aims: Community respiratory viruses are a common cause of infections in children. RSV is one of the most important pathogens of mild respiratory diseases, which occur at a younger age.The purpose of our study is to investigate the role of RSV in respiratory infections in children.

Methods: We reviewed the records of 131 respiratory tract infections in 131 hospitalized children. The survey was carried out between January 2007 and December 2008. Pharyngeal swabs was obtained from each child. RSV was isolated by PCR.

Results: The median age of children was 4 years (IR 0,12-16yrs) and female/male ratio was 70/61. The incidence of RSV infection was 15,3% (20/131). RSVA serotype was detected in 11 (55%), RSVB in 7 (35%) and combination of both in 2 children (10%). The median age in children with RSV infection was 0,62 years (IR 1,6-5yrs) The majority of RSV infections was clinically present as lower respiratory tract infections (bronchiolitis 60%, pneumonia 35%). Coinfections with other viruses were detected in 5 cases. Only 1 patient (5%) developed parapharyngeal abscess, as a complication of the RSV infection. No significant difference was found between RSV infection and lymphopenia (< 1.400/mm^3), neutropenia (< 1.500/mm^3), sex and seasonal distribution, although the majority of cases presented in winter. Younger age (≤2 years) was marginally significant associated with RSV infection (p:0,05).

Conclusions: Due to the limited literature concerning RSV infections, further epidemiological studies may help to a better understanding and management of respiratory tract infections in childhood.

P694

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V. Tsotoulidou[1], F. Athanasiadou[1], M. Emporiadou[1], E. Roilides[2], A. Papa[3], Z.-D. Pana[1], M. Goutaki[4], A. Haidopoulou[4], A. Tragiannidis[1], E. Hatzipantelis[1], T. Papageorgiou[1]

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Conclusions: Due to the limited literature concerning RSV infections, further epidemiological studies may help to a better understanding and management of respiratory tract infections in childhood.

P695

IMPACT OF (H1N1) 2009 INFLUENZA ON THE PAEDIATRIC DEPARTMENT OF A BELGIAN UNIVERSITY HOSPITAL

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Background and aims: A new strain of influenza virus was declared pandemic on June 11th, 2009. Considering available data regarding the epidemiological and clinical impact of the virus and uncertainties about its evolution, a surveillance and management process was defined in accordance to (inter)national recommandations for HealthCare Settings.

Methods: From August 1st to December 31th 2009, an identification process was implemented in the Emergency Department (ED): all children (0-16) with a positive screening for Influenza Like Illness (ILI) were isolated to guarantee the protection of HealthCare Workers *and* patients, and optimize the treatment.

Paediatric patients were determined as possible influenza cases after medical evaluation, and considered eligible for virological testings (Rapid Influenza Diagnostic Test (RIDT), Reverse Transcriptase PCR (RT-PCR) *if* RIDT negative *and* presenting with risk factors or requiring hospitalization).

Results: 149 positive ILI screening in the ED, 135 determined as (H1N1) 2009 possible cases.

59 hospitalized: 8 positive RIDT *or* RT-PCR, 23 negative RT-PCR, 27 negative RIDT not tested for RT-PCR (other diagnosis rapidly available), 1 not virologically tested.

76 discharged: 20 positive RIDT *or* RT-PCR, 9 negative RIDT *and* RT-PCR, 21 negative RIDT not tested for RT-PCR, 26 not virologically tested.

Conclusions: Impact on hospitalization ward remained limited and was highest regarding the ED paediatric evaluation process and the microbiological laboratory analysis, in weeks directly preceding and following the Belgian wave peak.

Nevertheless, a higher clinical attack rate in Belgium could have involved capacities limitations, and focussed on a need for better preparation even with a moderate pathogen.

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CLINICAL FEATURES OF PAEDIATRIC PATIENTS DURING THE (H1N1) 2009 PANDEMIC WAVE IN A BELGIAN UNIVERSITY HOSPITAL

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Background and aims: Isolation process for children presenting to Emergency Department (ED) with Influenza Like Illness (ILI) was implemented during the pandemic wave. We looked forward to assess the specificities of a new influenza virus, mainly circulating in school-aged population.

Methods: Epidemiological/clinical data of ILI paediatric patients were registered from August 1st to December 31th 2009. All children (0-16) determined as possible (H1N1) 2009 cases after ED medical evaluation were included in a medical chart review.

They were confirmed whith positive Rapid Influenza Diagnostic Test (RIDT) *or* Reverse Transcriptase PCR (RT-PCR); children with negative RT-PCR were excluded from the diagnosis.

Results: 135 children were included: median age 4.5 (0.3-16); 108 were virologically tested.

28 were positive (8 hospitalized). Main clinical findings at admission: fever (96.4%), cough (92,9%), rhinorrhea (75%), gastrointestinal symptoms (42,86%), dyspnea (14,3%). Risk factors were mainly related to respiratory diseases (39,3%). Main differences between hospitalized/discharged patients: dyspnea (37,5% *vs* 5%), gastrointestinal symptoms (62,5% *vs* 35%).

Out of 107 children not confirmed for influenza, 32 (23 hospitalized) were negative for RT-PCR, with fever (100%), cough (87,5%), rhinorrhea (68,8%), gastrointestinal symptoms (43,8%), dyspnea (31,3%). Risk factors were less related to respiratory diseases (28,1%). Main difference between hospitalized/discharged patients in this group: dyspnea (39,1% *vs* 11%).

Median age for confirmed patients: 7.5 (0.5-16) *vs* 2.9 (0.4-13) for excluded patients.

Conclusions: 28,6% of confirmed influenza patients (0-16) were hospitalized. Clinical patterns were atypical regarding gastrointestinal symptoms. (H1N1) 2009 diagnosis can´t be excluded in 70% (75, *no RT-PCR*) of not confirmed patients.

P697

LEGIONELLOSIS: REPORT OF A CASE IN NEWBORN INFANT

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Pneumonia due to *Legionella pneumophila* is well described in the adult literature. But only few cases of neonatal Legionellosis have been reported until now. We report a case of a neonatal Legionellosis.

On her 7th day of life a full term newborn with normal body weight was affected by a pneumonia. This was at first resistant to antibiotic-therapy(Ampicillin/Amikacin) . We detected Legionella urinary antigen.Diagnosis of Legionella pneumophila was made by polymerase chain reaction method from sputum .The clinical course of the disease was favourable, and a prompt recovery as observed after administration of an antibiotic - therapy(Erythromycin). We emphasize the importance of considering Legionellosis in cases of antibiotic-resistant neonatal pneumonia.

P698

THE ROLE OF VITAMIN D IN RECURRENT TONSILLITIS

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Aim: Exact etiology of recurrent tonsillitis in children is not clear. Aim of the research was to determine the role of vitamin D in recurrent tonsillitis. Serum 25-OH vitamin D levels and vitamin D receptor polymorphism among children with recurrent tonsillitis were analyzed.

Methods: An eighty-four children with recurrent tonsillitis and a seventy-one healthy children aging between 2 and 10 years were enrolled the study. Serum 25-OH vitamin D level was measured with ELISA (nmol/L) and vitamin D receptor gene polymorphisms (*Apa1, Taq 1, Fok1*) were researched by PCR. Serum 25-OH vitamin D level below 50 nmol/L, was accepted as insufficient. The vitamin D receptor gene polymorphism in each group was compared.

Results: Mean ages were 5.6±2.4 years in study group, and 6.1±2.7 years in control group. The average serum 25-OH vitamin D level was 142.7±68.1 nmol/L in study group and 192.3±56.1 nmol/L in control group ($p < 0.01$). In study group, 4.7% (n=4) of children had their serum 25 OH vitamin D levels below 50 nmol/L. Vitamin D receptor sub-genotypes was not significantly different between the groups.

Conclusion: Serum 25-OH vitamin D levels in recurrent tonsillitis group were lower than healthy children. But, there is no difference in vitamin D receptor gene polymorphism.

P699

CURRENT STATUS OF DIAGNOSIS AND TREATMENT OF CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA (CAP) IN EUROPE. CAP-PRI* SURVEY

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Background and aims: CAP is a common and potentially serious illness in European countries. Case definitions for CAP are not standardized. Aim of study - to review the current status of the availability and usage of the guidelines in diagnosis and treatment of CAP in European countries.

Methods: The questionnaire developed by the members of CAP-PRI was distributed to 22 centres in 20 European countries and 18 returned questionnaires from 16 countries were analysed.

Results: All of 16 responding countries reported available CAP guidelines. Three out of 18 (16.7%) responding centres use WHO guidelines, 5 (27.8%) centres use national, 5 (27.8%) guidelines approved in their own hospital and 1 centre doesn't use paediatric CAP guidelines. Chest X-ray examination, blood count and CRP are the most common diagnostic criteria (100%, 100%, 88.9%), whilst evaluation of clinical symptoms and other laboratory tests vary significantly. Antibacterial treatment of CAP varied among participating centres: amoxicillin (83.3%) and macrolides (94.4%) are most commonly used in out-patient settings whereas in hospital settings antibiotic treatment varies widely.

Conclusions: Our survey revealed the great variety of clinical and laboratory criteria used in diagnosis and treatment of CAP. In some countries guidelines differ by region, or even by hospital. This heterogeneity may reflect differences in epidemiology and, in particular, antibiotic resistance rates, but studies are now needed to assemble evidence on this.

*CAP-PRI

Community Acquired Pneumonia Paediatric Research Initiative is an international working group of members of ESPID, initiating and co-ordinating research in the area of childhood pneumonia.

P700

'DECLINE OF IGG-PERTUSSIS TOXIN MEASURED IN UMBILICAL CORD BLOOD AND NEONATAL SERUM'

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Background and aims: Maternal pertussis-specific antibodies are passively acquired by infants during pregnancy. IgG-pertussis toxin (IgG-PT) concentration of >20 U/ml (= >ln 3,0) is assumed to protect neonates against pertussis. To evaluate the amount at birth and course in the first two months of life of IgG-PT, we examined IgG-PT concentration in umbilical cord blood and at 3 times in the neonatal period.

Methods: IgG-PT was measured by validated IgG-specific enzyme-linked immunosorbent assays in umbilical cord blood and in dried blood spots on filter paper cards prepared from umbilical cord blood. These measurements were comparable. Children, born between April 2006-December 2008 with concentrations of IgG-PT >30 U/ml in umbilical cord blood were included. IgG-PT was again measured at the age of 5 days, 1 month and 2 months in dried blood spots. Mean concentrations of IgG-PT were calculated.

Results: The mean concentration of IgG-PT in umbilical cord blood was 60,1 U/ml (ln 4,1; 0,6 SD; N=103). At the age of 5 days, 1 month and 2 months, mean concentrations of IgG-PT were 40,6 U/ml (ln 3,7; 0,5 SD; N=103), 20,7 U/ml (ln 3,0; 0,7 SD; N=62) and 16,7 U/ml (ln 2,8; 0,9 SD; N=61) respectively.

	Umbilical cord blood IgG-PT	Umbilical cord blood IgG-PT Guthrie card	5 days IgG-PT Guthrie card	1 month IgG-PT Guthrie card	2 months IgG-PT Guthrie card
ln	4,1	4,0	3,7	3,0	2,8
SD	0,6	0,5	0,5	0,7	0,9
N	103	103	103	62	61
U/ml	60,1	56,4	40,6	20,7	16,7

[IgG-pertussis toxin concentration]

Conclusion: Only 4% of neonates had IgG-PT >30U/ml in umbilical cord blood, which declines to levels around the concentration needed for protection against pertussis (>20 U/ml) in the first two months of life. Hence, it is of great importance to further investigate safety of maternal immunization during pregnancy to prevent life-threatening pertussis in newborns.

P701

IMPACT OF RESPIRATORY TRACT INFECTIONS IN CHILDREN WITH DOWN SYNDROME

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Background and aims: Parents believe that recurrent respiratory tract infections (RRTI) have a large impact on children with Down Syndrome (DS), but data are lacking. We studied the impact of RRTI on development, behaviour, and health related quality of life (HRQoL) in 8-year-old DS children.

Methods: During a 3-year period, all members of the Dutch DS Foundation with an 8-year-old child with DS were asked to fill in the Child Behavior CheckList and TNO-AZL Children's Quality of Life Parent Form. Also, a psychological assistant administrated the McCarthy Scales of Children's Abilities. Based on parental report, the children were divided into increased RRTI (RRTI+) and no increased RRTI (RRTI-). Linear regression analyses were performed to assess the effect of RRTI on the outcomes, correcting for the influence of confounders.

Results: The influence of RRTI was significant for most outcome measures, corrected for the influence of confounders. Compared to RRTI- children (n=176; missing data n=12), RRTI+ children (n=149, 46%) showed lower mean developmental age (3.67 vs. 4.08 years), more behavioral problems and lower scores on most HRQoL scales (*p*-values< .05).

Conclusions: Our study shows RRTI have significant impact in 8-year-old DS children: it causes relatively more delayed development, more behavioural problems, and lower HRQoL. Since RRTI are potentially preventable, further studies should focus on causes and improved treatment of RRTI in children with DS, such as pathogens, extent of immunodeficiency, prophylactic antibiotics, and additional immunizations.

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P702

CHARACTERISATION OF BACTERIAL PATHOGENS CAUSING SEVERE ACUTE OTITIS MEDIA (AOM) IN GERMAN CHILDREN POST-INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7)

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Background and aims: AOM is a frequent childhood disease, however, tympanocentesis is not routinely performed and swabs from perforated cases may be contaminated, limiting aetiology data. This non-interventional epidemiological study assessed aetiology and antimicrobial susceptibility of bacterial AOM pathogens in Germany.

Methods: 112 children aged ≥3-< 60 months visiting, or referred to, ENT specialists for spontaneous tympanic rupture or clinically indicated tympanocentesis were enrolled. Middle ear fluid (MEF) samples were collected by tympanocentesis or by sampling spontaneous otorrhoea directly from the perforated area of the tympanum after thoroughly cleaning the ear canal. Samples were cultured for bacterial characterisation.

Results: 100 samples were analysed from 100 children (median age 36 months) meeting inclusion criteria. The most common symptoms at presentation were ear discharge (70%) and ear pain (68%). 74 children had received ≥1 dose pneumococcal vaccine. Bacteria were cultured from 53% of samples; *Haemophilus influenzae* (Hi; 21%), *Streptococcus pyogenes* (Spyo; 13%) and *Streptococcus pneumoniae* (Spn; 10%) were most common, with 1 sample positive for both Spn and Hi. Spyo and Spn were only isolated in MEF from spontaneous otorrhoea (n=76). 86% of Hi samples were non-typeable (NTHi) and 60% of Spn samples were serotype 3. All Spn-isolates were susceptible to all antibiotics tested (except 1 with intermediate penicillin susceptibility). Hi-isolates showed some resistance to various antibiotics; notably, 10% were amoxicillin resistant.

Conclusions: NTHi was the main bacterial AOM pathogen in Germany 4-5 years post-PCV7 introduction, which should be considered when choosing antibiotics. Vaccination against Hi, Spyo and Spn may substantially reduce AOM.

P703

SEVERETY OF VIRAL CO-INFECTIONS IN HOSPITALIZED INFANTS WITH RESPIRATORY SYNCYTIAL VIRUS INFECTIONS

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Background and aims: Virus is the most common agent of low respiratory tract infections in infants. The first cause of hospitalization during the first year of life is respiratory syncytial virus (RSV) infection and its association with other respiratory viruses is frequent. The clinical meaning of virus co-infections remains unclear. The aim of this study is to analyse the clinical severety of viral co-infections comparing to single RSV infections.

Methods: A historical cohort was studied, including hospitalized infants with RSV acute infection. In all patients nasopharyngeal secretion samples were collected to search eight respiratory viruses through molecular biology methods. Severity of single RSV infections was compared with that of co-infections. The following outcomes were analyzed: duration of hospitalization and of oxygen therapy, need of intensive care unit and of mechanical ventilation. Results were adjusted for confounding factors (prematurity, age and breastfeeding).

Results: A hundred and seventy six infants were studied, with a median age of 4.5 mon:ths and diagnoses of bronchiolitis and/or pneumonia. A hundred and twenty one had single RSV infection and 55 had co-infections (24 RSV+adenovirus, 16 RSV+human metapneumovirus and 15 other less frequent virus associations).The four severity outcomes which have been studied showed similar effects in the group with single RSV infection and in the co-infection groups, independent of the associated virus with RSV.

Conclusion: The results of this study suggest that virus co-infections do not alter the prognosis in hospitalized infants with acute RSV infection.

P704

SAFE APPLICATION OF CONVALESCENT PLASMA IN AN 1 YO INFANT WITH SEVERE INFLUENZA A (H1N1) 2009 VIRUS INFECTION

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In severe influenza infections as Spanish influenza, influenza A(H5N1) or influenza A (H1N1) 2009 treatment of patients with convalescent plasma infusion may reduce mortality (Hung et al, Clin Infect Dis 2011;52:447-456).

We present an 1 yo preterm (34 weeks of gestation) infant suffering from severe influenza A (H1N1) 2009 infection. Clinical deterioration occured despite optimal antiviral treatment leading to respiratory failure and prolonged HFO ventilation. Oseltamivir was given for 6 days followed by a 5 day course of intravenous zanamivir without clinical improvement. We offered treatment with convalescent plasma with a neutralizing antibody titer of >1:1000, harvested by apheresis from a female volunteer who recovered from H1N1 2009 infection. Hundred milliliters of convalescent plasma were infused intravenously to the infant over a period of 4h. The infusion was well tolerated. Viral loads were measured before application, directly after application and on subsequent days within the next two weeks.

Treatment of severe H1N1 2009 infection in this infant with convalescent plasma was safe and lead to a favourable clinical outcome. Therefore, a prospective controlled clinical trial of convalescent plasma treatment in pediatric patients with severe influenza infection is urgently warranted.

P705

MULTI-VIRUSES INFECTION IN ACUTE LOWER RESPIRATORY TRACT INFECTION IN CHILDREN

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Objective: To investigate the mixed infection of viruses in acute lower respiratory tract infection（ALRTI）in children.

Methods: Totally 1914 children with clinical diagnosis of ALRTI during the period of March 2007 to March 2010 were recruited into this study. One nasopharyngeal aspirate specimen was collected from each patient.（RT）PCR methods were performed to detect common respiratory viruses including respiratory syncytial virus, human rhinovirus, influzenza virus type A, B and C, parainfluenza virustype 1-4, adenovirus, enterovirus, human coronavirus, human metapneumovirusand human bocavirus.

Results: Among 1914 cases, the overall positive rate of viruses was 70.3%. The positive rate was 83.0% in age group of < 1 year old, and 80.1% in 1~< 3 years old group, 60.8% in 3~< 6 years old group and 27.7% in ≥6 years old group, respectively. The mixed infection rate was 38.2%、36.4%、30.2% and 15.2% in age groups of < 1 year old, 1~< 3 years old, 3~< 6 years old and ≥6 years old, respectively. There was a significant difference of the mixed infection rate among different age groups (P=0.000).

Conclusion: Mixed infections with two or more viruses were detected in substantial patients with ALRTI. Further study are needed to explore the clinical significance of mixed infection of viruses in patients with ALRTI.

P706

AWARENESS AND ATTITUDES ABOUT ACUTE OTITIS MEDIA AMONG PEDIATRICIANS, FAMILY PHYSICIANS, EAR-NOSE-THROAT SPECIALISTS IN TURKEY (TR-AOM STUDY PART I)

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Aims: Acute otitis media(AOM) is the most common bacterial infection in children. Compliance to published guidelines for AOM is not at desired level. The aims of this prospective study was to assess the compliance to AOM guidelines in a large sample of pediatricians(PEDs), family physicians/general practitioners(FP&GPs) and ENT specialist in Turkey.

Methods: This is a web-based cross-sectional survey of a national convenient sample in Turkey. The questionnaire included questions about attitudes about the diagnosis of AOM and source of timing of AOM medical education.

Results: TR-AOM study includes 633 participants from different health care settings. 77.5% of PEDs, 71.5% of FP&GPs, 83.6% of ENTs have indicated they are using direct antibiotic therapy when they diagnose AOM. 30.0% participants from private clinics prefer to watch and see protocol and this rate is significantly higher than other settings. Major part of participants give their decisions according to journals/guidelines, second source of information is medical congress. 38.3% of the participants have been received continuing medical education. A 54.2% of PEDs, 51.4% of FP&GPs and 57.4% of ENTs stated that the first causative agent is S.pneumoniae and second one is NTHi. Among participants, 70.8% from state hospitals, 74.8% from university hospitals, 86.9% from private clinics, and 60.6% from primary care, thought that AOM is vaccine preventable disease.

Conclusion: Regarding to our results, continuing medical education about AOM guidelines needed to harmonize all interventions for all specialties. Vaccines seem to be hope for the prevention of AOM and further studies and education about vaccines for AOM needed.

P707

INFECTION FOLLOWING CEREBROSPINAL FLUID SHUNT INSERTION IN THE REPUBLIC OF IRELAND: A RETROSPECTIVE AUDIT

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Background: The Irish national paediatric neurosurgical service was established in 2008. A retrospective audit of infection arising following cerebrospinal fluid (CSF) shunt insertions, 2008 - 2009, inclusive, was conducted.

Methods: A standardised data collection form was completed for each procedure. US Centers for Disease Control and Prevention (CDC) definitions of surgical site infection (SSI) were utilised.

Results: Ninety-one children underwent 130 CSF shunt insertions, 65 (50%) using clindamycin & rifampicin-impregnated catheters. At admission, 63 (69%) were ≤1 year old and 62 (68%) weighed ≤10 kg. Post-operative infection followed 27 (21%) procedures; 12 episodes of SSI (25% MRSA) and 15 episodes of meningitis (0% MRSA). Eighty-eight percent of culture-positive SSIs were due to *S. aureus* and 77% of culture-positive meningitis episodes were due to coagulase-negative staphylococci. Average length of stay for infection following CSF shunt insertion was 27 days versus 17 days without. No infection-related deaths were recorded. SSI following shunt revision or replacement following temporary external ventricular drainage (EVD) (9%) was more common than following primary shunt insertion only (5%). Post-operative meningitis occurred in 18% of shunts replaced following EVD versus primary shunt insertion only (11%). Where antimicrobial-impregnated catheters were used, post-operative infection developed in 20% versus 23% for non-antimicrobial-catheters.

Conclusions: This study highlights the persisting problem of infection following CSF shunt insertion, despite use of antimicrobial-impregnated catheters particularly in young, small children. The predominance of coagulase-negative staphylococci causing meningitis following CSF shunt insertion has implications for empiric choice of therapy when treating suspected infection.

P708

INFECTION FOLLOWING EXTERNAL VENTRICULAR DRAIN INSERTION IN THE REPUBLIC OF IRELAND: A RETROSPECTIVE AUDIT

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Background: The Irish national paediatric neurosurgical service was established in 2008. A retrospective audit of infection arising following external ventricular drain (EVD) insertions, 2008 - 2009, inclusive, was conducted.

Methods: A standardised data collection form was completed for each procedure. US Centers for Disease Control and Prevention (CDC) definitions of surgical site infection (SSI) were utilised.

Results: Thirty-nine children (22 males) underwent 59 EVD insertion procedures, all impregnated with clindamycin and rifampicin. Twenty-one (35%) EVD insertions were because of suspected infection of an existing CSF shunt or EVD. On admission, 22 (56%) children were ≤ 1 year old and 22 (56%) weighed ≤ 10kg. Post-neurosurgical infection occurred following eight (14%) procedures. Eight episodes of meningitis occurred, of which five were culture-positive: Coagulase-negative staphylococci (2), *E. coli* (1), *C. albicans* (1) and one polymicrobial infection (*Enterococcus faecalis and Citrobacter freundii*). One child had three episodes of EVD meningitis. Gram-stain was not helpful in guiding empiric antimicrobial therapy as organisms were not seen on any of the eight CSF Gram stains. No episodes of superficial or deep incisional SSI were recorded. The average length of stay for EVD insertion complicated by infection was 44 days versus 24 days without. No infection-related deaths were recorded.

Conclusions: Despite the use of antimicrobial-impregnated catheters, EVD infection remains an important cause of prolonged hospital stay. The heterogeneity of microorganism isolated complicates selection of empiric therapy and highlights the continued need to adopt a multifaceted approach to infection prevention in paediatric patients.

P709

INFECTION FOLLOWING EXTERNAL VENTRICULAR DRAIN INSERTION IN THE REPUBLIC OF IRELAND: A RETROSPECTIVE AUDIT

K. Burns[1], J. Caird[2], D. Allcutt[2], M.T.A. Sattar[2], D. Crimmins[2], P. Gavin[3], K. Butler[3], M. Cafferkey[1], R. Cunney[1]

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Conclusions: Despite the use of antimicrobial-impregnated catheters, EVD infection remains an important cause of prolonged hospital stay. The heterogeneity of microorganism isolated complicates selection of empiric therapy and highlights the continued need to adopt a multifaceted approach to infection prevention in paediatric patients.

P710

RETROSPECTIVE REVIEW OF ACUTE CERVICAL LYMPHADENITIS AND PERI-PHARYNGEAL INFECTIONS IN CHILDREN

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Background and aims: Our aim was to describe the clinical presentation and analyze the management of acute cervical lymphadenitis and peri-pharyngeal infections in children.

Methods: This is a retrospective study of children aged 3 months to 18 years of age hospitalized in the general paediatric ward of the Créteil-Intercommunal Hospital between January 2003 and May 2010. The cases were selected based on the diagnosis (acute cervical lymphadenitis, suppurative cervical lymphadenitis, peri-pharyngeal abscess). The data collected were case history, clinical signs, laboratory tests, imaging, treatment and evolution.

Results: 75 children were hospitalized during this period. 57% had acute cervical lymphadenitis, 17.5% suppurative cervical lymphadenitis, 24.1% retropharyngeal or parapharyngeal abscess and 1.4% cervical necrotizing fasciitis. 72% were male. 83% were younger than 6 years. 96% had fever and 45% had stiff neck. 44% of abscesses occurred in children who had taken NSAIDs or corticosteroids versus 43% among children who had not. 47% of children over 3 years had a RADT for group A beta-haemolytic streptococci and 47% of the RADTs were positive. A neck CT scan with contrast in those children with stiff neck found an abscess in 65%. 10% of these children had a needle biopsy and 10% had surgical drainage. Bacteriology was positive in 10.6% with a predominance of Staphylococcus aureus and Streptococcus pyogenes. All patients received intravenous antibiotics and evolution was favourable regardless of surgery.

Conclusions: Neck CT scan with contrast, especially in children with stiff neck, is helpful in diagnosing and assessing the extent of the infection.

P711

STAPHYLOCOCCAL SCALDED SKIN SYNDROME A PAEDIATRIC EMERGENCY SITUATION - CASE REPORT FROM A SIX YEAR OLD GIRL

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The Staphylococcal scalded skin syndrome (SSSS) is more common in infants and small children, than in older children and adults. It is caused by staphylococcal toxins. Symptoms are burn-like bullae on the skin with following displacement. Fluid loss and super infection make the SSSS an emergency situation and life threatening disease. The top layer of the skin is involved in contrary to the differential diagnosis of Steven-Johnson-Syndrome. After recovery skin lesions heal without scars. Therapy consists of intravenous antibiotics, fluid management and prevention of further infections additional to pain treatment.

Case report: Six year old girl with large bullae at the sternal region. Initial treatment with Cefuroxime. Further bullae developed. At presentation we saw a seriously ill child. The lips bloody and dry, the mouth was unaffected from the inside. Tonsils hypertrophic and suppurative, conjunctivitis and multiple insect bites. In the history no special illnesses were reported. Blood count, signs of inflammation and other blood parameters (liver, kidney etc.) were normal. In the bullae Staphylococcus aureus was isolated, sensitive to Ampicillin/ Sulbactam.

Systemic antibiotic therapy with Ampicillin/ Sulbactam and Flucloxacillin, fluid balance, parenteral nutrition and pain management with Metamizol and Piritramid followed. Initial care of the child and the skin care were only possible in Ketanest/ Midazolam anaesthesia. The entire integument was involved except of the oral cavity. After ablation of the bullae the skin recovered completely without scars. In our case the invasion of staphylococcus may be assumed by tonsillitis or an infected insect bite.

P712

THE PRESENT STATUS OF TETANUS IN CHILDREN

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Background: Despite the widespread availability of a safe and effective vaccine against tetanus, this disease is still present in Romania with an incidence of 0.07 per 100,000 population and it is more rare in children.

Methods: A retrospective study (1990-2010) of hospitalized children with tetanus in 2nd Clinic of Infectious Diseases.

Results: We analyzed 18 cases (15 boys and 3 girls between 1 year 4 months to 13 years) with generalized tetanus. 10 children were incomplete vaccinated, and in one case the child had protective antibody titer. The incubation period was on average 7.9 days in cases with favorable evolution and 4.47 days in those who died. Patients who survived spent between 10 and 37 days (median 23 days) compared with 14 hours, 23 hours and 10 days in those who did not survived. The mortality rate was 16.7%. Death by cardiac arrest occurred in 2 cases and in one case by respiratory complications installed in the tenth day of hospitalization. All children received the vaccine and tetanus serum at admission, the wound was cleanedand wide debrided, they were treated with penicillin, diazepam and phenobarbital; 3 cases required assisted ventilation.

Conclusions:

1 - Tetanus must not be excluded on the basis of tetanus vaccination history or in the presence of a protective antibody titers;

2 - Factors associated with poor prognosis : short incubation period, period of onset < 48 h, tachycardia, fever> 39 ° C, frequent and durable muscle spasms, profuse sweating.

P713

STAPHYLOCOCCAL SUPERANTIGENS (ENTROTOXINS A, B, C &TSST1) IN SYNOVIAL FLUID OF PATIENTS WITH ARTHRITIS

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Objective: To determine the staphylococal super Antigens (SEA, SEB, SEC, TSST1) ELISA in synovial fluid of patients with arthritis:

Methods & materials: In a cross sectional study in pediatric and orthopedic ward of Rasoul/ hospitals in Tehran Iran (2008-2010).

Synovial fluid aspirated in 62 patients with arthritis. Staphylococal superantigens (SEA, SEB, SEC, TSST1) searched in synovial fluid by ELISA (ABcam USA) .Chi square values (CI 95%, $p< 0.05$) were calculated for all categorical variables.

Results: 27% (18/66) of cases diagnosed as bacterial arthritis upon positive culture / or direct gram stain smear in synovial fluid.

Positive culture obtained in 11 cases (17.7%) .Staphylococcal arthritis diagnosed in 7 cases (4 positive culture;3 positive direct smear).Staphylococcal superantigens detected in 39% of cases.SETA was the least common ones. No agreement observed between isolation of S.Aureus and presence of all S.aureus superantigens except SETA.

Conclusion: S.Aureus has a prominent role in arthritis. In cases without isolation of organisms from synovial fluid S.aureus toxins are detectable in synovial fluid. Failure in isolation of organisms are due to natural ungrowth of organism in synovial fluid, previous antibiotic usage or low technical methods for isolation.

P714

TOXIC SHOCK SYNDROME IN PICU: EXPERIENCE OF 20 YEARS

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Introduction: Toxic shock syndrome (TSS) is a rare complication of *Staphylococcus aureus* infection. Twenty per cent of the strains of *S. aureus* are capable of producing toxic shock syndrome toxin

Objective: We present an overview about patients with toxic shock syndrome (TSS) in our PICU at admission during the last 20 years.

Methods: 12 bed interdisciplinary PICU, University hospital;

Patients: 12 patients with TSS from 1990 to 2010; prospective, controlled study.

Patients were cohorted in groups of 3 years each to show changes by the time of observation. Time of ventilation, PICU and physiological scoring were monitored.

Results: 12 patients were elected in this study, mean age 9.5±7.9 years. Of this cohort 1 patient suffered from pneumonia, 2 patients suffered from small thermal injuries, which should be expected to heal uneventfully, and 9 occurred in young women with menstruation and tampon use. Their mean ICU duration was 14 days, mean time on ventilation was 3 days, PRISM III score at admission was 15. All patients survived. The patient with pneumonia was admitted 24 hours after the first symptoms and survived with residual symptoms.

Conclusion: TSS is a serious complication in children with uneventful bacterial infections. The patient's condition worsens very rapidly if shock therapy is delayed or inadequate and outcome might be poor as in the patient with late admission.

P715

" EFFECT OF HOME BASED CHILD CARE ON DIARREAL DEATHS IN A TRIBAL POPULATION: RESULT OF A FIELD TRIAL"

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Background: Melghat is tribal area in India with very high child mortality & malnutrition. The major causes of mortality & morbidity are infectious diseases like diarrhea due to scarcity of doctors. We developed Home Based Child Care (HBCC) model for tribal population to reduce children mortality and infectious diseases.

Aims:

1. To reduce diarrheal deaths by at least 35% in population of 14,120 of Melghat over 3 years.

2. To reduce case fatality rate of diarrhoea by at least 50% in population of 14,120 of Melghat over 3 years.

3. To reduce incidence of diarrheal diseases by 35% over 3 years.

Methods: Study-design was Randomised Control Trial . We selected 16 intervention (population 14,888) and 18 control (population 16,310) villages. Trained village health workers in intervention area treated diseases such as diarrhoea, dysentery, etc. Behaviour Change Communication programs were conducted.

Results: The incidence , number of deaths & case fatality rates due to diarrhoea in intervention area were reduced significantly from 1139 to 631 , 14 to 2, 1.23 % to 0.32% respectively ($p < 0.001$).Baseline mortality indices in control versus intervention areas were: NMR- 57.19 vs 50.93, IMR- 72.97 vs 94.9, & U5MR- 102.56 vs 143.52. After intervention NMR, IMR & U5MR were significantly decreased in intervention area to 29.2, 44.64 & 58.04 respectively($p < 0.05$).

Conclusions: HBCC resulted in significant decrease in children mortality due to diarrheal deaths & incidence of diarrhoea. Our model is replicable for reducing children mortality due to diarrhoea in other backward part of world.

P716

RHADOMYOLYSIS AND BRADYCARDIA IN A CHILD WITH DENGUE FEVER AFTER TRAVEL TO INDIA

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Rhabdomyolysis and relative bradycardia due to dengue virus infection are common features, but these clinical findings were rarely described in children, especially when presenting as an imported disease. We report about a fourteen year old boy with generalized severe muscle pain after a trip to India. During his trip he had developed fever and macrohaematuria was observed. On presentation, clinically, there were no pathological findings apart from bradycardia (< 60 bpm). The patient had thrombocytopenia and biochemistry showed marked elevation of creatine kinase (>14,000 U/l) and mild elevation of liver enzymes. Dengue virus infection was confirmed by serology and initial presumptive antibiotic therapy was stopped. With hydration therapy creatine kinase and transaminases revolved quickly and thrombocytes normolized. Persisting bradycardia indicated cardiac work-up, which showed no functional, morphological or electrophysical pathology.

There are reports about severe rhabdomyolysis and cardiac involvement in adult and paediatric patients with dengue fever, largely from endemic countries. To our knowledge, although the residual symptoms were mild, the clinical picture of rhabdomyolysis with presumable mild myocardial involvement has not been described in imported paediatric denguen fever.

The diagnosis could have been easily missed without taking a travel history. In the absence of classical clinical signs, dengue virus infection should be suspected in cases with symptoms of rhabdomyolysis and elevated creatine kinase in connection with fever after visiting dengue endemic countries.

P717

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P718

AUTOCHTHONUS PLASMODIUM VIVAX MALARIA IN 2 SIBLINGS. FIRST REPORTED PAEDIATRIC CASES AFTER 20 YEARS OF ERADICATION OF MALARIA IN GREECE

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Background and aims: During the last 10 years, less than 20 cases of autochthonous transmission of malaria have been reported in the EU, despite the presence of potential anopheline vectors in some countries.

Methods: We report the first two cases of autochthonous Plasmodium vivax malaria in children the last 20 years in Greece, hospitalised in our paediatric department in September 2010.

Results: An 8 year old boy of Gypsie origin was admitted because of fever with rigors lasting for several days. On examination he looked pale and had mild hepatomegaly and splenomegaly. FBC revealed WBCs within normal limits, thrombocytopenia and mild anemia. Bilirubin, LFTs and coagulation screen were normal. Examination of stained thick and thin blood films showed intracellular forms of parasites of Plasmodium vivax , verified with PCR testing.

Two days later his little sister aged 3 years, was admitted with similar symptoms. On examination she looked pale and her liver and spleen were enlarged. Blood smears revealed intracellular forms of parasites (rings, trophozoites, amoeboid forms, gametocytes) of *P.vivax* proved by PCR . There was no history of recent travel in malaria endemic countries.

Both children were treated with combined regiment of hydroxychloroquine followed by primaquine and completed the treatment uneventfully.Repeat PCR on the fifth day of treatment were negative.

Conclusion: Malaria is considered to be eradicated in Europe. The diagnosis is, therefore, likely to be delayed or missed in patients without a relevant travel history. These rare occasions pose a challenge to local and public health authorities.

P719

COMPARATIVE STUDY OF PEDIATRIC URINARY TRACT INFECTIONS CAUSED BY COMMUNITY-ACQUIRED EXTENDED-SPECTRUM BETA-LACTAMASE -PRODUCING AND NON-PRODUCING BACTERIA

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Introduction: Community-acquired extended-spectrum beta-lactamase-producing bacteria (CA-ESBL) are emerging as a cause of urinary tract infections (UTI) worldwide. However, risk factors and clinical parameters have not been defined for children with ESBL UTI. The aim of the study was to evaluate clinical characteristics and associated risk factors for UTI due to CA-ESBL.

Methods: A retrospective chart review combined with telephonic questionnaire. Children hospitalized in the Western Galilee Hospital with UTI due to CA-ESBL between 12/07-11/10 were included. Data were compared with a randomly-selected control group of children with non-ESBL UTI. The standard protocol of ampicillin+gentamicin was evaluated.

Results: Of 484 children with UTI, caused by *E. coli* and *Klebsiella spp*., 16 (3%) had UTI caused by CA-ESBL. There were no significant differences between the groups in demographics, creatinine, urinalysis and infection type (pyelonephritis/cystitis). Children with CA-ESBL UTI were hospitalized for a longer duration (5.8 vs. 3.5 days, p=0.004) and had higher rates of recent hospitalization (25% vs. 6% p=0.059), previous UTI (38% vs. 13% p=0.037), urinary tract anomalies (31% vs. 6% p=0.019) and UTI prophylaxis (37% vs. 2% p=0.001) compared with children suffering from non-ESBL UTI (n=48). Resistance rates for gentamicin were higher in the CA-ESBL group (56% vs. 8% p< 0.001); amikacin resistance was low (6% vs. 0% p=0.25).

Conclusions: Children with urinary tract anomalies, previous hospitalization or UTI and those receiving antimicrobial prophylaxis appear to be at higher risk for CA-ESBL UTI. Children with these risk factors may be better treated empirically for UTI with amikacin instead of gentamicin.

P720

ANTIBIOTIC RESISTANCE PATTERNS IN ESCHERICHIA COLI URINARY TRACT INFECTIONS IN HOSPITALISED CHILDREN FROM ARAD COUNTY, ROMANIA

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Background and aims: E. Coli is the major bacteria incriminated for urinary tract infection in children. The increase of the antibiotic resistance of the E. Coli strains in Arad County is an alarming phenomenon.The aim of the study was to establish a local guideline in urinary tract infection with E. Coli in hospitalized children in Arad County based upon the variation of antibiosensitivity and antibioresistance of this bacterial pathogen.

Methods: The group consisted of 82 E. Coli strains, isolated from children with acute urinary tract infections. The children were admitted in the Pediatric Clinic of Arad during a period of 4 years, from January 2006 to December 2009. The retrospective study used clinical data. The diffusimetric antibiotic test was performed according to the existing standards at the moment.

Results: The E. Coli strains developed the highest sensitivity for Norfloxacin (57 /69,51%), Ciprofloxacin (55/67,07%), Ofloxacin (55/67,07%), Gentamicin (52/63,41%) and Nitrofurantoin (50/60,97%). The lowest sensitivity was noticed for Ampicillin (0/0%), Cephalexin (7/8,53%) and Colistin (11/13,41%). A high resistance was confirmed for Colistin (48/58,53%), Amoxicillin + Clavulanic Acid (33/40,24%), Co-trimoxazole (27/32,92%) and Ampicillin (25/30,48%)., while Amikacin (0/0%), Norfloxacin (4/4,87%) and Nitrofurantoin (4/4.87%) had the lowest resistance.

Conclusions:

1 The Fluoroquinolones, Gentamicin and Nitrofurantoin have the maximum therapeutic benefit.

2 The use of antibiotics that induce high resistance must be stopped in our region (Ampicillin, Colistin, Co-trimoxazole and Amoxicillin + Clavulanic Acid).

P721

ANTIMICROBIAL THERAPY IN URINARY TRACT INFECTION AMONG CHILDREN IN FIRST TWO YEARS OF LIFE

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Background and aims: Urinary tract infection (UTI) is the most common bacterial infections affecting humans. Toddler UTI represent a major issue, because of the renal function impairment that recurrent infections can lead to. The aim was to compare data from our 2006 study and a 2009 one regarding UTI.

Methods: We studied in 2006 a cohort of 41 children and in 2009 a group of 34 with UTI in first two years of life, focusing on the types of germs, their sensitivity to antibiotics, and association with other factors. All of the cases were without renal malformations at ultrasonography. All the cultures were performed using standardized bag collectors.

Results: *E.coli* was resistant in 87% of cases to Ampicillin, and more than 60% to TMP/SMX (2009). In 2006, 54.5% of the *E. coli* presented resistance to 2 antibiotics (Ampicillin, TMP/SMX). In 2009, *Proteus* has 72% resistance to Colistin, higher than in 2006, and also for Ampicillin, and aminoglycozides. *Klebsiella* was proven resistant to: Ampicillin, aminoglycozides, and Nalidixic acid (2006). In 2009 *Klebsiella* showed increased resistance to Ampicillin-86%, TMP/SMX-87%.

Conclusions: Male patients were most frequently affected (65.85%) in the age group of 0 - 2 years in 2006 and the same in 2009 - 67.7%. UTI was produced generally by the same germs that has in time increased resistance to Ampicillin, TMP/SMX and some aminoglycozides. The strains responsible for the community acquired infections were initially sensitive to the first choice antibiotics, but most of them developed highly resistance to these treatment.

P722

DETERMINATION THE CUT-OFF VALUE OF URINARY SOLUBLE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS-1 LEVELS FOR DIAGNOSIS OF URINARY TRACT INFECTIONS

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Objective: To evaluate whether soluble triggering receptor expressed on myeloid cells (sTREM-1) in urine can serve as a biomarker for discrimination between bacterial urinary tract infection from other causes of urinary signs and symptoms.

Design: Prospective study of diagnostic accuracy.

Methods: Urine was collected from 79 children suspected to have urinary tract infection for the first time, early in their admission. In 52 of them the diagnosis were confirmed and in 8 patients were rejected. 19 patients had probable or possible diagnosis till discharge. Urinary sTREM-1 levels were measured by enzyme-linked immunosorbent assay.

Results: Urine sTREM-1 level were higher in patients with confirmed diagnosis (median 500 pg/ml,range 30-5600 pg/ml) than those with rejected infection(median 406 pg/ml,range 50-2000pg/ml). The diagnostic accuracy area under the receiver operating characteristic curve, using sTREM-1 to differentiate between the presence and absence of bacterial urinary tract infection, was 0.72(95% confidence interval, 95%CI= 0.53-0.91; p< 0.046). A sTREM-1 cutoff value of 132.5 pg/ml correlated with sensitivity and specificity values of 79.2 %(95% CI= 65.9-89.2) and 62.5%(95% CI= 24.5-91.5), respectively. Positive likelihood ratio was 2.11 and negative likelihood ratio was 0.33.

Conclusion: Measuring sTREm-1 in urine may be a valuable additional approach to accurately diagnose urinary tract infection and identify patients who need more harmful investigation and prolonged follow up. Therefore a larger study especially with more rejected cases as control is needed.

P723

URINARY TRACT INFECTION: DIAGNOSTIC DILEMMAS AND EMERGING TRENDS

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Background and aims: Urinary Tract Infection may be difficult to recognise in children because the presenting symptoms and signs are non-specific. Urine collection and interpretation of urine tests in children are not easy and it may not always be possible to unequivocally confirm the diagnosis. We evaluated our practise of diagnosis and management.

Method: 73 culture positive samples were identified using microbiology database over 2009-2010. We retrospectively analysed the case notes and microbiology database. 36 samples were clean catch specimen and these were included in our analysis. In 36 (49%) patients cotton wool was used to collect urine sample and were excluded.

Results: 30% were male and 70 % female. 28/36(77%) children had first episode.

On dipstick urinalysis, 18/33(54%) were positive for leukocyte esterase, 10/33(30%) were positive for nitrites and only 8(22%) were positive for both.

28/36(77%) had more than 5 leucocytes on microscopy. 8 children who had no leucocytes were < 2 years.

EColi 32/36(88%) was the commonest. Other organisms included Enterobacter, Klebsiella, Entercoccus and Proteus.

69% were resistant to amoxicillin, 33% to Trimethoprim and 30% to Co-amoxiclav.

Conclusion: In children with confirmed UTI, dipstick showed only half were positive for leukocyte esterase and one-third for nitrites. Negative microscopic findings were seen in children less than 2 years. This study highlights the practical difficulties of diagnosing UTI on dipstick especially in younger children.

Resistance to commonly used antibiotics showed an increase. Knowledge of local strains of organism and resistance to antibiotics would aid to choose the appropriate treatment.

P724

PREDICTIVE ABILITY OF PROCALCITONIN FOR ACUTE PYELONEPHRTITIS AND LATE RENAL SCARS IN CHILDREN WITH UTI: META-ANALYSIS ON INDIVIDUAL DATA

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Background: Urinary tract infections (UTIs) are common bacterial infections in childhood, and may lead to acute pyelonephritis (APN) and then late renal scarring (LRS). Prompt high-quality diagnosis of APN and later identification of children with LRS are important to keep them from future complications. DMSA scan is the gold standard imaging but is not routinely performed. An easier tool, such as procalcitonin, would be then useful. We thus aimed to investigate the predictive ability of procalcitonin for both APN and LRS, in children with UTI.

Methods: A systematic review and meta-analysis of individual patient data gathered all data on children with UTI, procalcitonin measurement and DMSA scan.

Results: 1011 patients (APN in 61%, LRS in 26%, 33% of boys,) were included from 17 studies (13 centres). Procalcitonin as continuous, class and binary variable was associated to both APN and LRS ($p < 0.001$), and had a significant higher ($p< 0.05$) AUC ROC than CRP and white blood cell (WBC) count for both too. A procalcitonin >=0.5 ng/mL yielded to an aOR=7.9 (95%CI, 5.8-10.9) with a 71% sensitivity (95% CI, 67-74), and a 72% specificity (95%CI, 67-76) for APN. A procalcitonin ³0.5 ng/mL was significantly associated to LRS (aOR=3.4; 95%CI, 2.1-5.7) with a 79% sensitivity (95%CI, 71-85), and a 50% specificity (95%CI, 45-54).

Conclusion: PCT had an interesting predictive ability (better than CRP, and WBC) to selectively identify both children who had APN in the early stage of UTI, and then those with LRS.

P725

PREDICTION OF HIGH-GRADE VESICO-URETERAL REFLUX AFTER A FIRST UTI IN CHILDREN: EXTERNAL VALIDATION OF A CLINICAL DECISION RULE

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Background: Predicting vesico-ureteral reflux (VUR) >=3 at the time of the first urinary tract infection (UTI) would make it possible to restrict cystography to high-risk children. We previously derived the following clinical decision rule for that purpose: cystography should be performed in cases with ureteral dilation and a serum procalcitonin level ≥0.17 ng/mL, or without ureteral dilatation when the serum procalcitonin level ≥0.63 ng/mL. The rule yielded a 86% sensitivity with a 46% specificity. We aimed to test its reproducibility.

Methods: A secondary analysis of prospective series of children with a first UTI. The rule was applied to each patient, and predictive ability was calculated.

Results: The study included 413 patients (157 boys, VUR >=3 in 11%) from eight centers in five countries. The rule offered a 46% specificity (95% CI, 41 to 52), not different from the one in the derivation study. But, the sensitivity significantly decreased to 64% (95%CI, 50 to 76), leading to a difference of 20% (95%CI, 17 to 36). In all, 16 (34%) patients among the 47 with VUR >=3 were misdiagnosed by the rule. This lack of reproducibility might come from difference regarding inflammatory parameters (CRP, PCT) between derivation and validation population, and from a lack of robustness of inter-observer variability of the ultrasonographic criterion (ureteral dilation) included in the rule.

Conclusions: The rule built to predict VUR >=3 partially failed to be reproduced, some refinement regarding the time of PCT measurement and the inter-observer variability for ureteral dilation might be warranted.

P726

CAN URINARY NITRITE RESULTS BE USED TO CONDUCT ANTIMICROBIAL OPTION FOR URINARY TRACT INFECTION IN CHILDREN?

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Background and aims: Urinary tract infection (UTI) is a common disease in children. Rapid diagnosis and proper treatment can prevent its serious complications such as chronic renal failure. This study was performed to determine the relationship between urinary nitrite result and bacterial resistance to antimicrobial drugs in UTI of children.

Methods: In this cross-section study 119 children younger than 12 years with UTI were evaluated in Qazvin children hospital. Patients were divided into negative and positive nitrite groups depend on urinary nitrite test result. Rate of antibiotic resistance in the two groups were compared.

Results: Sixty seven patients were in the negative nitrite group and 52 in the positive nitrite group. In the nitrite negative group resistance rate to ceftriaxone, trimethoprim sulfamethoxazole, ampicillin, gentamicin, amikacin, nalidixic acid, cephalothin and nitrofurantoin were 7.5%, 31.3%, 50.7%, 11.9%, 9%, 3%, 14.9% and 11.9%, respectively. These values in the nitrite positive group were 21.2%, 28.8%, 63.5%, 7.7%, 5.8%, 1.9%, 9.6%, and 3.8%, respectively($P>0.05$).

Conclusions: This study showed that there is no correlation between urinary nitrite results and bacterial resistance to antimicrobial drugs. Therefore, initial antibiotic selection should not be determined based on the urinary nitrite result.

P727

EMERGENCE OF ESBL PRODUCING ORGANISMS IN PAEDIATRIC UTI

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Background and aims: Limited data are available regarding community-acquired infections due to extended spectrum beta-lactamase producing gram-negative pathogens (ESBL-GN), particularly in children. We studied the evolution of ESBL-GN recovered from children with UTI in a 170-beds tertiary care paediatric hospital in Brussels and analysed the potential impact on empirical antibiotic treatment.

Methods: ESBL-GN were recorded prospectively for the years 2003-2009. Patients with sampled urine growing an ESBL-GN in the first 24 hours were community acquired. UTI cases were defined as positive microscopic examination and culture obtained from catheterised sample, mid-stream or in very rare occasions bags in children with microscopic examination showing more than 500 leucocytes and a dipstick performed directly on the sample showing both positive leukocyte esterase and nitrites. Epidemiological and clinical data were completed retrospectively.

Results: During the study period, 20 demonstrated UTI caused by ESBL-GN were community-acquired, all occurring from 2006 onwards. Among these 20 children, 13 had risk factors for UTI (urinary tract abnormalities or recurrent UTI); 11 had pyelonephritis and were treated IV. Empirical therapy (amoxi-clavulanate, second generation cephalosporin) was inappropriate in 3 children, all with cystitis, all of them showed a favorable evolution. *E. coli* was isolated in all but one case due to a *K. pneumoniae*.

Conclusion: ESBL-GN, particularly *E. coli,* emerge as a cause of community-acquired UTI in children. Further studies are needed to determine how these common paediatric infections will be treated empirically in the future.

P728

FACTORS RELATED TO AND CLINICAL OUTCOME OF URINARY TRACT INFECTIONS CAUSED BY EXTENDED-SPECTRUM ß-LACTAMASE BACTERIA (ESBL)

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Aims: The isolation of ESBL has been increasingly reported and sometimes raises questions of management. The aims of this study are to determine whether there are factors related to isolates in urine cultures (UC) and what is their clinical outcome.

Methods: Retrospective study of the ESBL isolates from a prospective registry of positive UC, conducted in the pediatric emergency department of 2 academic tertiary care hospitals between 01/01/2008 and 31/12/2010. All UC were collected by a sterile method. All cases were followed.

Results: We analyzed 41 ESBL-positive UC. Thirty (73.2%) were female. The mean age was 37.17 months (1-127), with 51.2% younger than 12. Twenty cases (48.8%) had one or more nephrourological comorbid conditions: 17 previous urinary tract infections (UTI), 9 vesicoureteral reflux, 10 received antibiotic prophylaxis, 8 other. The final diagnoses were: 24 (58.5%) pyelonephritis, 14 (34.1%) lower UTI, 3 asymptomatic bacteriuria (7.4%). The most common bacteria was Escherichia coli, 38 (92.7%). The antibiogram showed sensitivity to aminoglycosides 28 cases (68.3%), 26 (63.4%) to cotrimoxazole and 12 (29.3%) to quinolones. Nine patients (22%) were admitted and treated with parenteral antibiotics. The remaining 32 were treated as outpatients, 29 with oral antibiotics and 3 without treatment. None of these cases were subsequently hospitalized. There were no bacteremias. All progressed well clinically.

Conclusions: Almost half of our patients with ESBL-UC had nephrourological comorbid conditions. Despite antibiotic resistances, all patients did well. Although clinical follow-up is required, these patients can be managed initially with the usual pattern of other UTI.

P729

AN EPIDEMIOLOGIC-CLINICAL STUDY ON THE URINARY TRACT INFECTIONS IN CHILDREN

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Material and method: We carried out an epidemiologic clinical study on the urinary tract infections (UTI) in the 0-16 year-old children, admitted to the 2nd Pediatric Clinic of the Emergency County Hospital Craiova from 01.01.2009 to 31.12.2010. We decided on 3 groups of study: G1 (0-1 year), G2 (1-6 years), G3 (>6years).

Results: 76 children with UTI were admitted (1.5% of all the admitted cases). G1: 20 cases (26.3%), F/M=9/11, U/R = 11/3. G2: 14 (18.4%), M/F=7/7, U/R= 16/26. G3: 42 (56.3%), F/M=34/8 (sex ratio 4.25), U/R=16/26.

Clinical findings G1: fever in 16(80%), unrest 8(40%), vomiting 4(20%), food rejection 4(20%), convulsions in 1(5%); G2: fever in 10(71.4%), abdominal pains 8(57.1%), dysuria 6(42.9%), pollakiuria 4(28.6%); G3: dysuria 36(85.7%), pollakiuria 30(71.4%), abdominal/lumbar pains 32(76.2%), fever 25(59.5%), hematuria 10(23.8%). UTI location in G1: 20(100%) upper; G2: upper 10(71.4%), lower 4(28.6%); G3: upper 19(45.2%), lower 23(54.8%).

Etiology G1: E. coli 12(60%), Klebsiella 6(30%), Proteus 2(10%); G2: E. coli 6, Proteus 3, Klebsiella 1; G3: E coli 15, Staphylococcus aureus 2, Klebsiella, Proteus 1 case each. Favoring factors G1: phimosis 3, renal malformations 2, dystrophy 4, prematureness 2; G2: phimosis 1, renal malformations 1, severe psychomotor retardation 1; G3: renal lithiasis 16, severe psychic retardation 1 case.

Conclusions: More than half of the UTI cases were registered in G3. UTI slightly prevailed in males in G1 (sex ratio M/F 1.2) and significantly in females in G3 (sex ratio F/M 4.25). E. coli was the most frequent stem isolated in UTI.

P730

HIGH EXRPESSION OF TLR2, TLR4 ON PERIPHERAL BLOOD MONOCYTES IN CHILDREN SUFFERING FROM URINARY TRACT INFECTIONS

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Background: Urinary tract is one of the most intractable mucosae sites for bacteria to colonize. Toll-Like Receptors (TLRs) appear to play a potential role in innate immunity protecting the mucosal barrier against bacterial attacks. The aim of the study was to determine TLR2 and TLR4 expression during the acute phase of Urinary Tract Infections (UTIs) in children.

Methods: 67 children free of immunologic or any other chronic illness were enrolled in the study: 36 patients (0,5-14 years of age, 16 boys) who suffered from acute UTIs and 31 age and gender matched healthy controls. 9/36 patients had anatomic genitourinary anomalies. Percentages of T and B lymphocytes, Natural Killer cells (NK), along with expression of TLR2 and TLR4 on monocytes were estimated using flow cytometry. Serum immunoglobulins and IgG subclasses were measured by nephelometry.

Results: Phenotypic analysis showed that the percentage of CD14+/TLR2+ was markedly elevated among patients(mean ±SDEV: 87,9%±10,9%) compared to controls (mean ±SDEV: 79%±12%) and the difference was statistically significant ($p< 0,05$). In addition, a significantly higher percentage of CD14+/TLR4+ was observed in patients (mean±SDEV: 88,1%±10,3%) compared to controls (mean ±SDEV: 80%±10%)($p< 0,05$). No significant differences in the TLR2 and TLR4 expression between the patients with genitourinary anomalies and those without, were found. Percentages of T, B, NK and levels of immunoglobulins and IgG subclasses in both patients and controls were normal.

Conclusions: TLR2 and TLR4 are highly expressed on peripheral blood monocytes during acute UTIs and may play a pivotal role in their pathogenesis mediating rapid immune response.

P731

POPULATION BASED STUDY ON THE IMPACT OF THE 7V-PCV ON NASOPHARYNGEAL CARRIAGE OF *STREPTOCOCCUS PNEUMONIAE* IN HEALTHY JORDANIAN INFANTS (2009-2010)

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Background and aims: Colonization of *Streptococcus pneumoniae* in infants is a serious health problem, since dissemination to other body parts can cause serious infections. Aims are to study the impact of the 7v-PCV on NP-carriage of pneumococci among healthy infants attending the DCC of Ajlun, north Jordan; determine carriage rates, resistance, and coverage of PCVs.

Methods: A 2+1 scheme of vaccination was performed at ages of 2, 4 and 10 months. NP-swabs were taken from 415 healthy infants in Ajlun at ages of 2, 10, and 13 months of age between May 2009 and September 2010. Identification done according to morphology, bile solubility and optochin sensitivity.

Results: Carriage, resistance and coverage rates are shown in the table. The impact of vaccination was noticed on reducing the resistance of Penicillin, Cefotaxime, Clarithromycin, and Clindamycin by 6%, 2.4%, 11.4%, and 17.7%, respectively. Coverage of the 7v-PCV after the last injection was reduced by 18.3%, while an increase of the 19A from 2.8% to 10.7% was noticed. *erm*(B) was detected in 50%, *mef*(A) in 36.4%, both *erm*(B) and *mef*(A) 4.5% and 9% were negative for both.

Conclusions: The high carriage rate in early ages combined with high resistance are serious problems, but it is necessary for predicting the possible impact of different conjugate vaccines.

Phase	PEN R (%)	CETA R (%)	CLI R (%)	CLA R (%)	SXT R (%)	Coverage of 7v-PCV (%)	Coverage of 10v-PCV (%)	Coverage of 13v-PCV (%)	Carriage (%)
Phase I	82.6	7.3	40.4	22.0	56.0	32.1	32.1	50.5	26.3
Phase II	87.9	4.8	55.7	36.3	58.1	33.9	33.9	55.7	29.9
Phase III	82.0	4.9	44.3	18.0	62.3	14.8	15.6	36.9	29.4

[Resistance, coverage of PCVs and carriage rates]

P732

DOSE-RANGING PAEDIATRIC STUDY: IDENTIFICATION OF A NOVEL MF59-ADJUVANTED 2A2B QUADRIVALENT INFLUENZA VACCINE

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Background and aims: Influenza B viruses from 2 antigenically dissimilar lineages often co-circulate, and there is no cross-protection between these lineages. Ideal paediatric vaccines are safe and offer long-term protection against all circulating influenza virus strains. This study aimed to assess the safety and immunogenicity of different combinations of MF59 adjuvant and/or a second B strain added to high or low doses of TIV.

Methods: 410 healthy children aged 6-35 months were randomly assigned to receive vaccines including combinations of 7.5µg or 15µg doses of the WHO recommended influenza strains, 0%, 12.5%, 25%, 50%, 100% of the MF59 adjuvant dose approved for elderly adults in FLUAD, and, for the quadrivalent vaccine, the addition of 7.5µg or 15µg of a second B strain. Antibody levels were measured by haemagglutination inhibition at Days 1, 29, and 50. Adverse reactions were recorded for 7 days after each vaccine dose, and adverse events were reported throughout the study period.

Results: The addition of a second B strain was immunogenic and did not affect immunogenicity of the other strains. MF59-adjuvanted formulations, even at low levels of MF59, induced superior antibody responses compared with non-adjuvanted influenza vaccines. A higher immune response was observed with increasing MF59 dose. There was no increase in adverse reactions with increasing MF59 dose, antigen dose, or the addition of a second B strain.

Conclusion: MF59-adjuvanted quadrivalent influenza vaccine appears a viable combination for use in young children. MF59 dose response supports the use of half the adult MF59 dose in children.

P733

MF59®-ADJUVANTED H1N1 VACCINES IN HEALTHY CHILDREN 6 MONTHS TO 17 YEARS OF AGE: 6 MONTH FOLLOW-UP SAFETY DATA

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Background and aims: The A(H1N1) influenza disease burden in the paediatric population highlights the need for effective and safe vaccination for this age group. This study reports the 6 month follow-up safety data after 2 vaccine doses of egg-derived (Focetria®) or cell-culture-derived (Celtura®) MF59-adjuvanted H1N1 vaccines and a non-adjuvanted comparator in children and adolescents 6 months to 17 years of age.

Methods: Safety data from 2 clinical studies involving 1530 children (Focetria n=778 enrolled, Celtura n=752 enrolled) were included in the analyses. Study participants were randomly assigned to receive, at a 21 day interval, two doses of either 3.75µg antigen with 50% of the standard MF59 dose, 7.5µg antigen and the standard MF59 dose, or 15µg antigen of H1N1 vaccine without adjuvant (only older age cohorts 3-17 yrs). Safety analyses at the 6 month follow-up included SAEs, onset of chronic disease, and adverse events leading to study withdrawal.

Results: 6 month follow-up data were available for 85%-98% of subjects across vaccine groups. Overall, 75 SAEs, 13 AEs that led to withdrawal, and 13 cases of onset of new chronic diseases were reported in the combined age cohorts, of which 5 SAEs, 6 AEs and 2 cases of onset of chronic diseases were considered as possibly related to the vaccine (mainly typical post vaccination reactions). No deaths were reported.

Conclusions: The 6 month follow-up safety data of the present study support the good safety profile for MF59-adjuvanted H1N1 vaccines in healthy children and adolescents 6 months to 17 years of age.

P734

SAFETY PROFILE OF M59®-ADJUVANTED VACCINES VERSUS NON- ADJUVANTED VACCINES: POOLED DATA FROM PAEDIATRIC CLINICAL TRIALS

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Background and aims: Immune responses conferred by conventional non-adjuvanted trivalent inactivated vaccines are often suboptimal in children, highlighting the need for safe and effective vaccines in this population. In the elderly, MF59® has been successfully used as an adjuvant in the seasonal influenza vaccine Fluad®, and may overcome current limitations in paediatric vaccines. This study aimed to assess the safety profile of MF59-adjuvanted influenza vaccine (Fluad) and non-adjuvanted influenza comparators, based on pooled data from paediatric trials.

Methods: Safety data from 6 studies from the clinical development program of Fluad in children were integrated and divided into age groups: 6 to < 36 months, 3 to < 9 years, and 9 to < 18 years. Local and systemic adverse reactions were recorded for 7 days after vaccination, and (S)AEs were recorded throughout entire study periods.

Results: The total safety population consisted of 4,840 children, 2,575 were vaccinated with MF59-adjuvanted vaccine and 2,265 with a non-adjuvanted flu comparator. For all age groups, overall reactogenicity was higher following MF59-adjuvanted vaccine than for non-adjuvanted vaccines. However, most reactions were mild to moderate and self limiting. AE rates were similar between MF59-adjuvanted and non-adjuvanted vaccines in children 6 < 36 months, and 3 to < 9 years, and higher in non-adjuvanted vaccine groups in children 9 < 18 years. Overall, only few SAEs were reported. One death occurred in the non-adjuvanted comparator group, considered as not vaccine related.

Conclusion: Integrated analyses from 6 paediatric trials support the general safety and tolerability of MF59-containing vaccines.

P735

THE ADHESION TO THE SECOND DOSE OF INFLUENZA ON CHILDREN YOUNGER THAN 9 YEARS OLD IN THE INFLUENZA PANDEMIC

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Objective: To assess adherence to influenza vaccine - 2010 (two doses) , compared to 2009 in children aged 6 months - 9 years old in private vaccination.

Methods: Retrospective descriptive study from thegathering of information in the database of private vaccination about the influenza vaccination (two doses) at the age of 6 months - 9 years old. The data are related to 7 Brazilian states and the vaccination occurred between January and December of 2009 and Mach and December of 2010.

Results: In 2009, from 2373 vaccinated children, 1015 (43%) received two doses. 52% were male. 30 (3%) were aged between 7 months - 1 year and 11 months, 872 (86%) between 2 - 5 years and 11 months, and 113 (11%) between 6 - 9 completed years. In 2010, from 3666 vaccinated children, 3097 (84%) took two doses; 1490 (48%) were male and were distributed on the following age groups: 596 (19%) from 7 moths - 1 year and 11 months, 1513 (49%) from 2 years - 5 years and 11 months, and 971 (32%) from 6 - 9 years old.

Conclusion: Pandemic caused by H1N1 in 2009 induced mainly hospitalization and deaths in the pediatric groups, hence, there have been innumerous educative acts from the public and private health sectors, urging people to vaccinate. Our casuistry showed, in 2010, a greater adherence by families who sought the private sector to vaccinate their children, realizing the full vaccination schedule (two doses) proposed by the Brazilian Ministry of Health

P736

REACTOGENICITY AND SAFETY OF MULTICOMPONENT MENINGOCOCCAL SEROGROUP B VACCINE (4CMENB) ADMINISTERED WITH OR WITHOUT ROUTINE INFANT VACCINATIONS IN DIFFERENT SCHEDULES

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Background: An investigational serogroup B meningococcal vaccine containing 3 recombinant-proteins plus outer-membrane-vesicles (4CMenB) is in late-stage development. We studied the reactogenicity of this vaccine when administered at 2, 4 and 6 months of age (concomitantly with and separately from routine-vaccines) and at 2, 3 and 4 months of age (concomitantly with routine-vaccines).

Methods: An open-label, parallel-group, multi-centre study was conducted with randomisation of 1885 participants 2:2:1:1 to receive

i) 4CMenB at age 2, 4 and 6 months concomitantly with routine-vaccines (7-valent pneumococcal-vaccine and a combined DTaP/HepB/IPV/Hib-vaccine)

ii) 4CMenB at 2, 4 and 6 months administered separately from routine-vaccines (given at 3, 5 and 7 months)

iii) 4CMenB with routine-vaccines at 2, 3 and 4 months or

iv) routine-vaccines alone.

Local and systemic reactions were recorded for 7 days after each vaccination.

Results: Fever (≥38°C) was found in 44%-61% of participants after each dose of 4CMenB given concomitantly with routine-vaccines, in 26%-41% receiving 4CMenB alone and in 23%-36% with routine-vaccines alone. A similar pattern was seen for the percentage of participants with irritability (66%-79% 4CMenB and routine-vaccines, 53%-63% 4CMenB alone, 44%-57% routine-vaccines only). Local reactogenicity was similar between all groups. Four seizures (none febrile) were reported within 48 hours after vaccination; one after 4CMenB and routine vaccines, one after 4CMenB alone and two after routine-vaccines alone.

Conclusion: 4CMenB when administered alone had a reactogenicity profile which was comparable to that produced by routine-vaccines, but systemic reactogenicity was increased when the study-vaccine was combined with routine-vaccination. No major safety concerns were raised.

P737

IS RECENT INFLUENZA VACCINATION A RISK FACTOR FOR HOSPITAL ADMISSION WITH INFLUENZA?

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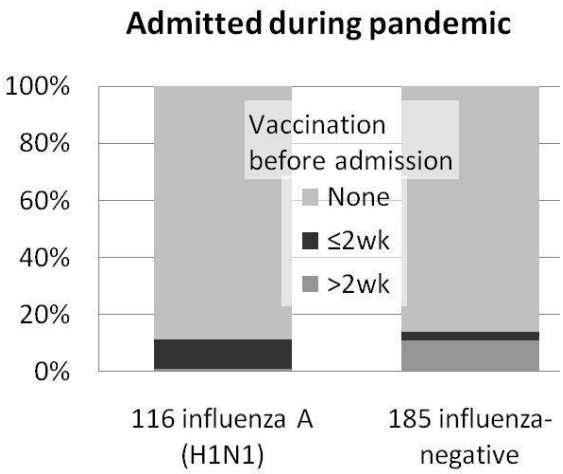
Background and aims: We have previously reported that adjuvanted pandemic influenza A (H1N1) vaccine (Pandemrix®) was efficacious against hospitalisation after more than 14 days. We observed that several children hospitalised with influenza were vaccinated less than 14 d before admission.

Methods: We compared children hospitalised with pandemic influenza to influenza-negative children hospitalised during the same time period (28 Oct - 4 Dec 2009) regarding rates of and time since vaccination.

Results: The results are presented in the figure.



[Vacc1]

Significantly (P< 0,05) more influenza-positive children than influenza-negative children were vaccinated during the 2-week period preceding admission.

Conclusion: The 2 weeks immediately following vaccination may constitute a window of increased risk during an on-going epidemic.

P738

THE USE OF A FLUORESCENT MICROSPHERE-BASED MULTIPLEX IMMUNOASSAY FOR THE QUANTITATION OF VACCINE SERUM ANTIBODIES

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Background and aims: To improve multiple testing of humoral immunity against vaccine components of the national immunisation program, rapid and simple fluorescent microsphere-based multiplex imunoassays (MIA) were developed or adopted and optimized. The MIAs included the diphtheria- and tetanus toxin and 4 pertussis vaccine antigens as hexaplex, mumps, measles, rubella and varicella as tetraplex, Hib and MenA CYW-135 polysaccharide as pentaplex and 13-valent pneumococci assay.

Methods: The various purified vaccine antigens were covalently coupled to activated carboxylated microspheres. Capsular polysaccharides were first conjugated to poly-L-lysine. Validation of the MIA was assessed serologically and compared to (internationally) standardized ELISAs.

Results: Reproducibility of bead conjugation was high for all MIAs (R: 0.97-0.99) and conjugated beads could be stored at 4 ºC for 24 months. The specificity was demonstrated by a low percentage of heterologous inhibition and a high percentage of homologous inhibition. The sensitivity of the MIA was much better than ELISA. Only one or two single serum dilutions could cover > 90% of the total antibody concentration range. Assay reproducibility was high for all individual MIAs with low intra- and inter-assay variability. Most importantly, the correlation of the MIA with ELISA was good to excellent (R: 0.91-0.99).

Conclusion: Serum IgG antibodies against various vaccine components can be measured easy, specific, reproducible and rapid with a MIA. The good correlation with the classic ELISA and its successful application in a large sero-surveillance and vaccine studies demonstrated that the MIA is a fast alternative method for the detection of vaccine-specific antibodies.

P739

COMPARISON OF TIMELINESS OF PRIAMRY COURSE OF DTPA IN VICTORIA AND NEW SOUTH WALES

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In Australia, Pertussis notifications are at persistently high levels across the country despite excellent participation in routine recommended immunitsation.

Basic cocoon strategies based on immunising parents of newborn babies with DTPa are currently funded free of charge in New South Wales and Victoria. Despite this, it is very important that the imunisation of infants with the primary course of DTPa be both timely and complete.

This study builds on previous research on the timeliness of the Primary Course of DTPa vaccine in Victoria, which looked at timeliness of DTPa based on the dosing window of the three doses of Rotateq (rotavirus vaccine).

It examines the sustainability of timeliness of the primary course of DTPa in Victoria and compares the timeliness of the primary course of DTPa in new South Wales, which uses the two dose Rotarix (rotavirus vaccine).

Immunisation is predominately delivered throuhg General Practice in New South Wales but in Victoria immunisation is provided almost equally through General Practice and local council immunisation sessions.

There has been no specific education or promotion of timeliness of vaccine doses in either state.

It draws comparisons between timeliness of vaccination and models of provision of immunisation and makes recommendations about possible change to improve immunisation delivery.

P740

AN EVALUATION OF THE DEPARTMENT OF HEALTH ´BOOSTRIX FOR NEW PARENTS´ IMMUNISATION PROGRAM IN EASTERN MELBOURNE, VICTORIA

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Boostrix (a vaccine containing pertussis, diptheria and tetanus antigens) has been available free of charge from General Practitioners, local council immunisation sessions and maternity hospitals for new parents for the last 18 months. It is intended as a coccoon strategy for new infants prior to them receiving their own immunisations.

This study assesses the penetration of this program into the eligible parent population of Eastern Melbourne, Victoria, Australia.

Methodology: Parents presenting to General Practice or council immunisation session with their 2 month old infant for the first routine infant immunisation are asked to complete a simple questionaire. Questions are asked about heir knowledge about the ´Boostrix for New Parents´ program, whether they or their partner has been immunised with Boostrix vaccine as part of the program and where was the immunisation given. They are offered the vaccine on completion of the questionaire if not already immunised. Survey lasted 6 weeks.

Initial findings indicate reasonable knowledge of the program, adequate upatake in mothers but poor uptake in fathers.

New born babies are susceptible to pertussis until they complete their primary immunisation course at 6 months of age. Providing immunisation against pertussis to parents with free boosters and encouraging vaccination in close contacts provides some protection to the infant. Free vaccine programs are only useful if the vaccine is used as intended, in a timely and appropriate fashion- evaluation of such programs gives information about the reach of a program and can influence program and process changes to improve future vaccine delivery.

P741

DEFINITION OF A CORRELATE OF PROTECTION FOR INACTIVATED INFLUENZA VACCINES IN CHILDREN LESS THAN FIVE YEARS OF AGE

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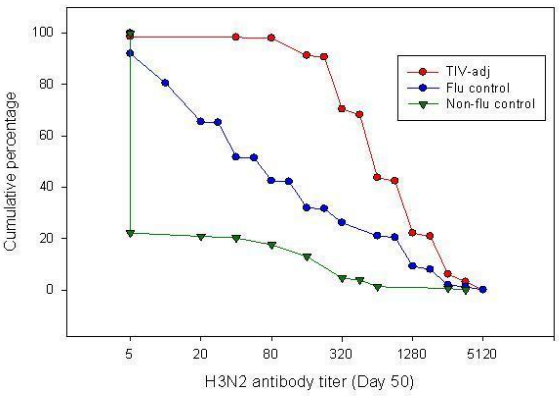
Background: Although an HAI titer of 1:40 has been recognized as an immunologic correlate corresponding to a 50% reduction in the risk of contracting influenza in adult populations, this relationship has not been evaluated in children.

Methods: 4707 influenza vaccine naive children 6-72 mo old were randomized 2:2:1 to MF-59 adjuvanted influenza vaccine (Novartis), subunit TIV (control, GSK) or placebo during the 2007-8 and 2008-9 influenza seasons. Cases identified by active surveillance were confirmed by RT-PCR. Immunogenicity at day 50 (21 days after dose two) was evaluated in a subset of 777 children.

Results: H3N2 Immunogenicity and efficacy results were evaluated against the Prentice criteria which confirmed that the immunogenicity data warranted estimation of an immunologic correlate. The Dunning model fitting H3N2 antibody titers and cases observed in the immunogenicit subset revealed that a cut-off titer of 1:110 was associated with the conventional 50% clinical protection rate whereas titers of 1:215, 1:330 and 1:629 predicted protection rates of 70%, 80% and 90% respectively. The conventional adult 1:40 HAI titer was only associated with 22% protection.



[Reverse Cummulative Distributions]

Conclusion: The use of the conventional 1:40 HAI correlate of protection derived from adult challenge studies is not appropriate when evaluating influenza vaccines in children. Although a cut-off of 1:110 may be used to predict the conventional 50% clinical protection rate, a titer of 1:330 would predict an 80% protective level which would seem to be more desirable from a public health perspective.

P742

THE B-CELL RESPONSE TO PRIMARY AND BOOSTER DOSES OF MENACWY-CRM VACCINE ADMINISTERED AT 2, 4 AND 12 MONTHS OF AGE

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Background and aims: A new quadrivalent meningococcal vaccine conjugated to CRM (MenACWY-CRM) is immunogenic in young infants. In this study we assessed the memory B-cell and antibody responses after a primary course and a booster dose of MenACWY-CRM in infants.

Methods: 216 healthy infants were primed at 2 and 4 months of age and boosted at 12 months of age with MenACWY-CRM. Blood samples were obtained from all children at 5, 12 and 13 months of age. The memory B-cell response was measured by ELISPOT and serum antibodies measured using a serum bactericidal assay with human complement (hSBA).

Results: At 5 months of age, after primary immunisation, serogroup-specific memory B-cells were detectable in fewer than 25% of children, although protective hSBA antibody titres (≥1:8) were detectable in more than 94% of children against serogroup C and W-135, in 87% against serogroups Y, and in 58% against serogroup A. At 12 months of age, before booster immunisation the percentages with hSBA ≥1:8 were 2% for serogroup A, 40% for serogroup C, 59% for serogroup W-135 and 54% for serogroup Y. One month after the booster dose of MenACWY-CRM over 50% of children had detectable memory B-cells, more than 98% had protective antibody titres against serogroups C, W-135 and Y, and 91% against serogroup A.

Conclusions: These data indicate that few antigen-specific anticapsular memory B-cells can be detected after two doses priming with MenACWY-CRM, however, these cells rapidly proliferate after booster immunisation and induce a strong bactericidal antibody response.

P743

SAFETY OF ADJUVANTED PANDEMIC INFLUENZA VACCINES: BACKGROUND RATE OF NARCOLEPSY IN EUROPE

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Aim: To calculate background rates of narcolepsy in Europe and assess rates before (< April 2009) and during (May-September) the pandemic and after the beginning of the vaccination campaign (October 2009).

Methods: Seven European countries united in the VAESCO consortium used population and health care databases to calculate background incidence rates (IRs). Countries used standardized Jerboa® software locally on common input data to produce uniform aggregated data, which could be transferred centrally for calculation of incidence rates (IR) and pooling.

Results: 193 million person years (PY) including 18 million PY in 2009 and 2010 from Finland, IPCI (NL) and GPRD (UK) were captured. Overall crude and non-validated narcolepsy rates varied between 1.00 and 2.04 per 100,000 PY per country. Age-specific incidence rates differed between countries. The pooled age standardized rate was 1.30 (95%CI: 1.10-1.52) per 100,000 PY. Overall rates remained within confidence limits of a 10-year secular trend after start of the vaccination campaign. In 2009 narcolepsy rates increased in 5-19 year olds in Finland and 20-59 year olds in IPCI while rates decreased in GPRD. Rates started increasing before the vaccination campaign.

Conclusion: Background rates show different age distributions between countries. The observed increase of narcolepsy rates in Finland and the Netherlands was significant but started prior to the immunization campaign and involved different age groups. In the Netherlands the affected age group did not correspond with the group targeted for vaccination, in Finland it did. A European case control study is underway.

P744

GUILLAIN-BARRÉ SYNDROME AND ADJUVANTED PANDEMIC INFLUENZA A (H1N1) 2009 VACCINES-A MULTINATIONAL CASE CONTROL STUDY IN EUROPE

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Aim: To investigate a potential association of the 2009 pandemic influenza A (H1N1) with Guillain-Barré syndrome (GBS).

Methods: Five European countries participated in a prospective case-control study between November 2009 and March 2010 using a common protocol and a distributed data model. GBS case status was classified according to the Brighton Collaboration definition. Controls were matched to cases on age, sex, index date and country. Those who received pandemic influenza vaccines in the 42 days before the index date were considered exposed Conditional logistic regression analysis was adjusted for influenza like illness, upper respiratory tract infections (ILI/URTI) and seasonal influenza vaccination. Country-specific data were pooled using a fixed-effects model.

Results: 104 cases were matched to one or more controls. Case recruitment and vaccine coverage varied considerably between countries; the most common vaccines used were adjuvanted (Pandemrix® and Focetria®). The unadjusted pooled risk estimate for all countries was 2.8 (95%CI: 1.3-6.0). After adjustment for ILI/URTI and seasonal influenza vaccination pandemic influenza vaccines were not associated with an increased risk of GBS (OR_{adj}: 1.0, 95%CI: 0.3-2.7).

Conclusion: This study shows that a potential increase in relative risk of GBS after pandemic influenza vaccine is unlikely to exceed 2.7. The unadjusted increase in GBS risk following pandemic influenza vaccines could be fully explained by confounding by ILI/URTI and seasonal influenza vaccination. When assessing the association between pandemic influenza vaccines and GBS, it is therefore important to make statistical adjustments for exposure to ILI/URTI and seasonal influenza vaccination.

P745

CONGENITAL AND NEONATAL VARICELLA: IMPACT OF THE NATIONAL VARICELLA VACCINATION PROGRAM IN AUSTRALIA

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Objective: Routine varicella zoster vaccination for children aged 18 months began in Australia from November 2005. Our aim was to compare the current incidence and outcomes of congenital and neonatal varicella in Australia with similarly collected data from 1995-7.

Methods: Active national prospective surveillance for congenital and neonatal varicella using the Australian Paediatric Surveillance Unit for 3.5 years from June 2006. Monthly reporting by ~1300 clinicians according to pre-defined case criteria.

Results: During the study period the mean monthly return rate of APSU report cards was 93.7%. Two cases of congenital varicella (0.19/100,000 live births per annum) and 16 cases of neonatal varicella (2.0/100,000 live births per annum) were identified. During 2008 and 2009 no cases of congenital varicella were reported and neonatal varicella rates declined to 0.7/100,000 live births per annum, a reduction of >85% compared to rates during both 1995-7 (pre-vaccination era) and the first year of the current surveillance study. Eleven of 16 neonatal cases followed pre-natal maternal infection and 7 infections were acquired from other children, 4 of whom were living in the same household. Ten (62.5%) infants with neonatal varicella were admitted to hospital, one developed varicella pneumonitis requiring ventilatory support, but none died. Only one infecting contact had been vaccinated.

Conclusions: There has been a substantial reduction in congenital and neonatal varicella in Australia following the introduction of universal varicella vaccination in 2005.

P746

VACCINE EFFECTIVENESS AGAINST COMMUNITY-ACQUIRED SEVERE ROTAVIRUS GASTROENTERITIS AMONG YOUNG CHILDREN, IN BELGIUM: A HOSPITAL-BASED, PROSPECTIVE, CASE CONTROL STUDY

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Background and aims: In Belgium, 2 rotavirus (RV) vaccines are licensed (Rotarix™ and RotaTeq™); vaccination is recommended since October 2006 and reimbursed since November 2006. This study evaluates direct vaccine effectiveness (VE) against severe rotavirus gastroenteritis (RVGE) among young children.

Methods: Case-control study in 39 Belgian hospitals between FEB2008 and JUN2010. Confirmed cases were children hospitalized with PCR-confirmed RVGE and age-eligible (>=14 weeks of age and born after 01OCT2006) to be vaccinated against RV. For each case, at least one age and hospital-matched control without GE was enrolled. VE was calculated as (1-matched odds ratio of vaccination) x 100, using condition logistic regression with 95% confidence intervals (CI).

Results: The VE analysis included 213 confirmed cases and 276 matched controls and showed no significant differences between groups in terms of previous hospitalisations due to GE, or medical history. Cases were significantly more frequently formula-fed, had a larger household size and their mother had lower educational level than controls. Forty-eight % of cases and 91% of controls had received any RV vaccination.

The VE against RVGE of Rotarix™ full-series-vaccination compared to unvaccinated children was 90.2% [95% CI: 81.0-94.9%]. VE was 91.0% [95% CI: 74.5-96.8%] in children aged 3-11 months and 89.6% [95% CI: 75.5-95.6%] in children aged >=12 months. G2P[4]-specific VE was 85.0% [95% CI: 64.7-93.8%].

Conclusions: RV vaccination proves highly effective for prevention of RVGE hospitalizations in young children in Belgium. The significant differences between cases and controls suggest tackling health inequalities as a priority for further RV prevention.

P747

EPIDEMIOLOGY OF THE UNVACCINATED: A BEHAVIOUR CHANGE COMMUNICATIONS FRAMEWORK AND TOOLKIT FOR THE WHO EUROPEAN REGION

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Background and aims: The European Region has documented pockets of low immunization coverage for childhood vaccines, such as measles, mumps and rubella (MMR), oral polio vaccine (OPV) and pertussis which have led to growing susceptible populations being able to sustain disease transmission leading to outbreaks. In many countries, populations are excluded from services or refuse to be vaccinated.

To address the behavioural barriers to vaccination faced by such segments of the population, Member States need to better understand the epidemiology of the susceptible populations and appropriately create demand for vaccines, change risk perception and ensure equity to immunization services.

Method: The WHO Regional Office for Europe is developing a Toolkit that comprises of formative research questionnaires and moderator guides, a behaviour change communications framework, and a menu of best practices and lesson learned from social marketing and vaccine communications programmes around the world. The behavioural determinant framework is adapted from tried-and-tested social marketing approaches. The framework helps shape a response to the motivational, ability and opportunity determinants of vaccination behaviour of at-risk, susceptible or vulnerable populations.

Findings: Member States will be equipped with the Toolkit and trained to epidemiologically and socially profile and segment susceptible populations, and appropriately respond according to their circumstances, behavioural barriers and communication/media preferences. The Toolkit components will be piloted in Bulgaria in 2011.

Conclusions: The Toolkit will reframe the response to reaching the remaining susceptible populations in the WHO European Region and, in turn, assist the Region in meeting elimination and eradication goals.

P748

PEDIATRICIANS' AND OBSTETRICIANS-JINECOLOJISTS' KNOWLEDGE AND ATTITUDES TOWARD HUMAN PAPILLOMAVIRUS (HPV) INFECTION AND VACCINATION

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HPV vaccines were licanced for use in muslim country Turkey. We invastigated whether pediatricians and obstetricians-jinecolojists (O-J) would recommend the HPV vaccine, obstacles they encountered and characteristics associated with not recommending HPV vaccine to all eligible patients. A cross-sectional survey was conducted in 12 cities of Turkey. The study questionnaire was completed by face to face with physicians. Overall 378 physicians (193 pediatrician, 185 O-J) with a mean age of 39 ± 7 years participated in our survey. Most of the participitants knew the HPV related clinical condions and cancers. Eighty-seven percent of physicians responded that HPV vaccine is the main route of preventing HPV infection and 81% of them stated that usage of condom would protect HPV acquisition. Also 24% of physicians thought that non-penetrating sexual activity was not risk for HPV acguisition. Among the all physicians 43% of them stated that they recommended the vaccine to whom demanding HPV vaccination, only 20% recommended it to their all patients and 3% would give it to none of their eligible patients. The main obstacles were cost, efficacy and safety of vaccine. Among the all physicians 9% of them would not recommended HPV vaccination to their own daughter since they mostly thought that HPV vaccine is not efficient and they believe that their daughters will made monogamic marriage.This study highlights key factors that effect vaccine acceptability in physicians and may help HPV vaccination campaigns organizations.

P749

PEDIATRICIANS' AND OBSTETRICIANS-JINECOLOJISTS' KNOWLEDGE AND ATTITUDES TOWARD HUMAN PAPILLOMAVIRUS (HPV) INFECTION AND VACCINATION

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P750

MODELLING THE HEALTH IMPACT OF 13-VALENT RELATIVE TO 10- VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN THE UNITED KINGDOM

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Background and aims: Seven-valent pneumococcal conjugate vaccine (PCV7) has had a profound public health impact by preventing disease caused by seven *S.pneumoniae* serotypes. PCV13 covers six additional serotypes while PCV10 covers only an additional three. The study objective was to evaluate the health impact of PCV13 versus PCV10 paediatric vaccination in the United Kingdom (UK).

Methods: A static steady state model was developed to estimate the impact of PCV13, and PCV10 on invasive pneumococcal disease (IPD), pneumonia, and acute otitis media (AOM). Disease cases were estimated using 2009/10 UK incidence and serotype coverage (prior to PCV13 introduction), vaccine effectiveness, and indirect effects. Direct effects for PCV13- and PCV10-covered serotypes were assumed to be similar to PCV7. Indirect (herd immunity) effects were assumed only for PCV13 as PCV10 has not demonstrated a consistent statistically significant reduction in nasopharyngeal carriage in vaccinated individuals. Assumptions were tested in sensitivity analyses.

Results: It is estimated that PCV13 will have a greater impact than PCV10 on all types of pneumococcal disease. Compared to baseline disease levels, PCV13 paediatric vaccination would eliminate an additional 28.8% of IPD (61.7% vs. 32.9%), 11.9% of pneumonia (25.5% vs. 13.6%) and 3.6% of AOM (7.8% vs. 4.2%) in vaccinated children over PCV10. Assuming herd immunity effects, PCV13 could eliminate up to 32.9% of IPD and 13.4% of pneumonia in unvaccinated individuals.

Conclusions: Continuing national PCV13 paediatric vaccination in the UK would provide a substantial further reduction in IPD, pneumonia, and AOM cases when compared to PCV10.

P751

EFFECTIVENESS OF THE HIB CONJUGATE VACCINE AGAINST PNEUMONIA IN YOUNG CHILDREN IN UKRAINE

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Objective: *Haemophilus influenza* type b (Hib) conjugate vaccine was included into vaccination calendar of Ukraine at the end of 2006. The vaccine is recommended at 3, 4, 5 months of age, together with DTaP and IPV, with a booster given at 18 months of age.

Aim: To demonstrate effectiveness of Hib vaccination program against radiologically-confirmed pneumonia in children.

Methods: Surveillance for radiologically-confirmed pneumonia at seven Kiev hospitals and four hospitals in Dnipropetrovsk was done. Children < 2 years old with pneumonia admitted to participating hospitals between April 2007 and June 2009 were included into a case-control evaluation. Four controls were matched to each case by age and outpatient clinic. Conditional logistic regression, adjusted for presence of underlying medical conditions or contraindications for vaccination, was used to estimated odds ratios for vaccination (OR) and vaccine effectiveness ((1-OR)*100%).

Results: We enrolled 188 case-children and 735 matched controls. Fifty one percent of cases and 67% of controls received ≥1 doses of Hib vaccine; 26% of cases and 37% of controls received ≥3 doses. The effectiveness of ≥1 doses Hib vaccine was estimated at 45% (95%CI 18-63%).

Conclusions: This is the first evaluation of the impact of routine Hib vaccination in the countries of Eastern European region, where Hib disease burden is not well documented. Our study showed that Hib infections are important causes of hospitalized radiologically-confirmed pneumonia in young children in Ukraine.

Acknowledgement: The financial support for this evaluation was provided by the WHO Regional Office for Europe and the Hib Initiative (www.hibaction.org).

P752

THE INTRODUCTION OF HPV VACCINATION IN THE DUTCH NATIONAL IMMUNISATION PROGRAMME IN 2009-2010; COMMUNICATION CAMPAIGN AND COVERAGE

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Background: In 2009 HPV immunization was started in the Netherlands with a campaign for older girls (born in 1993-1996) and later, 2010, introduced as routine vaccination in the National Immunisation Programme for girls 12-years old (cohort 1997 and onwards).

Methods: A letter including a leaflet, immunization cards and a personal invitation to hand over to their daughter, was sent to the parents. Additional information could be found on a special website. The HPV vaccinations were offered in mass immunization sessions organized in the place of residence by public health services.

Results: After a vaccine uptake of about 80% in the first week, the coverage dropped below 50% in parallel to enormous negative media attention. This was partly provoked by antivaccine lobbyers.

In response our communication strategy was adapted to deal with incertainties and emotions, use modern communication tools (webfora,chat sessions) and interaction with the target group was sought. Thus it was realized that girls were supported to informed decision making based on correct information.

Conclusions: HPV vaccination, which is targeting a new age group, a disease different from those covered by the NIP sofar, asks for changes to a modern communication policy. The coverage is shown to gradually improve.

P753

IMMUNOGENICITY OF A PROPHYLACTIC QUADRIVALENT HPV VACCINE IN FEMALES WITH PAEDIATRIC RHEUMATOLOGICAL DISEASES

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Aim: To determine the immunogenic response of quadrivalent (4v)HPV [6,11,16,18] vaccine in female paediatric rheumatological diseases (PRD) patients.

Methods: All participants received 3 doses of 4vHPV vaccine, with a single opportunistic blood sample taken > 1 month post the final dose. Immunosuppression was graded as: level 1 (none or NSAIDs only); level 2 (corticosteroids); level 3 (methotrexate; azothiorpine; cyclosporin); or level 4 (biologic therapies: etanercept; infliximab). Anti-HPV serology was performed using competitive Luminex based immunoassays (cLIA Merck, Wrest Point, PA).

Results: From March 2008- March 2010 36 female PRD patients were assessed: 28 juvenile idiopathic arthritis (JIA); 4 Systemic Lupus Erythematosus; 2 Juvenile Dermatomyositis; 1 Scleroderma and 1 Sjogrens disease. The mean age was 14.2 years (standard deviation (S.D) 1.3 years). The level of patient immunosuppression was: 6 level 1; 3 level 2; 16 level 3 and 11 level 4. Mean time for serology testing was 96.3 days (S.D. +/- 135 days). All results were above the HPV type serostatus cut-offs. The geometric mean titre (GMT) for type 6 was [1287.3 mMU/ml (95% Confidence intervals (CI) 725.3-1849.4); type 11 [1952.7 (923.3-2980.2)]; type 16 [7458.5 (4240.7-10676.4)] and type 18 [2295.5 (1159.8 - 3431.3)]. One participant, with underlying active disease, had a 6 week duration JIA flare, which commenced 2 days post dose 3 4vHPV. No other significant adverse events were reported.

Conclusion: PRD participants, including those on significant immunosuppressive therapy, mounted robust immune responses to 4vHPV vaccine. Long-term follow-up will help determine whether booster doses are required.

mMU= milli Merck units

P754

ABSENCE OF NARCOLEPSY CASES IN MF59®-ADJUVANTED INFLUENZA VACCINE CLINICAL TRIAL AND MF59®-ADJUVANTED H1N1 PANDEMIC VACCINE PHARMACOVIGILANCE DATABASES

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Background and aims: Narcolepsy with cataplexy, putatively an autoimmune disease, has been reported in temporal association with administration of AS03®-adjuvanted H1N1 pandemic vaccine.[1] We searched for narcolepsy cases in a pooled MF59®-adjuvanted influenza vaccine clinical trials database and separately, the pharmacovigilance (PV) database of MF59-adjuvanted egg-derived H1N1 pandemic vaccine.

Methods: Narcolepsy cases were sought using narrow and broad MeDRA Preferred Terms. Potential cases were reviewed against American Academy of Sleep Medicine criteria.[2]115 clinical trials of adjuvanted and unadjuvanted seasonal, H1N1 pandemic and H5N1 influenza vaccines comprised 79,004 subjects in 73 uncontrolled clinical trials (40,059 subjects) and 42 controlled clinical trials (38,945 subjects. Rates in subjects receiving MF59-adjuvanted or non-adjuvanted vaccine, meeting narrow and broad definitions were calculated per 1000 subjects and per 100 subject-years and Odds Ratios (OR), by logistic regression analysis, adjusted for observation-days and vaccine doses, and for various temporal windows after vaccination. The PV database was searched for all spontaneous reports (serious and non-serious) received through 31 July 2010 occurring in temporal association with receipt of egg-derived MF59-adjuvanted H1N1 vaccine (Focetria®).

Results: No case meeting accepted clinical definitions of narcolepsy was found in either database, under narrow and broad search criteria. Adjusted ORs for broad search terms indicated no difference in risk for MF59-adjuvanted and unadjuvanted subject groups for the various clinical trials groups and temporal windows.

Conclusions: Within the limits of the available prospectively and passively collected data, we found no indication of an increased risk for narcolepsy in recipients of MF59-adjuvanted influenza vaccines.

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THE IMPACT OF COCOONING VACCINATION STRATEGIES ON TRANSMISSION OF PERTUSSIS TO NEWBORNS WITHIN HOUSEHOLD SETTINGS

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Background and aims: Despite more than 50 years of mass vaccination, pertussis remains the most frequent infectious disease targeted by vaccination in developed countries. Pertussis infection is especially severe in young infants. We quantified transmission of pertussis in households, using data from 140 households with a clinically confirmed infection.

Methods: Data on transmission of pertussis within households was captured in a population-based, nationwide, prospective study performed in the Netherlands between February 2006 and November 2008. We developed a four-type stochastic SEIR model to generate quantitative estimates of transmission rates.

Results: Our model showed that the introduction of an infected mother is expected to lead to infection of the infant in 40% of such households. In case that the father or the another person is the primary infected person, the probability of infection of the infant decreases to 15% and 20%, respectively. Furthermore, the analyses show that after vaccination of mothers the probability of infection of the infant can be reduced from 40% to 5% if the mother is the primary case, from 15% to 8% if it is the father, and from 20% to 13% if it was the other household person.

Conclusions: Our results indicate that transmission levels are high within households, that fathers are significantly less infected than mothers, and that mothers may be more infectious to their infants than fathers and siblings. Vaccination of mothers in particular may be an effective means of preventing infection of their infants.

P756

VACCINE UPTAKE DETERMINANTS IN THE NETHERLANDS

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Background: Participation in nationwide vaccination programmes is not self-evident. Insight in determinants of vaccine uptake is important to guide future communication activities.

Methods: The study population consisted of children born in 2005 according to the national vaccination register Præventis. A hierarchical, or multilevel, logistic regression model was used to quantify associations between vaccination status (individual level) and proxy variables for ethnic background (country of birth parents, individual level), socioeconomic status ('status score' 2006, postcode level) and religious objection to vaccination (percentage voters for Reformed Political Party 2006, municipal level).

Results: Most children of whom parents were not both born in the Netherlands had a lower combined full uptake of all vaccines together. Although children of whom both parents were born in Turkey or Morocco did not have a lower full uptake for single vaccines, the combined full uptake was lower. The same counts for children of whom one parent was born in the Netherlands and one in another western country and children of whom one parent was born in a western and one in a non-western country. A possible explanation could be that foreigners are known to change their residence more often. Postcode areas with a higher socioeconomic status and municipalities with less religious objection to vaccination were associated with a higher full vaccine uptake.

Conclusions: Ethnic background, religious objection to vaccination and socioeconomic status to a lesser extent are important determinants of full vaccine uptake among children in the Netherlands. Future research should focus on reasons behind these differences.

P757

MUMPS OUTBREAK AMONG A HIGHLY VACCINATED STUDENTPOPULATION, THE NETHERLANDS, 2009-2011

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Background and aims: In December 2009, a mumps outbreak started among university students in the Netherlands. In March 2010, transmission during a student party caused a sudden increase in the incidence. Individuals aged 27 and below have been offered two doses of MMR in the Dutch immunisation programme. The coverage of this has consistently been over 90%.

Methods: We analysed mumps notification data between 1-12-2009 and 19-1-2011. A case of mumps was a person with at least one of the following: acute swelling of a salivary gland, orchitis or meningitis, with either laboratory confirmation of mumps or contact with a laboratory confirmed mumps case.

Results: In the study period, 590 notified mumps cases occurred. The median age was 22 years. Of cases, 57% was male and 61% was a university student. For 51 persons complicates were reported (9% of all cases), mainly orchitis (45 cases, 14% of male patients). Eleven persons (2%) were hospitalized, most frequently due to orchitis (7 cases). Information about vaccination status was available for 87% (513) of cases. Of these, 16% were unvaccinated, 10% were vaccinated once, and 74% were vaccinated at least twice. Genotype G5 is the circulating strain in this outbreak.

Conclusions: A mumps outbreak is ongoing mainly among university students who received two doses of MMR in the past. Orchitis is the most frequently reported complication. Subsequent sub-fertility is of concern. Further research into reasons for vaccine failure, mumps virus transmission in vaccinated populations, and chronic sequelae of mumps orchitis is required.

P758

ADVERSE EVENTS IN HEALTHY YOUNG CHILDREN REPORTED FOLLWING MASS VACCINATION AGAINST PANDEMIC INFLUENZA A(H1N1) IN THE NETHERLANDS

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Background and aims: In the Netherlands, vaccination against pandemic influenza A(H1N1) started in November 2009. Safety surveillance is essential in such vaccination campaigns. Children aged 6 months up to 4 years without chronic illness were vaccinated with Pandemrix®, administered in two doses through mass vaccination. We investigated the tolerability of two doses Pandemrix® in these children.

Methods: Among parents of children eligible for vaccination, 1500 questionnaires were distributed during both, the first and second mass vaccination session. We asked for the occurrence, time interval, and duration of local reactions and systemic adverse events (AEs).

Results: 1013 questionnaires were returned, with responses of 36.7% and 29.5% after the two subsequent doses. In 40.1% of the children local reactions were reported, with pain at the injection site most frequently. Systemic AEs were reported in 51.0%. Of all children, 30.5% experienced fever (mean temperature 38.8°C), in 86.2% starting within two days after vaccination. Four high fever cases (>40.5°C) were reported, three following the first dose. Pallor was most frequent reported after the first dose, for other systemic AEs there was no difference between doses. The incidences of fever, crying, sleeping problems, and vomiting decreased with age, and pain increased with age.

Conclusions: Fever was frequently reported in children aged 6 months up to 4 years after vaccination with Pandemrix®. No difference in incidences of systemic AEs, including fever and mean temperature, was seen between the first and second dose. Besides the few very high fever cases, no severe AEs were reported.

P759

REPORTED ADVERSE EVENTS IN GIRLS AGED 13-16 YEARS AFTER VACCINATION WITH THE BIVALENT HUMAN PAPILLOMAVIRUS (HPV) VACCINE IN THE NETHERLANDS

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Background and aims: In 2009, human papillomavirus (HPV)-vaccination was offered to girls born in 1993-1996 in a catch-up campaign. The execution of mass vaccination in a new target group necessitated intensified safety surveillance. To monitor the tolerability, we investigated the occurrence of frequent adverse events (AEs) within 7 days after vaccination with the bivalent HPV-vaccine.

Methods: A total of 6000 girls were asked to participate (about 1500 from each birth cohort). One week after each of the required three successive doses, participants received by e-mail a Web-based questionnaire focused on local reactions and systemic AEs.

Results: One or more questionnaires were returned by 4248 girls. Local reactions were reported by 92.1% of the girls after the first dose, 79.4% after the second dose, and 83.3% after the third dose, and 91.7%, 78.7%, and 78.4% reported systemic AEs after the three doses, respectively. Pain in the arm was the most frequently reported local reaction, and myalgia the most often reported systemic AE. Proportions of local reactions and most systemic AEs were significantly lower after the second and third dose compared with the first dose (OR 0.33-0.76). Older girls reported higher proportions of AEs than younger girls. No serious or unexpected AEs were reported.

Conclusions: After vaccination with the bivalent HPV-vaccine, 13-16-year-old girls reported high proportions of short-term AEs, which was age and dose dependent. However, these AEs were mostly mild and all transient. These results are being communicated to health care professionals and public to help increase confidence in vaccination.

P760

PREVENTION OF PERINATAL HEPATITIS B VIRUS TRANSMISSION IN THE NETHERLANDS, 2003-2007: EFFECTIVENESS OF DIFFERENT VACCINATION SCHEDULES

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Background and aims: In the Netherlands, over time different hepatitis B vaccination schedules have been recommended for children born to HBV-infected mothers. We assessed whether the schedule without a birth dose of vaccine was associated with more frequent perinatal infection than the schedule without a birth dose. We also studied determinants of anti-HBs titers.

Methods: We included infants born to HBV infected mothers between 1.1.2003 and 30.6.2007 in the Netherlands. Risk factors for perinatal transmission and determinants of the anti-HBs titer were studied using logistic and linear regression.

Results: Of 2657 infants in the national database, 91% were registered to have received HBIg and at least three hepatitis B vaccinations. In Amsterdam, this coverage among 413 children at risk was 96%. Serological test results for 2121 infants (80%) indicated that 13 (0.6%) were HBsAg positive. A mother of Chinese descent was the only risk factor for perinatal HBV infection (RR 9.1, 95%CI 3.1-26.8). Receiving a birth dose of hepatitis B vaccine later than in the first week of life was not associated with an increased risk of perinatal HBV infection. A shorter period between last vaccination and testing, and having received more doses of hepatitis B vaccine were independently associated with a higher anti-HBs titer.

Conclusions: Infants born to Chinese mothers were at increased risk of perinatal HBV infection. Among infants receiving HBIg at birth, administration of the first dose of hepatitis B vaccine after first week of life was not associated with an increased risk of perinatal HBV infection.

P761

MUMPS EPIDEMIC IN AN ORTHODOX PROTESTANT COMMUNITY IN THE NETHERLANDS 2007-2009 SPREAD TO CANADA

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Background and aims: A mumps virus epidemic occurred in the Netherlands between August 2007 and May 2009. We aimed to assess its characteristics and burden of disease, and to study the association with a subsequent mumps outbreak in Canada.

Methods: In the Netherlands, five data sources were used: notifications (from December 2008 onwards; 56 cases), laboratory confirmation (177 cases), a general practitioner (GP) database (275 cases), hospitalisation data (29 cases), and weekly virological reports (96 cases).

Results: The estimated incidence based on GP data was 81.4/100.000 per year. The median age of cases in the notification database, laboratory database, and GP database ranged between 13-15 years. The proportion of cases that was unvaccinated ranged from 65-85% in the notification, laboratory, and GP database. Orthodox protestant religion was the main reason for not being vaccinated. The outbreak strain was of genotype D. In Canada, an identical mumps virus strain to the Dutch outbreak strain was detected between February and October 2008 in an orthodox reformed community with historical and social links to the orthodox protestant community in the Netherlands.

Conclusion: During most of this outbreak, mumps was not notifiable in the Netherlands, making it difficult to assess its impact and epidemiology. Based on different surveillance data we conclude that during 2007-2009, a considerable proportion of the unvaccinated Dutch Orthodox Protestant population was infected with a genotype D mumps virus. The outbreak strain spread to Canada.

P762

PERINATAL HEPATITIS B TRANSMISSION: EVALUATION OF THE SCREENING AND IMMUNIZATION POLICY IN ANTWERP (BELGIUM)

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Background and aims: Perinatal hepatitis B transmission still occurs in industrialized countries. The goal of this study was to determine in one hospital in Antwerp compliance with the 2004 recommendation (Belgian Superior Health Council) for prevention of perinatal hepatitis B virus transmission from Hepatitis B surface antigen (HBsAg) positive mothers to their offspring.

Methods: Data were obtained from women who gave birth in the studied hospital in 2006: name and birth dates, child's birth weight, address, telephone number, nationality, HBsAg status of the mother and date of screening. HBsAg screening was also assessed by taking a telephone questionnaire from the women. Currently, we evaluate the immunization policy at birth and during the first year of life. The HBsAg positive women who agreed to participate are visited at home to fill in a second questionnaire.

Results: Of the 1462 mothers, HBsAg screening was performed in 778 (53%) women during, and in 168 (11%) after the pregnancy. When we compare the nationality, age of the mother, family income, level of education and work of the mother and number of consults at the general practioner/gynaecologist between screened and non-screened women, no significant difference was observed. Ten (0.7% of the 946 documented women) were HBsAg positive, all from foreign origin, but no measures were communicated to the respective treating physicians.

Conclusions: HBsAg screening was not documented or not performed for a substantial part of the studied population. Based on current findings, there is room for improvement in the compliance with the recommendation.

P763

INVASIVE PNEUMOCOCCAL DISEASE IN TWO BIRTH COHORTS VACCINATED, RESPECTIVELY, WITH 2+1 PCV-7 OR PHID-CV-10 DOSES

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Background: In Quebec, a 2+1-dose pneumococcal conjugate vaccine program was implemented in December 2004. PCVC-7 was first used and PHiD-CV-10 was introduced in the summer of 2009. So far, there is no data on the clinical effectiveness of PHiD-CV-10.

Methods: Cases of invasive pneumococcal disease (IPD) were identified by the provincial reference laboratory in two birth cohorts as of June 30, 2010:

(i) approximately 43,800 children born in the period July-December 2008 (PCV-7 cohort representing 43,800 person-years of observation);

(ii) 44,300 children born in the period July-December 2009 (PHiD-CV-10 cohort representing 33,225 person-years of observation).

Results: During the study period, IPD cases caused by PCV-7 serotypes were infrequent in children < 5 year-old, whereas 7F and 19A incidence was on the rise. Two vaccine-type (VT) and 19 non-vaccine-type (NVT) cases occurred in the PCV-7 cohort. Two VT and 6 NVT cases occured in the PHiD-CV-10 cohort. In both cohorts, 2 VT cases were identified before the age of completion of the 2-dose primary immunization series and no other case thereafter, suggesting high level of vaccine effectiveness. In the PCV-7 cohort, 13 IPD cases, including seven 19A cases were observed in the age group 6-11 months, whereas only 2 cases neither of which were 19A, were observed in the PHiD-CV-10 cohort.

Conclusion: This is the first information on the clinical impact of PHiD-CV-10 use. As with any ecological study, results should be interpreted with care. Surveillance will continue to include more births and extended follow-up.

P764

PERSTENCE OF BACTERICIDAL ANTIBODIES ONE YEAR AFTER A BOOSTER DOSE OF SEROGROUP C MENINGOCOCCAL VACCINE GIVEN TO PREVIOUSLY IMMUNISED ADOLESCENTS

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Background and aims: Bactericidal antibodies induced by immunization of infants with serogroup C *Neisseria meningitidis* (MenC) vaccines wane rapidly during childhood. Adolescents are at particular risk from meningococcal disease, so may benefit from a booster dose of vaccine. This study investigates the serological response to such a booster.

Methods: English schoolchildren who had received a monovalent MenC glycoconjugate vaccine in 1999-2000, aged 9-12 years, were given a booster dose of either a reduced dose plain polysaccharide vaccine (MenC-PS) or a glycoconjugate vaccine (MenC-CRM) at age 13-15 years (mean 3.7 years after priming). Both vaccines contained 10 microgrammes MenC polysaccharide per dose. Rabbit serum bactericidal antibody titre (rSBA) was assessed before, 28 days after and one year after the booster.

Results: There were 50 children in each group. Geometric mean titre (GMT) for rSBA before booster vaccination was 302 (95%CI 156-587) in MenC-PS group and 153 (95%CI 79-298) in the MenC-CRM group. 28 days after the booster, GMT was 10226 (95%CI 8239-12693) in MenC-PS group and 16384 (95%CI 13201-20335) in the MenC-CRM group. One year after the booster, GMT was 3875 (95%CI 2810-5344) in MenC-PS group and 4211 (95%CI 3053-5808) in the MenC-CRM group. Before the booster, rSBA titres were ≥1:8 (the correlate for protection) in 88% MenC-PS group and 84% MenC-CRM group. One year after the booster, all children in both groups had rSBA titre ≥1:8.

Conclusions: A booster dose of MenC vaccine given to adolescents produces a marked rise in bactericidal antibody, which remains elevated one year later.

P765

HPV-VACCINATION OF BOYS OR ADDITIONAL COHORTS OF GIRLS: WHERE IS THE GREATEST BENEFIT FOR CERVICAL CANCER PREVENTION IN ITALY?

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Background: Cervical cancer (CC) vaccination has been implemented in Italy primarily targeting girls aged 12. To further reduce the CC burden should a limited budget preferentially be used to extend vaccination to boys or improve coverage in young adult women?

Methods: A published cohort model adapted to Italy estimated the CC reduction from different vaccination strategies: vaccinating females at the age of 12, 15 or 25 or vaccinating boys at the age of 12. The maximum benefit from vaccinating boys is assumed to equal the CC reduction that would results from vaccinating all non-vaccinated of the same age girls. Each cohort size was 280,000. Vaccine efficacy (VE) was based on clinical trial results (including cross-protection of other non-vaccine HPV-types) and HPV-type distribution. VE was differentiated for pre- and post-sexual debut. Vaccine protection was assumed life-long. Sensitivity analysis was performed on vaccine coverage (VC), vaccinated boys and girls overlap, and all HPV cancer types inclusion.

Results: Under a fixed budget and 70% VC, vaccinating 12, 15, 25 years-old females or 12 years-old boys would prevent 937, 884, 647 or 401 CC respectively. Vaccination of boys will only add more health gain if 12 years-old girls VC is low with low overlap between vaccinated boys and girls and vaccinated boys have numerous partners, resulting in large indirect vaccine effect. The results are strengthened after accounting for other HPV-types.

Conclusion: For a fixed additional budget extending vaccination of female instead of boys will maximise the number of CC prevented.

P766

GLYCOPROTEIN VACCINES, A NEW GENERATION OF CONJUGATED VACCINES WITH IMPROVED PROPERTIES

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Background: Conventional conjugate vaccines are produced in a complex process, which includes fermentation of virulent pathogens for polysaccharide antigen harvesting, production of carrier proteins, chemical conjugation of polysaccharides and protein carrier, and removal of impurities. The chemical process varies considerably between different products and has several disadvantages: products are highly variable in terms of structure, polysaccharide chain length and protein glycosylation degree. Polysaccharides and carrier protein may be chemically modified, with the risk of losing part or all of the protein´s inherent antigenic properties.

Methods: GlycoVaxyn has developed an *in vivo* process in *E. coli*, in which polysaccharides of distinct target pathogens are produced and enzymatically transferred to specific glycosylation sites on carrier proteins of choice. This *in vivo* one-step process results in a glycoprotein with reproducible, uniform higher-order and native structure and antigenically preserved carrier epitopes. In a first-in-human trial, 40 subjects were vaccinated with a *Shigella dysenteriae* O1 glycoprotein vaccine linked to the detoxified recombinant *Pseudomonas aeruginosa* exotoxin A (EPA).

Results: Vaccination with the highly homogeneous glycoprotein vaccine resulted in a strong and lasting antibody response against both polysaccharide and carrier. Post vaccination sera from 12 representative subjects showed a 10 - 20-fold increased capacity to neutralize *Pseudomonas aeruginosa* exotoxin A (ETA), which correlated strongly with the elicited anti-EPA titers.

Conclusions: The novel glycoprotein vaccine elicits a robust immune response against the strain-specific polysaccharide and the carrier protein, including confirmed functionality. This novel technology opens the way to development of new vaccines that combine polysaccharide and protein antigens.

P767

IMMUNOGENICITY AND SAFETY OF 10-VALENT PNEUMOCOCCAL NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* PROTEIN-D CONJUGATE VACCINE (PHID-CV) PRIMARY VACCINATION IN MALIAN AND NIGERIAN INFANTS

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Background and aims: To assess immunogenicity and safety/reactogenicity of PHiD-CV when administered in a 3-dose primary series to Sub-Saharan African infants.

Methods: In a phase III, randomised, open, controlled study (110521/NCT00678301), infants received a 3-dose primary vaccination at age 6-10-14 weeks with PHiD-CV co-administered with DTPw-HBV/Hib vaccine and oral poliovirus vaccine (OPV) (PHiD-CV group) or DTPw-HBV/Hib co-administered with OPV (Control). Immune responses were measured using GSK's 22F-ELISA, OPA assay (pneumococcal serotypes) and ELISA (protein-D, DTPw-HBV/Hib). Solicited (local/general) and unsolicited symptoms and SAEs were recorded.

Results: 357 infants (Mali N=238; Nigeria N=119) were vaccinated in the PHiD-CV (N=239) and Control (N=118) groups. One month post-dose 3, for each vaccine pneumococcal serotype, ≥97.2% of PHiD-CV vaccinees had antibody concentrations ≥0.2µg/mL except for 6B (82.0%) and 23F (87.6%); ≥93.3% had OPA titres ≥8 except for serotypes 1 (87.6%) and 6B (85.4%). Robust anti-pneumococcal antibody responses were observed in PHiD-CV vaccinees; serotype-specific antibody GMCs ranged from 0.95µg/mL (6B) to 10.01µg/mL (18C). All PHiD-CV vaccinees had measurable antibodies against protein-D (GMC=3791.8 EL.U/mL). All infants were seroprotected/seropositive against DTPw-HBV/Hib antigens except two for hepatitis B (PHiD-CV group) and one for Hib (Control group).

Safety/reactogenicity profiles were comparable between groups but differed between countries (higher incidences of redness, swelling, irritability in Mali; higher incidences of drowsiness, loss of appetite in Nigeria). Five infants reported seven SAEs (PHiD-CV group); none were considered causally vaccination-related.

Conclusions: PHiD-CV co-administered with DTPw-HBV/Hib and OPV in 3-dose primary series to Sub-Saharan African infants was well-tolerated; all vaccine antigens elicited robust immune responses.

P768

PERSPECTIVE OF INVASIVE PNEUMOCOCCAL SEROTYPES IN QATAR IN RELATION TO CONJUGATE VACCINE PCV-7 & PCV-13

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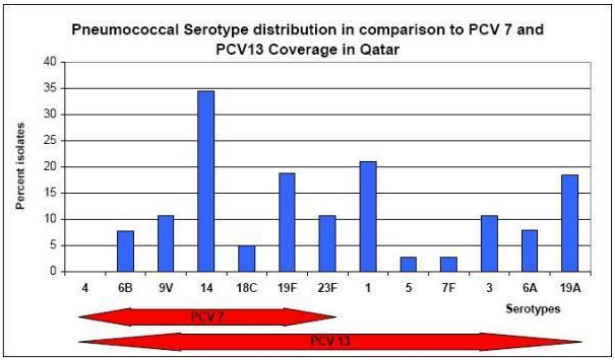
Background and aims: PCV-7 vaccine was introduced in Qatar in Feb 2005 and was replaced by PCV-13 in Nov 2010. This study is aimed to have an overview of invasive pneumococcal diseases (IPD) caused by vaccine and non-vaccine serotypes. It was also aimed to estimate the coverage rate by PCV-7 and to predict if introducing additional serotypes as part of PCV-13 will reduce IPDs. Seroepidemiological data will also guide future strategies to control serotypes not covered in the PCV-13 vaccine.

Methods: A total of 163 Streptococcus pneumoniae isolates (75 from children ≤5 years) from IPDs (from blood, CSF and sputum) from 2005 through Sep 2010, were analyzed. Capsular serotyping was carried out at the Streptococcal Reference Laboratory, CDC,Atlanta, using standard procedures.

Results: The estimated coverage of serotypes in children below 2 years or children 2 to 5 years of age by the PCV-7 vaccine was approximately 35% and 53 % respectively. Introduction of PCV-13 is estimated to increase coverage to 62% and 92% respectively. Additional serotypes not covered in PCV-13 that caused IPDs were serotypes 8, 12F, 35 B, 11A, 18F, and 10A.



[Pneumococcal serotype distribution]

Conclusion: Introduction of PCV-13 in Qatar will have a clear benefit for children's health as it will significantly increase the serotype coverage and reduce the morbidity and mortality due to IPDs in children aged five years or less. However changing seroepidemiology of IPDs, continuous surveillance of pneumococcal serotypes together with a robust vaccine delivery system will ensure control of IPDs in children in Qatar

P769

IDENTIFICATION OF ROTATEQ® VACCINE IN PAEDIATRIC PATIENTS WITH ACUTE GASTROENTERITIS FOLLOWING ROUTINE VACCINATION

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Background and aims: Rotavirus is the predominant cause of acute gastroenteritis in young children worldwide. Two live-attenuated vaccines were introduced into the Australian National Immunisation Program in July 2007. Rotarix® is a monovalent vaccine containing a human G1P[8] strain. RotaTeq® is a pentavalent vaccine containing five human-bovine reassortant strains: G1P[5], G2P[5], G3P[5], G4P[5] and G6P[8].

The aim of this study was to identify and characterise rotavirus strains isolated from children recently vaccinated with RotaTeq® who were subsequently admitted to the Royal Children's Hospital, Melbourne, Australia with symptoms of acute gastroenteritis.

Methods: Rotavirus was detected using a gene-specific RT-PCR which amplified regions of the genes encoding the capsid proteins VP4, VP6 and VP7. Amplicons were sequenced and compared to the reference sequences for RotaTeq® and wild-type rotavirus strains.

Results: Of the 79 faecal samples collected between 1/7/2007 to 1/7/2010 from recently vaccinated children who developed acute gastroenteritis, 13 samples were identified as containing RotaTeq® vaccine. Nine of the thirteen vaccine associated samples contained at least two of the five RotaTeq® vaccine strains. In four samples, a G1P[8] strain was detected that was derived via reassortment between two RotaTeq® vaccine strains G1P[5] and G6P[8]. Eighteen samples were identified as wild-type rotavirus strains and the remaining 48 samples tested negative for the presence of rotavirus.

Conclusion: This study shows that reassortment between the five component strains of the RotaTeq® vaccine does occur and this event may result in a strain with increased virulence. Thus, continued monitoring of rotavirus associated acute gastroenteritis is required.

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PROPHYLACTIC PARACETAMOL IN INFANTS DECREASES FEVER FOLLOWING CONCOMITANT ADMINISTRATION OF AN INVESTIGATIONAL MENINGOCOCCAL SEROGROUP B VACCINE WITH ROUTINE IMMUNIZATIONS

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Background: Adding new vaccines to routine infant schedules necessitates concomitant administration, with consequences on reactogenicity profiles, notably temperature. As prophylactic paracetamol has been reported to interfere with immune responses (Prymula et al. Lancet 2009; 374: 1339-50), we present data showing effective temperature control by prophylactic paracetamol without compromising immunogenicity in a study of a novel, multicomponent, meningococcal serogroup B vaccine, 4CMenB.

Methods: Subsets of healthy infants (n = 183-184) from a large randomised, multicentre, partially observer-blind study received three doses of routine vaccines (DTaP-HPV-IPV/Hib and PCV7) at 2,3,4 months of age, administered concomitantly with 4CMenB or 4CMenB with prophylactic paracetamol at 0, 4-6 and 8-12 hours postvaccination. Immunogenicity at 5 months was measured by standard assays for routine vaccines, and serum bactericidal assay using human complement (hSBA) to three MenB strains selected for the vaccine antigens. Rectal temperature was monitored for 7 days after each dose.

Results: Postvaccination, temperatures ≥38.5ºC and ≥39.5ºC were observed after any dose in 69.0% and 8.2% with concomitant 4CMenB, and 39.3% and 3.3% with 4CMenB and prophylactic paracetamol. At 5 months, there were no significant differences in immune responses to routine vaccines between the groups. Three doses of 4CMenB elicited hSBA titers ≥5 in 75-100% of subjects against the three test strains, unaffected by paracetamol administration.

Conclusions: Prophylactic paracetamol decreased fever after 4CMenB with concomitant vaccines with minimal impact on immune responses to concomitant vaccines which probably have no clinical significance.

P771

ISOLATION OF H.INFLUENZAE TYPE-B FROM CHILDREN SUSPECTED TO MENINGITIS FOR VACCINE PRODUCTION ON THE BASES OF BACTERIAL BIOMASS AND PRP

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Background and aims: Heamophilus influenzae type-b (Hib) is a gram - negative bacterium that causes meningitis infections in infants. In the present study various strains of H.influenzae from infants suspected to meningitis were isolated , identified,characterized and were used through out our experiments .

Methods: Different culture media namely BHI, TSB and GCB which this medium is modified and prepared in our own laboratory, were compared to determine the highest bacterial yield. All media were added supplements 10mg/ml hemin & 0.01/ml IsovitaleX containing V factor. In this study we modified CPS-b production according to our technical and instrumental availabilities replacing ultra centrifugation to phenol chloroform to remove contaminants like endotoxin and proteins to the minimum level and also decreased the number of some chemical treatment while some steps were added in purification process.

Results: The result showed very closed amount of biomass for all strains ,however modified preparation of GCB had slightly higher yield and ultimately we chose this medium for cultivation and extraction of CPS-b. The average amount of PRP for three strains showed 108mg/lit, however strain ATF2 showed the highest amount with 192mg/lit and the least PRP was produced by strain H.inf1, with 16 mg/lit. The amount of protein along with nucleic acid was estimated at optical density 280 and 260nm were under 5% and 10% respectively .

Conclusion: The method used in our study is very efficient and simple for production of CPS-b with high purity and can easily be scale up for PRP.

P772

IMMUNOGENICITY AND SAFETY OF INTRADERMAL INFLUENZA VACCINES WITH DIFFERENT AMOUNT OF ANTIGENS IN OTHERWISE HEALTHY CHILDREN

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Background and aims: Use of influenza vaccine in healthy children is debated mainly because the conventional inactivated trivalent vaccine (TIV) is not always adequately immunogenic. The intradermal (ID) administration of TIV is used in adults in order to increase immunogenicity. This study was planned to evaluate the immunogenicity and safety of ID-TIV vaccine in pediatric age.

Methods: Primed healthy children aged 3-14 years were randomized to receive ID-TIV vaccine at the dose of 9 µg (n=38) or 15 µg (n=37) for each antigen using a pre-filled syringe with micro-injection system. As controls, 37 age-matched healthy children receiving the virosomal-adjuvanted influenza vaccine (VAIV) were enrolled. On blood samples drawn at enrollment and after 28 ± 3 days, antibody response was evaluated by hemagglutination inhibition assay. Safety in the month following vaccination was analysed.

Results: Seroconversion and seroprotection rates against H1 and H3 antigens were >90% in children receiving ID-TIV vaccine independently from the dose and 86.5% in those vaccinated with VAIV. Response to B antigen was significantly better in children receiving ID-TIV vaccines than VAIV (57.9% with ID-TIV 9 µg, 62.2% with ID-TIV 15 µg, 32.4% with VAIV; ID-TIV 9 µg or 15 µg vs VAIV, $p< 0.05$). All the vaccines were equally safe without differences between groups, although children receiving ID-TIVs had more local reactions.

Conclusions: ID-TIV administration can improve immunogenicity of influenza vaccination in pediatric age, particularly against B antigen. The antigens' dose of 9 µg seems adequate to obtain an optimal immune response with a favorable safety profile.

P773

AN ANALYSIS OF THE IMPACT OF THE THIRTEEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE SEROTYPE CATCH-UP PROGRAM USING UNITED STATES CLAIMS DATA

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Introduction: In February 2010, the Advisory Committee on Immunization Practices recommended 13-valent pneumococcal conjugate vaccine (PCV13) for routine US infant vaccination and an additional catch-up dose of PCV13 to children aged 14-59 months previously fully vaccinated with PCV7. A recent US analysis predicted catch-up would reduce cases of pneumococcal disease and deaths while remaining cost-saving. In this study, we modeled the estimate of actual penetration of PCV13 catch-up to identify the extent of excess disease that could be eliminated with more complete catch-up.

Methods: Analysis of US claims data from April 2010 through September 2010 estimated 39% of the eligible cohort would ever receive PCV13 catch-up; previously the authors assumed 87%. Applying this updated figure to the previously published 10-year Markov model and holding all other inputs constant, we estimated cases of invasive (pneumococcal meningitis or bacteremia [IPD]) and non-invasive disease (pneumonia and otitis media) avoided due to catch-up, and excess cases that could be eliminated with a more complete catch-up program.

Results: Compared with no catch-up, the model estimated that current US catch-up would prevent 11,155 IPD cases, 322,272 pneumonias, 1.6 million AOM cases, and 4,512 deaths over 10 years. The model further suggests an additional 1,485 IPD cases, 81,341 pneumonias, 658,062 AOM cases, and 44 deaths could be avoided over 10 years by increasing catch-up penetration equivalent to fourth-dose compliance levels.

Discussion: Our model predicts vaccine preventable cases of pneumococcal disease and related deaths could substantially decrease with additional penetration of ACIP catch-up recommendations.

P774

THE DIAGNOSIS OF CHRONIC HEPATITIS B INFECTION AMONG CHILDREN BORN IN ENGLAND AFTER INTRODUCTION OF UNIVERSAL ANTENATAL HBV SCREENING PROGRAMME

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Background: Unlike most other countries, the United Kingdom has adopted a selective vaccination policy for hepatitis B virus (HBV), targeting high-risk groups only. This study assessed the risk of chronic hepatitis B among children born in England from 2001 onwards, after the introduction of universal antenatal HBV screening

Methods: Paediatric gastroenterology and infectious disease consultants in England were contacted as part of enhanced national surveillance to report all cases of chronic HBV diagnosed in children aged < 16 years and to complete a questionnaire.

Results: Of 85 children diagnosed with chronic HBV who were born after 01 January 2001, 59 (69%) had been born in England, including 51 (86%) children with mothers diagnosed with HBV infection through the antenatal screening programme. Most children (49/51, 96%) received at least partial vaccination after birth, including 28 (55%) high-risk cases who also received Hepatitis B Immunoglobulin. Two of three children born to antenatally-screened, HBV-negative mothers were later infected horizontally from a family member, while the third one was infected vertically after the mother acquired HBV in late pregnancy. The maternal antenatal screening status was not known for the 5 remaining children. The estimated minimum vertical transmission rate among children born to HBV-infected mothers in England was 0.28% (95% CI: 0.21-0.36%)

Conclusion: The current antenatal screening programme appears to be effective in reducing the risk of vertical HBV transmission, while horizontal transmission among diagnosed cases is rare. Appropriate management and follow-up of children born to HBV-infected mothers remains a key public health priority.

P775

COST-EFFECTIVENESS OF A COCOONING STRATEGY IN NORWAY

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Background and aims: Norway has the highest reported incidence of pertussis in Europe.Immunity against pertussis wanes over time so adolescents and adults become susceptible and act as a reservoir for pertussis transmission.

Until completion of the primary vaccination course newborns remain vulnerable to pertussis which could be potentially fatal at this age.

Parents are the source of pertussis transmission to infants in 52% of the cases. Immunisation of newborns' parents (e.g. cocooning), would potentially reduce the risk in infants.This analysis assesses the cost-effectiveness of such immunisation strategy.

Methods: A decision-tree model was used, and data on pertussis morbidity and costs was collected for infants below 1y and adults (20-39-year). Infant's and parents' cohort sizes were 60,000 and 120,000 respectively. Pertussis in older age groups is highly under-reported, and for parents an under-reporting factor of 10 was assumed.

Health benefits and costs were estimated for both cohorts. Incremental cost-effectiveness ratios (ICER) were calculated from payer and societal perspectives. A univariate sensitivity analysis was performed.

Results: The cocooning strategy (55% coverage) was found to reduce by 24% the incidence of pertussis among infants and 49% among parents. The strategy was estimated to be cost-effective from payer's (NOK 338,158/QALY) and societal perspective (NOK 167,712/QALY). The sensitivity analysis shows the ICER to be most sensitive to the underreporting factor. Lower under-reporting factor (5), would still lead to an ICER below NOK 500,000/QALY (e.g. the Norwegian threshold).

Conclusion: This study estimated that pertussis cocooning strategy would likely be cost-effective in Norway.

P776

ECONOMIC EVALUATION OF SECOND GENERATION PNEUMOCOCCAL CONJUGATE VACCINES IN NORWAY

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Background and aims: A seven-valent pneumococcal conjugate vaccine (PCV7) was introduced in the Norwegian childhood immunization programme in 2006, and since then the incidence of invasive pneumococcal disease (IPD) has declined substantially. Recently, two new second generation pneumococcal conjugate vaccines have become available, and an update of the economic evidence is needed. The aim of this study was to estimate incremental costs, health effects and cost-effectiveness of the pneumococcal conjugate vaccines PCV7, PHiD-CV and PCV13 in the Norwegian setting.

Methods: An age-compartmental cohort model was used to estimate lifetime costs and consequences of vaccination strategies. Using the most relevant evidence and assumptions for a Norwegian setting, we calculated incremental costs, health effects and cost-effectiveness. We performed sensitivity analyses for key parameters, tested key assumptions in scenario analyses and explored overall model uncertainty using probabilistic sensitivity analysis.

Results: The model predicts that both PCV13 and PHiD-CV provide more health gains at a lower cost than PCV7. Differences in health gains between the two second generation vaccines are small for IPD but more substantial for acute otitis media and myringotomy procedures. Consequently, PHiD-CV saves more disease treatment costs and indirect costs than PCV13.

Conclusion: Compared to PVC13, PHiD-CV entails lower costs and greater benefits if the latter is measured in terms of quality adjusted life years. PVC13 entails more life years gained than PHiD-CV, but those come at a cost of NOK 8.2 million (~€ 1.0 million) per life year. The results indicate that PHiD-CV is cost-effective compared to PCV13 in the Norwegian setting.

P777

IMPACT OF A ROTAVIRUS VACCINATION CAMPAIGN ON HOSPITALISATIONS IN FRANCE: THIRD-YEAR SURVEY OF THE IVANHOE STUDY

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Objective: To determine the real-world impact of rotavirus vaccination, controlling for epidemic-to-epidemic variation in disease burden.

Methods: An active hospital-based surveillance system initiated 5 years before vaccine introduction (May 2007) enabled the occurrence of acute rotavirus diarrhoea (ARD) to be modelled. Inclusion in a poisson regression model of an indicator variable for vaccination quantified the impact of a vaccination campaign with Rotateq$^{\grave{O}}$ offered to all children born in Brest by paediatricians, mother and child health centres and general practitioners from the Brest Urban Community (BUC). The principal endpoint was the number of hospitalisations for ARD in infants under 3 years old living in the BUC during 2009/2010 epidemic season.

Results: More than 7150 infants received at least one dose. Vaccine coverage was 55% and 51% for one and 3 doses respectively. Timely administration of doses 1 and 3 was respected in 97% of cases.

Modelling allows estimating that number of hospitalizations for ARD has been divided by 2,8 (95% CI: 2,2 - 3,5) during the last epidemic season (2009/2010). The observed number of cases was 40 whereas the expected number was 110. Comparatively, in the previous 2008/2009 season the number of hospitalizations has been divided by 1,8 (95% CI: 1,5-2,2).

Relative risk reduction for ARD hospitalization was 95% (95% CI: 87% - 98%).

Conclusion: We observed an increasing impact of rotavirus vaccination on hospitalization in the third year survey on this vaccination campaign.

P778

ADOPTION OF ROTAVIRUS VACCINATION BY PHYSICIANS IN FRANCE. EXPERIENCE OF THE IVANHOE STUDY

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Objective: To measure French physicians' knowledge, attitudes and beliefs (KAB) about rotavirus disease and vaccination and to compare those KAB with rates of offering the vaccine in their office.

To assess barriers to use and factors associated with offering the vaccine.

Methods: We conducted in October 2010 a cross sectional survey of paediatricians, General Practitioners (GPs) and mother and child health centres physicians (MCHP) who were investigators in the Ivanhoé study, a prospective cohort study of rotavirus vaccination in Brest City. A questionnaire based upon the Health belief model was administered by phone to all investigators. For GPs, we used in multivariate analysis the rates of vaccination in their office as primary outcome to explore factors associated with offering the vaccine.

Results: Responses rates were respectively 100%, 62% and 83% for paediatricians, GPs, MCHP. More than 7150 infants were vaccinated during the cohort study (Paediatricians: 60%, GPs:18%, MCHP:22%). Paediatricians were more likely to report to systematically offer the vaccine (100%vs 76%) and to agree that rotavirus infection were common (85 vs 40%) and potentially severe (100 vs 76%) than GPs. The most commonly endorsed barriers were the lack of reimbursement (94%) and the absence of recommendation by the health authorities (50%). For GPs, in multivariate analysis lower vaccination rate was significantly associated with higher age, the perception of complexity of recommendations for timing of rotavirus doses and addition of another vaccine to already overloaded vaccine schedule ($p < 0.001$).

Conclusion: Those results should help health authorities before implementing rotavirus vaccination.

P779

TIMELINESS AND COMPLIANCE OF ROTAVIRUS VACCINATION IN AUSTRALIA

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Background and aims: Two licensed rotavirus (RV) vaccines are funded under the Australian National Immunisation Program for all children born since May 2007. A two-dose vaccine, RIX4414, (*Rotarix*™, GlaxoSmithKline Biologicals) is funded in New South Wales (NSW). A three-dose vaccine, RV5 (*RotaTeq*™, Merck and Co.) is funded in Queensland (QLD). We examined the compliance and timeliness of vaccination during 2007-2009.

Methods: Data from the Australian Childhood Immunisation Register (ACIR) was used to quantify the proportion of children completing the full vaccination series (CVS) regardless of age, mean age at each dose, and timeliness of receiving the two- dose or three-dose vaccine.

Results: Overall proportion of CVS was ~80%. Mean (median) age for the two-dose series was 1.5 (2) and 3.8 (4) months, and 1.7 (2), 3.8 (4) and 6 (6) months for the three dose series.

Table 1: Percentage of children vaccinated, by median age and those who successfully completed the vaccination series regardless of age

Year	Two dose vaccine in NSW* (Rotarix™)				Three dose vaccine in QLD* (Rotateq™)				
	Total Number of children	% of children receiving 1st dose by 2 months	% of children receiving 2nd dose by 4 mo	% of children complete vaccination at any age	Total number of children	% of children receiving 1st dose by 2 months	% of children receiving second dose by 4 mo	% of children receiving 3rd dose by 6 mo	% of children fully complete vaccination at any age
07/08	98,367	79.8%	74.3%^	81%	97,847	76.2%	75.2%	68.9%^	78.1%
08/09	83,384	82.2%	77.9%^	83.9%	82,388	84.5%	80.0%	74.0%^	82.0%

*States investigated have similar modes of vaccine delivery (HCP, councils, others) and % indigenous populations
^p value <0.001 between last scheduled dose at cut off of median age of vaccination,
^p value <0.001 between last scheduled dose at cut off of median age of vaccination

[Table 1 - completion of vaccine series]

Table 2: Timeliness of two-dose vaccine and three-dose vaccine in NSW and QLD

Rotavirus Vaccines	Children vaccinated	Dose 1	Dose 2	Dose 3
Two-dose vaccine in NSW (Rotarix™)	Children born 2007-08	98%*	92%*	N/A
	Children born 2008-09	97%^	93%^	N/A
Three-dose vaccine in QLD (Rotateq™)	Children born 2007-08	98%	92%**	88%**
	Children born 2008-09	98%	94%^^	90%^^

*p value <0.001; ** p value <.001; ^p value <0.001; ^^ p value <.001 N/A -not applicable
Note: Timeliness was defined as the proportion of all children who received vaccine prior to median age at administration. 2 month, 4 month and 6 month for 1st, 2nd, and 3rd doses respectively.

[Table 2 - timeliness]

Conclusions: Overall completion of the full series of RV vaccination is high, although vaccination rates fall as a series progresses. A higher compliance with a two-dose schedule and decreased timeliness with increasing doses is suggested. Further investigation is warranted.

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IMPACT OF VACCINATION WITH RIX4414 ON ROTAVIRUS GASTROENTERITIS (RVGE) IN CHILDREN AGED < 5 YEARS IN AUSTRALIA

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Background and aims: Two licensed rotavirus vaccines are funded under the Australian National Immunisation Program (NIP) for all children born from 1 May 2007. We examined the impact of RIX4414 (*Rotarix*™, GlaxoSmithKline Biologicals) vaccination on rotavirus gastroenteritis (RVGE) hospitalizations in two states/territories: New South Wales (NSW), and the Australian Capital Territory (ACT).

Methods: A database analysis of state-based electronic hospital admissions was conducted to assess the trend of incidence rates of RVGE pre-introduction (1998-2006) with post-vaccination (2008-2009).

Results: RIX4414 coverage increased after initial introduction, rising to 83.4% in NSW and 91% in ACT within the first year of implementation[1]. In 2009, incidence of RVGE in children < 1 year decreased from a baseline of 35.85 to 2.69 per 10,000 child/year in NSW and 44.09 to 4.25 in ACT. The reduction of RVGE incidence was observed in all age groups (0-5 years). The overall reduction of RVGE in children < 5 years in 2009 compared with baseline was 90.1% in NSW and 92.1% in ACT.

Conclusions: This study demonstrates significant reduction of RVGE hospitalizations after introduction of mass vaccination with RIX4414 in two Australian states/territories. Reduction of RVGE hospitalizations was observed in all children < 5 years of age, even those were not eligible for vaccination according to their age, suggesting herd immunity.

Reference: 1. Hull B, Deeks S, Menzies R et al. Immunisation Coverage Annual Report, 2007. *Communicable Diseases Intelligence*.2009;33(2):170-87.

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TETANUS VACCINATION STATUS IN REFUGEE CHILDREN IN GENEVA, SWITZERLAND

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Background: Data on tetanus vaccination coverage in recently arrived refugee children in Switzerland are missing, and are essential to formulate vaccination strategies.

Materials and methods: We retrospectively collected data from refugee children followed in our hospital for general care. Tetanus antibodies were measured by ELISA either at arrival or one month after booster vaccination, according to local recommendations.

Results: 94 children were evaluated between January 2009 and May 2010. Most were from Eastern Europe and Africa. According to reported history, only 30% were up-to-date with their vaccination at arrival, and only 4% had available vaccination records. Antibody levels against tetanus were measured at baseline in 13 patients, and after booster vaccination in 57 children. Few patients (6% of the total children, 15% at baseline, and 3.5 % post-booster) were insufficiently immunized despite prior reported tetanus vaccination in their own country. Measuring antibody levels after booster vaccination saved children, in average, from two unnecessary additional tetanus vaccines.

Age (years)	Number of patients	<500 U/l	500-1000 U/l	1000-10000 U/l	>10000 U/l	Immediate vaccination needed	Protection < 5 years	Protection 5-10 years	Protection > 10 years
<2	2	0	0	1(50%)	1(50%)	0	1(50%)	1(50%)	0
2-5	13	0	0	3(23%)	10(77%)	0	2(15%)	9(70%)	2(15%)
5-10	19	1(5%)	1(5)%	6(32%)	11(58%)	2(10.5%)	1(5%)	14(74%)	2(10.5%)
10-16	23	0	0	9(39%)	14(61%)	0	0	13(57%)	10(43%)

[Te titers after booster and length of protection]

Conclusion: Immunologically proven protection against tetanus in refugee children is heterogeneous, but most children in our study are sufficiently immunized. Vaccine-related antibody measurement allows individual tailoring of vaccine schedules and avoids risk of hyperimmunization.

P782

VACCINATION COVERAGE AND ATTITUDES TOWARDS VACCINATION OF HEALTH CARE PERSONNEL OF A MAJOR PEDIATRIC HOSPITAL IN ATHENS

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Background: Healthcare personnel (HCP) is constantly at risk for exposure to and transmission of vaccine-preventable diseases.

Aims and methods: To evaluate vaccination coverage and attitude of HCP towards immunization, 101 questionnaires were filled by 66 residents in pediatrics and 35 medical students (age 22-38 years) of the largest pediatric hospital in Greece. Vaccination was recorded from immunization booklets.

Results: Natural infection was recorded for measles (11.9%), rubella (16.8%), mumps (17.8%) and varicella (79.2 %). Additionally, 55.4% of HCP was fully immunized for measles, and 47.5%, 44.6% and 5.0% for rubella, mumps and varicella respectively. Most HCP was fully immunized for tetanus in childhood but only 35.6% maintained this status as adults. Immunization for Hepatitis B was 63.4% with a worrying 7.0% of unvaccinated/incompletely vaccinated. Flu vaccination remains low (48.5%) with only 36.7% on a yearly basis. In agreement, just 27.7% were immunized in last year's H1N1 pandemic. Unanimous (99%) is the acceptance of vaccinations which aim to protect both patients and HCP (95.0%). Nevertheless, 69.3% worry of long term adverse events following vaccination; 44.1% have reservations on the administration of vaccines as H1N1-Flu (20.8%), Rota (9.9%) and HPV (7.9%) and 9.9% believe that HCP is in less danger of infectious diseases than general population.

Conclusions: A gap exists between HCP's positive thinking towards immunization and implementation on themselves. The considerable percentage of misconceptions about vaccine's safety keeps lowering the expected levels of vaccination coverage. Continued education efforts must be strengthened to avoid spread of vaccine-preventable diseases especially in health care settings.

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VACCINATION COVERAGE AND ATTITUDES TOWARDS VACCINATION OF HEALTH CARE PERSONNEL OF A MAJOR PEDIATRIC HOSPITAL IN ATHENS

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Conclusions: A gap exists between HCP's positive thinking towards immunization and implementation on themselves. The considerable percentage of misconceptions about vaccine's safety keeps lowering the expected levels of vaccination coverage. Continued education efforts must be strengthened to avoid spread of vaccine-preventable diseases especially in health care settings.

P784

ROLE OF INFLUENZA VIRUS IN ACUTE RESPIRATORY INFECTIONS AMONG PRESCHOOL CHILDREN: RESULTS OF AN OBSERVATIONAL STUDY

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Background and aims: Acute respiratory infections (ARI) and asthma are the main reasons for medical visits by preschool children. They can be associated with many respiratory viruses. Few studies have been focusing on influenza virus in this population. This study aims at assessing the burden of influenza and the coverage of influenza vaccine in preschool children attending a reference pediatric hospital with respiratory symptoms.

Methods: A prospective observational study was carried out at a Pediatric Hospital at, Curitiba, Brazil, from Jul/12 till Oct/19/2010. Children with influenza-like illness, pneumonia, asthma, bronchiolitis, tracheobronchitis or wheezing starting< 7 days before the medical visit were enrolled to analyze demographic, clinical and immunization data. Nasopharyngeal sample was tested with RT-PCR multiplex.

Results: 248 children aged 24 to 59 months (51.6% male) were recruited. Samples of 136 children (54.8%) were positive for at least one virus. The most frequent were rhinovirus (n=33, 13.3%), adenovirus (n=24, 9.7%) and influenza (n=21, 8.5%). From these 21 flu strains, 11 were subtype B (4.4% of all children), 9 were subtype AH3N2 (3.6%) and 1 was A non-typed (0.4%). 225 children (94.5%) had received monovalent H1N1 flu vaccines and 13 (5.5%) had received trivalent vaccine.

Conclusions: Flu was detected in 8.5% of preschool children in this study (95%CI= [0.05 - 0.12]). These data certainly underestimate the burden of influenza since vaccine coverage was very high (96%). However, the isolation of B or H3N2 strains in 8% of the children confirms the interest of the trivalent seasonal vaccine.

P785

THE YEAR AFTER H1N1 INFLUENZA PANDEMIC:PREVENTION OF THE SECOND WAVE, PARANÁ, BRAZIL

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Background and aims: In 2009 Parana was the state of Brazil where occurred the most cases of influenza (H1N1), with significant morbidity and mortality especially in children and young adults. The aim of this study is to analyze the magnitude of the influenza illness in Parana especially in pediatric and adolescents patients and compare the behavior of the disease after the vaccination campaign.

Methods: This is descriptive study using epidemiological surveillance data (SINAN NET system) of Health Public Service of Parana State, Brazil, from April/27/2009 till Dec/31/2010.

Results: A total of 78272 cases of influenza H1N1 were detected in 2009, with 344 deaths. In 2010 a vaccination campaign was carried out to the most vulnerable groups. The coverage achieved was 100%. Comparing the profile of the disease in the years 2009 and 2010 was observed: the number of cases decreased to 1862 with 18 deaths representing a significant reduction (97.9%) of influenza cases. The proportion of influenza among children and adolescents was approximately 40% in 2 years studied. The proportion of laboratory diagnosis increased from 7.2% to 12.1%. The lethality rate increased from 0.4% to 1.1%. The proportion of deaths in children and adolescents was from 11.4 to 33.4%.

Conclusions: To manage the pandemic was a challenge. The increase of the lethality showed that influenza illness needs a continuous surveillance and rapid approach. The commitment of government agencies, health professionals and society has contributed to the large participation in the vaccination campaign. Strategies used to pandemic control have been successful.

P786

INVASIVE MENINGOCOCCAL DISEASE IN QUEBEC 8 YEARS AFTER THE IMPLEMENTATION OF A PUBLIC SEROGROUP C MENINGOCCOCAL IMMUNIZATION PROGRAM

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Background/aims: In the province of Quebec, Canada, an increase in the incidence of serogroup C invasive meningococcal disease (IMD) occurred in 2001-2002. A mass-immunization campaign against serogroup C launched in 2001 was followed by a universal immunization program. In the perspective of changes in vaccination program, the dynamic of serogroup distribution was analyzed.

Methods: Review of 1997-2010 surveillance data on IMD isolates submitted to the Laboratoire de Santé Publique du Québec.

Results: Overall, 858 IMD were identified: 66%, 22%, 8%, and 3% were due to serogroups B, C, Y, and W135, respectively. 28% of cases were in children < 5 years of age and 18% in 15-19-year-olds. Serogroup B was consistently the most prevalent in < 5-year-olds. Over the last 3 years, serogroup B was responsible for 83% of all IMD: 97% in < 1-year-olds, 100% in 1-14-year-olds, and is decreasing from 95% in 15-19-year-olds to less than 60% in those ≥40-year-old. During 1997-2010, the incidence of serogroup B IMD (per 100 000) was stable in < 1-year-olds (12.4 to 12.3) and in 1-4-year-olds (1.2 to 2.1), and increased 6-fold (0.4 to 2.4) in 15-19-year-olds. *N.meningitidis* B:17:P1.19 (mostly corresponding to ST-269), first identified in 2003, is since accounting for 35% of all serogroup B IMD: 26% in < 5 year-olds, 38% in 10-14-year-olds, 51% in 15-24-year-olds and 38% in 25-39-year-olds.

Conclusion: Serogroup B is responsible for the vast majority of IMD in Quebec. An emerging clonal complex affecting mainly adolescents and young adults is spreading across the province.

P787

PAEDIATRICIANS OPINION REGARDING SEASONAL INFLUENZA VACCINATION: IMPLICATIONS FOR VACCINE PROMOTION

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Background and aims: Vaccination has been shown to reduce morbidity and mortality associated with influenza infection. Physicians own behaviours are known to be strongly associated with their recommendations to patients. We assessed knowledge, attitudes and practices of paediatricians regarding seasonal influenza and its prevention by vaccination.

Methods: In Spring 2010, a self-administered anonymous mail-based questionnaire was sent to all 565 paediatricians in the province of Quebec, Canada.

Results: Response rate was 65% (367/565). Most respondents strongly agreed (40.3%) or agreed (37.5%) that it is very useful to vaccinate children against seasonal influenza. Most paediatricians surveyed also indicated a high willingness to recommend seasonal influenza vaccination to their patients (42.3% strongly agreed and 39,7% agreed). The majority of them (91.3%) reported having been vaccinated against seasonal influenza in 2008-2009 and 55.7% in 2010, right after pandemic A(H1N1) influenza vaccination occurred in Quebec. At the time of the study, 88.8% of paediatricians had the intention to be vaccinated for the next flu season. The main reason mentioned by paediatricians who did not intend to be vaccinated was that they were not at risk to contract seasonal influenza. Paediatricians' intention to recommend seasonal influenza vaccine to their patients was highly correlated to their own vaccination behaviour ($p < 0.0001$ with Cochran-Armitage trend test).

Conclusions: Public health interventions to promote seasonal influenza vaccination among paediatricians should stress out the threat posed by seasonal influenza to healthcare workers and the patients.

P788

ANTIBODY PERSISTENCE IN CHILDREN VACCINATED WITH ONE DOSE OF ASO3-ADJUVANTED A/H1N1/2009 VACCINE AND THE EFFECT OF SEASONAL 2010-2011 INFLUENZA VACCINE

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Background and aims: In Canada, two doses of ASO3-adjuvanted A/H1N1/2009 vaccine (Arepanrix®1.9µgHA) were recommended to children < 9 years. In the province of Quebec, one dose of vaccine was recommended. We assessed the persistence of antibody one year after a single dose of adjuvanted vaccine and the immunogenicity of seasonal 2010-2011 vaccine.

Methods: Children ≤9 year-old vaccinated in 2009 with ASO3-adjuvanted vaccine were eligible to participate. In 2010, participants naïve to seasonal vaccine received two and non-naïve, one dose of seasonal vaccine. Blood samples were collected before and 21-28 days post-each dose. HAI test was used.

Results: 155 children participated. Before seasonal vaccination, 80% of participants had a titer ≥1:10 and 46% a titer ≥1:40 to A/California/7/2009 (H1N1). Post-first dose of seasonal vaccine, 98.4% and post-dose two, 100% had a titer ≥1:40. A 16.5-fold GMT increase was observed post-first dose but none post-second dose. All 25 participants aged < 36 months with a titer < 1:40 to B/Brisbane/60/2008 (Victoria lineage) before vaccination remained under this threshold post-first dose. Twelve of these children received previously a seasonal vaccine containing B Yamagata lineage. Post-second dose, 87% of naive participants had a titer ≥1:40 to B/Brisbane/60/2008. The response to A/Perth/16/2009 (H3N2) was in the previously reported range (≥75% 1:40). No SAE were reported.

Conclusions: One dose of adjuvanted vaccine induced a long lasting immunity against A/California/7/2009 (H1N1) virus. One dose of seasonal vaccine was insufficient to induce an adequate immune response to B/Brisbane/60/2008 strain in children < 3 years naive to B Victoria lineage.

P789

RAPID REDUCTION IN INVASIVE PNEUMOCOCCAL DISEASE (IPD) AFTER INTRODUCTION OF PCV7 TO THE NATIONAL IMMUNIZATION PLAN (NIP) IN ISRAEL

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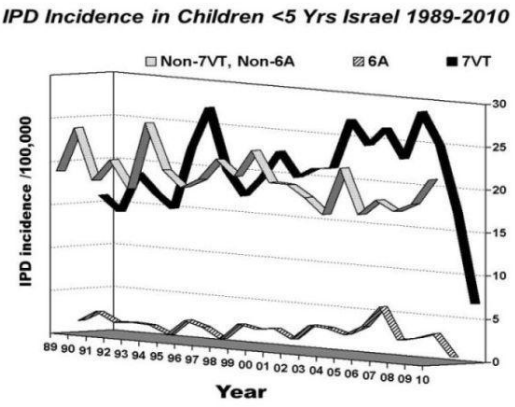
Background and aims: PCV7 was licensed in Israel in 2007, with scattered use till 2009, and was introduced to Israel NIP in July 2009, as a 2, 4, 12m schedule, with catch-up (2 doses, 2nd year). IPD nationwide active surveillance has been conducted since 1989.

Methods: All 27 medical centers performing blood cultures in Israel participated by reporting monthly all IPD cases (defined by positive blood/CSF cultures). Capture-recapture methods were used to evaluate completeness. ~50% of isolates were submitted to serotyping until recent years, and >95% since 2000. Extrapolation by year, ethnic group, age, and serogroup was conducted to insure appropriate age-specific serotype-specific incidence assessment.

Results: During 1989-2010, 5,821 cases were reported (**FIGURE**). PCV7 serotypes+6A (VT) contributed ~50% of IPD. VT incidence increased during 1989-2008, causing overall IPD increase. In 2004-8, mean IPD incidence/100,000 was 47.2 and 85.3 for < 5 and < 2 years, respectively. In 2010, VT incidence decreased by 72.9% and 78.7% compared with 2004-8 in < 5 and < 2 years respectively, (P< 0.001). The respective overall IPD reduction was 37.7% and 41.4% with no replacement so far. In 2010, 73% of isolates causing remaining IPD < 5 years were PCV13 serotypes.

Conclusions: PCV7 introduction to NIP as a 2+1 schedule with catch-up in < 2 years, showed a rapid decrease in IPD < 5 yrs. PCV7 was replaced by PCV13 in November 2010.



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P790

IMMUNOGENICITY OF AN INVESTIGATIONAL MULTICOMPONENT MENINGOCOCCAL SEROGROUP B VACCINE (4CMENB) ADMINISTERED WITH OR WITHOUT ROUTINE INFANT VACCINATIONS IN DIFFERENT SCHEDULES

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Background: When administered at 2, 4 and 6 months of age an investigational multicomponent meningococcal serogroup B vaccine (4CMenB) elicits bactericidal antibodies against reference MenB strains containing the vaccine-antigens. We studied the immunogenicity of 4CMenB when administered concomitantly or without routine-vaccines and in a 2, 3 and 4 month schedule.

Methods: An open-label, parallel-group, multi-centre study was conducted with randomisation of participants 2:2:1:1 to receive

i) 4CMenB at age 2, 4 and 6 months concomitantly with routine-vaccines (7-valent pneumococcal glyco-conjugate-vaccine and a combined diphtheria-toxoid, tetanus-toxoid, inactivated-polio, acellular-pertussis, hepatitis B and Haemophilus influenzae type b-vaccine)

ii) 4CMenB at 2, 4 and 6 months separately from routine-vaccines (given at 3, 5 and 7 months)

iii) 4CMenB and routine-vaccines at 2, 3 and 4 months

iv) routine-vaccines alone.

The proportion of participants with human-complement serum bactericidal antibody (hSBA) titre≥1:5 (serological correlate of protection) was calculated.

Results: At least 99% of participants receiving 4CMenB at 2, 4, 6 months (concomitantly or without routine-vaccines) or at 2, 3, 4 months (with routine-vaccines) developed hSBA titres ≥1:5 against strains 44/76 and 5/99. For NZ98/254 the correlate was reached or exceeded in 79% (2, 4, 6 months with routine-vaccines), 87% (2, 4, 6 months without routine-vaccines) and 81% (2, 3, 4 months with routine-vaccines). Percentages of participants responding to routine-vaccines given concomitantly with 4CMenB were non-inferior to routine-vaccines alone for all antigens except pneumococcal-serotype 6B.

Conclusion: 4CMenB is immunogenic against reference strains when administered concomitantly with routine-vaccines at 2, 4, 6 or 2, 3, 4 months.

P791

PREDICTED IMPACT OF UNIVERSAL MASS VACCINATION WITH MMRV VERSUS MMR IN THE NETHERLANDS ON VARICELLA INCIDENCE AND COMPLICATIONS

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Background and aims: Varicella affects the majority of people, causing complications in around 5%, causing an increased burden to healthcare systems. The objective was to assess the impact of universal mass vaccination with MMRV (measles, mumps, rubella, varicella) vaccine versus MMR (measles, mumps, rubella) vaccine on the incidence of varicella and its complications.

Methods: Varicella incidence is highest among < 5 year-olds in the Netherlands due to increased daycare attendance versus other countries. Infant vaccination programs are well-established and MMR coverage is high (95%). A dynamic transmission model for the Netherlands, including a Dutch empirical contact matrix, compared varicella cases before and after vaccination. The model assumed 100% replacement of MMR within 5 years. Dutch age-specific complication rates were applied.

Results: After vaccination, varicella incidence decreased by 83% overall, resulting in a 92% decrease in varicella complications; from 1,105 to 98 per million person-years (MPY) after MMRV vaccination. Before vaccination, 83% of varicella cases were among 1-4 year-olds (11,278 varicella cases per MPY of total population), causing 942 varicella complications per MPY in this age group. At the new equilibrium, the highest incidence was significantly lower; 1,445 varicella cases per MPY among the 20+ year-olds resulting in 45 varicella complications per MPY in this age group.

Conclusion: Replacement of MMR with MMRV allows sustained mass vaccination against varicella, predicted to significantly reduce varicella incidence and consequently the incidence of varicella complications.

P792

TEN-YEAR PERSISTENCE OF ANTI-HBS ANTIBODIES IN 12-13 YEAR OLDS PRIMED IN INFANCY WITH 3-DOSES OF HBV-VACCINE (10µG/DOSE) IN ROUTINE SETTING

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Background and aims: The long-term persistence of antibodies against HBV surface antigen (HBsAg) has been demonstrated in countries with high endemicity. The present study evaluated the persistence of anti-HBs antibodies in adolescents vaccinated 10 years ago in a routine clinical setting and residing in a western-European region of low endemicity. In addition, immune memory was assessed through a booster immunization.

Methods: This open-label study (112682/NCT00984139) was conducted in 20 centres in Germany. Adolescents aged 12−13 years received a challenge HBV vaccine dose, 10 years after priming with three-doses of the same monovalent paediatric HBV vaccine (10µg HBsAg) within 18 months of birth. Blood samples were collected before vaccination to assess persistence of antibodies and one month after challenge vaccination. Anti-HBs antibodies were measured using ELISA.

Results: In total, 306 subjects were vaccinated; 284 were included in the per-protocol cohort for immunogenicity. Prior to challenge dose, 91.8% of subjects had detectable anti-HBs antibodies, 78.0% of subjects had anti-HBs antibody concentrations ≥10mIU/ml and 24.8% had concentrations ≥100mIU/ml. One month post-challenge dose of monovalent paediatric HBV vaccine, these values increased to 99.6%, 98.9% and 93.7%, respectively. Anti-HBs Geometric Mean Concentrations increased 161-fold from 33.6 to 5425.5mIU/ml and 97.2% of subjects demonstrated an anamnestic response to the challenge dose. The HBV challenge vaccine was well-tolerated.

Conclusions: Routine three-dose primary vaccination with monovalent HBV vaccine during infancy results in strong immune memory against HBV in over 95% of vaccinees for at least 10 years.

P793

IMMUNOGENICITY AND SAFETY OF BOOSTER VACCINATION WITH REDUCED-ANTIGEN-CONTENT OR FULL-STRENGTH DIPHTHERIA-TETANUS-ACELLULAR-PERTUSSIS-IPV VACCINES IN PRE-SCHOOL CHILDREN, PRIMED WITH A 2+1 SCHEDULE

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Background: The use of reduced-antigen-content diphtheria-tetanus-acellular pertussis-poliomyelitis (dTpa-IPV) vaccines as boosters in preschool children is increasing, in Italy, where *POLIOBOOSTRIX*™ (ie. *Boostrix*-Polio™ GSK) is approved from 4 years of age.

This Phase IIIb study (NCT00871000) compared the immunogenicity and safety of dTpa-IPV with DTPa-IPV (*Tetravac*™, Sanofi Pasteur), when co-administered with a measles-mumps-rubella-varicella vaccine (MMRV; *Priorix Tetra*™, GSK).

Methods: Subjects aged 5-6 years who had received in infancy a DTPa-based vaccine in a routine setting, according to the Italian 3-5-11 recommended schedule were randomized (1:1) to receive either dTpa-IPV or DTPa-IPV vaccine, co-administered with MMRV. Serological testing was performed on samples collected before and one month post-vaccination. Safety assessments included solicited local and general adverse events (AE), unsolicited and serious AE.

Results: 303 subjects received either reduced-antigen-content dTpa-IPV (N=151) or a DTPa-IPV vaccines (N=152). One-month post-booster, non-inferiority of dTpa-IPV compared to DTPa-IPV was demonstrated according to the pre-defined criteria, and all subjects were seropositive and seroprotected. Reduced-antigen dTpa-IPV vaccinees reached anti-D concentrations >1.0IU/ml in 99.3% of cases. Anti-pertussis booster responses were: 89.8% (PT), 94.9% (FHA), 94.2% (PRN) in dTpa-IPV subjects and 92.2%, 95.7%, n/a%, respectively for DTPa-IPV subjects. Post-vaccination seropositivity rates reached 98-100% against the MMRV antigens. During the 4-day follow-up, grade 3 local AE were recorded at 10.6% dTpa-IPV and 16.4% DTPa-IPV of injection sites. No SAE were recorded.

Conclusions: The dTpa-IPV vaccine demonstrated comparable immunogenicity and reactogenicity versus DTPa-IPV.

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ACCEPTANCE OF SUPPLEMENTARY PNEUMOCOCCAL AND MENINGOCOCCAL GROUP C IMMUNIZATIONS IN SWITZERLAND

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Background: No data are available on the acceptance of supplementary pneumococcal (PCV) and meningococcal group C conjugate vaccine (MCV) immunizations introduced in Switzerland in 2006. PCV is recommended in a 2+1 schedule (2,4,12 months) or 2 catch-up doses (12-24 months), MCV as single dose (12-15 months). We aimed to assess acceptance of PCV and MCV immunizations compared to generally recommended immunizations (diphtheria-tetanus-pertussis-Hib-poliomyelitis/hepatitis B = DTP+; measles-mumps-rubella = MMR) in children 24 months of age in the regions of Basel and Geneva.

Methods: After sample size calculation, 650 children born January-April 2007 were to be recruited based on available birth-date lists. Informed consent was requested from parents in chronological order.

Results: 592 (Basel: 271, Geneva: 321) children were recruited in 2009 and their documented immunizations administered up to 24 months of age were analyzed. At 12 months compliance (Basel/Geneva) with 3 doses of DTP+ was 92% (95%CI:89-95)/96% (93-98) compared to 69% (63-74)/78% (73-82) with 2 doses of PCV ($p < 0.001$). Between 12-24 months, compliance with $\geq$1 dose of MMR was 89% (86-93)/94% (91-96), 78% (73-83)/76% (71-81) with 4th dose of DTP+, 72% (67-77)/82% (78-86) with $\geq$1 dose of PCV, and 59% (54-65)/64% (59-69) with $\geq$1 dose of MCV (PCV vs MMR, MCV vs MMR, DTP+ vs MCV:$p < 0.001$; DTP+ vs. PCV:$p=0.88$).

Conclusions: Shortly after introduction, acceptance with supplementary PCV and MCV immunizations was reasonably good (60-80%) in Swiss children at 24 months of age in the Basel and Geneva areas. However, further efforts are needed to improve immunization coverage.

P795

EXCESSIVELY HIGH IMMUNE RESPONSES IN 4-YEARS OLD DUTCH CHILDREN PRE AND POST THE 5TH CONSECUTIVE ACELLULAR PERTUSSIS VACCINE?

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Since antibody levels wane rapidly after vaccination, long-term B- and T-helpercell (Th) immune responses might play a major role in protection against pertussis. We investigated the effect of the preschool aP booster on cellular immune responses in whole-cell (wP) or acellular (aP) pertussis primed children.

Memory B-cells were detected by pertussis protein-specific ELISpot-assays, and T-cell cytokines as well as plasma IgG, IgA and IgE levels were determined by fluorescent bead-based multiplex immunoassays.

Three years after 4 infant wP or aP vaccinations anti-pertussis IgG levels have waned, but memory B- and T-cells were detectable. In aP vaccinated children, antibody levels as well as B- and T-cell responses for pertussis and tetanus were higher compared to wP vaccinated children. After the 5th aP vaccination especially the Th2 cytokines but also those of Th1 and Th17 remained high, but did not show a typical memory response. Furthermore, increased numbers of memory B-cells and higher pertussis-specific IgG levels but also higher total IgE concentrations were found after the preschool booster in aP vaccinated children compared to wP vaccination.

Long-term pertussis-specific memory B- and T-cells were identified in children despite waning antibody levels. However, high Th2 cytokines, unusual T-cell kinetics and IgE levels might be correlated to the higher but still rare incidence of severe local side effects found after the fifth aP vaccination. We speculate that a combination of four high-dose infant vaccinations combined with a preschool booster induce exaggerated cellular immune responses and possible immune unresponsiveness and adverse reactions.

P796

INTRODUCING UNIVERSAL VACCINATION AGAINST HEPATITIS B IN THE NETHERLANDS

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Currently, public vaccination programmes for hepatitis B in the Netherlands focus on

1) children whose mothers carry the virus,

2) children with at least one parent from a country where hepatitis B is relatively prevalent, and

3) people at elevated risk of infection through behavioural risks.

Although these targeted programmes have resulted in the alleviation of the considerable disease burden associated with acute and chronic infection, since about 1988 the reported number of new cases of hepatitis B has remained more or less constant. A dynamic transmission model was developed that incorporates the essential features of hepatitis B and its prevention, suggesting that over a period of 50 years about 5000 extra deaths would be prevented by adding universal vaccination of either infants or prepubertals. Therefore, the Minister of Health has decided to implement universal vaccination by October 2011. The Health Council has recommended to investigate the social and psychological determinants of acceptance of universal vaccination against hepatitis B in order to better plan the introduction in the NIP. In the presentation we explore which lessons can be learnt from HPV and influenza A/H1N1 and which approach is most appropriate in a public debate on universal vaccination against hepatitis B.

P797

THE IMPLEMENTATION OF REMINDER AND RECALL SYSTEMS FOR IMPROVED HEPATITIS B VACCINE UPTAKE IN AT RISK BABIES IN THE UK

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Background: The UK has not adopted universal hepatitis B immunisation but uses an at risk approach. This is based on 0.3 % incidence of hepatitis B infection in pregnant women from antenatal screening data. For babies this means that only those whose mothers are positive for the hepatitis B virus are offered the vaccine under the National Health Service. Uptake and completion of this vaccine course is lower than for other vaccines offered routinely to all children.

Aim: To look at two types of reminder and recall systems to see if these help in improving the uptake of the vaccine to those babies at risk.

Methods: A hospital based remind and recall appointment system involves automatic follow-up appointment at the hospital with Paediatrician antenatally for mother and for baby after birth to check on completion of vaccine doses. The community based remind and recall system uses the community nurse as main contact and a database with alert system for recall when vaccine is due.

Results: Nationally uptake for second and third doses of the vaccine ranges from 40 - 60% depending on region. With our recall systems, one in South East, the other in West Midlands, we had 98-100% uptake for all doses including one year booster.

Conclusions: We propose that the reminder and recall systems are used nationally in the UK in order to ensure that those babies who need these vaccines get them and complete the schedule. Acknowledgements: Dr Tariq Ahmad. Consultant Paediatrician. UHCW NHS Trust, UK.

P798

IMPACT OF PNEUMOCOCCAL VACCINATION IN DENMARK DURING THE FIRST 3 YEARS AFTER PCV7 INTRODUCTION IN THE CHILDHOOD IMMUNIZATION PROGRAMME

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Background and aim: From October 1st 2007 the 7-valent pneumococcal conjugate vaccine (PCV7) was implemented in a 2+1 dose schedule in the national immunization program for infants. Vaccine coverage has reached 86%. To assess the impact of PCV7 we evaluated direct and indirect effects on incidence of invasive pneumococcal disease (IPD) and pneumococcal serotype distribution.

Method: We compared disease incidence in pre-PCV7 (years 2000-2007) and PCV7 periods (years 2008-2010) based on national surveillance data, IPD laboratory-based surveillance and vaccination registry.

Results: In the whole population the overall incidence of IPD declined from 19.4 to 17.8 cases per 100,000 persons (incidence rate ratios (IRR) 0.92; 95% confidence interval (CI) [0.84-1.02]) and vaccine serotypes incidences (VT) changed from 7.7 to 3.8 (IRR 0.49; 95%CI [0.40-0.59]) comparing pre-PCV7 and PCV7 periods. In children aged 0-2 years the overall incidence of IPD decreased from 54.8 to 25.5 (IRR 0.47; 95%CI [0.29-0.77]) cases per 100,000 and for VT from 36.7 to 4.1 (IRR 0.11;95% CI [0.06-0.22]) comparing pre-PCV7 and PCV periods. The incidence of non-vaccine serotypes (NVT) increased from 11.8 to 14.0 cases pr 100,000 in the whole population (IRR 1.18; 95%CI [1.05-1.32]) and dominant serotypes in the PCV7-period were serotypes 1 and 7F.

Conclusions: We report a marked decline in the incidence of VT IPD in both vaccinated and non-vaccinated individuals, the latter suggesting the development of herd immunity. The incidence of NVTs in the whole population seems to increase slightly with dominant serotypes that are covered by the recently introduced 13-valent vaccine.

P799

THE IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINATION IN CHILDREN IN ENGLAND AND WALES FOUR YEARS AFTER THE INTRODUCTION OF PCV7

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Background and aims: The seven-valent pneumococcal conjugate vaccine (PCV7) was introduced into the UK in September 2006 as a 2/4/13 month schedule. Since 1996, enhanced national surveillance in England and Wales (E&W) has provided a baseline against which to evaluate the impact of PCV7 on vaccine type (VT) and non-vaccine type (NVT) invasive pneumococcal disease in vaccinated cohorts.

Methods: Trends in reported IPD were measured over a six year pre-PCV7 period and changes in VT and NVT IPD four years post-PCV7 were estimated after adjusting for changes in proportions with known serotype or age, changes in population size and trends in bacteraemia ascertainment.

Results: IPD decreased for all VT serotypes by 98% in children under 2 yrs and increased by 68% for NVT serotypes in this agegroup. The overall reduction in IPD in children < 2 years was 56%. Many more individual NVT serotypes increased than decreased post-PCV7 consistent with vaccine-induced replacement. This overall reduction was less, and the increase in NVT IPD more, than reported in the United States. Key serotypes showing replacement were 7F, 19A and 22F. Increases in NVT IPD were not associated with antimicrobial resistance.

Conclusions: PCV7 has reduced VT invasive pneumococcal disease in targeted agegroups although the overall impact has been reduced due to the serotype replacement seen and subsequent increase in NVT disease. Changes in surveillance sensitivity, inclusion of non-hospitalised cases and natural changes in serotype-specific incidence can also have a major effect on the conclusions drawn about the impact of PCV7 vaccination.

P800

OPSONOPHAGOCYTIC ACTIVITY (OPA) OF ANTIBODIES INDUCED BY ALTERNATIVE REGIMENS OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7) IN ISRAELI INFANTS

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Aims: We compared the OPA of antibodies induced by three alternative regimens of PCV7: 2, 4, 6 and 12 mos (3+1), at 4, 6 and 12 mos (2+1), or at 2, 4, and 6 mos (3+0).

Methods: 543 infants were recruited. Sets of samples taken at 7 and 13 mos (N=34-42) were randomly selected to represent each group. OPA against vaccine serotypes (VSTs) 4, 6B, 9V, 14, 18C, 19F and 23F, and against non-VST 6A, was determined by multiplex OPA assay. IgG antibody concentrations were determined by enzyme immunoassay.

Results: Two dose and 3 dose regimens induced comparable geometric mean opsonic titers (GMOPAs) at 7 mos for all serotypes, except 6B. 79-100% of the 7 mo samples were OPA positive (titer ≥4) for VSTs and 27-41 % for 6A. At 13 mos, 88-100% in the 3+1 and 2+1 groups were OPA positive for VSTs and 60-85% for 6A. The two boosted groups had similarly high GMOPAs, except for 6B and 6A, for which GMOPAs were lower in the 2+1 group. The GMOPAs of the 3+0 group had declined at 13 mos, but 60-94% of samples were still OPA positive for VSTs and 25% for 6A. In general, the OPA titers correlated with the IgG concentrations (r= 0.4-0.9).

Conclusions: 3+1 and 2+1 regimens induced similar titers of opsonic antibodies for majority of the PCV7 serotypes. After the 3+0 regimen the titers declined in 6 months after vaccination. Majority of the boosted children had OPA for 6A at 13 mos.

P801

COMPLIANCE OF PREGNANT WOMEN WITH FLU A H1N1-2009 VACCINE AND FACTORS ASSOCIATED WITH ACCEPTATION OR REFUSE TO VACCINATION, BRAZIL

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Background and objectives: Influenza can cause substantial morbidity and mortality in pregnant women. In 2010, monovalent Flu vaccine A/H1N1-2009 was offered free of charge to Brazilian pregnant women. The aim of this study is to describe Flu vaccine compliance and reasons associated with immunization´s acceptance or refuse.

Methods: Descriptive and prospective study including 300 postpartum women attended at a private hospital. Data were collected by a nurse, using a pre tested questionnaire, during October/2010.

Results: Mothers average age was 30.5 y; 231 (77%) women were married; 164 (54.7%) first birth; 192 (64%) had superior scholar level and 240 (80%) had a job. During prenatal, 234 (78%) received information about flu vaccine and 287 (95.7%) were immunized; 210 (73.2%) women had knowledge regarding neonatal protection through maternal vaccination. Factors associated with acceptance were: government campaign = 133(44.3%), medical recommendation = 163(54.3%) during prenatal visits. From 13 women that refused immunization, the reasons were: negligence (4), lack of time (4), lack of medical prescription (3) or contraindication (2), but 69.2% would have gotten the vaccine if they had been informed about newborn protection.

Conclusions: Pandemic fear and government campaign were strongly related to high acceptation of Flu vaccine; but 54.3% of pregnant women only got the shot after medical recommendations. Even among mothers of high economic and education level, almost 1/3 did not know the benefits of Flu vaccine for their children. Physicians and lay people should receive more information about the indirect protection to children when pregnant women receive Flu vaccine.

P802

MAINTENANCE OF IMMUNE RESPONSE THROUGHOUT CHILDHOOD FOLLOWING SEROGROUP C MENINGOCOCCAL CONJUGATE VACCINATION IN EARLY CHILDHOOD

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Background: Serogroup C meningococcal (MenC) conjugate vaccines were introduced into the UK routine infant immunisation schedule in 1999, along with a “catch-up” campaign for those aged 1-25 years. Previous cross-sectional studies demonstrated children immunised in early childhood have lower MenC bactericidal antibody 5 years after immunisation than children immunised in late childhood, however the kinetics of antibody decline have not been evaluated in a longitudinal study of a single cohort.

Method: Stored sera obtained at multiple time-points between 2001 and 2010 from children who had received a single dose of MenC vaccine at age 1-3.5 years, were analysed for MenC serum bactericidal antibody using rabbit complement (rSBA).

Results: The MenC rSBA geometric mean titre (GMT) at age 3.5 to 5 years, approximately one year after immunisation, was 8.0 (95% confidence interval [CI] 6.5 - 9.9, n = 292). Over the subsequent 9 years, rSBA GMT declined to 3.3 (CI 2.5 - 4.4, n = 98) at age 11.5-13.5 years. The percentage of children with rSBA titres ≥1:8 (threshold for protection) also declined from 38% (CI 35% - 41%) to 15% (CI 12% - 19%).

Conclusion: MenC rSBA titres wane rapidly following vaccination in early childhood, without evidence of natural boosting of antibody levels through cross-reactive antigens. In the UK, consideration should be given to a routine adolescent booster of MenC vaccine to protect this cohort of children who are entering the potentially high risk period of adolescence, and to prevent a resurgence in nasopharyngeal carriage and maintain herd immunity.

P803

PERSISTENCE OF THE IMMUNE RESPONSE AT 5 YEARS OF AGE FOLLOWING INFANT IMMUNISATION WITH INVESTIGATIONAL QUADRIVALENT MENACWY CONJUGATE VACCINE FORMULATIONS

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Introduction: Meningococcal serogroup C (MenC) conjugate vaccines are used routinely for infant immunisation in Canada and Europe. Quadrivalent serogroup A, C, W-135 and Y meningococcal (MenACWY) conjugate vaccines are licensed in Europe and North America, and recommended for routine immunisation of adolescents in the United States.

Methods: In an open-label, randomised controlled trial in the UK and Canada, we evaluated persistence of immune response after different schedules of two MenACWY-CRM conjugate vaccine formulations with MenC conjugate and MenACWY polysaccharide vaccines at 40 and 60 months of age. Two control groups were recruited at 60 months, immunised as infants or toddlers with MenC vaccine according to country-specific schedules.

Results: 382 children enrolled in 12 groups (22 to 40 per group) were followed up. By age 60 months, 3-11% of children primed and boosted with MenACWY-CRM had serum bactericidal antibody (using human complement [hSBA]) titres ≥1:8 against serogroup A meningococci, 14-45% against serogroup C, 57-84% against serogroup W-135 and 42-69% against serogroup Y. These proportions were similar for children primed with MenC and boosted with MenACWY-CRM except for serogroup C (59%). In age-matched controls, percentages with hSBA titres ≥1:8 were 0-3%, 29-53%, 33-36% and 10-29% against serogroups A, C, W-135 and Y, respectively.

Conclusions: Immune responses against all serogroups wane following infant immunisation with MenACWY-CRM vaccines, most markedly against serogroup A. Better persistence of serogroup C hSBA titres was observed in schedules with MenC conjugate vaccine priming doses, however use of a booster MenACWY vaccine could provide broader protection against meningococcal disease.

P804

PERSISTENCE OF THE IMMUNE RESPONSE AT 5 YEARS OF AGE FOLLOWING INFANT IMMUNISATION WITH INVESTIGATIONAL QUADRIVALENT MENACWY CONJUGATE VACCINE FORMULATIONS

A. Khatami[1], M.D. Snape[1], E. Davis[1], H. Layton[1], T. John[1], P.M. Dull[2], C.C. Gill[2], T. Odrjlin[2], S. Dobson[3,4], S.A. Halperin[5], A.J. Pollard[1]

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Conclusions: Immune responses against all serogroups wane following infant immunisation with MenACWY-CRM vaccines, most markedly against serogroup A. Better persistence of serogroup C hSBA titres was observed in schedules with MenC conjugate vaccine priming doses, however use of a booster MenACWY vaccine could provide broader protection against meningococcal disease.

P805

REPORTED INCIDENCE OF NARCOLEPSY IN CHIILDREN AND ADOLESCENTS AFTER PANDEMRIX/AREPANRIX VACCINATION

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Background and aims: Several cases of narcolepsy following Pandemrix vaccination reported in children in Sweden and Finland required further investigation. We collected information from 7 countries on reported incidence of narcolepsy after vaccination with AS03 adjuvanted pandemic vaccine in the age-group showing the clearest signal.

Methods: All cases of narcolepsy reported through spontaneous adverse event reporting systems by 24 January 2011 in individuals aged 4 to 19 years after Pandemrix/Arepanrix vaccination in 2009 were identified. Denominator was retrieved from vaccination registers or coverage surveys.

Results: Spontaneously reported incidence of narcolepsy varied considerably, being highest in Iceland and Finland and lowest in Canada. Incidence exceeded the expected in Finland, Iceland, Sweden and Germany but remained within expected limits in Norway, UK, and Canada.

Country	Reported cases, N	Vaccinated, N	Cases / 100 000 vaccinated
Iceland	3	31 958	9,4
Finland	54	668 000	8,1
Sweden	58	1 193 000	4,9
Norway	8	510 000*	1,6
UK	2	295 000**	0,7
Germany	5	928 000´	0,5
Canada	2	1 974 865´´	0,1
* 4-18-year-olds ** 5-16-year-olds ´0-17-year-olds ´´5-18-year-olds			

[Narcolepsy cases among children 4-19-years of age]

Conclusions: The unexpected number of narcolepsy cases reported in children and adolescents after Pandemrix/Arepanrix vaccination in some countries warrant more epidemiological studies to investigate whether there is increased risk of narcolepsy associated with AS03 adjuvanted (H1N1)v vaccine.

P806

FEBRILE SEIZURES FOLLOWING MEASLES-CONTAINING VACCINES IN CHILDREN AGED 4 TO 6 YEARS

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Background and aims: In the US, children receive 2 doses of measles-mumps-rubella (MMR) and varicella (V) vaccines, the first between 1-2 years and again between 4-6 years. We previously reported the combination vaccine MMRV doubles the risk for febrile seizures 7-10 days after vaccination among 1-2 year olds when compared with same-day, separate MMR + V. Whether MMRV is associated with increased febrile seizures among 4-6 year olds has not been investigated.

Methods: Among 4-6 year old members of Vaccine Safety Datalink from 2000 to 2008, we identified seizures in the emergency department and hospital, and outpatient fever visits during days 7-10 and 0-42 following MMRV and MMR + V. Incorporating medical record review results, we assessed seizure risk following MMRV or MMR + V.

Results: From 2006-2008, 84,653 children aged 4-6 years received MMRV, while 64,663 received same-day MMR + V from 2000-2008. Neither seizures nor outpatient fever visits peaked during days 7-10 or 0-42. There were 4 seizures 7-10 days after MMRV and 0 after MMR + V; 1 of 4 post-MMRV seizures was diagnosed as febrile. During days 7-10, seizure risk after MMRV was 1/84,653 (95% CI 1 per 3,343,615, 1 per 15,194) and 0/64,663 (95% CI 0, 1 per 17,529) after MMR + V.

Conclusion: This study provides reassurance that among 4-6 year olds, MMRV was not associated with increased risk of febrile seizures. For the 7-10 days after MMRV, we can rule out an absolute risk greater than 1 febrile seizure per 15,000 doses.

P807

PROTECTIVE BUT LOWER LEVEL OF ANTIBODIES AFTER SINGLE CONJUGATED MENINGOCOCCAL SEROGROUP C VACCINATION IN CHILDREN WITH DOWN SYNDROME

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Assaying specific antibody production against well-defined antigens can be used as a model to assess T-cell dependent and independent responses; conjugated protein-polysaccharide vaccines like Meningococcal serogroup C conjugate (MenC) show characteristics of both responses.

Blood samples of 19 Down syndrome (DS) children (mean 10.6, range 5.3-17.4 years) were taken 3 months (n=7; range 39-107 days) or around 1 year (n=12; 275-447 days) after a single dose of MenC. MenC polysaccharide (PS) specific IgG, IgA and IgM levels were measured using an antibody-capture enzyme-linked immunosorbent assay (JClinMicrobiol1994;32:1475) and were compared to values in healthy adults 1 month (n=12) and 1 year (n=11) after single MenC vaccination.

MenC specific IgG, IgA and IgM serum levels in DS children were 5.5 (geomean, range 1.4-41), 0.71 (0.03-11), and 0.61 (0.10-7.5) µg/mL 3 months post-vaccination, and 26 (5.6-59), 5.6 (2.1-11), and 5.2 (1.7-35) µg/mL ($p = 0.014, 0.028, 0.12$) in healthy adults. One year after vaccination, DS children had IgG, IgA, and IgM levels of 2.7 (0.8-15), 0.19 (0.02-1.2), and 0.28 (0.15-0.76) µg/mL, and healthy adults 4.5 (0.68-19), 0.8 (0.13-3.8), and 0.7 (0.16-5.1) µg/mL ($p = 0.20, 0.019, < 0.001$; all Mann-Whitney tests). So, DS children reached protective, but lower levels after single MenC vaccination compared to healthy adults.

Impaired specific antibody responses to polysaccharide-type and protein-type vaccines have been described in DS, suggesting both B-lymphocyte and T-lymphocyte problems. Not unexpectedly therefore, our data show that protein conjugation does not fully overcome the impaired antibody production to this polysaccharide antigen.

P808

THE BURDEN OF CHILDHOOD CHRONIC HEPATITIS B INFECTION IN ENGLAND WHERE A SELECTIVE IMMUNISATION STRATEGY HAS BEEN ADOPTED

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Background: Childhood chronic hepatitis B virus (HBV) infection is associated with long-term complications including cirrhosis, hepatocellular carcinoma and death. Unlike most countries, the UK has adopted a selective immunisation strategy targeting high-risk groups only. This study describes the burden of childhood chronic HBV diagnosed in England.

Methods: Paediatric gastroenterology and infectious disease consultants in England were contacted to report all cases of chronic HBV infection diagnosed in children aged < 16 years and to complete a questionnaire.

Results: In England, 332 children were diagnosed between 1989 and 2010, with around 30 cases diagnosed annually between 2005-09. In 2009, the estimated prevalence of diagnosed HBV cases per 100,000 was: 1.3 among 0-4 year-olds, 2.3 among 5-9 year-olds, and 4.1 among 10-14 year-olds. Of the 164 children born in England, 81% acquired the infection through vertical transmission. Of the 59 children with chronic HBV who were born in England after introduction of national antenatal screening, 85% were detected through screening, of whom 96% had received at least one dose of HBV vaccine. The remaining 168 children were born mainly in Asia (49%), Africa (34%) and Eastern Europe (11%), particularly Afghanistan (13%), China (11%), Somalia (10%) and Pakistan (10%). Most children (78%) born abroad had also acquired the infection through vertical transmission.

Conclusions: Chronic hepatitis B in children remains a rare diagnosis in England, and there is no evidence of any increase in diagnosed cases in recent years. These results provide useful data to guide future recommendations for screening high-risk groups.

P809

LACK OF ANTIBODY RESPONSE TO THE INFECTING SEROTYPE AMONG CHILDREN WITH INVASIVE PNEUMOCOCCAL DISEASE

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Objectives: To assess the frequency of non-protective (< 0.35 ug/ml) antibody response to the infecting serotype in children with invasive pneumococcal disease (IPD).

Methods: The Health Protection Agency provides clinicians in England, Wales and Northern Ireland with free IgG testing for 12 pneumococcal serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) since the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) into the UK childhood immunisation programme.

Results: Blood samples were submitted for 737 children aged < 5y with IPD, including 145 cases (19.7%) caused by PCV7 serotypes. Of these, 37 (25.5%) had non-protective antibody concentrations against their infecting serotype, despite receiving more doses of PCV7 post-infection than responders (mean 1.7 vs. 1.2; P=0.0044). Infections with serotype 6B (78% vs. 43%; P< 0.0001), 9V (25% vs. 6%; P=0.001), 18C (35% vs. 14%, P=0.005) and 4 (25% vs. 10%; P=0.012) were more common among non-responders compared with responders. In 328 children infected by one of the other 5 non-PCV7 serotypes, a higher proportion (48.5%; P< 0.001) did not develop protective antibodies to their infecting serotype, particularly 19A (59/109, 54.3%), 7F (50/93, 53.8%) and 1 (34/71, 47.9%). There was a strong correlation between antibody response to the infecting serotype and age at infection (P< 0.0001).

Conclusions: Among infections caused by PCV7 serotypes, a proportion of children will remain unresponsive to the infecting serotype despite receiving multiple PCV7 doses after infection. Further studies are warranted to determine whether such children are at continued risk of IPD.

P810

LACK OF ANTIBODY RESPONSE TO THE INFECTING SEROTYPE AMONG CHILDREN WITH INVASIVE PNEUMOCOCCAL DISEASE

S. Ladhani[1], E. Stanford[2], P.A. Waight[1], E. Newton[2], G. Laher[2], M.P. Slack[3], E. Miller[1], R. Borrow[2]

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Conclusions: Among infections caused by PCV7 serotypes, a proportion of children will remain unresponsive to the infecting serotype despite receiving multiple PCV7 doses after infection. Further studies are warranted to determine whether such children are at continued risk of IPD.

P811

M59®-ADJUVANTED H1N1 VACCINES IN CHILDREN 3-17 YEARS: SAFETY AND IMMUNOGENICITY FOLLOWING A 1-YEAR BOOSTER VACCINATION

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Background and aims: There is a need for effective and safe paediatric vaccines that offer broad, robust and long lasting protection. The aim of the present study was to assess the immunogenicity and safety after a 1-year booster dose of an egg-derived MF59-adjuvanted H1N1 vaccine (Focetria®). We also report 12 month follow-up safety data after the first 2 vaccine doses.

Methods: 410 children aged 3-17 years were randomly assigned to receive, at a 21 day interval, two doses of either 3.75µg antigen with 50% of the standard MF59 dose, 7.5µg antigen and the standard MF59 dose, or 15 µg antigen of H1N1 vaccine without adjuvant. A third vaccine dose was administered after approximately 1 year (data available for 25%-60% of the children across groups) using the MF59-adjuvanted seasonal influenza vaccine. Antibody levels were measured by hemagglutination inhibition, local and systemic adverse reactions were recorded for 7 days after the booster injection and adverse events were reported throughout the study period.

Results: Geometric mean titers ranged from 11-15 at study start, 122-252 after 1 year (pre-booster vaccination), and 2042-2260 at 3 weeks following the booster dose. Vaccinations were well tolerated with reactions mainly mild to moderate in severity. In the 6-12 month follow-up period, 8 SAEs and 6 cases of onset of chronic diseases were reported, none related to the study vaccine.

Conclusions: Results of the present study further support the use of MF59-adjuvanted H1N1 vaccine as a highly immunogenic and safe vaccine for active immunization against H1N1 influenza.

P812

NATURAL ANTIBODIES AGAINST SEVERAL PNEUMOCOCCAL VIRULENCE PROTEINS IN CHILDREN IN THE PRE-PNEUMOCOCCAL VACCINE-ERA: THE GENERATION R STUDY

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Background and aims: The current pneumococcal vaccines do not protect against all serotypes of *Streptococcus pneumoniae*. A shift towards non-vaccine serotypes causing colonisation and invasive disease has occurred and studies on protein-based vaccines are undertaken. We assessed the association between specific antibodies against pneumococcal virulence proteins and colonisation and respiratory tract infections (RTI). Additionally, we assessed to what extend colonisation induces a humoral immune response.

Methods: Nasopharyngeal swabs were cultured for pneumococcus at 1.5, 6, 14 and 24 months of age. Serum samples were obtained at birth, 6, 14 and 24 months (n=57) in the pre-pneumococcal vaccine-era. IgG, IgA and IgM levels against seventeen pneumococcal protein vaccine candidates were measured using a bead based flow cytometry technique (xMAP®, Luminex Corporation). Information regarding RTI was questionnaire-derived.

Results: IgG levels to all proteins were high in cord blood, decreased in the first 6 months and increased thereafter, contrary to the course of IgA and IgM levels. Specific antibodies were induced upon colonisation. Increased levels of IgG against BVH-3, NanA and SP1003 at 6 months, NanA, PpmA, PsaA, SlrA, SP0189 and SP1003 at 14 months and SlrA at 24 months were associated with a decreased number of RTI in the third year of life but not with colonisation. Maternal antibodies did not protect against pneumococcal colonisation and infection.

Conclusions: Certain antibodies against pneumococcal virulence proteins, some of which are induced by colonisation, are associated with a decreased number of RTIs in children. This should be taken into account for future pneumococcal vaccine studies.

P813

BRIDGING THE GAP: APPROACHES TO INFER EFFECTIVENESS OF MENINGOCOCCAL VACCINES TO PREVENT SEROGROUP B, A, C, Y AND W-135 DISEASE

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Background and aims: Meningococcal vaccines to prevent invasive serogroup A, B, C, Y, W-135 disease in infants/toddlers are not licensed the United States (U.S.). As such, in young children, inferred effectiveness would be indicated by the presence of measurable meningococcal-specific functional antibodies in serum. Immunological bridging of seroresponse to effectiveness against endemic meningococcal disease is complicated by the genetic and antigenic diversity of disease isolates.

Methods: Proposed approaches to infer effectiveness of meningococcal conjugate and sub-capsular vaccines was discussed at a Vaccine and Related Biologic Products Advisory Committee (VRBPAC) meeting held on April 6-7, 2011.

Results: The role of bactericidal antibodies in immunity to meningococcal disease was supported by historical data, efficacy studies with OMV vaccines in Chile, Cuba, Norway and Brazil, and effectiveness of OMV vaccines in New Zealand. An approach to bridging hSBA test strains to endemic disease isolates were described for two candidate meningococcal B vaccines.

Conclusion: Bactericidal antibodies to capsular polysaccharides and protein antigens, using hSBA as serological marker, is an acceptable immune measure to infer effectiveness of U.S. meningococcal conjugate and sub-capsular vaccines, respectively, for use in infants and young children. Use of a microbiologic marker to determine the proportion of disease isolates susceptible to vaccine induced bactericidal antibodies is an acceptable approach to bridge clinical immunogenicity to estimated meningococcal B vaccine effectiveness.

P814

ARE OMV VACCINES THE ANSWER FOR EPIDEMIC OR ENDEMIC SEROGROUP B DISEASE CONTROL?

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Background and aims: A New Zealand epidemic prompted MeNZB trials, a strain-specific outer membrane vesicle vaccine targeting the epidemic strain (B:4:P1.7-2.4). A three dose mass campaign (2004-06) followed licensure for 6month-19year olds (coverage 83%). Infants < 6 months were offered four doses from 2006 (coverage 50%). Measurable serum bactericidal antibodies (SBAb) are deemed necessary for disease control.

Methods: School children (8-12 years: Trials A and B) and infants (6-8 months) provided serum at intervals after three MeNZB doses to evaluate SBAb persistence. Disease surveillance data were reviewed.

Results: Geometric mean SBAb titres (GMTs) post-dose three are presented (95% CI). Trial A school children GMTs: 1 and 14 months: 18(12-26), 3(2-4). Trial B school children GMTs: 1 and 4 months: 18(13-25), 4(3-6). Infant GMTs: 1 and 7 months: 27(19-39), 2(2-3). Titres after dose three significantly influenced antibody persistence.

Auckland had the highest meningococcal rates in 0-19 year olds (1997 peak $31/10^5$) which fell following MeNZB (annual rates 2004-2009: $10.6/10^5$, $5.3/10^5$, $3.5/10^5$, $2.3/10^5$, $2.0/10^5$, $1.6/10^5$). Epidemic strain rates in 0-4 year olds, concentrated in South Auckland, also fell (2004-2009: $50/10^5$, $8.0/10^5$, $24/10^5$, $21/10^5$, $6.0/10^5$, $6.0/10^5$).

Conclusion: Rapid decay of SBAb in infants and school children and low vaccine coverage in young infants constituted an informal MeNZB withdrawal in 2006/07 without disease resurgence. Consequently, MeNZB was withdrawn in June 2008.

With no evidence of herd protection, rapid antibody decay in infants and the demonstrated requirement of measurable antibody for protection, it is likely multiple boosters of MeNZB would be required to maintain protection.

P815

KINETICS OF PRIMARY AND ANAMNESTIC IMMUNE RESPONSE TO 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7) IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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Aim: We evaluated the kinetics of PCV7-induced immune responses post-primary and booster immunization in children with idiopathic nephrotic syndrome (INS) in remission.

Methods: 33(17 male) INS patients aged(range) 10(4-17)years and 16(10 male) controls aged 14(7-20)years, all PCV7 naïve, were vaccinated with PCV7 (Prevenar, Wyeth Vaccines). INS subjects received an anamnestic PCV7 dose 12-14 months later. Patients were divided in 2 groups according to therapy. Group A patients were on no treatment or low-dose alternate-day prednisone. Group B patients were receiving additionally mycophenolate mofetil and/or cyclosporine A. Pneumococcal serotype (PS)-specific IgG antibodies were detected (ELISA) pre- and 1 month post-primary and anamnestic immunization .

Results: Baseline antibodies were similar between groups for all but one PS. Primary immunization induced protective antibodies ≥0.35ug/ml for >5 PS in 93% of patients and 100% of controls. Geometric mean concentrations (GMCs) were significantly lower in group B compared to controls for PS 4, 9V and 18C (2.17 *vs* 6.89, 3.98 *vs* 13.13, 1.70 *vs* 8.55ug/ml respectively, $p < 0.05$). At booster baseline, 72% of patients *vs* 100% of controls had retained protective antibodies for >5PS. Anamnestic immunization, given only in patients, increased antibody levels for all PS compared to pre-booster levels ($p < 0.001$); however, no further significant increase in GMCs was observed compared to post-primary IgG levels.

Conclusions: PCV7 induced protective immunity in INS children although with inferior immunogenicity for patients on immunomodulatory treatment compared to controls. Anamnestic immunization did not improve primary immune responses, but could be important for maintainance of protective circulating antibodies.

P816

EVALUATION OF MEASLES IMMUNE RESPONSE IN CHILDREN AND ADULT IN BAGHDAD

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Backround and aim: To evaluate the specific immune response against measles vaccine and natural virus infection among children and adult in Baghdad including factors of age ,number of vaccine doses and persistence of specific of antibodies after different period of vaccination.

Methods: Study was made on 165 blood samples were taken from children and adults, including 95 vaccinated , 70 with natural measles infection and 34 they are infected in spite of vaccination, using microneutralization assay.

Results: The prevalence of protective level of neutralizing antibody titer (≥ 1:128), was found in 79% of vaccinated group and 94.2 % for participants with a history of measles cases with protective level 97-100% for (6-15) years of vaccinated group and then decreased with increasing ages, while persistent (95-100%) for the different age groups infected with measles and the neutralizing antibody titers after five and six vaccine doses was a (1:838 (SEM) 100) and (1:938 (SEM) 93) respectively.

Conclusion: The prevalence of protective level of neutralizing antibody was found higher in participants with a history of natural infection than vaccinated group and individuals with multiple vaccine doses have better protection than two recipients.

The WHO estimates that vaccination could avoid 80 million cases of measles and 4.5 million deaths worldwide each year (CDC,2007) . In Iraq as part of Eastern Mediterranean Region (EMRO) of the WHO measles vaccination was begun in 1985 as a single of live attenuated measles vaccine and the MMR was conducted in 1988.

P817

MULTIPLE, NON-CONSERVED, INTERNAL VIRAL LIGANDS NATURALLY PRESENTED BY HLA-B27 IN HUMAN RESPIRATORY SYNCYTIAL VIRUS-INFECTED CELLS

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Human respiratory syncytial virus (HRSV), a member of the *Paramyxoviridae* family, is the single most important cause of serious lower respiratory tract illnesses such as bronchiolitis and pneumonia in infants and young children that require hospitalization with an attendant economic burden. Infections of this virus occur in people of all ages, but HRSV poses a serious health risk in immunocompromised individuals and in the elderly. In the United States alone, HRSV is estimated to cause more than 13,000 deaths each winter among adults who have underlying immunosuppressive and/or cardiopulmonary conditions. Also HRSV is a major cause of nosocomial infection in hospital or healthcare service units. The cytotoxic T lymphocyte response is critical for the clearance of HRSV infection, and requires prior recognition of short viral peptide antigens that are presented by human histocompatibility complex (HLA) class I molecules on the surface of infected cells. Using mass spectrometry analysis of complex HLA-bound peptide pools isolated from large amounts of HRSV-infected cells, we identified nine naturally processed HLA-B27 ligands. The isolated peptides derive from six internal, not envelope, proteins of the infective virus. The sequences of most of these ligands are not conserved between different HRSV strains, suggesting a mechanism to explain recurrent infection with virus of different HRSV antigenic subgroups. In addition, these nine ligands represent a significant fraction of the proteome of this virus, which is monitored by the same HLA class I allele. These data have implications for vaccine development as well as for analysis of the CTL response.

P818

CONSTRUCTION, EXPRESSION, AND IMMUNIZATION OF ENTEROVIRUS-71 VIRUS-LIKE PARTICLES

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Background and aims: EV71 is a cause of hand, foot and mouth disease (HMFD) combined with severe paralysis or encephalitis or possibly death in children. Numerous large outbreaks of EV71 caused HMFD have occurred recently in Asia, especially in China Mainland in 2010, 1,795,336 cases were reported in which the fatal cases were 888. So it is important to find a method for preventing infection with EV71 since there is no antiviral agent or vaccine for humans.

Methods: Transform P1-pGAPZa-A and 3CD-pGAPZa-A recombinant plasmids into SMD1168 and get the recombinant strain expressing P1 and 3CD proteins which form EV71 VLPs. Identify the expression proteins by Tricine-SDS-PAGE and Western-blot, visualize the VLPs by electronmicroscope. Further evaluate the potential of the purified VLP as a vaccine by the immunization of BALB/c mice. Total IgG and neutralization antibody were tested to evaluate humoral immunity. Lymphocyte proliferation assay and the cytokines produced by the stimulated splenocyte were tested to evaluate cytoimmunity response.

Results: The P1 protein was cleaved by 3CD prolease into VP0, VP1 and VP3 , which assembled into regular and homogeneous VLPs with diameter 20nm through the electron microscope. The VLP-immunized mice produced high total IgG and neutralization antibody titre. The splenocytes collected from the VLP-immunized mice exhibited significant cell proliferation and produced high levels of INF-γ, IL-2 and IL-4 after stimulation.

Conclusions: The EV71 VLPs could induce the mice's specific IgG and neutralization antibody and stimulate the cytoimmunity indicated that VLPs may be a valuable vaccine candidate to prevent EV71 epidemics.

P819

NEONATAL HEPATITIS B IMMUNISATION PROGRAMME - LOCAL SUCCESSES AND CHALLENGES

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Hepatitis B infection can be transmitted from infected mothers to their babies at or around the time of their birth. Such babies at risk of developing chronic hepatitis B infection, however, appropriate and timely immunisation can prevent this in over 90% of cases.

In 1998 English Health Authorities were directed to ensure arrangements were in place, by April 2000, to screen mothers and immunise their babies.

Ten years on many English Primary Care Trusts are struggling to ensure that services and systems are in place to provide full timely immunisation of babies at risk of Hepatitis B.

The collection of hepatitis B immunisation uptake has been part of the COVER (Cover of Vaccination Evaluated Rapidly) system since April 2005. In 2009 uptake of all four doses of vaccine in at risk children reaching two years of age averaged less than 55%; with a quarter of Trusts failing to submit data.

In October 2008 the Primary Care Trust recognised that the number of children reported as having completed the neonatal hepatitis B immunisation programme was low and actions were instigated to improve service delivery, immunisation uptake and data collection.

Multiagency multidisciplinary working has been necessary to facilitate what is now an improved but resource intensive system. Local uptake data has improved from between 0-60% uptake to 100% uptake in the year 2009/10.

Although the numbers of babies at risk in the PCT are low, this contributes to the challenges of delivering this targeted immunisation programme.

P820

TO STUDY THE CLINICO LABORATORY PROFILE AND BURDEN OF ROTAVIRUS INFECTION IN PEDIATRIC PATIENTS IN AN URBAN SET UP

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Materials and methods: A retrospective cohort study comprising 136 inpatients between 2008 and 2010 was conducted at our hospital.Inclusion criteria were presentation with acute diarrhea and stool positive for rotavirus antigen. Patients presenting with diarrhea but stool negative for rotavirus antigen were excluded. The data included other clinical symptoms in association with diarrhea like fever vomitings and hydration status. The laboratory parameters included Total leucocyte count (TLC) and C - reactive protein (CRP). The average length of stay in hospital among those vaccinated and non vaccinated pediatric patients were also studied.

Result: The rotaviral infection was seen in 132 (97%) patients in age group of less than 3 years. Four patients (3%) with age above 10 yrs tested rotaviral antigen positive. Vomiting was seen in 112 (82%) ,fever in 80 (58.8%) and 16 (11.7%) had severe dehydration. The TLC was out of range in 42 (30.8%) and CRP elevated in 68 (50%) patients.4 (2.94%) had history of rotavirus vaccination. The average length of stay in vaccinated children was 1-2 days and in non vaccinated children was 2-7 days.

Conclusion: The rotaviral infection was prevalent in children less than 3 years. Vomiting had significant correlation with rotavirus. Fever was less common clinical association. Most of the patients presented with some dehydration. The TLC was elevated in almost one third of the pediatric patients. The CRP showed a positive correlation with rotavirus infection. Average length of stay in pediatric patients was significantly reduced in vaccinated children compared to non vaccinated children.

P821

OSTEOMYELITIS AND SPLENIC LESIONS FOLLOWING BACILL CALMETTE-GUERIN (BCG) VACCINATION

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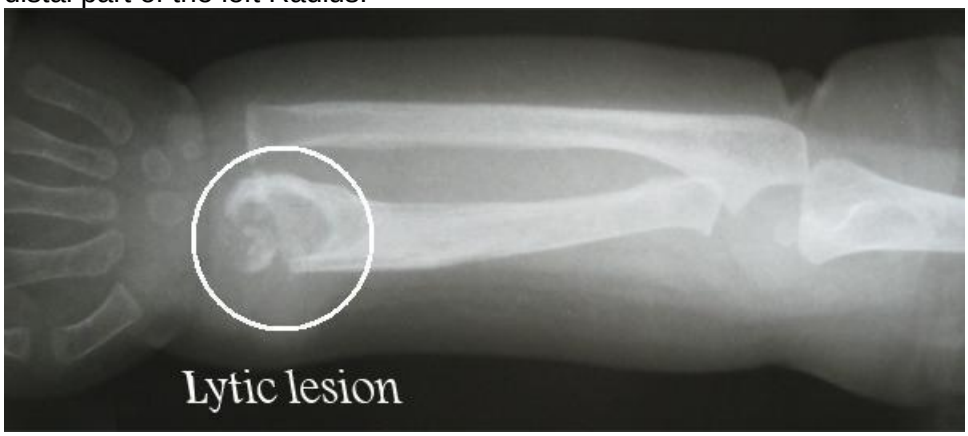
Background and aims: Bacill Chalmette-Guerin (BCG) vaccine is administered in developing countries to prevent tuberculosis, and it has been considered safe. Adverse reactions include regional lymphadenopathy, localized abscesses, osteomyelitis and disseminated disease are uncommon.
Methods: An 8-month-old girl with no previous significant medical problems was admitted in our hospital due to left wrist swelling and discoloration without any pain. There was no history of fever, poor feeding, trauma or insect bite.
Results: Lymphadenopathy or fever was not detected. A complete blood count revealed 10600 WBCs/mm^3 (lymphocytes =57%). ESR was 38 mm/h. Liver function tests showed AST increasing up to 59 IU/L.

The X-ray examination showed a lytic lesion in the left wrist that suggested osteomyelitis in distal part of the left Radius.



[Left hand radiography]

After open surgical drainage; gram smear was negative but acid fast bacilli staining was positive. Histopathological examination revealed a chronic granulomatous inflammatory reaction with central necrosis. The diagnosis was confirmed by positive PCR for BCG. The immunologic tests were normal. Ultrasonography revealed multifocal granulomatous lesions in the spleen.
The patient received Clarithromycin, Isoniazid (INH) and Rifampicin (RIF) for tow months and INH + RIF for further seven months. She had normal liver enzyme levels, ultrasonography of spleen, good growth and development with no remarkable health problem during six months follow up after treatment.
Conclusions: In our country all newborns are received single dose BCG vaccine at the birth. Therefore the adverse effects of vaccination should be considered exactly.

P822

VACCINE AGAINST ROTAVIRUS (RV) IN BRAZIL: EVIDENCE OF HERD IMMUNITY?

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Background and aims: Some researchers have raised the hypothesis of a possible indirect protective effect of vaccine against rotavirus to unvaccinated individuals by reducing viral transmission in the community. Considering the introduction of the vaccine on a large scale in Brazil (Rotarix^{GSK}) in 2006, this study aims to evaluate the possible effect of herd immunity of the vaccine.

Methods: We used the following data sources: Hospital System, the National Health System (SIH) and the Information System of the National Immunization Program (SI-API/CGPNI).

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Results: The VR has as target the children under six months of age (1 month and 15 days to 5 months and 15 days old).

Coverage for rotavirus vaccine in Brazil in 2008 was 95.8% for the 1st dose and 83.4% for the 2nd dose. Comparison of the rate of hospitalization for diarrheal diseases from 2004 to 2005 (pre-vaccine) with the rate from 2007 to 2008 (post vaccine) showed a reduction of 19.18% among children under 1 year and 67.2% between 1 and 4 years.

Conclusions: The results of reducing hospitalization rates observed for the age group 1-4 years suggests that the vaccine could be inducing herd immunity, as has been proposed by some researchers. However, it is necessary to monitor for longer periods as well as perform specific studies to investigate the plausibility of this hypothesis.

P823

PHASE I RANDOMISED CONTROLLED CLINICAL TRIAL OF SAFETY AND IMMUNOGENICITY OF A MENINGOCOCCAL B BIVALENT LP2086 VACCINE IN HEALTHY TODDLERS

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Background and aims: Neisseria meningitidis is a leading cause of meningitis and septicaemia globally, particularly in young children and adolescents. A bivalent factor H-binding protein (rLP2086) vaccine is being developed with an aim to provide broad protection against serogroup B meningococcal (MnB) infection. This study assessed the safety and immunogenicity of the bivalent rLP2086 vaccine in toddlers.

Methods: Ninety nine healthy toddlers aged 18 to 36 months were randomised (2:1) to receive rLP2086 vaccine (20, 60, or 200µg in ascending dose level cohorts) at 0, 1, and 6 months or control vaccine. Safety was assessed by parental reporting of local and systemic reactions using electronic diaries. Unsolicited AEs were also reported. rLP2086-specific immunoglobulin G binding and human serum bactericidal antibody (hSBA) titres against diverse strains expressing different LP2086 subfamily variants were assessed.

Results: The vaccine was generally safe and well-tolerated. Upper respiratory infection and cough were the most commonly reported adverse events in all groups. Tenderness was the commonest local reaction. Three toddlers (200µg group) developed severe erythema and 4 toddlers (60µg and 200µg groups) developed severe fever (>40.0°C). hSBA responder rates (titre ≥1:4) against strains with homologous and similar subfamily proteins were high after dose 3 (87.5%-93.3% at 60µg; 84.2%-89.5% at 200µg).

Conclusions: Results of this study suggest that the rLP2086 vaccine has an acceptable safety profile, is immunogenic in toddlers, and represents a candidate vaccine for broad protection against MnB disease in young children.

P824

PHASE II RANDOMISED CONTROLLED TRIAL OF SAFETY AND IMMUNOGENICITY OF A MENINGOCOCCAL B BIVALENT VACCINE (RLP2086) IN HEALTHY ADOLESCENTS

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Background and aims: *Neisseria meningitidis* serogroup B (MnB) is a major cause of invasive meningococcal disease, but a broadly protective vaccine is not commercially available. This study aimed to assess the immunogenicity, safety, and tolerability of a bivalent factor H binding protein vaccine (rLP2086) in adolescents, an age group at increased risk for MnB disease.

Methods: 539 healthy adolescents aged 11-18 years were randomized to receive placebo or rLP2086 (60µg, 120µg, or 200µg) at 0, 2, and 6-9 months. rLP2086-specific Immunoglobulin G (IgG) titres and human serum bactericidal assay (hSBA) against diverse strains expressing variants from the 2 different LP2086 subfamilies were assessed. Safety was assessed by solicited local and systemic reactions and unsolicited adverse events. .

Results: hSBA titres and geometric mean IgG titres increased after each rLP2086 vaccination. Among subjects receiving the 120ug and 200ug dose, hSBA titres ≥4 were achieved in 96%-100% (subfamily A) and 69%-92% (subfamily B) of participants. Mild-to-moderate injection site pain was the most common local reaction. Systemic events including fatigue and headache tended to increase with increasing rLP2086 dosage but were generally mild-to-moderate. Adverse events were similar among the control and vaccine arms. One related SAE was reported after dose 3 (200µg) that resolved without sequelae. No other serious adverse events were related to rLP2086 vaccination.

Conclusions: These results suggest that rLP2086 is immunogenic across diverse MnB strains and has an acceptable safety profile. Thus, rLP2086 represents a promising vaccine for broad protection against MnB disease in adolescents.

P825

IMPACT OF TEMPORARY WITHDRAWAL OF THE ROTAVIRUS VACCINE IN SPAIN

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Background and aims: DNA fragments of a porcine circovirus 1 (PCV-1) were detected in the monovalent rotavirus vaccine, Rotarix® (GlaxoSmithKline), and later also of PCV-1 and PCV-2 in the RotaTeq® (MSD) vaccine in 2010. The Spanish Medicines and Health Products Agency (AEMPS) did not authorize the release of new batches of both vaccines onto the Spanish market since March 29 and June 10, 2010, respectively, due to problems of "good manufacturing practice". On November 4, 2010, AEMPS again allowed the release of batches of the RotaTeq® vaccine. Until March 2010, the average vaccination coverage against rotavirus in Spain had reached 40%. The aim of our study is to estimate the impact of the temporary withdrawal of these vaccines from the Spanish market in terms of disease burden and associated costs.

Methods: The birth cohort in 2010 in Spain was 506.700 children. Previously published and updated incidence rates were used. The average indirect cost of an episode of acute gastroenteritis caused by rotavirus in Spain is 194.6 Euros (www.rotacost.org). The average direct medical cost is estimated at 549 Euros (Reveal study). We have assumed vaccine efficacy of 90.5%.

Results: (Table)

Table 1. Avoidable impact estimate if rotavirus vaccination had not been interrupted in Spain. Two vaccine coverage scenarios are assumed (0 to 5%) during the months of suspension of release of new vaccine lots.

	Estimation of 5% vaccine coverage	Estimation of 0% vaccine coverage
Total number of acute gastroenteritis episodes due to rotavirus	2,541	2.984
No. of hospitalizations	685	783
No. of visits to the ER	859	994
No. of visits to the paediatrician	699	799
Direct medical costs	494.546 euros	565.196 euros
Indirect medical costs	1.486.952 euros	1.687.745 euros
TOTAL AVOIDABLE COSTS	1.981.498 euros	2.172.941 euros

[Table 1]

Conclusions: The impact of the temporary withdrawal of rotavirus vaccines in Spain in terms of disease burden and costs may have been outstanding. The cost in terms of negative publicity about vaccines may have been even greater. It will be important to assess the actual impact.

P826

ACUTE GASTROENTERITIS HOSPITALIZATIONS BEFORE AND AFTER ROTAVIRUS VACCINE INTRODUCTION IN NORTH-WEST SPAIN (GALICIA)

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Background and aims: Rotavirus vaccines were licensed in Spain between late 2006 and early 2007. Rotavirus vaccination was recommended but not reimbursed by the Spanish National Health System. The significant coverage rates reached in some areas allowed describing variations in severe acute gastroenteritis (AGE) incidence in young children before and after vaccine introduction.

Methods: Hospital discharge data was obtained from the National Surveillance System of Hospital Data of the Region of Galicia. Rotavirus vaccination estimated coverage increased from 12% in period July2006-June2007 to 51% between July2008-June2009. The annual hospitalization rates before and after rotavirus vaccine introduction for children ≤2 years of age for all-cause AGE and rotavirus-AGE admissions were calculated.

Results: In the 3-yearly periods pre-vaccination, July2004-June2007, the median all-cause AGE hospitalization rate was of 892,8 per 100.000 children ≤2years. Rates in the post-vaccination periods (excluding the transition period 2007-2008) July2008-Jun2009 and July2009-June2010 decreased by 32% (606,9 per 100.000) and 51% (436.2 per 100.000), respectively. Considering rotavirus-AGE, hospitalizations rates decreased by 24% in 2008-2009 (372.03 per 100.000) and 52% in 2009-2010 (233.4 per 100.000) compared to the median rate for the pre-vaccination period (487.9 per 100.000).

Conclusions: Compared to pre-vaccination years, a decrease in all-cause and rotavirus AGE hospitalization rates was observed. The greater decline in period 2009-2010 vs 2008-2009 and the linear increase in vaccine uptake since vaccine introduction, could lead to the hypothesis that non-systematic vaccination has significant impact on severe AGE, although this should be confirmed by continued surveillance given the variability in rotavirus trends over time.

P827

HIGH ROTARIX™ VACCINE EFFECTIVENESS AGAINST DIFFERENT ROTAVIRUS GENOTYPES: MODEST RELATIVE INCREASE IN THE PREVALENCE OF G2P[4] IN REMAINING RVGE CASES

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Background and aims: In Belgium, rotavirus (RV) vaccination is recommended since October 2006 and reimbursed since November 2006. This study evaluated the RV genotype-specific vaccine effectiveness (VE), and the genotype distribution over 2.5 RV seasons (February 2008 to June 2010) in Belgium.

Methods: Sequencing methods were used to determine the genotype of RV strains in both vaccinated (n= 70) and unvaccinated (n= 89) children, isolated in 39 Belgian hospitals. Confirmed cases were children age-eligible to be vaccinated against RV (≥14 weeks of age and born after 1-October-2006) and hospitalized with PCR-confirmed RVGE.

Results: The VE against RVGE caused by homotypic G1P[8] RV strains in children receiving a Rotarix™ full series vaccination compared to unvaccinated children was found to be 95% [95%CI 77-99%]. Against RVGE caused by heterotypic G2P[4] RV strains, the VE was found to be 85% [95%CI 64-94%]. G4P[8]-specific VE was 90% [95%CI 19-99%]; and G3P[8]-specific VE was 87% [95%CI -5-98%]. Comparison between the genotype distribution among vaccinated and unvaccinated children revealed that less G1P[8] RV strains were isolated in vaccinated children than in unvaccinated children (11/70 vs. 29/89), whereas more G2P[4] RV strains were isolated from vaccinated children (46/70 vs. 34/89).

Conclusions: Subtle differences in VE against G1P[8] and G2P[4] RV strains in addition to natural seasonal fluctuations of strains could explain the higher proportion of G2P[4] strains in the remaining RVGE cases in Belgium. RV vaccination proved highly effective for the prevention of RVGE hospitalizations caused by different RV genotypes, including heterotypic G2P[4].

P828

BARRIERS TO REDUCING FURTHER THE GLOBAL INCIDENCE OF INVASIVE HAEMOPHILUS INFLUENZAE TYPE B DISEASE

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Background and aims: While Haemophilus influenzae type b (Hib) conjugate vaccines have reduced the global burden of Hib disease, there remain barriers to further reductions. The objective is to describe these barriers and point to ways of overcoming them.

Methods: We performed a literature review for the period 1996 to 2010 using “Haemophilus influenzae” and “vaccine”, and then searched for studies focused on effectiveness and carrier protein. 7424 papers used “Haemophilus influenzae”; 77,887 used “vaccine”; 1750 used both; 34 were focused on effectiveness and carrier protein.

Results: Protection against Hib disease is maintained over a number of years after primary vaccination in infancy, even if a booster is not administered. This may be partly due to herd protection with high vaccination coverage. There is no evidence that serotype replacement is occurring. Observed differences between countries are likely due to reporting differences. PRP-D induces the lowest antibody concentrations yet it eliminated Hib disease from Finland. It had a lower effectiveness in other countries like Germany. PRP-OMP is highly immunogenic after 1 dose only and only requires 2 doses to complete the primary course. PRP-CRM_{197}, HbOC and PRP- T appear to require at least a second dose and require 3 doses to complete a primary infant course. There may be immune interference between acellular pertussis vaccine and Hib conjugate vaccines, while carrier priming may improve the response.

Conclusions: Residual cases are more likely due to failure to vaccinate than vaccine failure; choice of carrier protein plays a minor role.

P829

ANTIBODY PERSISTENCE 54 MONTHS AFTER A BOOSTER DOSE OF COMBINED *HAEMOPHILUS INFLUENZAE* TYPE B-*NEISSERIA MENINGITIDIS* SEROGROUP C-TETANUS-TOXOID (HIB-MENC-TT) CONJUGATE VACCINE

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Background and aims: Persisting antibodies play a role in long-term protection against Hib and MenC disease. In this follow-up study, long-term antibody persistence was assessed 54 months after a booster dose of Hib-MenC-TT.

Methods: Previously (NCT00322335) subjects were randomised 1:2:1 to

1) Hib-MenC-TT group: primed with 3 doses (2, 4, 6 months) Hib-MenC-TT+DTPa-HBV-IPV, boosted with Hib-MenC-TT at age 13-14 months;

2) Neis Hib-MenC group: primed with 2 doses MenC-TT and 3 doses of DTPa-HPV-IPV-/Hib containing vaccines, boosted with HibMenC-TT at age 13-14 months;

3) MenC-CRM group: primed with 3 doses of MenC-CRM_{197}+DTPa-HBV-IPV/Hib boosted with DTPa-HBV-IPV/Hib at age 13-14 months (a 4^{th} dose of MenC-CRM_{197} was offered after completion of the booster study).

Blood samples were taken at 1, 18, 30, 42 and 54 months post-booster. Serum bactericidal activity was measured using rSBA-MenC and anti-PRP (Hib) was measured using ELISA. Serious adverse events (SAEs) considered possibly related to vaccine, occurring since booster, were recorded.

Results: Protective antibodies to Hib and MenC persisted in >99% and >77% of Hib-MenC-TT boosted children, respectively, up to 54 months post-booster vaccination (table). No vaccine-related SAEs were reported.

Table. Long-term persistence of immune responses to MenC and Hib (seroprotection / seropositivity rates) (ATP cohorts for persistence, 54 months post-booster)

		rSBA-MenC (95% CI)			Anti-PRP antibodies (95% CI)		
Group	Post-booster timepoint	n	% ≥1:8	GMT	n	% ≥0.15 µg/mL	GMC, µg/mL
1) HibMenC-TT group: (N=50)	Month 1	42	100 (91.6–100)	5310.3 (3907.3-7217.2)	49	100 (92.7-100)	59.41 (42.51-83.02)
	Month 54	49	77.6 (63.4-88.2)	90.4 (52.8-154.8)	49	100 (92.7-100)	1.55 (1.15-2.09)
2) Neis_HibMenC group: (N=108)	Month 1	92	100 (96.1-100)	9831.1 (7262.2-13308.8)	106	100 (96.6-100)	67.85 (51.59-89.24)
	Month 54	106	97.2 (92.0-99.4)	344.6 (255.9-463.9)	106	99.1 (94.9-100)	2.69 (2.15-3.36)
3) MenC-CRM control group: (N=56)	Month 1	–	–	–	52	100 (93.2-100)	47.10 (33.30-66.60)
	Month 54	51	64.7 (50.1-77.6)	36.7 (21.1-64.0)	52	100 (93.2-100)	1.80 (1.27-2.56)

N = number of children with available results.
GMC = geometric mean concentration
GMT = geometric mean titre

[ ]

Conclusions: One booster dose of Hib-MenC-TT given to toddlers after a Hib-MenC-TT or MenC-TT priming course in infancy induced protective antibody levels to Hib and MenC, persisting up to 54 months post-booster in the majority of children.

P830

SPECIAL IMMUNIZATION SERVICE (SIS) IN PADOVA: 8 YEARS OF EXPERIENCE

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Background and aims: Concerns on vaccines' safety are increasing, leading a lack of compliance in vaccination plans. Special Immunization Services (SIS) for children at risk of adverse reaction (AR) may improve immunization coverage. From 1999 a SIS has been activated at the Pediatric Emergency Unit of Padova. The aims of this study are to describe its experience, find out admission criteria and evaluate its role in improving vaccination coverage.

Methods: For each child evaluated for admission at SIS in the period 1 January 2002 - 31 July 2010, data on age, sex, type of vaccine required, previous AR to any vaccine were reported in a dedicated form. We performed a Univariate Analysis and a Multivariate Analysis to identify the most important admission to SIS's criteria.

Results: 489 vaccines (47.4 MMR or MMRV, 20.8% hexavalent) were administered to 352 children. All the children with a previous immediate AR to vaccination were admitted to SIS. The other admission to SIS's criteria resulted to be anaphylaxis and non-anaphylactic allergies (OR = 13.54 with CI (95%)= 1.78 to 103.23 and p value < 0.01 and OR= 2.01 with CI (95%) = 1.09 to 3.68 and p value < 0.02 respectively). We observed 6 (1.22%) mild but no severe AR. 99.9% of children admitted to the SIS completed their vaccination plan.

Conclusions: No serious AR after vaccination at SIS have been reported. The most important admission's criteria was previous AR to vaccination. SIS is an important means to complete the vaccination plan of high-risk children.

P831

LOCALIZED ADVERSE EVENTS AFTER BCG: CLINICAL CHARACTERISTICS AND IMMUNOLOGICAL EVALUATION

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Background and aims: Localized adverse events after BCG are rare and usually associated with incorrect vaccine administration or high reactogenicity of strain used. However, they might be the initial manifestation of an undiagnosed immunodeficiency. This study aims to evaluate clinical and immunological aspects of patients with localized adverse events after BCG.

Methods: A prospective follow-up study of patients with localized BCG adverse events was conducted from 2009 to 2010, in São Paulo, Brazil. Clinical data was collected and treatment was established according to the Guidelines of the Brazilian Ministry of Health. Patients treated with isoniazid were evaluated with complete blood count, immunophenotyping of lymphocytes, HIV and dihydro-rhodamine testing.

Results: Seventy-three patients were evaluated: supurative adenitis (n=31), local BCG abscess (n=23), lymphadenopathy>3cm (n=7), warts-like nodule (n=4), ulcer≥1cm (n=1), local bacterial infection (n=1), lupoid reaction (n=1) and 5 other diagnoses. The median age at the onset of symptoms was 2.5 months and treatment period ranged from 9d to 16months (median:3.3months). The median period until lesion resolution was 4.6 months (3d-29mo). Immunological evaluation was performed in 46 patients. Five patients presented immunological defects, including 4 with previous diagnosis of immunodeficiency: Chediak-Higashi Syndrome, Hyper-IgM Syndrome, liver transplantation (n=2), low CD4 count. None of them were HIV-infected. One patient who had consanguineous parents died of respiratory failure before immunological investigation.

Conclusion: Clinical characteristics of patients with localized BCG adverse events vary according to regional epidemiology. In our study, 10.8% of patients were immunodeficient. Primary immunodeficiency should be considered in localized BCG adverse events.

P832

LOCALIZED ADVERSE EVENTS AFTER BCG: CLINICAL CHARACTERISTICS AND IMMUNOLOGICAL EVALUATION

T.N.F. Moreira[1], M.I. de Moraes-Pinto[1], E.C. Santos-Valente[2], P.M. Fontes[1], A.S. Grumach[3], B.T. Costa-Carvalho[1], L.Y. Weckx[1]

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Conclusion: Clinical characteristics of patients with localized BCG adverse events vary according to regional epidemiology. In our study, 10.8% of patients were immunodeficient. Primary immunodeficiency should be considered in localized BCG adverse events.

P833

IMMUNOGENICITY AND SAFETY OF A HIB-MENC-TT BOOSTER VACCINE IN PRE-TERM AND FULL-TERM INFANTS IN THE SECOND YEAR OF LIFE

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Background and aims: Pre-term infants are at greater risk of morbidity from vaccine-preventable diseases with decreasing gestational age. The immunogenicity, reactogenicity and safety of combined *Haemophilus influenzae* type b-*Neisseria meningitidis* serogroup C (Hib-MenC-TT) booster vaccination was assessed in pre-term and full-term infants.
Methods: In this study (NCT00586612) 154 pre-term (n=50, < 31 weeks; n=104, 31-36 weeks) and 144 full-term Spanish infants (>36 weeks), previously vaccinated with Hib-MenC-TT (2, 4, 6 months) and DTPa-HBV-IPV and 7vCRM$_{197}$ vaccines, received a Hib-MenC-TT booster at age 16-18 months. Blood samples were collected pre- and 1 month post-booster. Serum bactericidal activity using rabbit complement (rSBA-MenC) and anti-PRP antibodies using ELISA were measured. Local/general solicited symptoms within 4 days and unsolicited AEs/SAEs within 31 days post-booster were recorded.
Results: One month post-booster, all subjects achieved anti-PRP ≥0.15µg/mL and ≥99.2% achieved rSBA-MenC titres ≥1:8 in all groups (Table). Hib-MenC-TT was generally well tolerated, with lower rates of drowsiness, injection-site reactions, and loss of appetite in pre-term infants (exploratory analysis). No vaccine-related SAEs were reported.

Table. Percentages of subjects with titres/concentrations greater than or equal to predefined cut-offs and GMTs/GMCs, for anti-PRP and rSBA-MenC (ATP cohort for immunogenicity)

Gestational age	Time-point	Anti-PRP			rSBA-MenC		
		N	% ≥0.15 µg/mL	GMC	N	% ≥1:8	GMT
<31 weeks	Pre-booster	38	89.5 [75.2–97.1]	0.75 [0.49–1.16]	38	71.1 [54.1-84.6]	84.2 [39.0–182.1]
	1 month post-booster	38	100 [90.7–100]	58.71 [40.55–84.98]	37	100 [90.5-100]	4570.8 [2784.1–7504.3]
31-36 weeks	Pre-booster	95	86.3 [77.7–92.5]	0.69 [0.53–0.89]	96	78.1 [68.5–85.9]	77.5 [53.0–113.2]
	1 month post-booster	94	100 [96.2–100]	47.31 [37.80–59.21]	96	99.0 [94.3–100]	5009.0 [3699.6–6781.9]
>36 weeks	Pre-booster	130	90.0 [83.5–94.6]	0.78 [0.62–0.97]	134	87.3 [80.5-92.4]	147.8 [110.9–197.1]
	1 month post-booster	134	100 [97.3–100]	54.63 [45.33–65.83]	137	99.3 [96.0-100]	5288.8 [4244.9–6589.4]

GMC/GMT = geometric mean antibody concentration/titre calculated on all subjects;
N= Number of subjects with available results; [ ] = lower and upper limits of 95% CI

[ ]

Conclusion: Hib-MenC-TT booster vaccination in the second year of life was immunogenic and well tolerated in pre-term and full-term infants when co-administered with other recommended vaccines. Robust booster responses in pre-term and full-term infants, indicating similar immune memory priming, suggest no delay in vaccination with Hib-MenC-TT is needed in pre-term infants.

P834

INFLUENZA VACCINE SINCE H1N1: A SURVEY OF PAEDIATRICIANS' ATTITUDES AND UPTAKE

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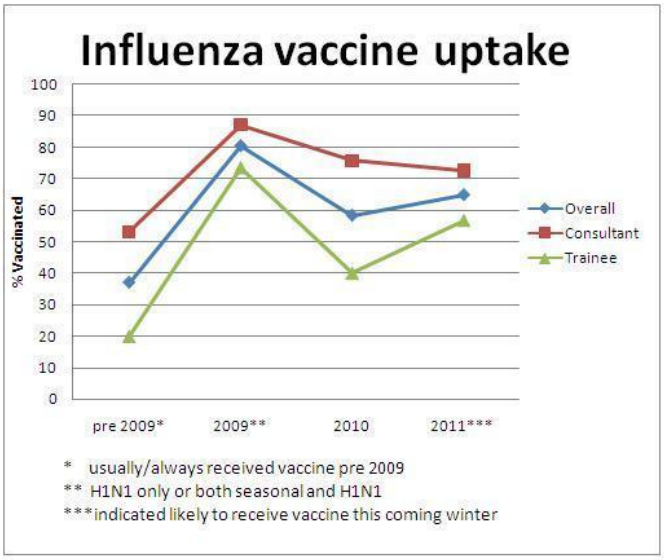
Background: Seasonal influenza vaccination is traditionally poor among paediatricians. We wished to establish if pandemic H1N1 has altered uptake and affected attitudes to influenza vaccination and to evaluate opinions on the vaccination of healthy children.

Methods: We carried out a survey of consultant and trainee paediatricians in Northern Ireland.

Results: 62 consultant and 60 trainee paediatricians responded. Significantly fewer trainees than consultants received the influenza vaccine in each year (p =0.037) [Figure 1]. Vaccine uptake more than doubled in 2009 compared with previous years (p< 0.001) then decreased again in 2010.



[Figure 1. Vaccine uptake.]

The commonest reasons for uptake (protect yourself; professional responsibility) and non-uptake (not at high risk; inconvenience) did not change. More people cited 'protecting patients' (20% Vs 14%) as a reason for getting the vaccine and 'concern about side effects' (15% Vs 3%) as a reason for not getting the vaccine during the pandemic compared with before the pandemic.There is evidence of some disagreement across the profession on the issue of vaccinating healthy children, with 30% of consultants and 18% of trainees indicating that they felt all children under 5 years should 'definitely receive the H1N1 vaccine'.

Conclusions: There is an opportunity to prevent a further decline in vaccine uptake among paediatricians, particularly trainees, with improved information on benefits and improved accessibility. There is a need for clarity, and engagement with paediatricians about decisions regarding H1N1 vaccine policy in children.

P835

LACK OF ASSOCIATION BETWEEN THIMEROSAL-CONTAINING VACCINES AND AUTISM: A CASE-CONTROL STUDY IN POLAND

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Background and aims: The controversial issue of the early human exposure to mercury compounds is ethylmercury, which is present in the thimerosal-containing vaccines (TCV). The objective of this analysis was to determine an association of TCVs exposure during the first 2 years of life with the risk of autism.

Methods: Study population included 96 cases diagnosed with childhood or atypical autism and 192 controls matched individually by year of birth, gender, and physician's practice. Data on autism diagnose and vaccination history were from GPs. Data on the other possible autism risk factors were collected from mothers. Logistic conditional regression was used to assess the risk of autism due to TCVs exposure.

Results: No significant association was found between TCVs exposure and autism. After adjusting to potential confounders, odds ratios of the risk of autism developing for infants vaccinated with TCVs were 1.33 (95%CI:0.52-3.39) for vaccination during the first 28 days, and 1.90 (95%CI:0.38-9.38) during the first six months of life.

Conclusion: Our study revealed no evidence of an association between TCVs and autism. Furthermore, there was no indication of a dose-response association between the thimerosal exposure and the risk of autism.

P836

INVASIVE BACTERIAL DISEASES ANDSTREPTCOCCUS PNEUMONIAE IN JAPAN

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Background: Japanese government finally introduced Hib vaccine in Dec 2008 and PCV7 in Feb 2010, despite the careful vaccine policy over the years,. The uptake of the vaccines is still around 20% for Hib and 10% for PCV, but we expect to see the changes soon. To estimate and to evaluate vaccine-preventable invasive diseases, we started a population-based surveillance in 2008.

Method: Surveillance area: Eastern Hokkaido

Study Period: 2008.1.1-2010.12.30

Population: 28511

Number of institutions: 7 (all in the surveillance area)

Target population: Children aged between 28days to 60 months

Result: The total of 95 bacteremia and 12 meningitis cases were reported. The distribution of the causal pathogen was: S.pneumoniae(69%), H.influenzae(22%), S.aureus(3%) and E.coli(2%) (Fig-1).

In 2010, we collected 22 cases of bacteremia and 3 cases of meningitis. The estimated incidence of invasive bacterial disease is 87.69/100,000 in 2010.

We received 67 S.pneumoniae strains. The serotype distribution is shown in (Table-1).

The overall serotype coverage for PCV7 was 61% and PCV13 was 86% (Table-2).

Serotype	2008	2009	2010	Total
23 F	4	3	5	12
14	1	3	1	5
6B	3	3	3	10
6A	5		5	9
19A	1		1	2
22F		1		1
23 A			1	1
28A	1			1
9A	3			3
9L		1		1
unknown	4	7	1	12
dead	2	4	4	11
Total	24	22	21	67

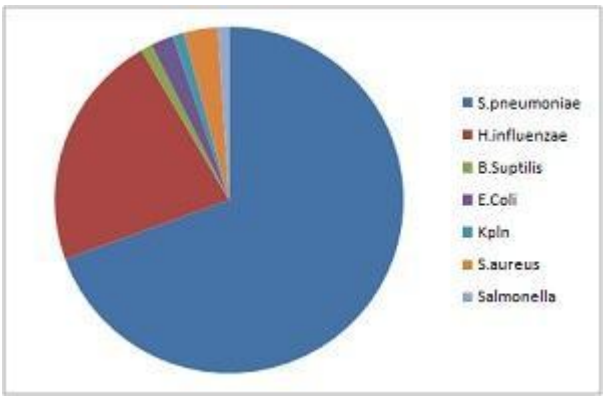
PCV7	4,6B,9V,14,18C,19F,23F
PCV13	1,3,4,5,6A,6B,7F,9V,14,18C,19A,19F,20F

[Fig-1. Distribution of Causal Pathogen]

[Table-1. Serotypes collected (2008-2010)]

	2008	2009	2010	Total
PCV7	44%	81%	56%	61%
PCV13	77%	81%	93%	86%

[Table-2. Serotype coverage(2008-2010)]



Conclusion: The estimated incidence of hospitalized bacteremia in Japan is higher than most of the developed countries. PCV7 coverage for all-over Japan was believed to be uniformly medium-high, but it was lower than expected. Vaccines of wider coverage are awaited.

P837

SURVEY REGARDING VACCINE COVERAGE IN GALICIA (2010)

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Background and aims: The Galician Vaccination Program has as its primary objective the achievement of high coverage rates of the vaccines included in the vaccination calender of the Autonomic Community of Galicia (Spain), in order to control and including, to eliminate these diseases though vaccination. To determine this coverage a biannual survey was conducted in different population groups to compare and contrast with data from the Vaccination Registry.

Methods: A sample of 3,607 children from 3-4 years, 8 years and 16 years of age was selected to carry out the survey. An in-person, household interview was conducted to collect vaccination history as recorded in the inmunization record and/or other accredited document.

The survey was conducted from a startified sample on two criteria:

- Urban or rural area

- Primary care sector

As a basis for the sample the database from the population information system of the Health Department (health card; estimated coverage > 99%) was used.

Results: No differences were observed in coverages between urban and rural areas.

Coverage rates for each vaccine refer exclusively to document coverages.

1. Children 3-4 years: documented vaccination >96%
2. Children 8 years: documented vaccination >97%, except for meningococcal C vaccine
3. Adolescents 16 years: documented vaccination > 93% except for Td vaccine

95% confidence intervals will be presented.

Conclusions: Excellent vaccination coverages were observed in all population groups.

P838

AEFI NOTIFICATIONS OF NARCOLEPSY/CATAPLEXY AMONG CHILDREN 5-16 YEARS OF AGE ASSOCIATED WITH PANDEMRIX VACCINATION AND A(H1N1) EPIDEMIC IN FINLAND

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Background and aims: To prevent population from severe A(H1N1) infection, THL recommended to vaccinate everyone. Adjuvanted Pandemrix^{R} was the only pandemic vaccine available. The epidemic peaked during weeks 41-51 in Finland in 2009. Vaccination took place during and after epidemic. Narcolepsy is a rare chronic neurologic condition with incidence of < 1/100 000 and strong genetic predisposition. Etiology of narcolepsy is unknown; infections are thought to contribute to onset. In Finland during 2006-9, 40-60 cases of narcolepsy occurred annually, of these ≤25% in those ≤19 years.

Methods: AEFI notifications reported to the national vaccine adverse event registry. Narcolepsy coded ICD-10 G47.4, defined as excessive daytime sleepiness with or without cataplexy, confirmed by sleep polygraphy and multiple sleep latency test.

Results: Total 62 AEFI reports on narcolepsy were received between May 2010 and 11 February 2011, only 3 of these in adults. Mean age was 12, range 4,5-37 years. 35 were female, 27 male. Onset of symptoms started mean 52 days (range 1- 240 days) after Pandemrix^{R} vaccination. In most cases, onset was abrupt and severe resulting in need of medical treatment.

Conclusions: In Finland, a cluster of narcolepsy cases was observed among children 4-19 years of age after Pandemrix vaccination increasing incidence to 8,8/100 000 begin_of_the_skype_highlighting 8/100 000 end_of_the_skype_highlighting vaccinated in this age group. Epidemiologic, immunologic and genetic studies are underway to explore the strength of association of narcolepsy following Pandemrix^{R} vaccination, A(H1N1) epidemic and other preceding or simultaneous infections and other risk factors.

P839

A PREDICTION TOOL FOR THE NET EFFECTIVENESS OF PNEUMOCOCCAL VACCINATION UNDER SEROTYPE REPLACEMENT

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Background and aims: Serotype replacement and herd immunity are the ever-intriguing issues in developing mathematical models for pneumococcal epidemiology and control efforts. Recently, increasing attention has been paid to the possibility of these two types of indirect effects having opposite effects on the population level effectiveness of a vaccination program. We propose using tools built on relatively simple probabilistic models to demonstrate potential effects of serotype replacement on the projected outcome of alternative pneumococcal vaccination programs.

Methods: Under a scenario of a complete elimination of the vaccine-types in carriage and their replacement by non-vaccine types, the projected effectiveness of a vaccination program is a function of two key serotype-specific quantities, the incidence rate of carriage and case-to-carrier ratio for invasive disease (IPD).

Results: Using data from Finland, we demonstrate that each of the three current pneumococcal conjugate vaccines (with 7, 10 or 13 serotypes) may be expected to decrease the IPD incidence among children < 5 years of age, with larger improved effectiveness with higher valency of the vaccine. However, in the population at large the reduction in IPD is much more moderate, and among the elderly the replacement may entirely erode the reduction in vaccine-type IPD.

Conclusions: These results highlight the importance of the interplay between the two quantities, the incidence of carriage and the case-to-carrier ratios among the groups of vaccine and non-vaccine serotypes. In particular, the comparison of the effectiveness of alternative vaccination programs should not be based on either of the quantities alone.

P840

INCIDENCE AND EPIDEMIOLOGY OF COMPLICATED VARICELLA ZOSTER VIRUS INFECTION IN IRISH CHILDREN: A NATIONAL SURVEY

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Background: Chickenpox and shingles are normally mild self-limiting illnesses but can be associated with severe morbidity and mortality in neonates, immunocompromised and children with underlying medical conditions. Safe, effective vaccines are used, in many countries, for routine universal vaccination or programmes targeting at risk children. The decision to introduce such vaccines for Irish children is under review.

Objectives: To estimate the incidence and characterise the epidemiology of complicated Varicella Zoster Virus (VZV) infection in Irish children.

Methods: Complicated VZV infection was defined as any child admitted to hospital with complicated VZV infection. Throughout 2007, data were collected prospectively from 211 paediatricians reporting to the Irish Paediatric Surveillance Unit, Hospital Inpatient Enquiry Systems and hospital infection control teams.

Results: 194 children with complicated VZV infection were identified: 184 chickenpox; 10 shingles. The majority were previously healthy (93%). The estimated incidence was 19.9/100,000. Median age for chickenpox, 28.5 months (range, 2 months - 14.9 years) and shingles, 8.5 years (range, 18 months -17 years). Complications included: infection (skin/soft tissue, 68 [37%]; pneumonia/empyema, 7 [4%]; septicaemia, 3 [2%]; bone/joint, 2 [1%]); neurologic, 30 (16%); and metabolic, 2 (1%). Median length of stay, 4 days (range 1-35 days). Three required ICU admission. No deaths were reported.

Conclusions: VZV infection causes significant morbidity in Irish children, the majority of whom are previously healthy. Prevention of such illnesses requires introduction of a universal vaccination strategy.

P841

THE DIFFERENCE IN REACTIONS ON AVIAN INFLUENZA VACCINES AMONGST CHILDREN AND ADULTS

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Goal: To ascertain the reactions among children compared to adults on avian influenza vaccines.

Background: The invasion of the avian influenza A (H5N1) virus was a great cause for worry around the globe. The concerns were more for children who were thought to be more vulnerable.

Methods: We made use of twenty healthy children from ages 4-12 for this study who were given a dose of the vaccine as trial. Twenty-one days after vaccination, immunogenicity was assessed by hem agglutination inhibition and micro neutralization assays. Safety information was collected for 180 days.

Results: We discovered that there were no side-effects, and the vaccine fulfilled all international immunogenicity criteria for licensure. The post/prevaccination geometric mean titer ratio was 18.75, the rate of seroconversion was 80% and the rate of seroprotection was also 80% 21 days after vaccination.

Conclusions: We were able to confirm that the vaccines were not harmful and that children had almost thesame reactions with adults.

P842

IMMUNOGLOBULIN DEFICIENCY IN CHILDREN WITH HIB VACCINE FAILURE

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Background: Immunoglobulin (Ig) deficiency in children with Hib vaccine failure is well-described, but its clinical significance is unknown.

Aims: To estimate the prevalence of Ig deficiency in children with Hib vaccine failure several years after infection and to determine their risk of recurrent infections.

Methods: Children who developed invasive Hib disease after immunization with Hib conjugate vaccine from 1992 to 2006 were identified through national surveillance. Participation involved completion of a questionnaire and a blood sample from the child.

Results: A completed questionnaire and blood sample was provided by 170 children at a median of 4 years after infection, equivalent to 1035 child-years of follow-up. Ig deficiency was present in 11.2% and was associated with age < 2 years at onset of Hib disease (63.2% vs. 39.7%, P=0.05) and receiving at least two antibiotic courses/year in early childhood (57.9% vs. 25.8%, P=0.004), but not with clinical presentation, severity of Hib infection or risk of other serious infections requiring hospitalization. In a logistic regression model, antibiotic use was independently associated with presence of an underlying medical condition (OR=7.3; 95% CI=2.3-22.7; P=0.001) and Ig deficiency (OR=5.4; 95%CI=1.8-16.0; P=0.003), while breastfeeding was protective (OR=0.30; 95%CI=0.14-0.65; P=0.002).

Conclusions: 4 years after infection, the prevalence of Ig deficiency in children with Hib vaccine failure is half that reported in the first few months after Hib infection. Young children with Hib vaccine failure may have quantitative as well as qualitative antibody defects, which predisposes them to recurrent minor and occasionally serious infections, but improves with age.

P843

PANDEMIC OF INFLUENZA AH1N1: QUALITATIVE ANALYSIS OF THE INFORMATION IN PRESS IN SPAIN

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Objective: To evaluate the information in Spanish press on the influenza A.

Method: Revision of the news published in Spanish newspapers that they suppose 39.6% of average printed copies (1.565.529) between April 2009 to January 2010.

We analyzed: Centers of mediatic attention (CMA) and Actors.

Results:

CMA: April-May 2009: The WHO describes the situation in Mexico like: “fear”, “preoccupation” and “alarm”. Possible closing of airports. Economic repercussion. Possible transmission by the pig meat ingestion. Fraudulent sale of antivirals.

June-July: Declaration phase 6 of pandemic. First death in Spain. Identify the groups for the vaccination (40%). Possible insufficiency of world-wide vaccine production.

August-September: Closing of schools. Benefits of the pharmaceutical industry. Vaccine Non availability at the beginning of the epidemic.

October-January 2010: Debate on the vaccine security. The vaccination campaign begins. Little affluence for the vaccination. 271 deaths by influenza A. WHO's criticing to exaggerate the pandemic.

Actors: The WHO declares the alarm, it gives contradictory information, coordinator of the performances, and finally responsible for the alarm.

European Union filters of the information by economic questions, and guarantor of the security of the vaccine.

Government of Spain: interlocutor of different sectors.

Experts: the majority is aligned with the sanitary authority and reinforces the sanitary device of mediatic form.

Conclusions: The WHO sends paradoxical, alarming and contradictory messages, but with much mediatic repercussion.

The UE has little informative presence.

The Spanish Government makes a policy informative intensive and contradictory.

P844

FINIP: A CLUSTER-RANDOMIZED TRIAL OF THE PNEUMOCOCCAL *HAEMOPHILUS INFLUENZAE PROTEIN* D CONJUGATE VACCINE (PHID-CV) IN FINLAND-UPDATE ON STUDY CONDUCT

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Background and aims: The FinIP trial was designed to demonstrate PHiD-CV vaccine (GlaxoSmithKline) effectiveness against *S. pneumoniae* and *H. influenzae* diseases in vaccinated and unvaccinated (indirect effect) populations.

Methods: In this phase III/IV cluster-randomized, double-blind field trial two thirds of clusters receive PHiD-CV; one third hepatitis A or B vaccine as control. The study is conducted in municipal health care centers (HCC, N=139) by well-baby clinics' (N=650) nurses (N>2000). Children < 19 months of age were enrolled to receive 2 to 4 doses according to age. Outcome data for invasive pneumococcal disease (IPD), hospital-diagnosed pneumonia, tympanostomy tube placements and antimicrobial prescriptions are obtained through national health registers.

Results: Together with parallel AOM and carriage study >47000 subjects were enrolled (initial target 91000). Participating 139 HCCs covered 77% of total Finnish birth cohort (90% targeted). Enrolment started in May 2009 and ended by September 2010 when pneumococcal vaccine was introduced into the national immunization programme. There were differences in enrolment targets achieved (median 64%, range 11-99%) in the HCCs. This variation was inversely associated with HCC size. Enrolment improved with calendar time. Recalculations of estimated accrual of IPD cases in enrolled cohort for the primary endpoint (vaccine-type IPD in infants) show that extension of the ongoing blinded follow-up is likely to ensure adequate power.

Conclusions: Enrolment of children varied across public health care centres. A survey has been started to assess parents' perceptions and attitudes on vaccine trials. Clinical population-randomized trials need to be pursued despite challenges in study conduct.

P845

SEASONAL INFLUENZA VACCINATION COVERAGE BY SEX, AGE AND RISK GROUPS IN THE VALENCIAN COMMUNITY IN 2009-2010 AND 2010-2011 SEASONS

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Background and aims: Seasonal influenza vaccination is one of the most effective preventive measures recommended for persons with risk factors, however, coverage in these groups continue without reaching the target set by WHO.

The aim of the study is to evaluate immunization coverage against seasonal influenza for 0-14, 15-59, 60-64 and over 64 years, by sex and risk groups in the Valencian Community in 2009-2010 and 2010-2011 seasons.

Methods: Retrospective study of vaccine acts against seasonal influenza registered at the Immunization Information System of the Valencian Community. We used the Population Information System to calculate the denominator.

Results: In the 2009-2010 season were declared a total of 781,286 doses of seasonal influenza vaccine in the Immunization Information System. 356,420 (45.62%) doses in men and 424,866 (54.38%) in women.

The largest number of vaccine acts were registered in the high risk group with 377,951 (48.38%), followed by medium risk with 281,965 (36.09%). Coverage in over 64 years was 56.66%.

In the 2010-2011 season were declared a total of 690,701 doses, 316,875 (45.88%) in men and 373,827 (54.12%) in women. In the high risk group were registered 348,475 (50.45%) doses and medium risk 256,906 (37.19%). Coverage in over 64 years was 52.43%.

Conclusions: Seasonal influenza vaccination coverage over 64 years in both seasons are less than the target by WHO, 70% for 2010.

P846

EVOLUTION OF IMMUNIZATION COVERAGES AGAINST HUMAN PAPILLOMAVIRUS FOR GIRLS AGED 14 YEARS IN THE VALENCIAN COMMUNITY

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Background and aims: The coverages against human papilloma virus (HPV) in our community have not reached the results expected. HPV immunization coverages are low, which means that this measure from the viewpoint of public health has a moderately effective.

The aim of the study is to evaluate the evolution of inmunization coverages against the human papilloma virus (HPV) in cohorts of girls born in 1994, 1995 and 1996 in the Valencian Community.

Methods: Retrospective study of vaccine acts of 14 year old girls vaccinated against HPV, reported in the Immunization Information System of the Valencian Community. The analysis has been done by dose and by birth year.

Results: The first dose of HPV vaccine given to the girls who were born in 1994, was administered at the health centers in 10 of the 22 health departments (45.45%). The rest of the departments made this vaccination at schools and coverages in these were higher .

Vaccination against HPV of girls born in 1995 and 1996 was given in all of the departments in health center.

Birth year	Dose 1	Dose 2	Dose 3
1994	85,47%	81,66%	74,66%
1995	64,70%	61,81%	57,26%
1996	54,85%	27,97%	Vaccination is not complete

[HPV Immunization coverage by dose and birth year]

Conclusions: In departments where vaccination was carried out in schools was achieved better coverage. Vaccination coverage against HPV has decreased for 14 year old girls born after 1994.

P847

IS THERE A RELATIONSHIP BETWEEN INFLUENZA VACCINATION COVERAGE OF HEALTH PROFESSIONAL AND COVERAGE OF RISK POPULATION IN THE 2010-11 SEASON?

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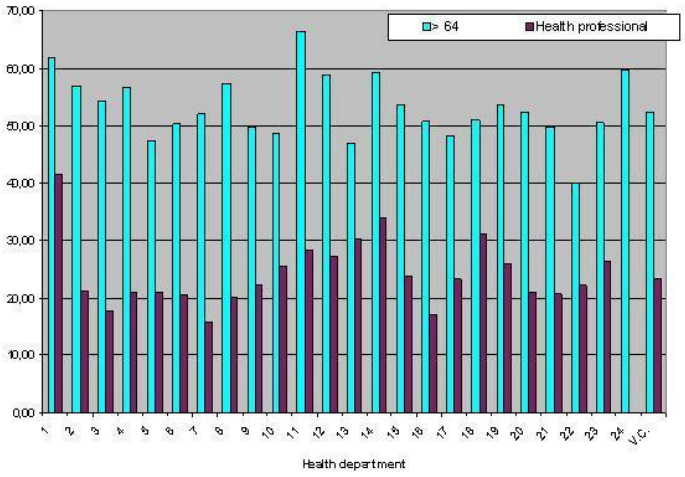
Background and aims: Factors that influence in the vaccination are: to be well informed, belong to a risk group, consider the flu vaccine safe, be recommended by the health professional and have been vaccinated in previous seasons, and have scientific information based on evidence.

Aim: To assess influenza vaccination coverage against seasonal influenza risk population and health professional in health departments in the Valencian Community in the 2010-2011 season.

Methods: Retrospective study of seasonal influenza vaccine reported in the Immunization Information System (SIV) in the 2010-2011 season in Valencian Community.The variables of the study are: health department, age, sex, risk group and healthcare workers.Source of data: Immunization Information System (SIV) and the Population Information System (SIP).

Results: 690,701 seasonal influenza vaccine acts recorded in the SIV during the study period, 316,874 (45.87%) in men and 373,827 (54.13) in women. 444,212 (64.31%) had a chronic illness, 16,693 (2.42%) were healthcare workers and 157,913 (22.86%) in over 60 years without any other risk factor. Coverages of health professional and over 64 years group, by health department in Valencian Community, are represented in the graph.



[Influenza Vaccination coverages in 2010-11 season]

Conclusions: Coverage over 64 years is not achieved in any department the value of the target set by WHO (70%) for this year. Coverage against seasonal influenza of health professionals is very low, there is no relationship between the high coverage in health professionals and coverage in over 64 years group, except in the department 1.

P848

WHO BCG REFERENCE REAGENTS EVALUATED BY ATP ASSAY AND CULTURAL VIABLE COUNT METHOD

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The first WHO Reference Reagents (RRs) for BCG vaccines of three different substrains - Danish 1331, Tokyo 172-1 and Russian BCG-I (Bulgarian Lot 254-2 produced from Sofia SL 222) have been established and adopted by the WHO ECBS in 2009/2010.

All three substrains were evaluated in an international collaborative study (Mei M. Ho *et al.,* Vaccine, 29 (2011)) using two viability assays (cultural viable count and modified ATP assay) and mPCR as an identity assay (Kevin Markey *et al.*, Vaccine, 28 (2010)).

The results of the ATP and CFU assays performed by the Bulgarian team are presented.

The modified ATP method was according to the international collaborative study protocol. The suitability of this rapid and sensitive method as an alternative method of the cultural viable count assay was evaluated. The routine method (BulBio-NCIPD) for the cultural viable count assay was applied.

The estimated ATP content of the BCG Lot 254-2 was mean 4.11±0.88 ng ATP/ampoule. In the collaborative study that content was 7.52±1.48 ng ATP/ampoule. As the ATP assay conditions varied among all participating laboratories, the distribution of the mean ATP content was wide.

The mean CFU of the Bulgarian candidate was 3.07±0.29 million/ampoule. In the collaborative study the estimated CFU confirmed the expected variable results due to the different culture media and methodologies applied (3.39±0.50 million/ampoule).

The intended uses of Bulgarian Lot 254-2 for use as a RR for BCG vaccine are as a comparator for viability assays, residual virulence/local reactogenicity assays and protection assay in animal models.

P849

VACCINATION COVERAGE AGAINST HUMAN PAPILLOMAVIRUS (HPV) IN MURCIA (SPAIN)

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Background and aims: Girls born in 1995 and 1996 were vaccinated against papillomavirus in schools. Girls born in 1994 were vaccinated at health centres. The primary endpoint was to compare the coverage achieved with the first dose with the two strategies that were used.

Methods: Girls born in 1995, 1994 and 1996 were vaccinated in October 2008, March 2009 and October 2009, respectively. Letters were sent out and were followed up with SMS reminders to girls born in 1994. We calculated girls who were vaccinated as a result of the reminders.

Results: Vaccination coverage of girls born in 1994, 1995 and 1996 was 60.1%, 89.8% and 78%. Girls born in Spain had a higher coverage than those born in Latin America in the 1994 and 1995 cohorts (62.4 vs. 53.3 and 91.8 vs. 89.7) while those born in Latin America had the highest coverage in 1996 (79.5 vs. 83.1). Reminder strategies increased vaccination coverage among girls born in 1994 by 5.1% (from 60.1 to 65.2%).

Conclusions: School vaccination strategy was found to achieve higher vaccination coverage. An incident relating to two possible adverse reactions had major media impact (subsequently being ruled out) and led to a fall in coverage starting in February 2009. Despite this, girls born in 1996 and vaccinated at school show an 18% higher vaccination coverage than those born in 1994 who were vaccinated at health centres. Reminder strategies are necessary for girls born in 1996 in order to increase the coverage.

P850

VICTIMS OF SEXUAL VIOLENCE UNDER 20 YEARS OF AGE REFFERED TO A BRAZILIAN SPECIAL IMMUNOBIOLOGICAL CENTRE - 2003-2009

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Background and aims: The Brazilian Special Immunobiological Centre (CRIE) is a government institution responsible for providing special immunobiological not provided by nacional vaccination programmes, in high risk situations.

In Brazil the vaccination against Hepatitis B is free from birth to 19 years of age. Victims of sexual violence that have been inadequately vaccinated are referred to the CRIE to receive immunoglobulin and vaccine anti-Hepatitis B.

The objective of this research was to define the profile of CRIE´s patients victims of sexual violence, who received immunoglobulin and vaccine anti-Hepatitis B in the period 2003 - 2009.

Methods: Reviewed data was collated between 2003-2009 from database of the National Program of Immunizations (PNI) of the Brazilian Government.

Results: From a group of 1329 victims of sexual violence assisted by CRIE, 506 were aged between 0-19 years of age, representing 38% of cases. Data showed that 91% of the group was female and 9% male with the highest incidence occurring in adolescents aged 15-19.

Conclusion: The numbers for sexual violence against children and adolescents are considerable in the state of Rio de Janeiro and approximately 38% of CRIE's assistance was to individuals who are entitled to free vaccination. The remaining 62% represent an age group not assisted by the government for vaccination against Hepatits B. This research will provide an explanation as to why this is the case.

P851

HUMAN T-CELL KINETICS FOLLOWING VACCINATION WITH THE TUBERCULOSIS VACCINE MVA85A

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Background/aims: A major effort is underway to develop new vaccines capable of generating T-cell protection against important intracellular pathogens including tuberculosis (TB), HIV and malaria. Viral-vectored prime-boost vaccine regimes can induce potent T-cell responses but little is known of the kinetics of such responses in humans or of the proliferative response *in vivo*.

Methods: 3 groups of 4 healthy Bacille Calmette-Guérin (BCG)-primed adults received a single intradermal dose of a TB vaccine candidate, MVA85A.

Group 1 volunteers underwent daily clinical assessments and interferon-γ ELISPOTs for 14 days post-vaccination.

Group 2 and 3 volunteers received a stable isotopic label (deuterated glucose) at either day 4 or 10 post-vaccination respectively. Vaccine-specific $CD4^+$ cells were separated from follow-up blood samples and gas chromatography-mass spectrometry (GC-MS) was used to estimate the fraction of labelled (and hence dividing) cells during the labelling period.

Results: MVA85A was safe and well tolerated. Immunogenicity was high: median IFNγ responses to pooled 85A peptides were 1,137 spot-forming units (sfu)/10^6 peripheral blood mononuclear cells (PBMC) at day 7 post-vaccine. IFNγ-secreting cells appeared in the blood abruptly at day 5/6 and rapidly rose to peak by ~day 7. Recently divided cells were detected at 1.8-7.8 times greater frequency amongst vaccine-specific $CD4^+$ PBMC than in non-responding $CD4^+$ cells even 4 days after labelling.

Conclusions: This study provides new data describing the cellular immune kinetics and clinical response to an MVA-vectored vaccine. Improving our understanding of the vaccine response could aid the design and evaluation of other T-cell inducing vaccine regimes.

P852

PURIFICATION OF TWO ANTIGENS EXTRACTED FROM BORDETELLA PERTUSSIS BY AFFINITY AND ABSORBTION CHROMATOGRAPHY

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Background and aims: Whooppig cough (Pertussis) is a severe , highly contagious respiratory disease especially for young infants. A pertussis vaccine mainly composed of two extracellular proteins of *Bordetella Pertussis* including of pertussis toxin (PT) and filamentous hemagglutinin (FHA) have been considered of two potential candidate for production of acellular vaccine . The aim of this study was to purify these two antigens from submerged culture of *B. Pertuusis* using affinity and absorbtion chromatography.

Methods: For this purpose *B. Pertussis* strain RIVM - 134 was grown in a 45-litre fermantor using a modified Stainer-Scholte medium supplemented with 1gr dimethyl (2,6-o-) β - cyclodextrin per litre . The two antigens (PT and FHA) were extracted from the supernatant of the culture after centrifugation and was concentrated 20 times and then submitted to chromatography for purification of the above two antigens.

Results: Pertussis toxin from one of the fractions in Fetuin - Sepharos 4B column and FHA from a certain fractions in Hydroxylapetite column were extracted , dialysed and protein concentration of 1200, 950 µg/ml were estimated for PT and FHA respectively. The entity of both antigens were confirmed by SDS - PAGE and immunoblotting techniques.

Conclusions: The results showed that the purification of PT and FHA are at their best when Fetuin-sepharose 4B and hydroxylapatite columns have been used.

P853

VARICELLA-ZOSTER-VIRUS (VZV) IGG ANTIBODY LEVELS AND AVIDITY IN SOLID ORGAN TRANSPLANT (SOT) RECIPIENTS AFTER VZV VACCINATION

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Background: The aim of the study was to investigate the varicella-zoster-virus (VZV) IgG avidity as a marker of memory priming and functional affinity of antibodies in solid-organ-transplant (SOT) recipients (20 liver, 3 heart, 5 kidney) several years after pre-transplant VZV vaccination with a single dose of Varivax (Aventis Pasteur, Lyon, France) compared to 36 healthy children with clinical and serological confirmed VZV infection and 14 healthy children after Varivax vaccination.

Methods: The serum samples of SOT were evaluated with an adapted ELISA.

Results: Median IgG antibody levels were 800 U/ml in wild-virus infected controls, 810 U/ml in vaccinated controls and 630 U/ml in SOT. Median relative avidity index (RAI) was 89% for wild-virus infected controls, 94% for vaccinated controls and 82% for SOT. A regression model for time post vaccination/wild-virus infection and different study groups displayed a peak for RAI between 50 and 100 months post exposition, with a delayed and decreased curve in SOT compared to controls. RAIs of SOT >180 months post vaccination were significantly lower than of controls. Of SOT, 13 patients had a RAI below 80%, whereas all controls had a RAI of at least 78%.

Conclusions: IgG antibody avidity in SOT may serve as an additional marker to evaluate humoral immunity against VZV. The role of humoral protection in the case of VZV exposure or re-activation has to be evaluated in long-term follow-up, since also cellular immunity may play a crucial role in defense against viral infections.

P854

HIGHER *STAPHYLOCOCCUS AUREUS* COLONIZATION IN 11-MONTH-OLD CHILDREN FOLLOWING PCV-7 VACCINATIONS IN INFANCY

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Background: Previously we observed in a randomized control trial (RCT) an increase in *S. aureus* carriage in PCV-7 vaccinated 11-month-old children (NCT00189020). A negative correlation between *S. aureus* and PCV-7-serotype carriage was suggested. We therefore investigated *S. aureus* colonization in a vaccinated population 3 and 4 years after PCV-7 implementation.

Methods: As a follow up of the RCT (2005), we performed in 2009 and 2010 two cross-sectional studies collecting nasopharyngeal swabs from PCV-7 vaccinated children 11 and 24 months of age, and from one of the parents of the latter group (n~330 per group). Swabs were cultured for *S. aureus* and *Streptococcus pneumoniae*: pneumococcal isolates were serotyped by Quellung method.

Results: *S. aureus* carriage rates increased from 5% in 2005, to 9% and 14% in 2009 and 2010, respectively, in 11-month-old children (2005 vs. 2009: p=0.03; 2005 vs. 2010: p< 0.001), but were stable over time in 24-month-old children (6-8%). *S. aureus* colonization in parents increased from 20% in 2005 to 32% and 34% in 2009 and 2010, respectively (p< 0.01). Pneumococcal carriage rates remained relatively stable between 2005 and 2010, although a strong shift from PCV-7 to non-PCV-7 serotypes was observed.

Conclusions: In line with the observations of the previous RCT, we observed increased *S. aureus* carriage rates after PCV-7 implementation in 11-month-old children and parents from 24-month-old children, but not in 24-month-old children. Clinical implications of our observations need to be further studied.

P855

CONTINUING INCREASE IN 19A AND 6C SEROTYPE CARRIAGE IN CHILDREN AFTER THE INTRODUCTION OF PCV-7 IN THE NETHERLANDS

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Background: Pneumococcal conjugate vaccine (PCV-7) was implemented in the Dutch NIP in 2006. We studied the ongoing effect of PCV-7 introduction on nasopharyngeal pneumococcal carriage over time.

Methods: In follow-up of a randomized controlled trial (RCT) (NCT00189020), we performed two cross-sectional studies in 2009 and 2010 collecting nasopharyngeal swabs at 11 and 24 months of age from PCV-7 vaccinated children and from one of the parents of the latter group (n~330 per group). Swabs were cultured for *S. pneumoniae* and serotyped by Quellung.

Results: In 11-month-olds PCV-7 carriage rates were 38%, 8% and 3% in 2005, 2009 and 2010, respectively, whereas in 24-month-olds vaccine serotype carriage was 36%, 3% and 3% ($p < 0.001$ for all comparisons vs. 2005). Carriage of non-PCV-7 serotypes increased in 11-month-olds from 29% in 2005 to 39% and 50% in 2009 and 2010, respectively ($p < 0.01$ for all comparisons vs. 2005) and from 30% to 45% and 61% in 24-month-old children ($p < 0.001$: vs. 2005). A significant increase in carriage of 19A was found in 11 and 24-month-old children over time (11 months: 2%, 10% and 12%, 24 months: 3%, 6% and 14%, respectively). Moreover, the latter serotype also became the most dominant serotype. Besides, 6C carriage increased as well as other non-vaccine serotypes over time. In parents a similar shift of serotypes was seen.

Conclusions: Within 4.5 years after introduction of PCV-7, vaccine serotypes are virtually eliminated in children and their parents. However, non-PCV-7 serotypes, in particular 19A, have emerged. Pneumococcal disease surveillance remains important.

P856

CATCH-UP VACCINATION OF HEALTHY TODDLERS WITH AN INVESTIGATIONAL MULTICOMPONENT MENINGOCOCCAL SEROGROUP B VACCINE (4CMENB) - EXPLORATION OF A TWO-DOSE SCHEDULE

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Background: An investigational multicomponent meningococcal serogroup B vaccine (4CMenB, Novartis) shows promise for vaccinating infants. We evaluated a two-dose schedule in toddlers, suitable for a catch-up vaccination, when administered separately and concomitantly with MMRV vaccine.

Methods: In this open-label study healthy toddlers with no history of 4CMenB vaccination either received MMRV at 12 months followed by two doses of 4CMenB at 13 and 15 months (separate), or MMRV and 4CMenB at 12 months and 4CMenB at 14 months (concomitant). Immunogenicity was assessed in subsets one month later by serum bactericidal assay using human complement (hSBA) against three reference strains. Solicited postvaccination reactions were recorded for seven days.

Results: Immune responses were similar in both groups; hSBA GMTs for separate and concomitant groups were 271 and 248 against strain H44/76; 599 and 627 against strain 5/99; 43 and 32 against NZ98/254, respectively. Seroprotection rates (% hSBA ≥ 5) against strains H44/76, 5/99, and NZ98/254 were 100%, 100% and 96% in the concomitant group, respectively, and 100% against all three strains in the separate group. 4CMenB injection-site reaction rates were similar (75-79%) for all doses, and higher than MMRV (49-60%). Systemic rates were 85-89% with concomitant vaccines, 77-81% with separate 4CMenB, and 68% with MMRV.

Conclusion: Two doses of 4CMenB two months apart were sufficient to elicit protective immune responses against all three reference strains for the component antigens, unaffected by concomitant MMRV administration, with minimal impact on reactogenicity, so facilitating 4CMenB catch-up vaccination in current toddler vaccination schedules.

P857

THIRD YEAR POST-ROTAVIRUS VACCINATION IN BELGIUM: IMPACT ON ROTAVIRUS-POSITIVE STOOL SAMPLES IN HOSPITALIZED CHILDREN

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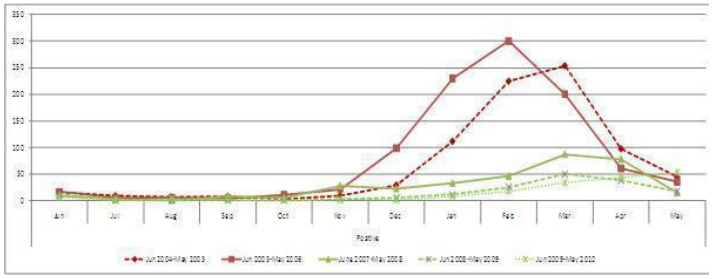
Background and aims: Rotavirus vaccination has been reimbursed in Belgium since November 2006. This study is the third year follow-up of previously reported impact of vaccination on rotavirus-positive stool samples in 9 pediatric centers across Belgium (rotavirus vaccine coverage (> 85%)).

Methods: Stool samples for rotavirus detection were collected from ≤ 5y old hospitalized children, within the same centers. Pre- (01/06/2004-31/05/2006) and post-vaccination periods (01/06/2007-31/05/2010) were compared. Absolute numbers and % reduction (95 % CI) are reported per year post-vaccination considering the average of the pre-vaccination period as a reference.

Results: The number of rotavirus-positive stool tests in children aged ≤5 years decreased from an average of 881 pre-vaccination to 368 (-58%) in the 1st year post-vaccination, to 202 (-77%) in the 2nd year and to 180 (-80%) in the 3rd year. In children aged between 2-24 months the percentage reductions were 64% (95% CI: 61-68), 81% (95% CI: 78-84) and 82% (95% CI: 79-84) in the 1st, 2nd and 3rd years respectively, compared with pre-vaccination. In addition an overall decline (-44%) in all-cause acute-gastroenteritis related hospital admissions was observed from 1700 per year pre-vaccination to 950 per year 3rd year post-vaccination.
Conclusion: Significant annual decline in number of rotavirus positive stool samples and in all cause acute GE related hospital admissions has been seen in young children after several years of vaccination in Belgium.

Figure 1: Monthly distribution of the number of rotavirus positive stool tests in hospitalized children age[s]d between 2 months and 24 months.



[Figure 1]

P858

CHANGING ETIOLOGY OF ACUTE GASTROENTERITIS AFTER INTRODUCTION OF ROTAVIRUS VACCINATION IN FINLAND: DECREASE OF ROTAVIRUSES AND INCREASE OF NOROVIRUSES

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Background and aims: Rotaviruses (RVs) and noroviruses (NoVs) are the two most important causative agents of acute gastroenteritis (AGE) in children, in this order. In Finland RV vaccines were launched in 2006, and universal immunization was introduced in September 2009. The coverage of RV vaccination was about 90% by 2010.

We studied the etiology of AGE before and after introduction of RV vaccination in Finland.

Methods: We collected stool samples from children seen in Tampere University Hospital (clinic or ward) because of AGE in 2006-2007 (n=341), 2007-2008 (n=418) and 2009-2010 (n=195). RVs and human caliciviruses (HuCVs) were detected by RT-PCR; HuCVs were further identified as NoVs or sapoviruses (SaVs).

Results: In the three seasons RVs were found in 128 (38%), 260 (62%), and 48 (25%) of the cases. NoVs were found in 116 (34%), 80 (19%), and 48 (25%), and SaVs in 4 (1%), 8 (2%), and 12 (6%) cases. In the season after the introduction of universal RV vaccination, 2009-2010, the most common RV genotypes seen in the hospital were G1P[8] (n=19), G4P[8] (n=17), and G2P[4] (n=6), and NoV genotypes were GII.4 (n=37) and GII.7 (n=9).

Conclusions: After universal RV immunization, RV AGE and all AGE seen in hospital have decreased remarkably. NoVs, especially subtypes of GII.4, have become equally common as RVs as causative agents and are likely to become the leading cause of AGE in children soon. We have not observed any increase of NoV AGE, however.

P859

PERCEPTION OF THE GALICIAN VACCINATION PROGRAM AND SATISFACTION WITH THE PROGRAM

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Background and aims: To evaluate the degree of satisfaction of users of the Galician Vaccination Program, and their perception regarding vaccines and the vaccination process.

Methods: We carried out an in -person, household survey of parents/guardians of a sample of children from 3-4 years, 8 years and 16 years of age to evaluate aspects related to vaccination, their point of wiew regarding vaccines and satisfaction with the program including:

- Perception of vaccines
- Opinion regarding the program
- Satisfaction with the vaccination process

The survey was conducted among parents/guardians of a total of 3,607 children.

As a basis for the sample the database from the population information system of the Health Department (health card) was used.

Results: A total of 3,023 people participated in the survey, a response rate of 83.81%

Among those surveyed, 88.7 to 90.9% believe that vaccines are beneficial. Between 75.7 and 83% of respondents described the Galician Vaccine Program as either good or very good. Between 78.6 and 88.2% of those surveyed did not have any complaints regarding the vaccination process.

Conclusions: In Galicia, the benefits of vaccines are well regarded, and parents/guardians have a good perception of the Galician Vaccination Program.

P860

OSCILLATIONS IN FREQUENCY AND GENOTYPE OF ROTAVIRUS DIARRHOEA PRESENTING TO A LARGE PAEDIATRIC EMERGENCY FACILITY IN PORTUGAL

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Introduction: Rotavirus (RV) vaccines (Rotateq and Rotarix ~50/50%) are provided via private practice in Portugal, with estimated coverage slowly rising (15-42%, form 2007-10). To identify trends we conducted annual wintertime surveillance of children presenting to our emergency service (ES).

Methods: During 5 epidemic seasons (January-June 2006-10), children < 3Y attending the ES with acute gastroenteritis (AG) had available stool samples tested for RV. Positive samples were genotyped.

Results: A total of 5939 AG cases (ICD-9 0093) were seen. 1947 (33%) children had available stool samples (range: 29%(2008)-37%(2009)); 723 (37%) were positive.

Consecutive annual RV+ proportions were 45%, 38%, 24%, 25% and 38% respectively. Genotyping results (2006-9) were obtained in ~75% of RV+ samples. G9P[8] the most frequent type in 2006(90%) dropped to 34%(2007), 1.9%(2008) and then 10%(2009). G1P[8] increased progressively to become the predominant type in 2009(62%). G3P[8], the predominant type in 2008(41%) was not detected in 2009. G2P[4] undetected in 2006, was found in a significant proportion of cases in 2007(22%) and 2008(31%). G4 P[8] was found for the first time in 2009(18%).

The mean age of RV+AG cases did not increase and no maintained shift in seasonality was observed. The proportion of presenting cases requiring admission was stable over the 5 years.

Conclusions: The proportions of AG that was RV+ fluctuated between seasons as did the frequency of co-circulating RV genotypes. No marked changes in seasonality and age distribution were seen. No clear evidence of impact was evident following relatively low level vaccine usage.

P861

MONITORING COVERAGE LEVELS OF HUMAN PAPILLOMAVIRUS (HPV) VACCINATION IN CASTILLA Y LEON (SPAIN)

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Background and aims: Human Papillomavirus (HPV) vaccine was firstly nation-wide recommended in 2007. Castilla y Leon introduced HPV vaccine on the Childhood Immunization Program in 2008.

The aim of this study is to describe HPV vaccination experience in the last three years.

Methods: Castilla y Leon is the biggest Spanish region, located at north plain, and it accounts for the lowest population density.

Vaccination program against HPV consists of school-based catch of 14 years old girls, followed by vaccine administration with a 0-2-6 months schedule at their Vaccination Centres.

Program evaluation was performed by collecting data of administered vaccines from public and private Vaccination Centres. Coverage levels were calculated using schooling girls lists and electronic medical records.

Results: In 2008 we achieved 94.2% full-schedule coverage for a target population of 9,816 girls. On 2009, coverage levels decreased to 84.4% (target population: 9,790).

Similarly to 2009, on 2010 (provisional data), full-schedule coverage remains on 82.5% of eligible girls (9,978).

Over 95% of girls who initiated vaccination received the three doses schedule.

Conclusions: The decrease in coverage levels from 2008 to 2009 could be related both to first vaccination campaign emphasis and to two cases of vaccine-related adverse events occurred in Spain in 2009. Although those adverse events were finally not due to the vaccine, in 2010 coverage levels showed no important variations referring to 2009.

New strategies need to be implemented in order to increase coverage levels, by communicating the excellent HPV-vaccines safety profile and addressing population concerns regarding these issues.

P862

COST-EFFECTIVENESS OF PERTUSSIS ADOLESCENT BOOSTER IN THE NETHERLANDS: A DYNAMIC MODEL BASED ANALYSIS

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Background and aims: Whilst good protection against pertussis is achieved in childhood in the Netherlands, adolescents and adults are susceptible to pertussis mainly due to waning of immunity. Adolescent vaccination is expected to reduce pertussis burden in this group, and potentially in infants and toddlers via indirect protection. This analysis assesses the cost-effectiveness of adolescent routine booster vaccination against pertussis in the Netherlands.

Methods: An age-stratified, compartmental dynamic model was developed and calibrated on serological data and empirical contact rates. Two scenarios were compared: (1) current pertussis vaccination schedule (2m, 3m, 4m, 11m and 4y, >95% coverage); (2) similar schedule with additional booster vaccination at age 12y, at 50% coverage. Total costs (including primary care, hospitalisation and productivity loss) and quality-adjusted life-years (QALYs) were estimated for each scenario. Unreported symptomatic cases (up to 95% of cases) were assumed to incur no costs but to have some quality-of-life impact. Vaccine price considered was €18.30 a dose plus €6 for administration.

Results: Pertussis booster vaccination at 12y is projected to reduce the incidence in children and adolescents (-1.5% < 4 yr, -8.4% 10-19 yrs), but increase it in adults (+0.9%). This translates into 424 QALYs gained annually at population level (16.5M). Implementation costs of €2.4M are partially offset by savings associated with reported symptomatic cases. The incremental cost per QALY gained is €6,250 when including increased costs of productivity loss in adults.

Conclusion: Model projections indicate that adolescent routine booster vaccination against pertussis reduces pertussis burden, and seems to be cost-effective.

P863

SAFETY OF MF59-ADJUVANTED INFLUENZA VACCINE: SYSTEMATIC REVIEW OF THE LITERATURE

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Background and aim: Influenza is a considerable health problem all over the world. Vaccination is important in children with chronic diseases, and other risk groups like elderly people or patients with reduce immune response, because the increased susceptibility and severity of infection with immunosuppressive therapy. However, immunosuppressive therapy may affect vaccine response. The new adjuvant vaccines open interesting perspectives for the prevention of the disease. The objective of this review is to evaluate the safety of MF59-adjuvanted influenza vaccine.

Methods: Systematic review (2000-11). We used database Medline, Embase, CRD and Cochrane Library. MESH terms were "influenza vaccines", “safety”, “adjuvants”, and free terms “MF59”, and “safety”. Inclusion criteria were clinical trials that assess the safety of MF59-adjunvanted vaccination. Quality were measured with CASP checklist.

Results: We found 125 references, and finally 13 clinical trials were included encompassing 5,633 people; 2,797 received the MF59-adjuvanted vaccine, and 2,836 received another vaccine or control.

Total local reactions ranged 10.4-60% in intervention group (I), vs. 8-31% in control group (C). The most frequent reactions were pain (6.6-90%I vs. 2.02-64%C) induration (0.5-22%I vs. 2-17%C), and erythema (1.5-30%I vs. 1.5-2%C).

Total systemic reactions ranged 0-33%I vs. 2.02-24%C. The most frequent reactions were chills (3-28%I vs. 2-10.2%C), malaise (2.4-33.3%I vs. 0-18.4%C), and headache (3-42%I vs. 2-41%C). Quality of clinical trials were high-moderate.

Conclusion: The analyzed studies show that the vaccine had a good safety and tolerability profile.There are not differences of reactions local and systemic between the groups. There no are serious effects adverse with the vaccine.

P864

EVALUATING THE EFFICACY OF 10-VALENT PNEUMOCOCCAL NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* PROTEIN-D CONJUGATE VACCINE (PHID-CV) AGAINST COMMUNITY-ACQUIRED PNEUMONIA IN LATIN AMERICA

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Background/aims: The **C**linical **O**titis **M**edia and **P**neumoni**A** **S**tudy (COMPAS) is the first pneumococcal conjugate vaccine (PCV) efficacy study conducted in Latin America. Measurement of a variety of pneumonia endpoints is important to assess the true public-health value of a PCV.

Methods: [1] 23,738 infants were randomised to receive either PHiD-CV and DTPa-HBV-IPV/Hib (PHiD-CV group) or HBV and DTPa-IPV/Hib (Control group) at 2-4-6 months of age, followed by PHiD-CV or HAV, respectively, at 15-18 months (both co-administered with DTPa-IPV/Hib).[1]

Results: Primary objective, based on first likely-bacterial-CAP episodes reported ≥2 weeks post-dose-3, was conclusive (22% VE [95%CI 8,34; p=0.002 with 1-sided alpha of 1.75%], according-to-protocol cohort).[2] The total vaccinated cohort results are tabulated below:

Occurrence of first episodes of CAP and vaccine efficacy anytime from the administration of dose 1						
	Number of first episodes				Difference in number of cases (Control – PHiD-CV)	Vaccine efficacy (95%CI)
	PHiD-CV (N=11,875)		Control (N=11,863)			
	n	%	n	%		
C-CAP	223	1.9%	289	2.4%	66	23% (9, 36)
B-CAP	341	2.9%	414	3.5%	73	18% (6, 29)
CXR-CAP	854	7.2%	947	8.0%	93	10% (2, 18)
S-CAP	2455	20.7%	2616	22.1%	161	7% (2, 12)

N = number of children in the total vaccinated cohort
n/% = number/percentage of children reporting at least one episode of CAP in a defined category
C-CAP = WHO-defined (consolidated) CAP
B-CAP = likely-bacterial-CAP (radiologically-confirmed CAP with alveolar consolidation/pleural effusion on chest X-ray, or with non-alveolar infiltrates and C-reactive protein ≥40 µg/mL)
CXR-CAP = any radiologically-confirmed CAP (child with abnormal pulmonary infiltrates on chest X-ray)
S-CAP = clinically-suspected CAP for which an X-ray was requested (regardless of final diagnosis)

[ITT results]

The observed efficacy against the specific C-CAP endpoint, proposed by the WHO to facilitate comparison of results across trials, suggests a PHiD-CV impact in the same range as seen with 7-, 9- and 11-valent PCVs in previous efficacy trials (in different settings). Despite lower efficacies, substantially higher numbers of cases were prevented with less-specific endpoints (such as S-CAP) than with more-specific endpoints (such as C-CAP). Endpoints such as S-CAP may potentially better reflect the overall public health impact of PHiD-CV vaccination.

Conclusion: The observed COMPAS results across various CAP endpoints demonstrate the clinical efficacy of PHiD-CV against pneumococcal infections; PHiD-CV could help address the pneumonia burden worldwide.

[1]Sáez-Llorens, ESPID 2011, Abstract 412; [2]Tregnaghi, SLIPE 2011

P865

DESIGN/SETTING OF COMPAS: A LATIN AMERICAN TRIAL EVALUATING THE EFFICACY OF 10-VALENT PNEUMOCOCCAL NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* PROTEIN-D CONJUGATE VACCINE (PHID-CV)

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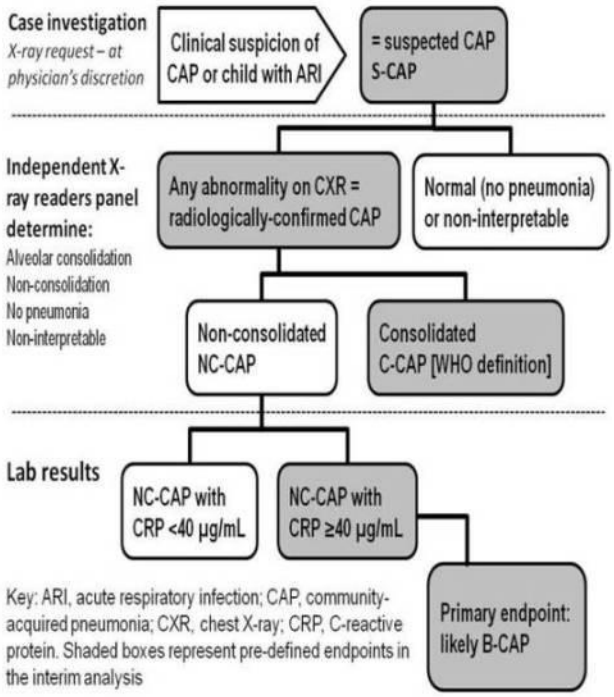
Background/aims: The **C**linical **O**titis **M**edia and **P**neumoni**A** **S**tudy (COMPAS) is the first pneumococcal vaccine efficacy study conducted in Latin America.

Design/setting: COMPAS, designed to demonstrate PHiD-CV efficacy against likely-bacterial- community-acquired pneumonia (B-CAP) and clinical AOM, is conducted in mainly urban areas of Argentina, Panama and Colombia, involving all major paediatric hospitals and primary care health sites in each study area. Participants have good public/private healthcare-access. Ethical/safety oversight is provided by an Independent Data Monitoring Committee (IDMC), to monitor SAE occurrence, assess potential treatment harm and make recommendations to GSK regarding safety measures, study design and/or reporting/analysis plans. Study design was approved by all ethical committees and consent was obtained from parents of participants.

Clinical suspicion of pneumonia was at the treating physician's judgment. Chest X-rays of suspected-CAP (S-CAP) cases are interpreted for determination of CAP-related study endpoints by a WHO-trained independent readers-panel, regardless of the on-site treatment-related interpretation. The first episode of B-CAP is the primary study endpoint. Consolidated-CAP (C-CAP) corresponds to WHO-defined CAP.

Discussion: The methodology employed should provide a robust assessment of the magnitude of the vaccine-elicited protection against pneumonia, an endpoint of major public health interest.



[COMPAS table]

Study type		**Phase III, double-blind/observer-blind, randomised, controlled multi-centre**
Participants		**~24,000 healthy infants aged 6–16 weeks at enrolment**
Study groups (children randomised 1:1)	**PHiD-CV group**	**PHiD-CV and DTPa-HBV-IPV/Hib vaccines at 2-4-6 months of age and booster dose of PHiD-CV and DTPa-IPV/Hib at 15–18 months**
	Control group	**Hepatitis B and DTPa-IPV/Hib vaccines at 2-4-6 months and hepatitis A vaccine and a DTPa-IPV/Hib booster dose at 15–18 months**
Primary objective (included in the interim analysis)		**To demonstrate efficacy of PHiD-CV against likely bacterial community-acquired pneumonia (B-CAP) cases, defined as radiologically-confirmed with either alveolar consolidation/pleural effusion on chest X-ray or with non-alveolar infiltrates but with C-reactive protein ≥40 µg/mL**
Key secondary objectives	**First**	**To demonstrate efficacy of PHiD-CV against clinically confirmed acute otitis media (C-AOM) cases in ~7,000 children enrolled in Panama**
	Other	**To assess efficacy of PHiD-CV against CAP with alveolar consolidation or pleural effusion on chest X-ray (C-CAP)** **To assess efficacy of PHiD-CV against vaccine-type invasive pneumococcal disease** **To assess PHiD-CV impact on nasopharyngeal carriage of *S. pneumoniae* and *H. influenzae***

[COMPAS Figure]

P866

GENOTYPE DISTRIBUTION AND ROTAVIRUS GASTROENTERITIS HOSPITALIZATIONS FOUR YEARS AFTER VACCINATION IN SAO PAULO, BRAZIL

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Background: Early effects, after implementation of rotavirus human vaccine in Brazil in 2006, were promising, showing a marked decline in rotavirus gastroenteritis (RVGE) hospitalizations among children aged < 5 years. A high predominance of G2P[4], probably reflecting natural annual fluctuation, was also observed. The aim of this study was to confirm the early impact of immunization on the incidence of severe RVGE and assess genotype distribution over time.

Methods: We performed a 7-year (2004 -2010) prospective surveillance, at two sentinel hospitals in Sao Paulo, monitoring the incidence of RVGE and acute gastroenteritis (AGE) hospitalizations among children younger than 5 years of age. Since 2006 genotypes of positive samples were determined by reverse transcription polymerase chain reaction.

Results: After vaccine introduction we observed a significant reduction in the proportion of rotavirus-positive results among children aged < 5 years hospitalized with RVGE of 42.2%*, 41.2%*, 72.2%* and 60.7%* (*p< 0.001), and a reduction in the number of all-cause hospitalizations for AGE of 29%, 28%, 39% and 40%, respectively from 2007 to 2010.

Genotype G2P[4] accounted for 8.8%, 58.8%, 73.7%, 75% and 66.7% of all cases identified, respectively, from 2006 to 2010.

Conclusions: Four years after vaccine implementation, a marked and sustained decline in RVGE hospitalizations was demonstrated among children aged < 5 years, confirming the early impact benefits of the vaccination. Although continued surveillance studies are still needed to correctly address this issue, it is unlikely to have persistent predominance of G2P[4], for four years, as an exclusive result of natural fluctuation.

P867

IMMUNOGENICITY AND TOLERABILITY OF AN INVESTIGATIONAL MULTICOMPONENT MENINGOCOCCAL SEROGROUP B (4CMENB) VACCINE IN HEALTHY ADOLESCENTS

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Background: Whole genome sequencing was used to identify three of four major protein components of an investigational multicomponent meningococcal vaccine (4CMenB).

Methods: In an observer-blind study in Santiago, Chile, 11-17-year-old adolescents were randomized to receive 1-3 doses of 4CMenB or placebo at baseline, one and/or two months later. Primary immunogenicity outcome was a titer ≥4 in a serum bactericidal assay using human complement (hSBA) against three test strains selected to evaluate the contribution of individual vaccine antigens. Tolerability was assessed by solicited local and systemic reactions within seven days of each study vaccination. Adverse events were monitored throughout the study.

Results: Overall, 1631 adolescents (56% female; mean age 13.8 ± 1.9 years) received 4CMenB and/or placebo. One month later 92-97% of recipients of one 4CMenB dose, 99-100% after 2 or 3 4CMenB doses and 29-50% of placebo recipients had hSBA titers ≥4 against the three test strains. Similar proportions of placebo and 4CMenB recipients reported solicited local (89-94%) and systemic (70-79%) reactions after the first study injection. At subsequent visits, reports of reactogenicity were less frequent in all groups, but placebo recipients were less likely to report reactogenicity outcomes than 4CMenB recipients.

Discussion: 4CMenB induced robust immune responses and had an acceptable tolerability profile following one, two, or three doses and all schedules administered. Three doses of 4CMenB imparted no additional benefits compared with two doses. No evidence of increased reactogenicity was observed with 2 or 3 doses compared with one dose of 4CMenB.

P868

LONG-TERM IMMUNOGENICITY AND SAFETY OF THE HUMAN PAPILLOMAVIRUS (HPV)-16/18 AS04-ADJUVANTED VACCINE IN ADOLESCENT GIRLS: RESULTS FROM A 5-YEAR FOLLOW-UP

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Background and aims: This study is an additional 6-year extension of a previously reported 4-year follow-up study of the HPV-16/18 AS04-adjuvanted vaccine in adolescent girls. Here, we present antibody persistence and safety results of the HPV-16/18 vaccine group, 5 years after the first vaccine administration.

Methods: Girls 10-14 years in the immunogenicity subset who received three vaccine doses and participated in the 4-year follow-up study (104918/NCT00316706) were invited to an additional 6-year follow-up. Anti-HPV-16 and HPV-18 antibodies (ELISA) results are presented in the according-to-protocol cohort (n=378). SAE and medically significant AEs are presented in the total vaccinated cohort (n=397).

Results: Five years after the first dose of HPV-16/18 vaccine, all girls were still seropositive for both HPV-16/18 antibodies. HPV-16 and HPV-18 geometric mean antibody titres (GMT, EL.U/mL [95% CI]) peaked at Month 7 (19719.8 [18110.6-21472.1], 8236.9 [7536.5-9002.4]), then gradually declined to a plateau from Month 24 (3291.6 [3006.7-3603.6], 1290.4 [1169.0-1424.5]) through Month 60 (2262.9 [2069.1-2475.0], 778.6 [703.1-862.1]). Plateau levels were higher than those at plateau phase in a phase IIB efficacy study (580299/007/NCT00518336) in young women aged 15-25 years, and well above natural infection levels.

Between Month 48 and Month 60, none of the reported AEs or SAEs were considered related to vaccination by the investigator and led to subject's withdrawal.

Conclusions: The HPV-16/18 AS04-adjuvanted vaccine administered to adolescent girls elicited a robust immune response that was sustained through 5 years after vaccination, suggesting long-term protection. The vaccine was generally well tolerated.

P869

COST-EFFECTIVENESS OF A PENTAVALENT HUMAN-BOVINE REASSORTANT ROTAVIRUS VACCINE (RV5) IN QUEBEC, CANADA

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Background and aims: This study assesses the cost-effectiveness of universal vaccination with RV5 over the first 5 years of life of a hypothetical cohort of 85000 children in Quebec, Canada.

Methods: A Markov model was developed to evaluate the cost per quality-adjusted-life-year (QALY) of vaccination from the healthcare and societal perspectives using CA$50,000 as the cost-effectiveness threshold. The basecase scenario assumed that 94% of the cohort received 3 RV5 doses at 2, 4, and 6 months of age with the remaining 6% receiving only 1 or 2 doses. Without vaccination, the annual rotavirus-related complications included 1 death, 3400 hospitalizations (CA$1246 per day), 6503 emergency department visits (CA$288 per visit), and 7990 outpatient visits (CA$99 per visit). The efficacy of RV5 was based on the Rotavirus Efficacy and Safety Trial's results. One way sensitivity analyses were conducted to assess the impact of varying the key parameters on the results.

Results: Universal vaccination reduced hospitalizations, emergency department visits, outpatient visits and all episodes of rotavirus gastroenteritis by 90%, 81%, 70% and 48.5%, respectively. In the basecase scenario, at a vaccination cost of CA$60 per dose, the cost per QALY saved was CA$22,924 from the healthcare perspective and cost-saving from the societal perspective. From the medical care payer perspective, the rates of healthcare utilization and the QALY loss values for episodes of rotavirus assumed were the most influential parameters.

Conclusion: In Quebec, RV5 could substantially reduce the complications of rotavirus gastroenteritis at cost per QALY ratios within the range typically regarded as cost-effective.

P870

ANTIBIOTIC RESISTANCE AND SEROTYPE DISTRIBUTION OF INVASIVE S.PNEUMONIAE AMONG CHILDREN ≤5 YEARS OF AGE BETWEEN 2005-2010 IN SAUDI ARABIA (KSA)

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Introduction: *S. pneumoniae* is one of the most common bacterial causes of morbidity and mortality worldwide, causing life threatening infections such as meningitis, pneumonia and febrile bacteremia. The severity and frequency of *S. pneumoniae* infection and emergence of drug-resistant isolates, have renewed the emphasis to prevent pneumococcal disease, however little is known in children under 5 years of age in KSA.

Methods: Cases of pneumococcal infections in children aged < 5 years, recorded in hospitals between 2005- 2010, were reviewed for serotyping and penicillin and erythromycin susceptibility. Case definition required isolation of Streptococccus pneumoniae from blood, cerebrospinal fluid, or any sterile biological fluid.

Results: A total of 311 eligible cases were collected from different regions across KSA, 250 isolates from blood and 61 from cerebrospinal fluid. The frequently isolated IPD serotypes were 23F, 6B, 5 and 1. There was significant rise of serotypes 19A, which accounts for 20 % of isolates of IPD in Western, 5 % in central regions in the last 2 years in KSA. The serotypes coverage for PCV7, PCV10, PCV13 in children < 5 years was 53%, 80% & 91% respectively across the Kingdom. 66% of IPD isolates were penicillin-resistant, and 62 % were erythromycin-resistant.

Conclusions: Continued surveillance is critical to measure the emerging of new serotypes and antibiotic resistance strains, and the potential impact of new PCVs.PCV13 provides the widest coverage among all IPD serotypes across KSA.

P871

HERPES ZOSTER IN CHILDREN AFTER INTRODUCTION OF UNIVERSAL CHILDHOOD VARICELLA VACCINATION IN GERMANY

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Background: Germany introduced universal varicella vaccination for children above 11 months in 2004. Different data sources showed increasing vaccine uptake and decreasing varicella case-numbers and complications since 2005. We assessed herpes zoster (HZ) in children aged 0-14 years since 2005 by analyzing two data sources.

Methods: Based on active sentinel-surveillance, approximately 1,200 doctor's practices transmitted case-based questionnaires on HZ or zero-reports monthly from April 2005 to November 2010.

Physicians' billing data on patients diagnosed with HZ-spezific ICD10-code B02 were quarterly available from 8 out of 17 regional Associations of Statutory Health Insurance Physicians from 2006-2008.

Logistic regression was performed to identify trends.

Results: Sentinel physicians reported a total of 1,875 HZ-cases aged 0-14 years (3.8 to 4.6 cases/100 physicians and month). Mean case-numbers per 100 physicians and month increased by age (0-4 years: 0.6; 10-14 years: 1.8). Between 2005 and 2010, mean case-numbers significantly decreased for children 0-4 and 5-9 years old, and increased in persons 10-14 years old.

According to billing data, mean quarterly HZ-incidence ranged between 0.54 and 0.62/1,000 person-years in age-group 0-14 and increased by age (0-4 years: 0.25; 10-14 years: 0.78/1,000 person-years). Time trends by age were similar to that observed by sentinel data, but were significant only for the 0-4-year-olds.

Conclusion: Both data sources showed similar age-specific patterns on HZ in children after introduction of universal varicella vaccination. However, only one source revealed statistically significant time trends, probably due to longer observation. Further monitoring is required to assess whether the observed trends remain stable.

P872

CHARACTERIZATION OF THE IMMUNE RESPONSE TO PNEUMOCOCCAL CONJUGATE VACCINE AFTER 23-VALENT POLYSACCHARIDE VACCINE (PPSV23) IN CHILDREN

S.T. Sigurdardottir[1,2], K.J. Center[3], K. Davidsdottir[4], V.A. Arason[4], B. Hjalmarsson[4], R. Elísdóttir[4], G. Ingólfsdóttir[1], R. Northington[5], P. Giardina[6], W. Gruber[6], E. Emini[6], D.A. Scott[6], I. Jonsdottir[1,2]

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Background: The objective was to characterize the immune responses to CRM197-conjugated pneumococcal polysaccharide vaccine (PCV13), in children vaccinated in infancy with a 9-valent pneumococcal- (serotypes 1, 4, 5 6B, 9V, 14, 18C, 19F, and 23F) and meningococcal-C-CRM197 conjugate (PCV9), followed by a toddler dose of PCV9 or PPSV23.

Methods: 7-year-old children, previously vaccinated with PCV9 in infancy and PPSV23 (PPSV23/PCV13, N=50) or PCV9 (PCV9/PCV13, N=37) at 12 months, were vaccinated with PCV13. IgG antibodies, avidity and opsonophagocytosis were measured before and 1 and 4 weeks after vaccination.

Results: IgG levels are shown in the Table. In both groups, >97% of vaccinees achieved IgG ≥0.35µg/mL one month after PCV13 vaccination for all serotypes. The PCV9/PCV13 group had higher IgG responses to PCV13 than the PPSV23/PCV13 group. Upper 95% CI limits of the PPSV23/PCV13:PCV9/PCV13 ratios were < 1 for serotypes 1, 4, 5, 9V, 18C and 23F. Opsonophagocytosis and avidity results support this finding.

Serotype	**1***	**4***	**5***	**6B***	**9V***	**14***	**18C***
PPSV23/PCV13	5.28	4.18	5.75	29.51	4.31	17.47	2.76
PCV9/PCV13	19.43	11.34	15.98	41.70	7.39	22.78	4.83
Serotype	**19F**	**23F**		**3**	**6A**	**7F**	**19A**
PPSV23/PCV13	9.78	7.89		3.28	11.16	7.13	14.62
PCV9/PCV13	11.60	12.25		2.87	14.07	8.05	17.07
*Serotypes in all three vaccines							

[Table: GMC IgG in µg/mL, 4 weeks after PCV13]

Conclusions: Our results indicate that PPSV23 vaccination of toddlers may compromise subsequent responses to pneumococcal vaccines. The clinical relevance of this is unclear.

P873

CHARACTERIZATION OF THE IMMUNE RESPONSE TO PNEUMOCOCCAL CONJUGATE VACCINE AFTER 23-VALENT POLYSACCHARIDE VACCINE (PPSV23) IN CHILDREN

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Methods: 7-year-old children, previously vaccinated with PCV9 in infancy and PPSV23 (PPSV23/PCV13, N=50) or PCV9 (PCV9/PCV13, N=37) at 12 months, were vaccinated with PCV13. IgG antibodies, avidity and opsonophagocytosis were measured before and 1 and 4 weeks after vaccination.

Results: IgG levels are shown in the Table. In both groups, >97% of vaccinees achieved IgG ≥0.35µg/mL one month after PCV13 vaccination for all serotypes. The PCV9/PCV13 group had higher IgG responses to PCV13 than the PPSV23/PCV13 group. Upper 95% CI limits of the PPSV23/PCV13:PCV9/PCV13 ratios were < 1 for serotypes 1, 4, 5, 9V, 18C and 23F. Opsonophagocytosis and avidity results support this finding.

Serotype	**1***	**4***	**5***	**6B***	**9V***	**14***	**18C***
PPSV23/PCV13	5.28	4.18	5.75	29.51	4.31	17.47	2.76
PCV9/PCV13	19.43	11.34	15.98	41.70	7.39	22.78	4.83
Serotype	**19F**	**23F**		**3**	**6A**	**7F**	**19A**
PPSV23/PCV13	9.78	7.89		3.28	11.16	7.13	14.62
PCV9/PCV13	11.60	12.25		2.87	14.07	8.05	17.07
*Serotypes in all three vaccines							

[Table: GMC IgG in µg/mL, 4 weeks after PCV13]

Conclusions: Our results indicate that PPSV23 vaccination of toddlers may compromise subsequent responses to pneumococcal vaccines. The clinical relevance of this is unclear.

P874

13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN CHILDREN PREVIOUSLY PARTIALLY IMMUNIZED WITH 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7): PHASE 3, OPEN-LABEL TRIAL

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Background and aims: As PCV13 is introduced, children who begin vaccination with PCV7 (serotypes 4, 6B, 9V, 14, 18C, 19F, 23F) may complete their vaccination with PCV13 (additional serotypes 1, 3, 5, 6A, 7F, and 19A). This open-label phase 3 study in Sweden evaluated immunogenicity and safety of PCV13 in children previously administered 1 or 2 doses of PCV7.

Methods: Healthy infants previously administered PCV7 at ages 3 months (group 1; n=118) or 3 and 5 months (group 2; n=116) received PCV13 at ages 5 (group 1 only) and 12 months (both groups). Serotype-specific IgG responses were assessed. Local reactions and systemic events were collected 7 days postvaccination. Adverse events were also collected.

Results: The Table shows serotype-specific IgG geometric mean concentrations before and after completion of the vaccine series. Local reactions and fever were mostly mild or moderate.

Conclusions: PCV13 was immunogenic and safe in infants and toddlers previously partially immunized with PCV7. One or two doses in infants or toddlers induced immune responses to the additional serotypes.

Serotype	Group 1 pre-12-month dose	Group 1 post-12-month dose	Group 2 pre-12-month dose	Group 2 post-12-month dose	**Serotype**	Group 1 pre-12-month dose	Group 1 post-12-month dose	Group 2 pre-12-month dose	Group 2 post-12-month dose
4	0.66	5.27	0.62	5.06	**1**	0.46	14.65	0.01	1.58
6B	0.83	9.63	0.65	8.75	**3**	0.40	1.85	0.05	1.34
9V	0.74	3.50	0.70	3.33	**5**	1.18	7.02	0.33	1.44
14	1.99	9.22	2.23	9.30	**6A**	0.71	6.14	0.24	2.48
18C	0.35	2.93	0.44	3.87	**7F**	1.08	5.86	0.02	3.55
19F	0.85	7.70	0.81	8.31	**19A**	1.06	7.25	1.55	13.16
23F	0.33	3.27	0.41	4.40					

[Pneumococcal serotype-specific IgG GMC (µg/mL)]

P875

A COMMON GP63 BASED VACCINE MIGHT BE AN IMPORTANT VACCINE CANDIDATE AGAINST ALL FORMS VISCERAL LEISHMANIASIS

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Leishmaniasis is an infectious disease complex caused by several species that are members of the protozoan parasite genus *Leishmania*. In humans, disease manifestation ranges from self-healing cutaneous lesions to life-threatening visceral leishmaniasis (VL). This disease complex affects 12 million people, and there are 1.5 million new cases annually. VL, caused by *Leishmania donovoni*, *infantum* and *Leishmania chagasi*, remains the main agent of morbidity and mortality in leishmaniasis. Visceral leishmaniasis is fatal if not treated, and development of a vaccine with long-term immunity remains a challenge. The attachment of *Leishmania* promastigotes to macrophages, crucial for intracellular parasitism and for the outcome of the infection, has been demonstrated by many investigators to be a specific receptor-mediated event . Emphasis has been placed on the critical role of two abundant surface molecules gp63 and lipophosphoglycan that independently mediate parasite attachment to macrophages. The current study has been undertaken with an idea to determine the regions of identity in the gp63 protein which will help in the development of a vaccine against all forms of VL.Our results of BLAST Cladogram, Phylogenetic tree analysis confirm that a high level of conservation and identity amongst gp63 residues may help in the designing of a common vaccine against visceral leishmaniasis caused by different species strains of Leishmania. T-COFFEE also showed that the level of similarity ranged from average to good in the strains we selected. The results reinstate our claim that a common gp63 based vaccine can be designed against all forms of visceral leishmaniasis.

P876

THE EPIDEMIOLOGY OF INVASIVE NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* (NTHI) DISEASE IN THE ERA OF ROUTINE HIB VACCINATION IN ENGLAND AND WALES

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Background: The reduction in invasive *Haemophilus influenzae* serotype b (Hib) disease following routine immunisation means that non-typeable *H. influenzae* (ntHi) are now the most common cause of invasive *H. influenzae* disease. Understanding the epidemiology of invasive ntHi disease is important because the infection may be prevented by a newly-licensed 10-valent pneumococcal conjugate vaccine that uses *H. influenzae* outer-membrane protein D as its primary carrier protein.

Methods: The Health Protection Agency Centre for Infections (CfI) conducts enhanced national surveillance of invasive *H. influenzae* disease in England and Wales through a combination of laboratory and clinical reporting schemes, and provides a national service for serotyping invasive *H. influenzae* isolates.

Results: Between 1994-2008, ntHi accounted for 45% of the 2,111 invasive *H. influenzae* cases diagnosed in children aged < 15 years. The average annual incidence of invasive ntHi disease was 0.60 cases/100,000 children, but there was a small, gradual increase of 2.9% per year (95% CI, 1.0-4.9%; P=0.003) in disease incidence over the 15-year period. Almost a third of childhood ntHi infections (242/814, 30%) presented in the first month of life, where they were responsible for 94% (227/242) of all invasive *H. influenzae* infections and presented mainly with bacteraemia (197/227 [87%]. After this period, ntHi cases were evenly distributed among the different age groups and caused two-thirds of all *H. influenzae* bacteraemic pneumonia (53/83 cases, 64%).

Conclusions: The incidence of invasive ntHi disease in children remains low, but the year-on-year rise in incidence merits further study, particularly among neonates.

P877

DEVELOPMENT OF A TRIVALENT VACCINE TO PREVENT GROUP B STREPTOCOCCUS INFECTION

G. Leroux[1], **K. Slobod**[2], C. Maes[1], F. Berti[2], R. Clemens[2]

[1]Ghent University and Hospital, Ghent, Belgium, [2]Novartis Vaccines & Diagnostics, Cambridge, MA, USA

Background and aims: Worldwide bacterial sepsis causes approximately 1 million neonatal deaths annually and group B streptococcus (GBS) is a leading cause. Newborn GBS infection follows maternal colonization. No vaccine is currently available but it is known that higher levels of maternal antibody to GBS correlate with reduced risk of neonatal disease. A trivalent GBS vaccine intended to prevent newborn GBS disease is being evaluated in phase I/II studies.

Methods: Purified capsular polysaccharides of GBS serotypes Ia, Ib and III were conjugated to CRM197 to prepare glycoconjugates (GC) for intramuscular injection. In a Phase I study 320 healthy, non-pregnant Belgian women were enrolled into 8 study groups examining dose (5/5/5 or 20/20/20 µg of each GC), formulation (unadjuvanted or aluminum hydroxide) and schedule (1 or 2 injections). 20 women received placebo (saline) as control. Women were monitored until day 61 for safety and GBS serum antibody using three serotype-specific ELISAs.

Results: Good tolerability and no vaccine-related SAE were reported. Geometric mean antibody (IgG) concentrations at day 61 ranged from 7-20 µg/ml for serotype Ia, from 3-7 µg/ml for serotype Ib and from 5-13 µg/ml for serotype III. Across all serotypes, antibody analysis demonstrated no benefit from higher dose, inclusion of adjuvant or a second injection.

Conclusions: Based on these clinical data, a single injection of an unadjuvanted trivalent vaccine at doses of 5 ug of each GC will be used in further studies planned in pregnant women.

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G. Leroux[1], **K. Slobod**[2], C. Maes[1], F. Berti[2], R. Clemens[2]

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Background and aims: Worldwide bacterial sepsis causes approximately 1 million neonatal deaths annually and group B streptococcus (GBS) is a leading cause. Newborn GBS infection follows maternal colonization. No vaccine is currently available but it is known that higher levels of maternal antibody to GBS correlate with reduced risk of neonatal disease. A trivalent GBS vaccine intended to prevent newborn GBS disease is being evaluated in phase I/II studies.

Methods: Purified capsular polysaccharides of GBS serotypes Ia, Ib and III were conjugated to CRM197 to prepare glycoconjugates (GC) for intramuscular injection. In a Phase I study 320 healthy, non-pregnant Belgian women were enrolled into 8 study groups examining dose (5/5/5 or 20/20/20 µg of each GC), formulation (unadjuvanted or aluminum hydroxide) and schedule (1 or 2 injections). 20 women received placebo (saline) as control. Women were monitored until day 61 for safety and GBS serum antibody using three serotype-specific ELISAs.

Results: Good tolerability and no vaccine-related SAE were reported. Geometric mean antibody (IgG) concentrations at day 61 ranged from 7-20 µg/ml for serotype Ia, from 3-7 µg/ml for serotype Ib and from 5-13 µg/ml for serotype III. Across all serotypes, antibody analysis demonstrated no benefit from higher dose, inclusion of adjuvant or a second injection.

Conclusions: Based on these clinical data, a single injection of an unadjuvanted trivalent vaccine at doses of 5 ug of each GC will be used in further studies planned in pregnant women.

P879

SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF 15-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV15) IN TODDLERS PREVIOUSLY IMMUNIZED WITH 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7)

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Background and aims: Widespread use of PCV7 in children has led to significant reduction in pneumococcal disease in children and adults. However, diseases caused by serotypes not included in PCV7 have increased. A 15-valent pneumococcal conjugate vaccine containing 7 serotypes in PCV7 and 8 additional serotypes (1, 3, 5, 6A, 7F, 19A, 22F, 33F) was developed and evaluated in toddlers 12 to 15 months old.

Methods: Approximately 90 toddlers who had previously completed a 3-dose series of PCV7 at 2, 4, and 6 months received a single dose of either aluminum-adjuvanted PCV15, non-adjuvanted PCV15, or PCV7. Injection site and systemic adverse events (AEs) were collected for 14 days postvaccination and serious AEs were collected for 30 days postvaccination. Solicited AEs included local (pain/tenderness, swelling, nodule, and redness), and systemic (fatigue, arthralgia, and myalgia). Serotype-specific IgG and OPA responses were measured immediately prior and 30 days postvaccination.

Results: Incidences of local and systemic AEs were comparable across treatment groups. The majority of reported events, irrespective of treatment, were transient and of mild to moderate intensity. No clinically significant differences were observed when comparing duration and severity of AEs. No vaccine-related SAEs or discontinuations from the study due to AEs were reported. Pneumococcal IgG concentrations and OPA titers increased postvaccination, with appreciable fold rises for all serotypes. Antibody levels were comparable between both V114 formulations and comparable to PCV7 for the shared serotypes.

Conclusions: Both formulations of PCV15 display acceptable safety profiles and induce IgG and OPA responses to all vaccine serotypes.

P880

ACCEPTABILITY OF UNIVERSAL INFANT HEPATITIS B VACCINATION AMONG PARENTS IN THE NETHERLANDS

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Background: As universal hepatitis B vaccination will be implemented into the Dutch National Immunization Programme starting October 2011, this study explores hepatitis B vaccine acceptance among parents of infants and which data sources parents use for retrieving vaccine information.

Methods: Thousand parents with a newborn baby, recruited through the Dutch National Immunization Programme Database, received a brief questionnaire covering general attitude and intention towards hepatitis B vaccination. Next, three focus group interviews were held with twelve parents. All groups included parents with a positive, neutral and negative intention towards hepatitis B vaccination. Interviews covered attitude, subjective norms and perceived behaviour control towards hepatitis B vaccination and which data sources parents used for retrieving vaccine information.

Results: 432 of 1000 invited parents returned the questionnaire. Most parents (81%) intended to accept hepatitis B vaccination as they do not want their child to miss other vaccinations (hepatitis B vaccine is combined with the DPTP-Hib vaccine). Moreover, many parents appeared to underestimate the incidence of hepatitis B. The majority of parents felt they needed more in-depth information about hepatitis B vaccination and from sources independent from the vaccination program (e.g. a consumers' association). Additionally, parents expressed their interest in the rationale behind the Dutch government's decision-making about universal vaccination (e.g. how it compares to policies in surrounding countries).

Conclusion: Most parents intended to accept hepatitis B vaccination for their child. However, vaccine information has to be more detailed and the reliability of the data source should be preserved by using clearly independent sources.

P881

SAFETY OF A THREE SUBUNIT INFLUENZA VACCINE IN HEALTH CARE WORKERS IN KURDISTAN: A CROSS SECTIONAL STUDY

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Background and aims: Influenza can cause severe morbidity and mortality. The most effective strategy for preventing influenza infections is annual vaccination. The safety and tolerability of several types of influenza vaccines have been investigated previously in different countries. In this study the safety of trivalent inactivated surface antigen (subunit) influenza vaccines Begrivac® (Novartis Company) was studied in health care workers.

Methods: This cross sectional study, started at August 2009 through July 2010 was conducted in the Sanandaj Center for Disease Control and Prevention and consisted of two parts: an early follow up for 2 weeks and late follow up 6 month after Vaccination. Nine hundreds persons were engaged in the study during one year of the study. In each case a questionnaire completed for the Person and all symptoms or abnormal physical findings were recorded.

Results: In part I of the study, post-vaccination complaints were as follows: Headache 5.3%, Fever 7.9%, Weakness 9.6%, Chills 10.1%, Sweating 10.5, Arthralgia 20.2%, Malaise 21.5%. All adverse events were mild. Swelling of injection site in 30.3% of cases and Pruritus of injection site in 32.9% of cases were observed. Redness and induration were also reported by 42.5% of subjects. Local reactions were mainly mild and lasted for 1-2 days. No systemic reactions were reported in part II. None of the subjects in part I or II experienced any inconvenience.

Conclusion: The trivalent inactivated split influenza vaccine Begrivac® was safe and well tolerated justifies the use of vaccine for the control of influenza.

P882

EVALUATION OF IMMUNE RESPONSE TO PNEUMOCOCCAL VACCINE IN VACCINATED SPLENECTOMIZEDTHALASSEMIC PATIENTS

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Introduction: 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.

Objectives: To obtain information on the immunity levels of pneumococcal antibody, in splenectomised beta-thalassemic patients in Jahrom.

Patients and 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 ($r=-0.573$, $P< 0.001$).

Conclusion: 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.

P883

THE PUBLIC'S KNOWLEDGE AND PERCEPTIONS ABOUT THE PANDEMIC INFLUENZA (H1N1) INFECTION AND VACCINE IN TURKEY DURING THE LAST H1N1 PANDEMIC

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Background and aims: Because of affecting health behaviors assessment of public´s knowledge and attitudes against the development and prevention of new outbreaks is essential. The aim of the study was to analyse the results of a recent survey about the public's level of knowledge and perceptions

regarding the pandemic influenza infection and vaccine during the last H1N1pandemic.

Methods: A total of 979 participants accompanying patients admitted to Marmara University Hospital were interviewed from February 22nd, 2010 to April 2nd, 2010. Each participant was given an anonymous, face-to-face, self-administered survey.

Results: Vaccination rate for 2009 pandemic influenza A (H1N1) among participants was low (14.6%). Vaccination refusal was mostly related to the perceived negative interview of scientists not being a specialist in infectious diseases (62.7%), so most of the respondents believed the vaccine was not safe (27.1%) and protective (54.7%). Vaccinated group was younger than unvaccinated group (p=0.002). The mean knowledge score in vaccinated group was higher than those in unvaccinated group (p=0,002). Vaccination rate of illiterate (21.9%) was similar those of university graduates (20.3%). When being illiterate was ignored, well-educated people tended to be vaccinated (p=0.010). Vaccination rate among participants receiving information from health provider was twice as high as those not receiving.

Conclusion: The survey clearly suggest that the percentage of people willingness to accept the vaccine will increase if accurate and clear information are given. Thus it will contribute to the control of the epidemic.

P884

IMPACT OF ROTAVIRUS VACCINATION AFTER 3 YEARS BY BIRTH COHORT: ADDITIONAL HERD BENEFIT OBSERVED?

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Background: Paediatric rotavirus vaccination has been reimbursed in Belgium since Nov,2006. Analysing rotavirus gastroenteritis cases by birth cohort before/after vaccine introduction allows assessment of a potential herd protection benefit in infants aged 0-3months. Rotavirus vaccine is administered at 8-12weeks time post-birth.

Methods: Data on rotavirus-positive stool tests in children hospitalised for acute gastroenteritis were collected from 9 paediatric wards in Belgium (20% of all paediatric beds) before (Jun,2004-May,2006) and after vaccine introduction (Jun,2007-May,2010). Birth cohorts were defined as follows: during pre-vaccination period (born before 1-Sep-2006); and during post-vaccination period cohort1 (born Sep,2007-Aug,2008); cohort2 (born Sep,2008-Aug,2009); and cohort3 (born after Sep,2009). The number of rotavirus-positive stool tests in infants aged 0-3months and 0-9months was calculated for each birth cohort.

Results: The number of rotavirus-positive tests clearly decreased in successive post-vaccination birth cohorts compared with the pre-vaccination birth cohort (Table) (Chi-square-test for trend, p< 0.001). This decrease occurred in infants old enough to be vaccinated (0-9months) but also in infants too young to be fully vaccinated (0-3months).

	Number of rotavirus-positive tests during pre- and post-vaccination period			
Age group (months)	Pre-vaccination	Post- vaccination		
		Cohort 1	Cohort 2	Cohort 3
0-3	102	43	31	23
0-9	229	111	65	47

[Table]

Conclusion: The number of rotavirus-positive cases decreased in cohorts born after introduction of rotavirus vaccination, even in infants too young to be fully vaccinated. This may indicate a herd protection benefit of rotavirus vaccination.

P885

RESURGENCE OF MUMPS: CHARACTERIZATION OF THE LARGEST MUMPS OUTBREAK OF THE LAST 2 DECADES IN ISRAEL, 2009-2010

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Background: In recent years, large mumps outbreaks, involving mainly adolescents and young adults, have re-emerged in several countries.

Methods: An epidemiologic study of a mumps outbreak in Jerusalem.

Results: The first cases occurred in ultra-orthodox boys´ schools in Jerusalem. Between 16.09.2009-31.12.2010, 2978 mumps cases were reported in the Jerusalem district, of 5100 cases nationally (58%). Most patients were students (70.1%); 64% males; median age 13.2 years; mean 14.9±9.8 years. Currently, 450 schools have been affected; school attack rates were 0.1-10%. Most patients were reported from the community. The clinical presentation included unilateral/bilateral parotitis. Patients with severe symptoms (390, 13%) were hospitalized (n=74) or evaluated in an emergency medical center (n=316); orchitis was diagnosed in 18 patients and neurologic symptoms in 12 patients. Hospitalized patients were less likely to be vaccinated than patients from the community. Mumps IgM antibody test - positive in 354 patients; PCR (urine) - 7 patients; genotype G5. The overall MMR vaccination status: 2 doses - 46.3%, 1 dose - 21% (8.5% age-appropriate), unvaccinated - 12.3%, missing - 20.5%. Most (94.1%) patients aged 7-20 years had received at least 1 dose of MMR vaccine (85.1%-2 doses) vs. 47.6% of those aged 21 years and older.

Conclusions: The outbreak was characterized by predominance of male students; the majority of whom had been previously vaccinated. The reported complication rate was relatively low. Vaccination status was associated with age and clinical course. The combination of limited mumps vaccine effectiveness and the specific school setting probably contributed to the disease spread.

P886

EVALUATION OF THE VACCINATION STATUS IN BRAZILIAN CHILDREN WITH CANCER

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Background and aims: More than 9,000 Brazilian children and adolescents were diagnosed with cancer during 2010. Their improved survival requests vaccination as an important strategy to prevent infections that threaten both the health and the life of these immunocompromised children. The aim of this study was to assess the immunization status in cancer patients followed at three pediatric oncologic centers in Northeast Brazil (Alagoas State).

Methods: Medical charts of 635 cancer patients (1 to18 years) were reviewed. Only 76 (12%) had vaccination charts available and were enrolled. Appropriate routine immunization was defined according to the Brazilian National Immunization Program. Special vaccines for immunodeficient or other high-risk children were provided for the Brazilian Special Immunobiological Agents Program.

Results: Vaccination charts were found to be up to date in 50/76 patients (65,8%) at the time of cancer diagnosis. After the cancer diagnosis 59 patients (77,6%) had not received vaccines and only one children (1,3%) received special and available free vaccines indicated for their immunocompromised condition (pneumococcal polysaccharide and Hepatitis A vaccine). Seasonal Influenza vaccine was received in only two patients and pandemic influenza vaccine (H1N1) in 4 patients. Children born before the year 2000 and with linfoproliferative neoplasias were more prone to have adequate immunization schedule at the time of cancer diagnosis.

Conclusions: Only 65,8% of these patients were up to date with routine free pediatric and adolescent vaccines when diagnosed with cancer. The immunization after cancer treatment is not a current practice of pediatric oncologists in this Brazilian study.

P887

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Conclusions: Only 65,8% of these patients were up to date with routine free pediatric and adolescent vaccines when diagnosed with cancer. The immunization after cancer treatment is not a current practice of pediatric oncologists in this Brazilian study.

P888

ANTIBODY PERSISTENCE 3, 5 AND 10 YEARS AFTER ADMINISTRATION OF A 5-COMPONENT ACELLULAR PERTUSSIS TDAP-IPV VACCINE TO 11-14 YEAR-OLDS

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Background and methods: Serial antibody persistence surveys were conducted among persons who as young adolescents had received intramuscular Tdap-IPV (REPEVAX®, ADACEL® POLIO) in a December 2000 - October 2001 randomized trial in which 50% of the 280 participants were administered concomitant hepatitis B vaccine. Sera were obtained 3, 5 and 10 years postvaccination from a subset of the study population: seroprotection levels and geometric mean concentrations/titers (GMC/GMT) of diphtheria, tetanus, pertussis, and polio antibodies were measured.

Results: Sera were obtained from 224 participants at 3 years postvaccination, 225 at 5 years and 174 at 10 years; 153 participants contributed at all timepoints. Ten years postvaccination, seroprotection at levels ≥0.01IU/mL for diphtheria and ≥0.01EU/mL for tetanus was evident in >98% and 100% respectively of participants, whereas 56% and 98% of participants presented with long-term protection levels for diphtheria (≥0.1 IU/mL) and tetanus (≥0.1 EU/mL) respectively. All maintained polio seroprotective titers of ≥1:8 for all 3 serotypes. Antibodies against PT, FHA, PRN and FIM 2&3 were detectable in 74%-98% of participants. GMCs or GMTs against all antigens were above or at prevaccination levels. No differences in antibody persistence were observed in participants who received concomitant hepatitis B vaccine compared with those who received Tdap-IPV alone.

Conclusions: Seroprotection against diphtheria, tetanus, and polio, and detectable acellular pertussis antibodies, were observed 10 years after Tdap-IPV administration. Concomitant hepatitis B vaccination did not affect antibody persistence. These data may aid decision making regarding Tdap-IPV re-dosing intervals.

P889

STARTING HPV-VACCINATION IN FLANDERS: ENHANCE IN USE OF THE VACCINATION REGISTRY VACCINNET AND PRELIMINARY DATA ON PARTICIPATION IN THE PROGRAMME

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Background and aims: In September 2010 HPV-vaccination was added to the vaccination programme of Flanders. Girls in the first year of secondary school are the target group for vaccination. We want to evaluate the participation in the programme with data from the vaccination registry in Vaccinnet. At the same time we want to see the impact of communication on the use of the registry by vaccinators.

Methods: At the start of the HPV-vaccination programme in Flanders, a communication strategy was set up both for the public (target group) as for vaccinators. The importance of registering vaccinations in the central registry was emphasized. Some months after the start, data from Vaccinnet were analysed to evaluate the impact on the use of Vaccinnet and to have an idea about the participation in the HPV-vaccination programme.

Results: At the start of this vaccination programme an increase in use of the vaccination registry Vaccinnet was seen. Analysis of the registered vaccination data for the first and second dose of HPV-vaccine gives a first idea about the participation of the target population. Preliminary results show registered vaccinations for about 80% of the target group of girls.

Conclusions: Communicating about the importance of registering vaccinations enhanced the use of the vaccination registry in Vaccinnet, which is important for the cervical cancer prevention programme in future. At the same time the vaccination registry, although not used by all vaccinators, shows an indication about the acceptability and participation of the target group in the vaccination programme.

P890

IMMUNOGENICITY OF A QUADRIVALENT MENACWY-CRM CONJUGATE VACCINE ADMINISTERED IN VARIOUS SCHEDULES TO ARGENTINEAN INFANTS AND TODDLERS

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Introduction: Although young infants are at highest risk for developing meningococcal disease, a quadrivalent conjugate vaccine is not available for routine use in this population. We present immunogenicity results from a large Phase III study using the final MenACWY-CRM formulation.

Methods: In a subset of a large randomised, multinational open-label study, we measured immune responses after primary and booster doses of MenACWY-CRM, administered concomitantly with routine immunizations using two (2, 6 and 12 months) or three priming doses (2, 4, 6 and 16 months) in healthy Argentinean infants. Immunogenicity was measured one month after priming, pre- and post-booster by serum bactericidal assay using human complement (hSBA).

Results: At 7 months, seroprotection rates (% with hSBA titres ≥ 8) after priming with two (n~274) or three (n~268) doses were 74% and 89%, 94% and 97%, 99% and 98%, and 97% and 98% against serogroups A, C, W-135 and Y, respectively. GMTs for serogroup A were 31 and 43 after 2 and 3 doses, respectively, but were similar in both groups for serogroups C, W-135 and Y. MenACWY-CRM with MMR/V+HepA+PCV7 at 12 months after two primary doses (n~100) or with DTaP-Hib at 16 months after three primary doses (n~115) achieved hSBA titres ≥ 8 in 95-100% of subjects against all four serogroups, with similar GMTs in both groups.

Conclusion: When administered concomitantly with routine vaccinations, two or three doses of MenACWY-CRM elicited similar robust immune responses to all serogroups, and were boosted at 12 or 16 months, respectively.

P891

HOSPITAL-BASED SURVEILLANCE OF ROTAVIRUS GASTROENTERITIS AND GENOTYPES DISTRIBUTION IN GREECE IN THE ERA OF PARTIAL VACCINATION

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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 RVGE among hospitalized children with AGE in a major Pediatric Hospital, examine possible impact of partial vaccination implemented gradually from 2007 (peak coverage was 25-28% in 2008-10 vs 4-15% in the previous 2 periods) and perform surveillance of rotavirus (RV) genotypes.

Methods: A prospective epidemiologic observational study included all children < 5y hospitalized for AGE (September 2006-August 2010). A rapid stool immunochromatographic test for RV antigen detection and seminested RT-PCR for genotype analysis on RV(+) samples were performed.

Results: Of all AGE cases (2589), 13.2% (342) were RV positive. RVGE rate was reduced significantly by 36% (95%CI: 16-51%, p< 0.001) in 2008-10 compared to 2006-08. A shift to older age was observed during the study period since the rate decreased in infants and increased in children over 24 months of age (p= 0.0267). No children with RVGE had been received any vaccine dose. G4P[8] was the most common genotype (71.1%) followed by G1P[8] (11.1%), G2P[4] (5.6%) and G9P[8] (2.2%). No association was observed between RV genotypes and hospitalization time or total disease duration. Mean age (38.4 months) of children with G2P[4] was higher compared to children with either G4P[8] or G1P[8] (17.0 and 13.6 months); p=0.035 and p=0.031 respectively.

Conclusions: This study indicates greater than expected benefits of partial RV vaccination in Greece. Circulating genotypes are among the 5 commonest worldwide.

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PERTUSSIS AFTER END OF A MASS VACCINATION PROJECT - END OF THE "VACCINATION HONEY- MOON"

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After 16 years of no vaccination against pertussis in Sweden, mass vaccination of infants and catch-up vaccination of children up to 10 years with a pertussis toxoid vaccine was performed in the Greater Gothenburg area 1995 - 1999. In 1999 56 % of all 10 year old children born in Greater Gothenburg had received 3 doses of the pertussis toxoid. No booster doses were given. This led to almost complete elimination of pertussis. The aim of the present study was to follow the incidence of pertussis after end of the mass vaccination project (1999 - 2009) as reflected by cultures and/or PCR. A reemergence was seen from the end of 1999 with a peak in 2004 followed by a decrease when booster doses to both 6 and 10 year old children were introduced in 2005 - 2006. From July 1, 1999 through December 31, 2009 a total of 1973 cases were diagnosed with culture or PCR. The disease was prevalent in all age groups. The highest documented incidence was seen in infants. 450 patients with verified pertussis had received 3 doses of pertussis toxoid in the mass vaccination project and some other trials (comprising a total of 69,423 children). The mean time from the last dose to the laboratory verification of pertussis was 5 years in these 450 cases. In conclusion, pertussis is still not eliminated from the area. Booster doses are needed but the numbers and optimal timing are not known.

P893

MEMORY B CELL RESPONSE TO A PCV-13 BOOSTER IN 3.5 YEAR OLD CHILDREN PRIMED WITH EITHER PCV-7 OR PCV-13

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Background/aims: Direct vaccine-induced host immunity to pneumococcal disease is determined by anti-polysaccharide antibodies and induction of immune memory. There is limited information about the role of memory B cells (MBC) in maintaining antibody levels following infant vaccination. We studied antigen-specific MBC in children 2.5 years after infant immunisation and after a booster dose of a 13-valent pneumococcal conjugate vaccine (PCV-13).

Methods: We recruited children who had participated in a previous multicentre RCT comparing PCV-7 and PCV-13 in infancy at the age of 3.5 years. Blood was taken before and 1 month post-booster. MBC were quantified using a stimulated ELISpot assay for serotypes 1,3,4,14,19A,23F.

Results: In total, 98 blood samples were available for analysis. Numbers of MBC specific for serotypes included in both the PCV-7 and PCV-13 (4,14,23F) were low at baseline and did not differ between the groups (except for serotype 14: higher in the PCV-13 group). MBC numbers post-booster were higher than baseline for these 3 serotypes with no differences between the groups. For serotypes only included in PCV-13 (1,3,19A), baseline MBC numbers were lower in the unprimed group for all 3 serotypes (6/0/9 versus 10/4/11 MBC/10^6 cells, significant only for serotype 3; $p< 0.01$). However, post-booster MC frequencies were similar for serotypes 1,3,19A in both groups (16-37 MBC/10^6 cells; $p>0.1$).

Conclusions: A PCV-13 pre-school booster results in similar post-booster MBC frequencies in individuals irrespective of prior priming with PCV-7 or PCV-13 for serotypes 1, 3 and 19A despite lower pre-booster MBC frequencies in the unprimed group.

P894

HEMAGGLUTINATION INHIBITION AND MICRONEUTRALIZATION ANTIBODIES IN INFANTS AND CHILDREN RECEIVING SEASONAL TRIVALENT INACTIVATED INFLUENZA VACCINE (TIV) OR MF59®-ADJUVANTED TIV (ATIV)

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Background and aims: Serological assessments of immunity to influenza and of responses to vaccination conventionally have been based on the hemagglutination inhibition assay (HI). We compare, for the first time, comparative HI and (micro-) neutralization (MN) responses to seasonal TIV and ATIV in children.

Methods: In a subset of 793 vaccine-naive 6-< 72 month old children enrolled in an efficacy trial of two age-appropriate doses of TIV, ATIV and control non-influenza vaccines, HI and MN antibodies were measured in sera obtained before vaccination, three weeks after each dose, and on Day181. The HI was performed according to standard procedures using whole live virus. The MN procedure was performed according to the CDC method using ELISA readout.

Results: Both GMT HI and MN titers were higher for ATIV than for TIV for all three viral subtypes, after both doses and at Day 181.

In 6-< 36 month olds, the fold increase of ATIV above TIV GMT responses was higher than in 36-< 72 month olds.

One ATIV dose stimulated higher MN titers than two doses of TIV for A/H3N2 and A/H1N1 subtypes, in both age groups.

HI and MN titers were similar in response to A/H3N2 and also for A/H1N1 antigens; the MN test was considerably more sensitive in measuring responses to the B antigen.

Conclusions: ATIV stimulated higher and more persistent MN as well as HI titers than TIV in vaccine-naive 6-< 72 month old children.

P895

SAFETY OF AN MF59®-ADJUVANTED SEASONAL INFLUENZA VACCINE IN 6-< 24 MONTH-OLD CHILDREN

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Background and aims: Infants are highly susceptible to influenza infections and safe vaccines for this age group are a medical priority.

Methods: A randomized, blinded controlled trial assessed safety and tolerability of two age-appropriate doses of MF59®-adjuvanted trivalent influenza vaccine (ATIV, Fluad®, Novartis), compared with TIV (Agrippal®, Novartis or Influsplit SSW®, GSK Biologicals) or non-influenza control (CTRL) vaccines (Menjugate® or Encepur Children®, Novartis) in a sub-group of 2042 influenza vaccine-naive 6 -< 24 month-olds for 2007-2010. After each vaccination, solicited reactions were collected for 7 days, all adverse events (AEs) for 28 days and selected AE and severe AE (SAE) for study duration.

Results: Relative risk ratios of local and systemic reactions for ATIV were 1.021 (95% CI: 0.971-1.074) vs. TIV and 1.026 (95% CI: 0.969-1.088) vs. CTRL. Overall solicited reaction rates with ATIV were 81% vs. 79% with TIV. Commonest local reactions across vaccine groups post first dose were erythema (21-35%) and injection site tenderness (13-20%) - most being mild and transient. Commonest systemic reactions were sleepiness, irritability and unusual crying; 11%-16% vaccinees had fever (≥ 37 ºC), < 1% had fever ≥ 40ºC. Four febrile seizures each with ATIV (< 1%) and TIV (1%), and 3 with CTRL (1%) resolved without sequelae. Reaction rates were lower after the second vaccination. Most frequently reported unsolicited AEs were upper respiratory tract infection (29-33%) and otitis media (23-24%); SAEs were reported by 8%-11% vaccinees.

Conclusion: ATIV is well tolerated and shows no major safety concerns in 6-< 24 month-old children.

P896

ANALYSIS OF THE POST-VACCINATION PERIOD IN HIGH RISK CHILDREN GIVEN PNEUMOCOCCAL CONJUGATE 7-VALENT VACCINE

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Background and aims: There is lack of in-country experience in registered in Russia in 2009 pneumococcal conjugate 7-valent vaccine (PCV7) use in children from high risk groups. The study aim is PCV7 reactogenity and tolerability assessment in high risk children.

Methods: Unreserved observation of post-PCV7-vaccination period in 146 children aged 6-24 months old with recurrent respiratory infections and otitis media (40%), resuscitation during newborn period (22%), HIV-infection (21%), premature birth (17%). 60 children were vaccinated by PCV7 alone, the rest has been given combined vaccination: Hib (52 kids), hepatitis A and B, DTP, Varicella, flu and MMR (34 children).

Results: Post-vaccination adverse events: fever 38ºC and local site reactions (hyperemia 1-3 cm) has been registered in 25 (17%) kids, mostly in children with recurrent respiratory tract infections and otitis media (16 cases).

Conclusions: PCV7 vaccination of infants from risk groups (recurrent respiratory infections and otitis media, HIV-infection, premature babies) is well tolerated with relatively low rate of adverse events both in PCV7-separated and combined with other pediatric vaccines immunization. Children with recurrent respiratory infections have higher frequency of adverse reaction compared to children from other risk groups.

P897

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P898

ANTIBODY TITRATION AND IMMUNITY TO HEPATITIS B VACCINE IN THALASEMIC PATIENTS ACCORDING TO THE DURATION AFTER VACCINATION

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Background and aims: Hepatitis B virus is one of the causes of acute and chronic hepatitis. Due to multiple hospitalization and transfusion, thalasemic patients are in the more risk for this infection. Duration the immunity after vaccination in this high-risk group and the need to booster vaccination is uncertain. Aim of this study is Antibody titration and immunity to Hepatitis B vaccine in thalasemic patients According to the duration after vaccination.

Material and methods: Four hundred fifty eight thalasemic patients attending in Kerman were evaluated in this study. All patients had been vaccinated with recombinant hepatitis B Vaccine according to the national vaccination program. On the base of the time after vaccination, patients were divided into 6 groups. According to their antiHBs antibody titer, non-immune group had antibody titer less than 10 international unit per liter (IU/L), semi-immune group had antibody titer 10-100 IU/L and complete-immune group had more than 100 IU/L of antibody.

Results: On the base of the time, one to more than 5 years after vaccination in six-groups, non-immunity was detected in percentage 3.28, 3.3, 5.7, 19.16, 33.3 and 58.2 respectively.

Conclusion: Three years after Hepatitis B vaccination in thalasemic patients anti HBs antibody levels is decreased significantly. At this time evaluation of the hepatitis B immunity and booster, vaccination should be considered.

P899

COLLABORATION BETWEEN ACADEMIA AND PHARMA IN THE DESIGN AND CONDUCT OF A VACCINE TRIAL BY INCORPORATION OF MUTUAL SCIENTIFIC INTERESTS

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Background and aims: A randomised controlled trial (RCT) evaluating the 10-valent pneumococcal non-typeable *Haemophilus influenzae* (NTHi) protein D conjugate vaccine (PHiD-CV; GlaxoSmithKline) was initiated by GlaxoSmithKline, focusing on immunogenicity and safety/reactogenicity. The clinical investigators were interested in evaluating nasopharyngeal carriage. This was incorporated in the final study design, enabling comparison of the effects of two pneumococcal conjugate vaccines on nasopharyngeal bacterial carriage rates in a RCT setting.

Materials and methods: Infants (n=780) were vaccinated with either PHiD-CV and DTPa-HBV-IPV/Hib (GlaxoSmithKline), PHiD-CV and DTPa-IPV-Hib (Sanofi Pasteur MSD) or 7vCRM (Pfizer) and DTPa-IPV-Hib. Blood samples and nasopharyngeal swabs for bacterial culture were collected at several time points up to 2 years of age. Collaboration between the laboratories of the two parties lead to incorporation of molecular techniques in the analysis; one PCR tool discriminating NTHi from *Haemophilus haemolyticus* and one quantifying bacterial loads were developed by GlaxoSmithKline.

Results: Recruitment proceeded as planned. This single-centre study was conducted by well-trained study staff with extensive experience in collecting blood and nasopharyngeal samples in infants. Short timeframes between sampling and culturing nasopharyngeal specimens further enabled high quality output, producing high yields of *Streptococcus pneumoniae* and NTHi. Clinic- and industry-based investigators collaborated to finalise the statistical analysis plan; it was agreed that PhD students would play a leading role in the trial conduct and writing of publications.

Conclusion: Collaboration between industry- and clinic-based investigators can lead to synergism in which both can have their questions addressed in a good quality RCT, performed within predefined timelines.

P900

FIRST EFFECTS OF IMMUNIZATION WITH HIGHER VALENT PNEUMOCOCCAL CONJUGATE VACCINES IN GERMAN CHILDREN ON NUMBERS OF REPORTED IPD CASES

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Background and aims: A general recommendation for vaccination with pneumococcal conjugate vaccine (PCV) was issued for German children up to the age of 2y in July 2006. In 2009, two higher valent PCVs were licenced in Germany: PCV10 in April 2009, PCV13 in December 2009 (PCV7 was replaced completely). In this study, we present data on cases of IPD sent in for serotyping in the five years following the start of PCV-vaccination, focusing on the effect on the new serotypes in PCV10 and PCV13.

Methods: Pneumococcal isolates recovered from children with invasive pneumococcal diseases (IPD) were sent to the National Reference Center for Streptococci. Identification of the isolates was confirmed and serotyping was performed using the Neufeld Quellung reaction.

Results: In 2009-2010, IPD cases in children < 2y caused by PCV7 serotypes had decreased by almost 90%, while cases caused by non-PCV7 serotypes almost doubled. Of particular interest, among the six new serotypes, less cases caused by serotypes 1,3 and 7F were reported from July-Dec. 2010 (n=11) as compared to the same time period in 2009 (n=18). Cases caused by serotype 19A were slightly higher (n=15 vs. n=13). Serotypes 5 and 6A (1 case each) were still very rare in the age group < 2y.

Conclusions: Five years after the general vaccination recommendation reported cases caused by PCV7 serotypes have almost disappeared. One year after the introduction of higher valent PCVs first effects are visible, with less reported cases among children < 2y due to serotypes 1, 3 and 7F.

P901

ANTIBODY RESPONSE TO VACCINATIONS OF CHILDREN IN ITHAKI ISLAND GREECE

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Objective: Our goal was to assess the specific antibody response against the vaccines of measles,rubella,mumps (MMR) and varicella in children living in Ithaki island.

Material and methods: We investigated the IgG antibody response in 90 patients (45 girls,45 boys) aged 12 months to 15 years .Antibody concentrations were measured by ELISA.

Results: All children were divided into two age groups:group A consisted of children from 12 months old to 7 years old and group B consisted of children older than 7 years All children were vaccinated with MMR,76 of which (84,4%) were given both doses of the vaccine.The varicella vaccine was provided to 57 children (63,3%); 22 were infected by the virus(24,5%) while 11 (12,3%) were not vaccinated.All children were satisfactorily covered against the rubella virus(group A 98,1% , group B 100%). Against measles group B was found with less positive antibodies 64,9% compared to group A 90,6%.Almost half of the children carried positive antibodies against mumps (group A 47,2% and group B 43,2%).From 57 vaccinated children against varicella the immunisation level was sattisfactory 84,2% group A while a 73,7% corresponds to older ages.

Conclusion: Parents were properly informed and responded positevely to the vaccination program .Against the rubella virus the children were higly immunized whereas against the measles the immunisation levels in ages > 7 years old (64,9%) were not sattisfactory. The immunization levels against varicella were satisfactory despite the small percentage of non vaccinated children.The low level of immunity response against mumps despite massive children vaccination with MMR is worth mentioning

P902

PREVALENCE OF DRAVET SYNDROME AMONG CHILDREN REPORTED WITH A CONVULSION AFTER VACCINATION, IN A NATIONWIDE TEN-YEAR COHORT

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Background and aim: This study is undertaken to assess the frequency of Dravet syndrome (DS) due to a SCN1A-mutations, in children reported with a convulsion after vaccination, in a nationwide ten-year cohort (1997-2006), and to analyse which clinical characteristics distinguishes children with and without DS.

Method: Medical data of all children, reported with convulsion(s) after vaccination in the first two years of life to the National Institute for Public Health and Environment in the Netherlands, were re-evaluated. In children with possible DS, additional medical information was requested. DNA-analysis of SCN1A was offered, if not yet performed, to those with a clinical history compatible with DS. The study has been approved by the medical ethics committee of the UMC-Utrecht.

Results: 1301 children were reported with 1368 convulsions after vaccination. Median age at initial reporting was 1.3 years. 103 (7.9%) children had been diagnosed with epilepsy. Of 239 children (median age 8.4 years) out of 285 children with possible DS, additional medical information could be retrieved. 15 children were diagnosed with DS, 4 as a result of this study, and had a SCN1A-mutation. Seizures in children with DS occurred at a lower age (4 vs. 11 months), were more often afebrile (64.3% vs. 25.4%) and reoccurred more often after following vaccinations (26.7% vs. 3.9%), than in children without a diagnosis of DS (p-values< 0.01).

Conclusion: At least 1.2% (15/1301) of children with a convulsion after vaccination in the first two years of life has Dravet syndrome due to a SCN1A-mutation.

P903

(PRE)SYNCOPE IN THREE MASS VACCINATION CAMPAIGNS IN THE NETHERLANDS; MENC IN 2002, HPV IN 2009, AND H1N1 IN 2009-2010

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Background and aims: In the Netherlands, three large vaccination campaigns were held, in 2002, 2009, and winter 2009/2010 against Meningococcal C (MenC), human papillomavirus (HPV) and pandemic influenza A(H1N1) infection, respectively.MenC (1 dose) targeted 1-18-year-olds, HPV (3 doses) girls 12-16-year-old and H1N1 (2 doses) children 0.5-4-years-old and parents/siblings of younger infants. Monitoring included immediate adverse events (imAE).

Methods: Questionnaires distributed to all vaccination sites addressed all imAE and numbers of vaccinees. Coverage- denominators (age, sex, and dose) were available from national vaccination registries.

Results: Reported imAE followed most frequently dose1. Presyncope/syncope were predominant (peak rates in pre-adolescents), sometimes with subsequent injury. Accompanying symptoms were nausea/vomiting, rash, or jerks.

	MenC	HPV	H1N1
Target group	1-18y	12-16y	0.5-4y + parents/siblings younger infants
Campaign Coverage	93%	51%	71%
Schedule	1 dose	3 doses	2 doses
Vaccinees monitored (%)	1,817,558 (63%)	143,278 (74%)	510,296 (70%)
Monitored doses	1,817,558	408,663	928,735
Any immediate AE/10,000 vaccinees (dose 1)	23.0	44.0	2.6
Any immediate AE/10,000 vaccinees (any dose)	23.0	77.0	3.4
Presyncope-syncope/10,000 vaccinees (dose 1)	21.4 (6-14y)	20.5 (12-16y)	26.5 (5-10y)
Presyncope-syncope/10,000 vaccinees (any dose)	21.4	48	33.4

[Comparison vaccination campaigns for imAE]

Conclusions: Most often reported imAE were presyncope and syncope. No serious imAE were reported. Careful follow-up of reports should avoid undue apprehension, false contra-indications, and the stigma of epileptic seizure in syncopal children with jerks. Attention should be paid to prevention of fainting and subsequent injury.

P904

INCREASED RISK LOCAL REACTIONS 4-YR-BOOSTER-DTAP-IPV IN THE NETHERLANDS; ASSOCIATION WITH TRANSITION TO INFANT ACELLULAR-PERTUSSIS VACCINES AND SPECIFIC TYPES OF (BOOSTER)VACCINES

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Background and aims: Acellular pertussis vaccine was added to the 4-yers-old booster DT-IPV since 1998. Infant schedule (4 doses) of the National-Vaccination-Programme, shifted from whole-cell to acellular pertussis combination-vaccines in 2004. In 2008 suddenly reports increased 4-fold, mainly for local reactions with/without fever. Types and brands of vaccines have differed, both for infants and for boosters. Our interest was their effect on adverse events (AE) after 4y-boosters.

Methods: Reports (n=1809) over 1995-2010 and 1991-2006 cohorts were categorised using the regular criteria for diagnosis (annual AE reports, www.rivm.nl). Coverage-denominators (date, age, sex, vaccine dose, type and lot number) were available from national vaccination registers.

Results: Reports numbered about 50 annually for cohorts 1991-1997, most frequenty fainting, local reactions and fever. With acellular booster at 4 years following infant whole-cell vaccine, reports increased to 85 (cohorts 1998-2003), mainly for local reactions and/or fever. For cohort 2004 the increase started in children under the old whole-cell pertussis schedule. Seemingly, many received acellular vaccines privately, ahead of the universal transition. For cohort 2005, with all children on infant acellular vaccines, reports increased further nearly 3-fold. Cohort 2006 saw a decrease, but still reports numbered much higher than 3 years before.

Conclusions: The increase in reports of local reactions following the 4-yr-booster DTaP-IPV was linked to the transition to acellular vaccines for infants. Questionnaire studies are being conducted. The types of booster-vaccine and infant-vaccine influence the risk. Because different vaccines have been in use concurrently, a case-control-study must be made based on the vaccination register.

P905

BOOSTER DOSE AT 12 MONTHS OF AN INVESTIGATIONAL MENINGOCOCCAL SEROGROUP B VACCINE (4CMENB) IN TODDLERS PREVIOUSLY PRIMED AT 2,4,6 MONTHS

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Background: Whole genome sequencing was used to identify three of four major protein components of an investigational multicomponent meningococcal vaccine (4CMenB).

Methods: In an observer-blind study in Santiago, Chile, 11-17-year-old adolescents were randomized to receive 1-3 doses of 4CMenB or placebo at baseline, one and/or two months later. Primary immunogenicity outcome was a titer ≥4 in a serum bactericidal assay using human complement (hSBA) against three test strains selected to evaluate the contribution of individual vaccine antigens. Tolerability was assessed by solicited local and systemic reactions within seven days of each study vaccination. Adverse events were monitored throughout the study.

Results: Overall, 1631 adolescents (56% female; mean age 13.8 ± 1.9 years) received 4CMenB and/or placebo. One month later 92-97% of recipients of one 4CMenB dose, 99-100% after 2 or 3 4CMenB doses and 29-50% of placebo recipients had hSBA titers ≥4 against the three test strains. Similar proportions of placebo and 4CMenB recipients reported solicited local (89-94%) and systemic (70-79%) reactions after the first study injection. At subsequent visits, reports of reactogenicity were less frequent in all groups, but placebo recipients were less likely to report reactogenicity outcomes than 4CMenB recipients.

Discussion: 4CMenB induced robust immune responses and had an acceptable tolerability profile following one, two, or three doses and all schedules administered. Three doses of 4CMenB imparted no additional benefits compared with two doses. No evidence of increased reactogenicity was observed with 2 or 3 doses compared with one dose of 4CMenB.

P906

HOSPITAL-BASED SURVEILLANCE OF ROTAVIRUS ACUTE GASTROENTERITIS IN CHILDREN AFTER INTRODUCTION OF ROUTINE ROTAVIRUS VACCINATION IN FINLAND WITH PENTAVALENT ROTAVIRUS VACCINE

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Background and aims: Rotavirus (RV) is the leading cause of severe dehydrating diarrhoea in children under-five and is associated with direct costs for medical care and indirect costs for family. RV vaccine was included in the Finnish National Vaccination Programme starting from September 2009. All infants aged 2 months would have received 3 doses of live attenuated pentavalent vaccine (RV5) free of charge. The aim of the study is to assess the incidence of children hospitalized with RV positive AGE (RV+AGE) during the RV seasons 2009/2010 and 2010/2011 in conjunction with increasing RV vaccination coverage.

Methods: Since December 2009 a prospective observational hospital-based surveillance study has been conducted in two paediatric hospitals in Finland (Oulu and Tampere). All children under-16 years-old, permanent residents and admitted for an acute gastroenteritis (AGE) were eligible for inclusion in the study. RVs were detected in stool samples by ELISA and RT-PCR.

Results: The results of the first season´s surveillance (December 2009- mid-June 2010) showed a low overall number of RV+AGE (total of 65 cases of RV+AGE; 20 in Tampere and 45 in Oulu). The season lasted from January to June with no peak. The vaccine coverage estimated in each area rapidly reached approximately 90%. No child fully vaccinated with RV5 was hospitalized for RV+AGE.

Conclusion: Compared to three previous RV seasons 2006-2009 in Finland, the number of RV+AGE hospitalizations was lower during this first season of routine rotavirus vaccination, very likely associated with the high RV vaccination coverage and high efficacy of RV5.

P907

EFFECT OF MEASLES, MUMPS, AND RUBELLA VACCINATION ON THE IMMUNITY OF NEWBORNS

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Background and aims: Despite high vaccination coverage for measles, mumps, and rubella, children are still at risk of infection due to clusters of unvaccinated individuals, e.g. orthodox protestant religious persons in the Bible belt, or to travel to countries with low vaccination coverage. Maternal antibodies help newborns fight infections in the first months of their life. However, the antibody levels of MMR-vaccinees seems to be lower than for naturally infected individuals. This lower level can be reflected in the maternal antibody levels of newborns.

Methods: A cross-sectional serological survey was conducted in the Netherlands. Herein, we compared maternal antibody levels in children born to vaccinated mothers with the levels in children born to orthodox protestant mothers, who often decline vaccination based on their religious beliefs.

Results: Children born to vaccinated mothers seemed to have lower levels of antibodies for measles and rubella at the moment of birth, compared to children born to orthodox protestant mothers. For mumps there was no difference. As a control we also modeled varicella zoster virus, for which no vaccination is given, and no difference was observed between the two groups.

Conclusions: MMR-vaccination resulted in a slight decrease in the maternal antibody levels for measles and rubella. To protect these young children, the vaccination scheme might be adapted such that the first vaccination is given at an earlier age.

P908

PERSISTENCE OF ANTIBODY AGAINST H1N1 AND RESPONSE TO TRIVALENT INFLUENZA VACCINE 13 MONTHS AFTER 2 DOSES OF MONOVALENT PANDEMIC VACCINES

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Background and aims: We investigated antibody persistence in children 13 months after two doses of $AS03_B$-adjuvanted or non-adjuvanted monovalent pandemic H1N1 influenza vaccine and assessed the immunogenicity and reactogenicity of a further dose of a seasonal trivalent influenza vaccine (TIV).

Methods: After a blood sample assessing persistence of levels of antibody against the 2009 pandemic H1N1 influenza virus (n=323), 302 children received a single dose of a seasonal trivalent influenza vaccine. Immunogenicity was assessed at day 21.

Results: Although antibody levels had waned across all groups, at 13 months post-vaccination significantly more participants had microneutralisation (MN) titres ≥1:40 in the $AS03_B$-adjuvanted vaccine group compared to the non-adjuvanted vaccine group. For children aged < 3 years at first immunisation these percentages were 100% (95% CI 94.1-100%) for the $AS03_B$-adjuvanted vaccine versus 32.4% (21.5-44.8%) for the non-adjuvanted vaccine. For those aged 3 to 12 years at first immunisation these percentages were 96.9% (91.3-99.4%) versus 65.9% (55.3-75.5) ($p< 0.001$ for both comparisons). Following TIV all participants had MN titres ≥1:40. $AS03_B$-adjuvanted groups had higher absolute haemagglutination inhibition (HI) titre levels than non-adjuvanted groups. In under five year olds, redness >50mm and any severe local reaction were more frequent ($p< 0.05$) in previous recipients of $AS03_B$-adjuvanted versus non-adjuvanted vaccine (40.8% vs 24.2%, and 14.1% vs 1.5% respectively).

Conclusions: Almost all children who received two doses of the $AS03_B$-adjuvanted H1N1 pandemic influenza vaccine maintained adequate antibody levels one year after vaccination. TIV is safe and immunogenic in the season following pandemic vaccine administration.

P909

ANTIBODIES INDUCED BY AN ACCELERATED INFANT COURSE OF HEPATITIS B VACCINE PERSIST WITHOUT BOOSTING IN PRIMARY SCHOOL AGE CHILDREN

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Background and aims: In 2006, UK guidance for the immunisation of children born to Hepatitis B (HBV) carrier mothers changed, recommending an additional (fifth) dose at pre-school age. Previous research conducted on a cohort whose last vaccine had been at 6 months of age suggested only half had anti-HBsAg concentrations >10 mI/mL by adolescence. We describe persistence of antibodies against HBV surface antigen (anti-HBsAg) and response to a booster in a cohort due their pre-school booster. Most had been immunised according to the current UK schedule, i.e. at 0, 1, 2 and 12 months of age.

Methods: Children commencing HBV vaccination as post-exposure prophylaxis at birth had blood taken before and 3-5 weeks after their 'pre-school' HBV booster tested for anti-HBsAg concentrations and evidence of past or current infection. The primary endpoint was the proportion of children with anti-HBsAg concentrations >10 mIU/mL at both timepoints.

Results: Twenty-eight children were enrolled (mean age 6.2, range 3.4-10.5 years). An analysis including only children with complete infant schedules and no significant delays or additional doses, demonstrated 19 of 22 children with pre-booster samples had anti-HBsAg concentrations >10 mI/mL (86.4%, 95% CI 65.1-97.1%). All 21 children with samples had concentrations >100 mI/mL post-booster (100%, 95% CI 83.9-100%). With all children included, the proportions were 84.6% pre-boost (n=26, 95% CI 65.1-95.6%) and 100% post-boost (n=25, 95% CI 86.3-100%).

Conclusion: Most children immunised according to the current UK schedule, with a dose at 12 months, maintain anti-HBsAg antibodies through early childhood without a pre-school booster.

P910

CONCOMITANT USE OF VAQTA WITH PROQUAD AND PREVNARIN 12 TO 23 MONTH OLD CHILDREN

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Background: Open-label, multicenter, randomized study evaluated immunogenicity, safety, and tolerability of concomitant (Group 1) vs nonconcomitant (Group 2) Vaqta (25U/0.5 mL) (hepatitis A; HepA) with ProQuad (MMR/varicella) & Prevnar (7-valent pneumococcal) in healthy, 12-23 month old children.

Methods: Group 1 received Vaqta/ProQuad/Prevnar concomitantly on Day 1; second doses of Vaqta/ProQuad at Week 24. Group 2 received ProQuad/Prevnar on Day 1; Vaqta at Weeks 6 & 30; ProQuad at Week 34.

HepA seropositivity rate (SPR: ≥10 mIU/mL), varicella zoster-virus (VZV) SPR (≥5 gpELISA units/mL), and geometric mean titers (GMT) to S. pneumoniae examined. Injection site & systemic adverse experiences (AEs) and daily temperatures collected.

Results: HepA SPR were 100% for Group 1 and 99.4% for Group 2 after two Vaqta doses; risk difference=0.7 (95%CI: -1.4,3.8, non-inferior) regardless of initial serostatus. Varicella SPR was 93.3% for Group 1 and 98.3% for Group 2; risk difference=-5.1 (95%CI: -9.3,-1.4; non-inferior). S. pneumoniae GMT fold-difference (7 serotypes) ranged from 0.9 to 1.1; non-inferior.

No statistically significant incidence differences of individual AEs seen when Vaqta administered concomitantly vs nonconcomitantly. Three (all Group 2 post-administration of ProQuad/Prevnar) of 11 serious AEs (SAEs) were considered possibly vaccine related: dehydration & gastroenteritis (same subject) on Day 52; febrile seizure on Day 9. No deaths reported.

Conclusions: Immune responses to Vaqta, Prevnar and ProQuad given concomitantly were non-inferior to each vaccine given nonconcomitantly. Concomitant administration of Vaqta with Prevnar & ProQuad had an acceptable safety profile in 12-23 month old children.

P911

IMMUNE RESPONSE OF PRETERM INFANTS TO HEPATITIS B VACCINE

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Background: Nearly one third of the word´s population have serologic evidence of past or present infection with the hepatitis B virus (HBV). This study evaluated the immune response in preterm infants to hepatitis B vaccine.

Methods: This study was conducted 71 preterm neonates with gestational age equal or less than 36 weeks and 6 day or birth weight equal or less than 2000 gram and 72 term neonates with gestational age equal or more 37 weeks and birth weight equal or more than 2500 gram. Excluding criteria was including neonates of HBsAg positive mothers, infants who received less than 3 dose of vaccine and infants who received immunoglobulin or blood products. In both preterm and term groups sampling for anti-HBS was done and titer 0f > 10 mIU/mL considered as immune response to hepatitis B vaccine.

Results: Neonates in both groups 100% response to vaccination. Immune response to vaccination have no correlation with gestational age (r=-0.112, p=0.182) and birth weight (r=-0.136, p=0.106). Mean anti HBS titer was 660.0±409.3 in preterm group and 565.4±567.9 in term group who deference was not significant (p=0.256).

In preterm group mean anti-HBS titer show not significant difference (p=0.316) between low birth weight (1500-2000g), VLBW(1000-1499 g), anal extremely low birth weight (< 1000 g) in preterm group. Mean anti-HBs titer show no significant difference between male and female (p=0.368), but in term group this difference was significant (p=0.007).

Conclusion: Immune response to hepatitis B vaccine was similar in preterm and term infants.

P912

ROTAVIRUS, NOROVIRUS AND ADENOVIRUS GASTROENTERITIS IN HOSPITALIZED CHILDREN, TURKEY

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Background and aims: This study aims to determine the prevalence and the distribution of Enteric viruses(especially rotavirus, norovirus and adenovirus) responsible for gastroenteritis in children.

Methods: A epidemiological study on common diarrheal viruses was conducted in Afyon City, Turkey between January and November 2009. One hundred and fifty faecal samples from children under 6 years of age(mean age, 2.18±SD 3.64 years, range: 1 - 72 months)(negative for the presence of pathogenic bacteria by standard culture methods) were tested by ELISA(Ridascreen and Biomeriux) and RTPCR methods for detection of-Norovirus G1,G2. Stool samples positive for group A rotavirus by commercial enzyme immunoassay were subjected to reverse transcription-polymerase chain reaction based genotyping of the outer capsid antigens, VP7 and VP4, determining G and P type specificities, respectively.

Results: Norovirus were detected in 22.8% of 92 children (< 6 years of age) and rotavirus and adenovirus were detected in 23.3 % and 6% of 150 hospitalized for gastroenteritis in Afyonkarahisar, Turkey, during 2009, respectively; predominant genotypes were GGIIb/Hilversum and GGII.4 Hunter for norovirus. The most common rotavirus strain was G2P[4] (n=16), followed by G9P[8] (n=7). Other strains were G1P[8] (n=3), G2P[8] (n=3), G1+2P[8] (n=2), G9P[4] (n=1), G2+9P[8] (n=1), G4+9P[6] (n=1), and G2P[4+8] (n=1). Of children with viral enteritis, 6.5% had a mixed norovirus-rotavirus infection.

Conclusions: Rotavirus is still the most common cause for gastroenteritis. Norovirus might be a more frequent agent in patients with vomiting prominent. The severity of infection by norovirus was lower but an increase was observed with rotavirus co-infection.

P913

ADENOVIRUS INFECTION IN IMMUNOCOMPROMISED KIDS PATIENTS

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Background: Every child is at risk of adenovirus infection, but kids patients with weak immune systems or with underlying respiratory or cardiac disease are most at risk for severe complications from any respiratory infection, including adenovirus infections. Features include dyspnea, dry cough, pulmonary rhonchi and rales, grossly bloody urine, and diarrhea. Treatment of adenovirus infection is supportive.

Aims: The primary aim of this study was to assess the relationship between adenovirus specific antibodies and immunocompromised children.

Methods: In the immunocompromised host, adenovirus infection caused severe localized disease including pneumonitis, colitis, hemorrhagic cystitis, hepatitis, nephritis, encephalitis, or disseminated disease with multiorgan failure. Our series of patients is representative of the spectrum of immunocompromised children at greatest risk for severe adenovirus disease, namely solid-organ and BMT recipients, neonates and children with immunodeficiency.

Results: Adenovirus usually causes a localized infection, but generalized infection occur edin immuno-compromised kids patients. In addition to leukopenia and mild elevations in aspartate aminotransferase levels, ammonia and glucose levels were within normal range as were serum electrolytes, pH, and blood gases, with no evidence of dehydration or metabolic disturbances. One hundred eighty-eight children (19%) had positive viral culture results during our studies comparative groups.

Conclusions: Adenovirus is a common pathogen in the pediatric population. Adenovirus is increasingly known to cause disease during the posttransplantation period in patients who have received hematopoietic stem cell transplants.

P914

CLINICAL AND LABORATORY FEATURES OF CHILDREN WITH H1N1 INFLUENZA A INFECTION IN AN EMERGENCY CARE DEPARTMENT

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Background: OnMarch 2009 a new outbreak of H1N1Influenza A(IA-H1N1) virus was detected in Mexico,and it rapidly spread throughout the world. On June of the same year,the WHO declared a IA-H1N1pandemics,which led to an overload of medical visits to Emergency Departments.IA-H1N1 is expected to continue to circulate in the next years.

Aims: To analyze the clinical and laboratory features of children with Influenza Like Syndrome(ILS), and to compare patients with confirmed IA-H1N1 infection with other causes of ILS.

Methods: A retrospective analysis of children 0-167 months admitted to a Pediatric Emergency Care Department from March 2009-April 2010 who had a diagnosis of ILS,and had a RT-PCR IA-H1N1 performed.Statistical analysis was done using Pearson x^2test, Fisher exact Test, t-Student and U Mann-Whitney tests.

Results: 236patients were included,mean age 66,5+/-45,3months. Eighty(33,9%)

patients had positive RT-PCR IA-H1N1.Positive results were significantly less frequent in the 54 children< 24m(p< 0,001).Patients with positive RT-PCR IA-H1N1 had a higher mean age(93,7+/-40,1 x 52,6+/-52,6m, p< 0,0001), higher prevalence of cough(p=0,008), headache(p=0,034),previous history of asthma(p=0,001) and lower leucocyte count(6077+/-1996 x10404=/-5280, p=0,025). No differences between positive and negative IA-H1N1patients were observed in: time from onset of symptoms,presence of fever,vomits,sore throat, diarrhea,abdominal pain,nasal congestion/rhinorrea,wheezing, respiratoydistress,O_2Saturation,hospital

admission rates,Hb/Ht,and RCP.No deaths occurred.

Conclusions: In this study we observed a higher prevalence of IA-H1N1 infection among patients>24 months,and in those with previous asthma.Except for cough, headache and normal leucocyte count, no other clinical or laboratory differences were observed between positive and negative IA-H1N1 ILS patients. Low morbidity and hospital admission rates were observed in this study.

P915

SENSIBILITY, SPECIFICITY AND PREDICTIVE VALUES OF A RAPID INFLUENZA TEST IN THE DIAGNOSIS OF H1N1 INFLUENZA A

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Background: From June 2009 to August 2010, the world faced a H1N1-Influenza A (IA-H1N1) pandemics. It is expected that the IA-H1N1 continues to circulate among the next few years,which leads to the need of a quick screening test to detect IA-H1N1 infection in high risk patients with Influenza-Like syndrome(ILS).

Aims: To evaluate the sensibility, specificity, positive and negative predictive values(PPV and NPV)of a rapid Influenza diagnostic test(RIDT-Quick View Influenza A+B Test) in comparison to IA-H1N1 rT-PCR

Methods: Retrospective 12months study of children 0-167months admitted to a pediatric Emergency Department from April2009-April2010 who had a diagnosis of ILS, and a concomitant RIDT and IA-H1N1 rT-PCR performed.

Results: 161patients were included, mean age 63,98+/-44,2(6-156)months, 51,6%male.Concordance between both tests results was observed in 123/161(76,4%).Among the 57 patients with positive IA-H1N1 rT-PCR,only 23(40,4%) had a positive RIDT. Among the 104 patients with negative IA-H1N1rT-PCR, 4(3,8%)had a positive RIDT:3 seasonal Influenza A and 1Influenza B. Sensibility, specificity, PPV and NPV of the RIDT were 40,4%, 96,2%, 85,2% and 74,6%, respectively. Among children < 2years(n=21),the values for the same tests were: 75%, 100%, 100% and 97,1%.

Conclusion: In this study,RIDT showed a high sensibility among children < 2 years, and may be a useful tool for screening of this high risk group of patients with suspected IA-H1N1 infection.The low sensibility in older patients limits its use in this age group.The high specificity in all age groups makes this test a valuable tool for initial management of patients with suspected IA-H1N1 and positive RIDT results during IA-H1N1 outbreaks.

P916

HEPATITIS D OUTBREAK IN A HEPATITIS B HYPER-ENDEMIC SETTLEMENT IN GREENLAND.ROUTE OF TRANSMISSION - MOLECULAR EVIDENCE

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Background and aims: Hepatitis B virus (HBV) infection is endemic in Greenland with 5-10% of the population being chronic carriers hepatitis B surface antigen-positive (HBsAg-positive). Until now hepatitis D (HDV) has seldomly been reported in Greenland and never among children. In 2006, following 3 cases of acute hepatitis among children from a settlement (Itilleq, N=135) on the west coast of Greenland, a population based sero-screening showed that 27% of the inhabitants in the settlement were HBsAg-positive hereof were 46% below 20 years of age, and 52% of the chronic carriers were HDV IgG-positive. On follow-up one year later five children, who were HBsAg-positive in 2006, had HDV-seroconverted from 2006 to 2007 indicating ongoing HDV transmission. In this study, we wanted to determine route of transmission of HBV and HDV infection in the settlement.

Methods: HBV and HDV-positive specimens were sequenced, the sequences BLASTed on NCBI-homepage and phylogenetic trees constructed.

Results: HBV and HDV sequencing showed that all HBV isolates were of genotype D2 and all HDV isolates of genotype I. All HBV isolates formed one definite cluster with 100% homology among examined children, which indicated transmission within the settlement and horizontal transmission among children. The HDV isolates formed three distinct clusters, one restricted to children and adolescents, the two restricted to adults.

Conclusions: Phylogenetic trees suggested horizontal transmission of HBV and HDV among children in the settlement and separate introductions as well as different routes of transmission among children and adults.

P917

HEPATITIS D OUTBREAK IN A HEPATITIS B HYPER-ENDEMIC SETTLEMENT IN GREENLAND.ROUTE OF TRANSMISSION - MOLECULAR EVIDENCE

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Conclusions: Phylogenetic trees suggested horizontal transmission of HBV and HDV among children in the settlement and separate introductions as well as different routes of transmission among children and adults.

P918

USE OF OSELTAMIVIR IN CRITICALLY ILL CHILDREN IN A PAEDIATRIC INTENSIVE CARE UNIT DURING THE 2009 INFLUENZA A (H1N1) PANDEMIC

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Background and aims: The 2009 influenza A (H1N1) pandemic saw an unprecedented rise in the empirical use of oseltamivir in critically ill children. Evidence for efficacy and guidelines on optimal use are lacking. We aim to describe and audit the prescribing practice of oseltamivir in a paediatric intensive care unit (PICU).

Methods: Retrospective case series of children treated empirically with oseltamivir in a London tertiary hospital PICU from September 2009 to January 2010, the peak of the pandemic flu season. Pharmacy records, controlled drug log books, and electronic drug charts were reviewed. Dose and duration of oseltamivir treatment were audited against local hospital policy.

Results: 89 children received oseltamivir; 14 had RT-PCR confirmed influenza A (H1N1) infection, 75 had other diagnoses. Thirty one (34.8%) patients received standard dose of oseltamivir; 27 (30.3%) received double the dose. Twenty one (23.6%) patients received a dose that could not be attributed to any known prescribing policy. H1N1 positive patients were more likely to be started on double doses of oseltamivir compared to H1N1 negative patients (64.3% vs. 30.7%; p=0.031). Mean duration of oseltamivir treatment for H1N1 positive patients was 6.9 days (range 1-19), compared to 1.6 days (range 0-5) for H1N1 negative patients. Five H1N1 positive patients had prolonged treatment beyond the recommended five days (8, 10, 14, 15 and 19 respectively).

Conclusions: Oseltamivir prescribing for suspected influenza is inconsistent, even within a single unit. Better defined risk factors, symptom profiles, and manifestations of severe H1N1 disease, are required to guide clinical practice.

P919

CRITICALLY ILL CHILDREN TREATED WITH EMPIRICAL OSELTAMIVIR IN A PAEDIATRIC INTENSIVE CARE UNIT DURING THE 2009 INFLUENZA A (H1N1) PANDEMIC

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Background and aims: During the 2009 influenza A (H1N1) pandemic, many children admitted to paediatric intensive care (PICU) were empirically treated with oseltamivir for clinically suspected influenza. H1N1 influenza causes a wide and atypical range of symptoms; severe manifestations are not well described. We describe the clinical spectrum of critically ill children who received oseltamivir.

Methods: A retrospective case series of children treated empirically with

oseltamivir in a London tertiary hospital PICU from September 2009 to January 2010 at the peak of the pandemic flu season. Demographics, presentation, treatment, and outcome for H1N1 positive and negative patients were compared.

Results: 89 children received oseltamivir; 14 had RT-PCR confirmed influenza A (H1N1) infection, 75 had other diagnoses. 71.4% of H1N1 positive patients had significant co-morbidities compared to 58.7% of H1N1 negative patients. 50.0% of H1N1 positive patients had pre-existing neurological conditions compared to 18.7% of H1N1 negative patients (p=0.011). H1N1 positive patients seemed more likely to have gastrointestinal symptoms. At presentation, H1N1 positive patients had lower platelet levels than H1N1 negative patients (194 x 10^9/L vs. 298.6 x 10^9/L; p=0.0082), and required more inotropes on admission (p=0.028). H1N1 negative patients were more likely to survive than H1N1 positive patients (92.0% vs. 71.4%; p=0.025). Using ROC analysis, H1N1 positive patients who survived trended towards higher platelet levels compared to those who died (AUC 0.75; p=0.18).

Conclusions: The majority of patients started empirically on oseltamivir did not have H1N1 infection. Severe H1N1 infection is associated with hypotensive shock, thrombocytopenia, and neurological co-morbidity.

P920

HERPES SIMPLEX ENCEPHALITIS IN CHILDREN - SHOULD WE CHANGE OUR APPROACH?

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Background and aims: Despite advances in therapy, herpes simplex encephalitis (HSE) remains a serious illness. Defects of the TLR3-interferon (IFN) axis in the antiviral innate immune response against HSV-1 and some genes (*TLR3*, *UNC93B1* and *TRAF3*) are associated with HSE. We analyzed the presence of HSE associated genes, treatment and outcome in children.

Methods: Descriptive study between January 2000 and December 2010. HSV-1 was detected by PCR from CSF. PBMC and fibroblasts were studied for their IFN responses to TLR3 and virus stimulations. Coding exons of the known HSE-associated genes were sequenced.

Results: Four cases, ages between 6 and 9 months, with seizures and extensive brain injuries, treated with acyclovir 21 days (starting on day 1 of disease). Patients 1 and 2 presented serious morbidity, with tetraparesis and epilepsy refractory to treatment did not received INF. Patient 3 had immune-mediated encephalitis 23 days after the initial infection, was treated with IFN (7 days) stopped for no clinical improvement and bicytopenia. Patient 4 started IFN at day 2 of the disease (21 days) being discharge without sequelae.

The functional studies were normal, except the fibroblasts from patient 3 which displayed impaired IFN-lambda production after stimulations of poly(I:C), response to which is thought to be TLR3-dependent. No mutation was found in the sequenced coding exons of *UNC93B1*, *TLR3* and *TRAF3*.

Conclusions: Although we present a small sample, the impaired IFN responses of patient 3 and the outcome observed on patient 4 may reveal the importance of IFN in the treatment of HSE.

P921

ENTEROVIRUS AND HUMAN PARECHOVIRUS INFECTIONS ARE A MAJOR CAUSE OF FEVER OF UNKNOWN ORIGIN IN YOUNG CHILDREN

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Background and aims: Enterovirus (EV) or Human Parechovirus (HPeV) infections in young children are usually self-limiting, but may cause serious symptoms, such as convulsions and cardiorespiratory instability. We investigated the incidence, clinical characteristics and management of EV and HPeV infections among young children with fever of unknown origin.

Methods: In 2008 345 children under 36 months of age presenting with fever of unknown origin and sepsis-like symptoms at the Juliana Children's Hospital in The Hague, the Netherlands, were evaluated in a prospective observational study. All received a sepsis work up including white cell count, CRP, blood culture and urine screening. Cerebrospinal fluid (CSF) was collected on indication. EV or HPeV DNA was detected by PCR in plasma and/or CSF. Urine cultures were performed when urine screening was positive. 115 children with urinary tract infection were excluded. Data of the remaining 230 children were analysed.

Results: EV/HPeV PCR could be performed in 163/230 children: 52 (32%) were EV positive, 31 (19%) HPeV positive, 10 (6%) had bacterial sepsis/meningitis and 70 (43%) were negative. Clinical characteristics at presentation varied only slightly between the four groups. EV and HPeV infections occurred predominantly in summertime. Bacterial infections resulted in longer hospital stays than viral infections.

Conclusion: EV and HPeV infections are a major cause of fever of unknown origin and sepsis-like symptoms in children under 36 months of age in summertime and are difficult to differentiate from bacterial infections. Early diagnosis EV and HPeV infections using PCR diagnostics reduces duration of hospital admission.

P922

HOSPITALIZATION DUE TO VARICELLA IN THE NETHERLANDS

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Objectives: In the Netherlands, incidence of physician's consultations and hospitalizations for varicella is low compared to other countries. Better knowledge about the severity of varicella among Dutch hospitalized patients is needed.

Methods: Hospital admissions due to varicella in 2003-2006 were obtained from the National Medical Register. Retrospectively, additional data were retrieved from the medical record of patients hospitalized with varicella in 23 Dutch hospitals using a standardized form.

Results: The study population (N=296) was representative for all varicella admissions in the Netherlands (N=1,658) regarding age, sex, duration of admission and type of diagnosis. Complications were recorded in 76% of the patients (37% had at least one relatively severe complication). Bacterial super infections of skin lesions (28%), (imminent) dehydration (19%), febrile convulsions (7%), pneumonia (7%) and gastroenteritis (7%) were most frequently reported. No varicella-related death occurred within the study population and 3% of the patients had serious rest symptoms.

Conclusions: It is not likely that the severity of varicella among hospitalized patients in the Netherlands differs from other countries. A considerable part of the varicella complications among hospitalized patients was rather moderate and can be treated effectively. These data are relevant in the decision-making process regarding whether or not to introduce routine varicella vaccination in the Netherlands.

P923

VACCINATION AGAINST PANDEMIC INFLUENZA (H1N1) AMONG PREGNANT WOMEN IN THE NETHERLANDS

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Background: At the end of 2009, the Dutch government advised pregnant women (second or third trimester) to get vaccinated against pandemic influenza A(H1N1). For future decisions on vaccination during pregnancy it is important to get insight in participation of pregnant women and reasons why they get vaccinated or not.

Methods: In April 2010, the RIVM invited 14,529 pregnant women by letter to participate in an internet survey of which 3,067 (21.1%) women participated; 29 women were excluded from the analysis because the expected date of delivery was before November 2009 or after May 2010 or the pregnancy ended premature before 9 November 2009 (before vaccination against pandemic influenza A(H1N1) was offered).

Results: Of the total group of respondents 58,5% received two vaccinations against pandemic influenza A(H1N1); additionally 5,3% of the respondents received only one vaccination. It must be noted that women with higher educational level were overrepresented (60%) and had a slightly higher participation. Vaccinated women responded more positive on statements regarding protection of the vaccine, less negative on statements regarding harmfulness of the vaccine and they expected a higher risk on (harmfull effects of) pandemic influenza than unvaccinated women. Furthermore, vaccinated women agreed more on statements that the advice of the government and health care professionals played an important role in their decision.

Conclusions: A considerable part of pregnant women in the Netherlands was vaccinated against pandemic influenza A(H1N1). Future multivariate analysis need to reveal which aspects were most important in their decision to get vaccinated or not.

P924

VARICELLA RELATED HOSPITALIZATIONS IN TURKEY, 2008-2010: A NATIONWIDE SURVEY AT PREVACCINE ERA (VARICOMP STUDY-1)

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Aim: While usually self-limiting, varicella can develop potentially serious complications requiring hospitalization. The aim of this study was to identify varicella complications in children and assess the hospitalization rates in the pre-vaccination era in Turkey.

Methods: We retrospectively evaluated medical records of hospitalizations due to varicella from 24 tertiary care centers of 14 cities between October 2008-October 2010.

Results: 640 children (3 days-216 months, 357 boys-283 girls, 23.4% have underlying conditions) have been reported during this two year time period (325 cases between October 2008-September 2009; 315 cases between October 2009-October 2010). 18.6% of children hospitalized with the diagnosis of serious varicella infection. 6.7% of children have been hospitalized due to poor feeding with/without dehydration. 38.4% have secondary bacterial infections (including GAS bacteremia), 17% have skin superinfections, 13.8% have neurological complications, 5.5% have hematological complications, 18.1% have respiratory complications (viral/bacterial pneumonia, acute asthma exacerbations). Febrile convulsion reported as 7.8%, acute cerebellar ataxia 5.2% and encephalitis as 4.5%. 10 patients needed to intensive care and mechanical ventilation. 66.4% of children have been received acyclovir. 5.1% have been received intravenous immunoglobulin. Median hospitalization stay was 5 days (1-45days). Prognosis was favorable except for 7 cases: 5 serious sequel and 2 deaths have been reported(0.4%).

In conclusion, mortality associated varicella in Turkey was low, the hospitalizations rates relatively high, and the number of serious complications remarkable. Introduction to varicella vaccine to expanded immunization program is a better option to prevent these complications. Further guidelines to define and treatment of complicated varicella infections also needed.

P925

ACUTE HUMAN PARVOVIRUS B19 (HPVB19) INFECTION IN A 6-YEAR OLD GIRL WITH SICKLE CELL DISEASE: A CASE REPORT

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HPVB19 infection is common and its clinical manifestations depend on the patient's immuno-haematological status. Fever usually lasts 7-10 days. It's rarely associated with arthropathy (8% in children vs. 80% in adults) and often causes acute bone marrow failure but rarely splenic sequestration in patients with chronic haemolytic anaemia.

An African 6-years girl with Sickle-cell disease was hospitalized because of high fever (40° C) and arthralgia at the right knee from the previous day.

At admission she was in good general conditions. The physical examination revealed only a palpable spleen pole and painful right knee. Inflammatory markers were mildly increased (GB 19250/mm3; N 14030/mm3; PCR 23 mg / L; PCT 0.2 ug / L). Haemoglobin was stable for her steady state values (Hb 7.9 g / dl). After microbiological investigations, she underwent antibiotic therapy with ceftriaxone.

During hospitalization she developed a significant hepatosplenomegaly, haemoglobin decreased (2 g/dl below steady-state values) and reticulocytes increased (356000/mm3), meeting the criteria for splenic sequestration diagnosis. She required transfusions of red packed cells.

Microbiological investigations revealed positive HPVB19 IgM and IgG, HPVB19 DNA in blood, Adenovirus IgM and IgG. Given the diagnosis of HPVB19 infection and persistent fever, she stopped antibiotic therapy and received intravenous immunoglobulins (IVIG) with progressive clinical improvement and discharge after 24 days of hospitalization.

To our knowledge, this is the first case of acute HPVB19 infection in a child with Sickle cell disease and more than 20 days fever, associated with splenic sequestration. In these cases, IVIG may represent an effective therapy.

P926

VIRAL CO-INFECTIONS IN INFANTS WITH COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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Background and aims: Infants frequently suffer from CAP and in most of them viruses are found as etiologic agents, sometimes together with bacteria. However, whereas the relevance of bacterial and viral co-infections is quite known, information on viral co-infections is very poor. This study was planned to increase our knowledge at this regard.

Methods: Hospitalized children aged < 12 months with radiographically-confirmed CAP were enrolled. A nasopharyngeal swab was performed and analyzed for the presence of 19 viruses by the Multiplexed Luminex xMAP Assay. Data regarding history, clinical and laboratory findings, and outcome were recorded.

Results: A total of 139 infants were studied. At least one virus was found in 118 (84.9%) cases. The most frequent viruses were RSV (62, 44.6%), rhinovirus (46, 33.1%), and hMPV (17, 12.2%), with influenza viruses identified in 10 (7.1%) cases. Viral co-infections were found in 40 (28.7%) infants (2 viruses in 33 infants and 3 in 7). Bocavirus (92.8%), coronavirus (100%), adenovirus (100%) and parainfluenza viruses (100%) were almost always detected with other viruses. No increase in CAP severity was observed in patients with viral co-infections, and RSV and influenza viruses were associated with the most severe CAP cases even when alone.

Conclusions: Viral co-infections in infants with CAP are common but seem without clinical relevance. The fact that RSV and influenza have a relevant role for frequency and severity in CAP of infants strongly supports the use of the available preventive measures against these pathogens since the first months of age.

P927

FACTORS CONDITIONING ANTIBODY RESPONSE (AR) TO A/H1N1 2009 PANDEMIC INFLUENZA VIRUS IN HEALTHY CHILDREN

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Background and aims: Strong immune response to pathogens is essential to reduce clinical relevance of infectious diseases. Recently, the A/H1N1 2009 influenza virus has emerged as a possible cause of pandemia. Severity of disease due to this virus ranged from mild to extremely severe. Knowledge of immune response to this virus in pediatric age and whether immunity against seasonal influenza viruses or other factors can influence it is scanty.

Methods: A blood sample to evaluate AR by means of hemagglutination inhibition (HI) assay was drawn 28 ± 2 days after the onset of symptoms of laboratory-confirmed pandemic influenza in 73 children. Association between AR and antibody levels against seasonal influenza viruses was evaluated. Moreover, influence of age and sex, viral load, upper (URTI) or lower respiratory tract infection (LRTI) as disease presentation in conditioning AR was studied.

Results: Seventy of the 73 (95.9%) enrolled children with pandemic influenza (mean age, 4.3 ± 3.8 years) had AR ≥40, the level usually considered protective. AR was independent from levels against seasonal influenza viruses as well as from age, sex, and viral load. On the contrary higher AR (>160) was significantly associated with LRTIs ($p < 0.001$) and with Rx-confirmed pneumonia ($p < 0.05$).

Conclusions: Previous immunity against seasonal influenza viruses does not influence AR against the A/H1N1 2009 influenza virus, suggesting the lack of immune cross-reactivity between the two A/H1N1 influenza viruses. Children with the more severe disease showed the highest AR, confirming the importance of immune response in conditioning outcome.

P928

FACTORS CONDITIONING ANTIBODY RESPONSE (AR) TO A/H1N1 2009 PANDEMIC INFLUENZA VIRUS IN HEALTHY CHILDREN

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P929

CLINICAL AND SOCIOECONOMIC IMPACT OF INFECTION DUE TO A/H1N1V INFLUENZA VIRUS IN PEDIATRICS

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Background and aims: Clinical and socioeconomic importance of A/H1N1v in pediatrics in comparison to other influenza A subtypes (A/H1N1s and A/H3N2) has not been precisely defined. In this study, clinical and socioeconomic impact of infection due to A/H1N1v was compared with that due to A/H1N1 and A/H3N2.

Methods: Clinical and socioeconomic data of children with influenza enrolled in the Department of Maternal and Pediatric Sciences in Milan, Italy, during influenza seasons 2007-2008, 2008-2009 and 2009-2010 were compared. Considering the prevalence of influenza subtypes, in 2007-2008 data from A/H1N1s, in 2008-2009 from A/H3N2 and in 2009-2010 from A/H1N1v cases were analysed.

Results: A total of 126, 486 and 389 children were evaluated in 2007-2008, 2008-2009, and 2009-2010, respectively. No difference was observed between the groups in clinical presentation and outcome. In children with A/H1N1v in comparison with A/H1N1s and A/H3N2 subtypes, age (5.4 vs 3.3 and 3.7 yrs; $p< 0.001$), absence from school (8.9 vs 5.7 and 6.3 days; $p< 0.001$) and duration of hospitalization (9.1 vs 6.5 and 5.5 days; $p< 0.05$) were significantly higher and parents lost a greater number of work days (6.9 vs 3.4 and 6.2 days; $p< 0.001$).

Conclusions: Clinical impact of A/H1N1v infection was similar to that of other seasonal influenza A viruses. The longer duration of hospitalization and absence from school together with the higher number of work days lost by parents seem to be more ascribable to the fear of complications of the new infection than to real difference in severity of infection.

P930

AN OUTBREAK OF INFLUENZA CAN INTERFERE WITH THE INCIDENCE OF VARICELLA? THE 2009 EXPERIENCE OF CURITIBA (SOUTHERN BRAZIL)

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Background and aims: Varicella is a highly contagious disease that has an increase in the number of cases usually in late winter and spring. However, during the winter of 2009, the population of Curitiba (capital of Paraná State - Southern Brazil) lived intensely the pandemic influenza A/H1N1. The aim of this study is to describe the influence of this influenza outbreak on the occurrence of varicella in Curitiba.

Methods: Data was obtained from the Municipal Public Health System computerized electronic medical record according to International Classification of Diseases.

Results: In the city of Curitiba the varicella vaccine is not yet available in the public health system for previously healthy children. Thus, from 2003 to 2008, the surveillance of varicella in Curitiba has shown a bi-annual preponderance in children and in winter-spring seasons (August-December). However, in 2009, the level remarkably decreased and remained below average until the end of the year (Chart 1). In this period of 2009 were reported around 16,000 cases and 49 deaths from the H1N1 flu in the city. Preventive measures were enhanced such as the strengthening of guidance for hand hygiene, avoid crowding and extension of the winter school holidays to 45 days.

Conclusions: In this study, we demonstrated the shift in the seasonal occurrence of varicella in Curitiba during the 2009 influenza pandemic. Preventive measures against an outbreak of influenza would be enough to cause a reduction of airborne transmission of diseases such as varicella or competition allows a viral interaction?

P931

AN OUTBREAK OF INFLUENZA CAN INTERFERE WITH THE INCIDENCE OF VARICELLA? THE 2009 EXPERIENCE OF CURITIBA (SOUTHERN BRAZIL)

M. Feliz[1,2], A.G.M. Arias[3], A. Miro[4], J. Oliveira[2], R. Feliz[5], M. Burger[3]

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Conclusions: In this study, we demonstrated the shift in the seasonal occurrence of varicella in Curitiba during the 2009 influenza pandemic. Preventive measures against an outbreak of influenza would be enough to cause a reduction of airborne transmission of diseases such as varicella or competition allows a viral interaction?

P932

HERPES ZOSTER IN CHILDREN

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Background and aims: Herpes zoster (HZ) is infrequent in healthy children, especially in the countries were vaccine is in current use. In Romania anti varicella zoster virus (VZV) vaccination is optional. The objective is to analyze epidemiological, clinical and evolutive aspects of HZ in children.

Methodes: Retrospective study on HZ in children (0- 18 years) admitted in Clinical Hospital of Infectious and Tropical Diseases "Dr.V.Babes" Bucharest between 01.2007- 12.2010. 39(10%) cases were identified from a total of 389 HZ cases.

Results: Age distribution per groups was 7(18%) in 0- 1, 6(15%) in 1-5, 10(25%) in 6-10, 16(41%) in 11- 18 years. Sex distribution was heterogeneous (17boys:22girls). Known VZV exposure was documented in 23(59%) cases. 6(86%) patients in the 0- 1 year group were borne from mothers with VZV infection in the last trimester of pregnancy. 23(60%) cases had toraco- brachial localization. Associated systemic symptoms were fever in 12(31%) and pain in 11(28%) cases. All patients were treated with Acyclovir 20-40 mg/kg (per os), for 7- 10 days. 8(21%) cases evolved with encephalitis, 1(3%) with S. aureus infection 4(10%), 3(8%) had disseminated HZ. 1 patient (3%) was HIV infected, 1(3%) had pulmonary TB, 2(6%) had different malignancies.

Conclusions:

1.HZ incidence in small children appears to be higher in our group compaired to the literature data from countries were vaccine is in use but further monitoring is necessary.

2.Imunological screening and vaccination before pregnancy would be useful in limiting the number of HZ caused by in utero contamination.

P933

CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF A/H1N1 PANDEMIC INFLUENZA IN CHILDREN

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Background: Between 2009-2010 evolved pandemic A/H1N1influenza virus. Children were mainly involved; patients with significant comorbidities had severe prognosis.

Objectives: To describe clinical, epidemiological and virological aspects of influenza cases in children addressed to the Clinical Hospital of Infectious and Tropical Diseases "Dr.Victor Babes“ Bucharest.

Material and methods: Between 08.2009-01.2010 we tested 243 patients aged between 0 and 18, of which 220 were hospitalized and 23 ambulatory supervised. Etiological diagnosis was established by RT-PCR of naso-pharyngeal swab.

Results: 138 of 220 hospitalized and 2 of ambulatory cases tested positive. The most common source of infection was the school community in 62(44.9%) cases. Clinical signs was the cough in 130(95.6%) patients, followed by fever in 110 (79.7%) patients with sudden onset in 126 (91.3%) of cases, rhinorrhea 99 (73.3%), myalgia 70(51.9%), digestive disorders 34(25%) patients. 100 patients(73%) had clinical and radiological appearance of influenza pneumonia. The most common complications were respiratory with bacterial overgrowth (usually pharyngitis, sinusitis, otitis) to 24.6% of cases. Duration of hospitalization was between 24 hours and 17 days, mostly between 4 and 8 days. Antiviral treatment was administered to 71(51.8%) patients in the first 48 hours of symptoms onset. The most affected age group is between 13-18 years 72 cases (52, 2%).

Conclusions: All cases were virologically confirmed influenza with A/H1N1. Teenagers were most frequently affected. The 0-5 years age group was the least affected (opposite to the known data). The outcome was similar to the classical forms of seasonal influenza. There were no deaths or severe cases.

P934

COMPLICATIONS OF VARICELLA ZOSTER: A RETROSPECTIVE STUDY IN A TERTIARY REFERRAL CENTRE

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Background and aims: Chickenpox is a common cause of hospital attendance in children but rarely leads to admission. VZV is not currently included in the Irish national immunisation programme. We aimed to evaluate the relative frequencies of different types of complications leading to admission, duration of inpatient stay as well as the epidemiology of VZV infection in children over a 40 month period.

Methods: Hospital Emergency Department and Microbiology records were searched for patients admitted in whom VZV infection was present. Data were collected by chart review.

Results: From February 2007 to July 2010 there were 33 admissions (17 male, 16 female), all occurring between January and August. All patients were under 7, with the majority of admissions being 3 years old or younger.

Skin complications (16) were the commonest reason for admission, with 13 cases of cellulitis. Neurological complications (febrile convulsion(2), ataxia (1), VZV meningitis (1)) and immunocompromise (3) were next most frequent. Respiratory (VZV pneumonitis (2), pneumonia(1)), gastroenterological (2), sepsis (2), occular (2) and osteomyelitis (1) made up the remainder.

There were 279 inpatient days in total, with 27 in ICU and 18 days ventilation. Skin complications contributed the largest number of inpatient days, but respiratory (18 days) and septic (25 days) complications had the longest average length of admission .

Complication leading to admission		N= 33
Skin (16)	Cellulitis	8
	Cellulitis + collection	4
	Submental abscess	1
	Superinfected lesion	1
	Eczema exacerbation	1
	Impetigo	1
Neuro (4)	Febrile convulsion	2
	Ataxia	1
	VZV meningitis	1
Prophylactic admission due to immunocompromise (3)	Nephrotic Syndrome	2
	JIA: etanercept + steroids	1
Respiratory (3)	VZV pnemonitis	2
	Pneumonia	1
Gastro (2)	Vomiting & diarhoea	2
Sepsis (2)	Group A strep	1
	S. aureus	1
Ocular (2)	Periorbital cellulitis	1
	Occular VZV lesion	1
Bone (1)	Osteomyelitis	1

[Table 1]

Conclusions: While there were no deaths, VZV infection resulted in considerable morbidity and cost for those admitted, with significant hidden economic cost not evaluated here. These admissions would be preventable by a national immunisation programme.

P935

SEVERITY AND MORTALITY IN "THIRD WAVE" INFLUENZA A H1N1/09 INTENSIVE CARE ADMISSIONS CONTINUE TO EXCEED THAT OF PREVIOUS SEASONAL INFLUENZA

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Background: Children admitted to intensive care (PIC) with influenza A H1N1/09 during 2009-10 had increased cardiovascular shock, duration of admission and mortality, compared to the previous 5 seasons of seasonal influenza A admissions. We studied the clinical characteristics of H1N1-infected children admitted during the "third wave" (April 2010 - March 2011) to determine whether H1N1 disease severity persisted. We also studied influenza B admissions.

Methods: We retrospectively reviewed clinical records of all children admitted to St Mary's Hospital, London, testing positive for influenza A/B.

Results: There were 27 H1N1 admissions this season (cf 43 during 2009-10). The median age decreased from 54 to 18 months. Respiratory presentations predominated. In the 6 H1N1 patients on PIC, length of stay increased: median PIC-free days at day 28 fell from 12.5 to 3. All 6 presented with shock, (cf 13 of 18), and 3 of 6 died (cf 6 out of 18). There were 20 influenza B admissions, and 22 between 2006-10. Together, 10 of 42 patients required PIC, of whom 5 had cardiovascular shock, and 3 died. Median PIC-free days at day 28 was 10.

Conclusions: This season, H1N1 admissions fell, and overall median age decreased to that of previous seasonal influenza cohorts. However for PIC patients, mortality and refractory shock remained significantly higher, worsening since last year's "first and second wave" admissions. Influenza B admissions rose this year. Severity in PIC admissions was intermediate between seasonal and H1N1 influenza A. As H1N1 evolves, ongoing surveillance of its pathogenicity remains important.

P936

PRIMARY HHV-6B INFECTION AND ACUTE HEPATIC FAILURE IN A FIVE MONTHS-OLD BOY

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Background: Human Herpesvirus-6 (HHV-6) is usually acquired in early childhood. Primary infection can be silent, or associated with a febrile syndrome, such as exanthem subitum. Severe manifestations have been described, especially in immunocompromised patients. We present an unusually severe case of HHV-6 primary infection in a young child.

Case presentation: A previously healthy 5 months-old boy was admitted after a 5 days history of rash and fever, followed by generalized jaundice two days later. At admission, he had hepatomegaly and showed abnormal liver function and coagulation tests. Acetaminophen blood levels, metabolic and autoimmune screenings were negative. Over the next 10 days, his condition worsened with a grade III hepatic encephalopathy and refractory coagulopathy (factor V: 22%). Whole blood PCR was positive for HHV-6B (3936 GEq/ml). Other infectious etiologies were excluded. He was treated with intravenous ganciclovir, but required liver transplantation two days later for acute liver failure. HHV-6 was found by PCR in the native liver tissue and the bile fluid. He was subsequently treated with ganciclovir for both HHV-6 infection, and CMV mismatch. HHV-6 PCR was negative 20 days after transplantation.

Discussion: The pathogenic role of HHV-6 in acute liver failure remains unclear. Positive HHV-6 PCR in whole blood can also be caused by genomic integration, but is usually associated with very high titers, unlike in our patient. Furthermore, HHV-6 PCR was positive on his liver tissue, and bile fluid. HHV-6 infection should be actively searched in acute liver failure, even in immunocompetent children, as recommended.

P937

SEVERE NEUROLOGICAL AND NEUROVASCULAR COMPLICATIONS IN CHILDREN WITH A HISTORY OF VARICELLA ZOSTER VIRUS INFECTION

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Primary infection with varicella zoster virus (VZV) is normally a mild childhood disease. 90% of infections occur before adolescence. Severe cases are more common in immuno compromised children, but can occur in healthy children, causing a combination of VZV pneumonia, myocarditis, hepatitis, severe skin infections and neurological complications.

We would like to describe the case histories of 2 patients with severe disabling neurological complications following VZV infection.

Case 1 is a 4 year old girl who presented with post VZV encephalitis, leading to reduced consciousness, seizures, cortical blindness and visual hallucinations. Her MRI showed extensive abnormalities of the posterior grey matter and basal ganglia. Over the course of 12 weeks her visual problems completely resolved but she still has problems with concentration.

Case 2 is a 15 year old boy who presented 10 weeks after uncomplicated chickenpox with basilar artery thrombosis leading to stroke. He initial presented in status epilepticus needing ventilation support. Whilst on intensive care he was identified as being in locked in state. His MRI revealed multiple acute infarcts infratentorially in both cerebral hemisphere as well as the ventral pons. Eighteen months later he is able to talk and walk although being mild quadriplegic.

Although rare, neurological complications of VZV can be severe and cause permanent disability. The neuroradiology and possible pathogenic mechanisms will be discussed.

P938

EVALUATION OF VARICELLA ZOSTER VIRUS IMMUNITY RELATIVE TO SELF-REPORTED HISTORY FOR VARICELLA DISEASE AMONG YOUNG WOMEN BEFORE THEIR MARRIAGE

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Introduction and objective: Varicella zoster virus (VZV) infection especially in pregnant women is a concern of congenital varicella syndrome. The purpose of this study was to assess the validity of self-reported history for varicella disease relative to serological evidence of varicella immunity in premarital women attending care at clinics located in Kerman province, south eastern Iran with no vaccination coverage.

Material and methods: Premarital women attending care appointments who needed blood drawn as part of their routine pre-marriage test**,** eligible to participate. Self-reported varicella disease history was obtained via questionnaire. Varicella serostatus was determined using a whole-cell enzyme-linked immunosorbent assay to test for varicella zoster virus-specific immunoglobulin G (VZV IgG) antibodies.

Results: Of the 722 study participants 353(49%) self-reported having had chickenpox disease, 290(40%) self-reported having had no chickenpox disease and 78 (11%) having self reported uncertain varicella disease history. Of 353 participants who self-reported having had chickenpox disease, 94%, had serological evidence of immunity to varicella. Only 15% of women, who self-reported having a negative or uncertain varicella disease history, were seronegative for varicella antibodies**. Conclusions:** Self-reported history of varicella can be a strong predictor of VZV IgG antibodies. Negative or uncertain history is poorly predictive of negative serostatus.

P939

TOXOPLASMA GONDII / CMV ANTIBODIES IN CHILDREN WITH PROFOUND SENSORY NEURAL HEARING LOSS

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Background: Cytomegalovirus (CMV) and toxoplasma Gondii (T.Gondii) infection are the two most common causes of sensorineural hearing loss in Iranian children**.**

Objective: We performed this study to determine the serum antibodies against CMV and T. gondii in children with profound SNHL **.**

Materials & methods: In a cross sectional study, we determined T.Gondii and CMV antibodies **(**Enzyme linked immunosorbent assay IgG&IgM**)** in serum of 34 children with profound SNHL aged between 3 and 168 months who were candidates for cochlear implantation at Rasool Akram Hospital,Tehran Iran (2008-2009).

Results: Mean age of patients were 33.6± 38.6 months. Positive T.Gondii IgM antibody found in 1 /34 (3%)cases. ; None cases (0%)had positive T.Gondii -IgG antibody. Poisitive CMV-IgM was found in 11/34 (32%) cases. Poisitive CMV-IgG detected in 13/34 (38%) of studied cases

Conclusion: CMV infection was more common in SNHL cases. 32% of cases had recent CMV infection (Positive IgM).Both T.Gondi and CMV infections might have a significant role in profound SNHL in children less than 3 years of age. However, in this study we were unable to differentiate congenital from acquired cases.

P940

JUVENILE RHEUMATOID ARTHRITIS IN CHILDREN WITH EBSTEIN-BARR VIRUS INFECTION

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Background and aims: Juvenile Rheumatoid Arthritis (JRA) is a disease of unknown etiology. The most plausible environmental exposure is infection and although several decades of study have produced few definitive candidate organisms, Epstein-Barr virus (EBV) remains an interesting target. To determine the possible role of EBV infections in the clinical course of JRA, we attempt to demonstrate the radiologic changes and the frequency prescription of biologic product (Etenercept) rather than classic therapy.

Methods: A total of 73 patients with JRA who were hospitalized in the Pediatrics Rheumatology Ward of Hangang Sacred Hospital in Seoul, Korea during the years 2002-2009, were assessed serologically (IgM and IgG specific viral capsid antigens) for EBV infection and their response to therapy was studied.

Results: The median age of the patients was 6 years (0.6 - 15.7 years). EBV infection was seen in 46 (63%) patients . Girls were 40 JRA (55%) and boys were 33 JRA (45%). Twenty one girls (53%) among female and twenty five boys (76%) among male were infected with the virus. EBV infection was seen in 16 cases, 12 cases and 18 in the pauciarticular, polyarticular, and systemic JRA, respectively. Fifty five percent of EBV-positive patients (23/46) with JRA did not respond to the classic therapy, compare with EBV-negative patients (7/27). Sixteen percent of EBV-positive JRA (7/46) developed radiologic change within 2 years, compare with EBV-negative JRA (0/27).

Conclusions: EBV virus is invlolved in the pathogenesis of JRA and patients with EBV are in greater risk of progessing JRA.

P941

ENTEROVIRAL ASEPTIC MENINGITIS IN TURKEY NATIONAL WIDE SURVEILLANCE, 2006-2009

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Background: Enteroviruses are responsible for 85-95% of cases of aseptic meningitis (AM). AM due to enteroviruses can cause long-term sequelae in children. Although there are small-scale or single-center regional serological studies about the causative agents of AM in our country, there is not an enteroviral AM surveillance in Turkey.

Aim: In the present study, we show the frequency of enteroviral AM in Turkey from May 2006 to January 2009.

Methods: Cerebrospinal fluid (CSF) samples were collected from patients with suspected meningitis from 40 centers in Turkey. A total of 1,193 CSF samples that were negative by bacteriological culture and PCR were enrolled in the study. Enteroviral RNA was detected in CSF by reverse transcription-PCR and specific genotypes of enteroviruses were identified by direct DNA sequencing of the VP1 region.

Results: Enteroviruses were detected in 13 (1%) of 1,193 CSF specimens analyzed. Identified enteroviruses were echovirus 14 (1), echovirus 9 (1), coxsackievirus B 4 (1), and unknown serotype (8). The patients' ages ranged from 1 month to 126 months. Frequency of symptoms and findings were as follows; fever (69%), nuchal rigidity (38.5%), Kernig sign (23.1%), Brudzinski sign (23.1%) lethargy (23%), rash (15.4%), and focal neurologic signs (7.7%).

Conclusion: In CSF samples collected over a period of about 3 years, the frequency of enterovirus detection was lower than expected. To the best of our knowledge, this is the first surveillance for enteroviruses associated with AM in Turkey.

P942

DOUBLE TROUBLE: DISSEMINATED HSV2 INFECTION IN BOTH MOTHER AND NEONATE

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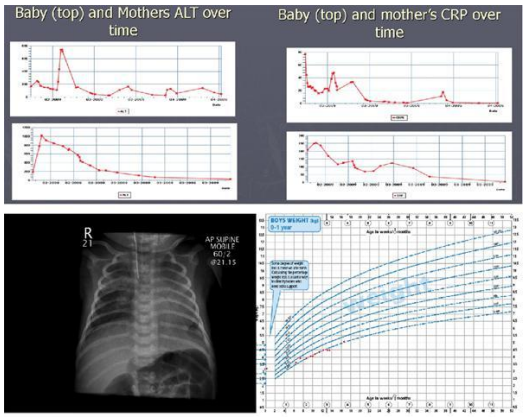
A 25 year old primigravida with no antenatal history of genital herpes or herpes contacts, as well as no other infections, had a ventouse delivery with epesiotomy. The neonate appeared well initially.

On day 3 post partum, the mother developed perineal pain and fever with hepatitis and by day 6 had developed a perineal abscess which was treated with antibiotics. By day 10 she developed vesicles on her palms, soles and buttocks, but not on her genitals. She also became confused with deteriorating GCS and required intensive care treatment.

The neonate was well until day 4, where he was noted to be pale and grunting. He had a full septic screen and was empirically treated with benzylpenicillin and gentamicin for sepsis. He subsequently deteriorated and required mechanical ventilation with inotropic support. On day 5 seizure activity was noted and cefotaxime and aciclovir were added. He developed acute hepatitis with coagulopathy and an ALT over 3000. He required transfer to a tertiary liver unit for ongoing management.

CSF PCR for mother and baby were both negative for HSV 1 and 2. Vesicle swabs and blood PCR from mother and baby´s eye and skin cultured HSV2. The baby also developed a dendritic ulcer requiring topical antivirals. Mother and baby survived and baby has currently no neurological sequele.

Conclusions: Disseminated HSV in neonates is fatal without treatment and neurological sequele are dependent on CNS involvement. There are few studies reviewing long term suppressive treatment with aciclovir to prevent relapses in HSV2.



[Figure]

P943

THE VICISSITUDES OF VIRUSES CAUSING ACUTE GASTROENTERITIS IN CHILDREN IN NORTHERN TAIWAN

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Backgroud and aims: This study assessed viral etiologies of acute gastroenteritis (AGE) in children hospitalized in Chang Gung Children's Hospital, Taiwan before and after the launch of rotavirus vaccine from April 2004 to March 2010.

Methods: Fecal samples from 678 patients (80.9% of the patients, ≤ 5 years of age) with AGE were collected, and reverse transcription-polymerase chain reaction (RT-PCR) or PCR and enzyme-linked immunosorbent assay (ELISA) were used to identify viral pathogens. Rotavirus vaccines were launched in 2006 in Taiwan; thus the study period was divided into pre-vaccine (2004 March to 2006 September) and post-vaccine (2006 October to 2010 March) periods. The prevalence of enteric viruses between the two periods is statistically analyzed.

Results: A total of 678 stool samples were collected and enteric pathogens were identified in 532 (78.5 %) of the patients, including 39 patients with concomitant bacterial infection. Infections by rotavirus, norovirus, astrovirus, sapovirus, enteric adenovirus, and multiple viruses were found in 29.1%, 15.6%, 3.4%, 0.9%, 10.2 %, and 13.6% patients, respectively. Comparison of the prevalence of each viral infection in pre-vaccine and post-vaccine periods are: rotavirus, 27.8% vs 30.5% (p=0.439); norovirus, 11.0% vs 20.6% (p=0.001); astrovirus, 2.3% vs 4.3% (p=0.091); sapovirus, 0 vs 1.7%; enteric adenovirus, 14.7% vs 5.2% (p< 0.0001); and multiple viruses, 16.1% vs 10.8% (p=0.041).

Conclusions: This study showed a decreasing trend of enteric adenovirus infection and multiple viral infection and an increasing trend of norovirus infection after the launch of rotavirus vaccines in Taiwan.

P944

SEASONALITY AND RATES OF HOSPITALIZATION FOR RESPIRATORY SYNCYTIAL VIRUS INFECTION AMONG SOUTHEASTERN BRAZILIAN CHILDREN

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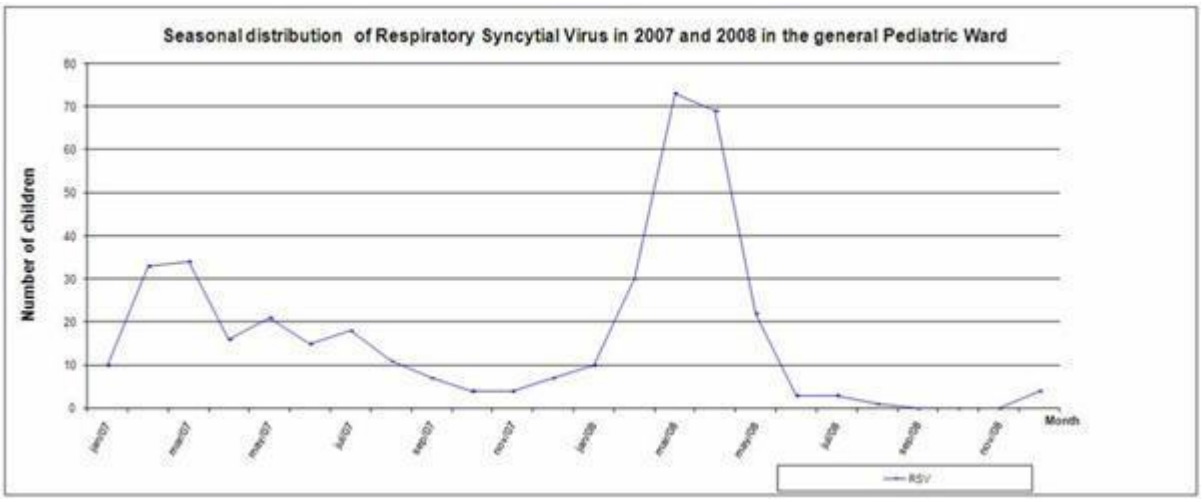
Background and aims: Respiratory syncytial virus (RSV) are the main cause of lower respiratory tract infection (LRTI) hospitalization reported worldwide. Reports from Brazilian cities are rare. The aim of this study was to identify the prevalence and seasonality of RSV in children hospitalized with LRTI and to determine their contribution to hospital admissions.

Methods: Children younger than 15 years of age, with the admission diagnosis of LRTI, at the "Hospital Universitário da Universidade de São Paulo", São Paulo, Brazil, were eligible for study, from January 2007 through December 2008. A nasal wash specimen for virus identification by indirect immunofluorescent assay was obtained after admission.

Results: Of 1583 children hospitalized for LRTI, RSV had a positive test in 395 (24.9%); 112 children were admitted to the intensive care unit (ICU). In both years, RSV activity increased in intensity during February, peaked during March (autumn), and waned during the winter months.



[Seasonal distribution of RSV]

Of the subjects included in the study, 80.3% were younger than 1 year of age, with similar distribution for males and females (1:0.79). The mean number of hospital days was 8.5. Overall 237 children had blood cultures performed; one of them had a pathogen isolated (*Haemophilus influenzae*). No child died among RSV positive case.

Conclusions: RSV are responsible for at least 24.9% of LRTI requiring hospitalization and are often severe, requiring admission to the ICU. Strategies for RSV prophylaxis in at risk children should consider results of local RSV seasonality.

P945

PEDIATRIC HOSPITAL ADMISSIONS DUE TO INFLUENZA A (H1N1) BEFORE AND AFTER THE 2010 VACCINATION CAMPAIGN IN BRAZIL

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Paediatrics, Federal University of Sao Paulo, Sao Paulo, Brazil

Background and aims: In 2009, influenza A (H1N1) strain spread rapidly around the world causing the first pandemic of XXI century. In 2010, there was a vaccination campaign against this new virus subtype aiming to reduce the morbidity and mortality of the disease in some countries like Brazil. Herein, we describe the clinical and epidemiological characteristics of patients < 19 years hospitalized with confirmed influenza A (H1N1) infection in 2009 and 2010.

Methodology: We retrospectively revised files from pediatric patients admitted to a university hospital with RT-PCR confirmed influenza A (H1N1) infection in 2009 and 2010.

Results: There were 37 hospitalized patients with influenza A (H1N1) in 2009 and 2 in 2010. In 2009, hospitalized children had more chronic disease (78%*x*31%;p< 0.001) and lower median age (4.9y*x*10.0y;p< 0.001) than those not hospitalized. Among the hospitalized patients, 78% had chronic disease, mostly pneumopathy (48%). The main signs and symptoms were fever (97%), cough (76%), dyspnea (59%). Complications occurred in 81% patients: acute respiratory failure (51%) and pneumonia (49%). The median length of hospitalization was 5 days, 27% required intensive care and 2 died. In 2010, 2 patients were hospitalized with influenza A (H1N1): one infant with adenovirus coinfection with one previous H1N1 vaccine dose who had respiratory sequelae and a 2 month-old with hospital-acquired infection.

Conclusion: Pediatric influenza A (H1N1) hospital admissions in 2009 were characterized by underlying chronic disease and young age. An impressive reduction in hospital admissions was observed in 2010, when the vaccination campaign took place in Brazil.

P946

PEDIATRIC HOSPITAL ADMISSIONS DUE TO INFLUENZA A (H1N1) BEFORE AND AFTER THE 2010 VACCINATION CAMPAIGN IN BRAZIL

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Conclusion: Pediatric influenza A (H1N1) hospital admissions in 2009 were characterized by underlying chronic disease and young age. An impressive reduction in hospital admissions was observed in 2010, when the vaccination campaign took place in Brazil.

P947

ISOLATION AND SEROTYPING OF ENTEROVIRUSES IN UNDER 14 YEARS ASEPTIC MENINGITIS PATIENTS ON HELA AND GMK2 CELL LINES

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This study was performed on 266 children under 14 years of age, presenting aseptic meningitis clinical symptoms. The role of enteroviruses in causing aseptic meningitis was evaluated in these samples. Then the serotyping of isolated viruses was done. These patients visited Bahrami, Emam Hossein, Shohada, Mofeed, Tehran children, Ali Asghar, Emam Khomeini, and Takhty hospitals. Questionnaires were completed and CSF specimens were transferred to Pasteur Institute of Iran in order to isolate viruses. The samples were cultured on HeLa and GMK2 cell lines and virus identification was done by L.B.M pooled antisera. In 15% of the patient presenting with clinical symptoms of aseptic meningitis, enterovirus was isolated. The patients were mostly younger than 1 year of age (42.5%) and were diagnosed during the summer (50%). There was a statistically significant correlation between season and enterovirus isolation ($p< 0.005$) and also between summer and other season in causing enteroviral and nonenteroviral aseptic meningitis ($p< 0.001$). Enteroviruses isolated in this study consisted of Coxsackie B group serotypes B5 (95%) and B4 (5%).

P948

GUILLAIN BARRE SYNDROME AND CEREBELLITIS FOLLOWING PRIMARY VARICELLA ZOSTER INFECTION IN A YOUNG IMMUNOCOMPETENT GIRL: A CASE REPORT

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Chicken pox (primary varicella zoster infection) is generally a mild and self-limiting illness amongst immunocompetent children. It has a peak incidence between the age of 1-4 and by age 5 around 75% of UK children have been infected.

Severe complications can occur however even in previously healthy children. Secondary bacterial infections are the commonest complication followed by neurological complications. Acute cerebellar ataxia occurs in about 1 in 4000 cases of varicella infection. Other less common complications include varicella encephalitis, aseptic meningitis, transverse myelitis, transient focal deficits and hemiplegia.

We report the case of a previously healthy 3-year-old girl, who presented with vomiting and acute ataxia 3 weeks post chicken pox infection. Over her admission she developed progressive ataxia, hypotonia, weakness and areflexia in upper and lower limbs. She also had a sinus bradycardia and urinary incontinence and later developed a bulbar palsy and shallow respiration . MRI brain was normal, lumbar puncture revealed a WCC of 11 (all lymphocytes,) with a normal protein and glucose.

Nerve conduction studies conducted at the tertiary neurology unit suggested Guillain Barre Syndrome in addition to Varicella Cerebellitis. She received intravenous immunoglobulin, made a good recovery and was discharged home 10 days later.

Whilst Guillain Barre Syndrome has been described previously in the context of varicella zoster infection, it is rare and most cases have been following reactivation in adults, as opposed to primary infection. We present a discussion of the neurological complications of primary varicella zoster, and its association with Guillain Barre Syndrome.

P949

ROLE OF INFECTIOUS AGENTS IN CHILDREN WITH COCHLEAR IMPLANT

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[1]Research Center of Pediatric Infectious, [2]Research Center for Diseases of Ear, Nose, Throat, Iran University of Medical Sciences, Tehran, Iran

Objective: To determine the role of infectious agents by serology& CMV/HSV-DNAs (PCR) in perilymphatic fluid of Idiopathic SNHL chidren with a cochlear implant.

Methods and materials:This cross sectional study was done in the cochlear implant center of the Rasul Hospital in Tehran (2006-2008) upon 108 cases. Idiopathic SNHL diagnoded in 15% (18/ 119) cases. During cochlear implantation surgery, perilymphatic fluid obtained and reserved in sterile microtubes , DNA extracted in all samples and searched for CMV/HSV-DNAs (Real time PCR).In deed adequate serum of 11cases searched for specific antibodies against CMV, Toxoplasma, HSV-1, Rubella .

Results: CMV- DNAs was positive in 11% (2/18); HSV -DNAs in 5.5%(1/18) of Idiopathic SNHL chidren .Positive CMV and HSV antibodies(IgG) detected in 100% ;positive T.Gondii-IgM in 63%;positive Rubella -IgG 10% (1 /11) of Idiopathic SNHLcases .

Conclusion:

In addition to known and proven other post natally infectious diseases in most SNHL cases ; We observed proven active infections (positive DNA-PCR which confirmed by serology) for CMV and HSV infection in 10% ;5.5% of Idiopathic SNHL cases. Acute T.Gondii infection (only serologicaly) was common (63%)in Idiopathic SNHL cases.Those 3 common indulent infections may acquired intrauterine or in post natal period.We recommend rapid diagnosis and suitable treatment of the indulent infections in SNHL children to decrease needing the cochlear implantation surgery.A neonatal screening program (in dried blood spots on Guthrie cards) might be helpful to detect the 3 common infections (;CMV /HSV/T.Gondii) in our country.

P950

CHARACTERISTICS OF PANDEMIC INFLUENZA A (H1N1V) INFECTION AMONG THE CHILDREN IN ISPARTA

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[1]Department of Paediatrics, [2]Department of Infectious Diseases, Suleyman Demirel University Faculty of Medicine, Isparta, Turkey

Background and aims: Influenza virus is the etiologic reason for seasonal flu, avian flu and swine flu. As a result of mutations, influenza virus acquires more invasive and contagious characteristics. In April 2009, World Health Organization defined a pandemic influenza A virus (H1N1v) which caused a global pandemic starting from Mexico and America. WHO declared “stage 6”, the highest level of pandemia warning. Our study evaluates the patients who are admitted to a University Hospital Pediatric Department with the pre-diognosis was H1N1v.

Methods: Demographic characteristics, clinical findings, laboratory results and radiological findings of 64 patients, who are admitted with the pre-diagnosis of H1N1v were analyzed and evaluated retrospectively. The nasopharyngeal specimens were confirmed in National Reference Laboratory for H1N1v.

Results: The avarage age of the patients was 32,4 months (1-188 months) and 22 of them (%38) were female cases. Nine of the cases (%14) were confirmed as H1N1v. Most common complaints were establihed cough (%85.9), fever (%65) and respiratory distress (%44). There was no significant difference between the laboratory test results (C-reactive protein, WBC number, Biochemical results) of H1N1v positive and negative groups. Five of the (%55) H1N1v positive pediatric patients had pre-existing diseases. Five patients needed intensive care during the observation and treatment. Two (%22.2) of them didn't survive.

Conclusion: Clinical findings of pandemical influenza and seasonal influenza were quite similar in pediatric age group. Pre-existing diseases increase the rates of morbidity and mortality

P951

MYOCARDITIS - UNUSUAL PRESENTATION OF CMV INFECTION

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Background and aims: Cytomegalovirus (CMV) infections are often asymptomatic or cause mild disease. However, the virus can cause serious complications such as myopericarditis. The authors present a case report of a 3 months old girl who presented with myocarditis due to CMV infection.

Methods: SAA, born at 36 weeks, with a past medical history of suspected type one nephrocalcinosis.

Results: She was brought to the emergency department (ED) with a 3-week history of difficulty in breastfeeding, a noisy breathing and one episode of cyanosis. Fever was denied. In the ED she presented respiratory distress, hepatomegaly, diminished heart sounds and intermittent gallop rhythm, with no murmur. No hypoxemia or fever were detected. The chest radiograph showed cardiomegaly and pulmonary vascular congestion. Complete blood count was normal, C-reactive protein negative and B-type natriuretic peptide was 17789 pg/ml. Echocardiogram demonstrated dilated cardiomyopathy with increased left ventricular dimensions, mild mitral regurgitation and an ejection fraction < 40%, no pericardial effusion.

CMV polymerase chain reaction (PCR) was positive in blood, urine and respiratory secretions, but negative in Guthrie´s card, as part of neonatal screen. Ganciclovir was initiated at 10 mg/kg/day for 14 days, following a maintenance therapy of a single daily dose of 5 mg/kg for a total of 23 days.

HIV was negative, lymphocyte populations, immunoglobulins, ammonia and lactate were normal. No retinitis. Head ultrasound had no alterations.

Two months after diagnosis CMV PCR in blood was negative and the ejection fraction was 51%.

Conclusions: Increased awareness of CMV infection complications is needed.

P952

PRELIMINARY ASSESSMENT OF THE EFFECTIVENESS OF HEPATITIS B PREVENTION IN CHILDREN WITH MATERNAL EXPOSURE

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Background and aims: In Poland, young women are 10 to 20 times more likely to have been exposed to HBV in early childhood. We have evaluated of the effectiveness of prevention HBV infection in children of women HBsAg positive.

Methods: 67 children (32 girls) of mothers HBsAg-positive from which 20 were infected during childhood. In the other 47 HBV was detected not later than in pregnancy. None of them had acute hepatitis B. HBV DNA was detect in 20 (12 copies/ml to over 580million copies/ml), HBe antigen in 3. Three out of 67 were treated in childhood(interferon, lamivudine or encorton).

67 children were vaccinated against hepatitis-B in the first day of life, 59 of them with HBIG.

Results: HBV DNA was detected only once in 9 children:7 between the 2nd and 4th month of life, 1 in the 6th and 1 in the 5th. The last patient was diagnosed with acute hepatitis-B.

HBs antigen was found in 1 child (1.5%) with acute viral hepatitis; HBe antigen in 3: 1 with acute hepatitis-B, 1 in the 2nd month of life and 1 in the 2nd and 3rd month. In neither of the last two children HBV infections were confirmed nor HBV DNA in further studies .

66 children (98.5%) produced Anti HBs: 3 to 10 IU/L and 6 above1000 IU /L

Conclusions: 1. Prevention of hepatitis B in children from maternal exposure is effective.

Maternal transmission of HBV infection is possible despite using prophylaxis, although the risk is low.

P953

HISTOPATHOLOGICAL FEATURES IN LIVER BIOPTATES AS A MARKER OF DISEASE PROGRESSION IN CHILDREN WITH CHRONIC VIRAL HEPATITIS

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Chronic viral hepatitis in children has usually asymptomatic course. Evaluation of liver bioptates may be the only method of revealing disease progression. Aim of the study was to analyze histopathological features in children with chronic viral B and C hepatitis.

Material and methods: Liver bioptates of 70 children (29 girls, 41 boys aged 5-17 years; 34 infected with HBV, 27 with HCV, 9 with HBV/HCV co-infection) were evaluated histopathologically according to modified Knodell numerical scoring system. Inflammatory activity (grading-G) and fibrosis (staging-S) were analyzed according to age, gender and type of infection.

Results: Minimal grading (0-3 points) was found in 16/70 (23%), mediocre (4-8) in 43/70 (61%), moderate (9-12) in 9/70 (13%) and high (13) in 2/70 (3%). Grading did not correlate with gender, age, nor type of infection. No fibrosis (S 0) was revealed in 7/70 (10%), minimal staging (1) - in 27/70 (39%), moderate (2) in 27/70 (39%), advanced (3) in 8/70 (11%). Cirrhosis (S4) was found in 1/70 (1%). Staging did not correlate with gender nor type of infection, whereas it increased with age (data on the border of statistical significance: p=0.06). Piecemeal necrosis was observed in 37/70 (53%), lymphadenoplasia in 26/70 (37%), steatosis in 12/70 (17%) and bridging necrosis in 15/70 (21%) of patients. None of these abnormalities correlated with age, gender nor type of infection.

Conclusion: Chronic viral hepatitis may lead to advanced inflammatory and fibrotic changes in the liver regardless of type of infection, gender and age. Fibrosis may increase with age.

P954

MOLECULAR AND CLINICAL CHARACTERIZATION OF ROTAVIRUS FROM DIARRHEAL INFANTS ADMITTED TO PEDIATRIC EMERGENY UNITS IN FRANCE, 2006-2010

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Background and aims: Rotaviruses are the major cause of acute gastroenteritis in young children worldwide, and require careful surveillance, especially in the context of vaccination programs (current vaccination coverage is under 10% in France). Prospective surveillance is required to monitor and characterize rotavirus infections, including viral and clinical data, and to detect the emergence of potentially epidemic strains.

Methods: Between 2006 and 2010, stool samples and clinical records were collected form 2727 children under 5 years old with acute diarrhea admitted to the pediatric emergency units of 15 French large public hospitals. Rotaviruses were detected, then genotyped by RT-PCR for P (VP4) and G (VP7) types.

Results: The genotyping of 2630 rotaviruses showed that G1 strains (62.9%) were predominant, G9 (23.0%) were decreasing, G2 (9.1%) were very changing, and G3 (4.1%) and G4 (2.5%) circulated locally. Most strains were associated with P[8] (91.2%). Overall, 63 uncommon strains or possible zoonotic reassortants were detected including G12 and G8 rotaviruses, some being closely related to bovine strains. No difference in clinical presentation and severity was found among genotypes.

Conclusions: In spite of the fluctuation of G2 strains, the relative stability of rotavirus genotypes detected in France may ensure vaccine effectiveness in the short and medium terms. Moreover, the likely emergence of G12 and G8 strains should be monitored during ongoing and future vaccination programs, especially as all genotypes can cause severe infections. Special attention should be paid to the emergence of new rotavirus reassortants not included in current rotavirus vaccines.

P955

VIRAL ETIOLOGY OF BRONCHIOLITIS AND INFECTIOUS ASTHMA AMONG HOSPITALIZED CHILDREN, SOUTHERN IRAN

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Introduction and objectives: This study designed to determines the role of respiratory viruses in bronchiolitis and infectious asthma in hospitalized children in Shiraz.

Materials and methods: From October 2006 to April 2007, we prospectively enrolled 140 patients 1 months of age to 16 years old hospitalized for acute wheezing in two teachig hospitals, affiliated to Shiraz University of Medical Sciences. The detection of common respiratory viruses (respiratory syncytial virus, influenza virus A and B, parainfluenza virus 1, 2, 3 and adenovirus) was performed using classical immunofluorescence antigen and cell-culture detection assays on nasal aspirates, whereas the detection of rhinovirus and/or enterovirus was assessed by a multiplex RT-PCR detection assay.

Results: Fifty eight patients have been diagnosed as bronchiolitis, 75 patients as asthma and 7 patients undetermined diagnosis. A potential causative viral agent was detected in 41 (29.3%) of the cases. RSV (17%) and parainfluenza viruses (6.4%), rhinovirus (2.9%), adenoviruses (2%) and influenza B combined with RSV (1%) were the causative agents, resulting in about 57%, 24%, 9.5%, 9.5% and 0% of 41 virus-positive bronchiolitis cases, respectively.

Conclusion: RSV have been the most common cause of bronchioloitis and infectious asthma occurring in children which strongly suggests the identical nature of infection-related wheezing episodes occurring in children of different ages.

P956

CHICKENPOX AND HENOCH-SCHÖNLEIN PURPURA - A DIAGNOSTIC CHALLENGE

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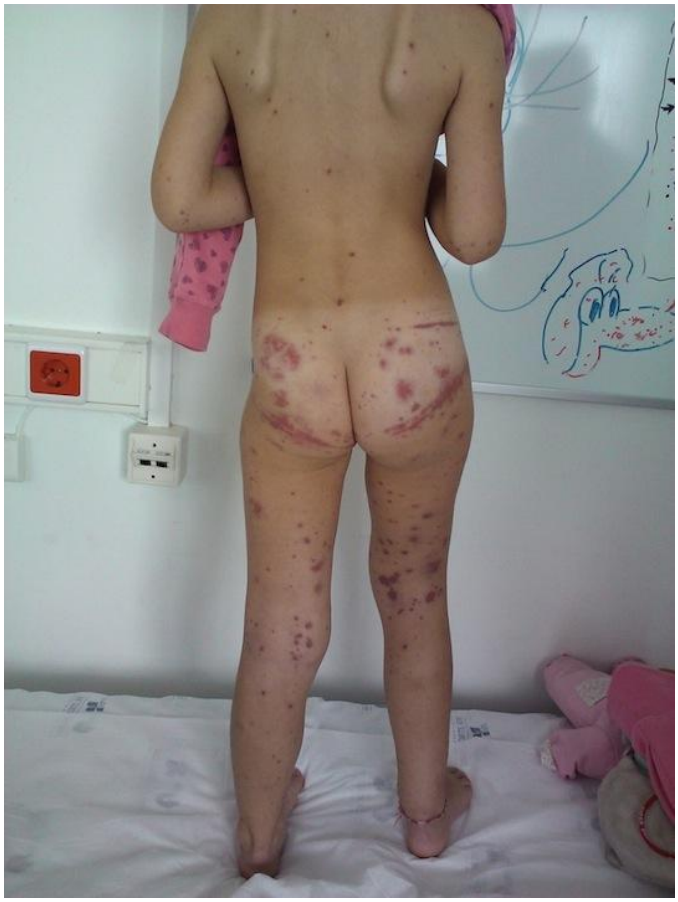
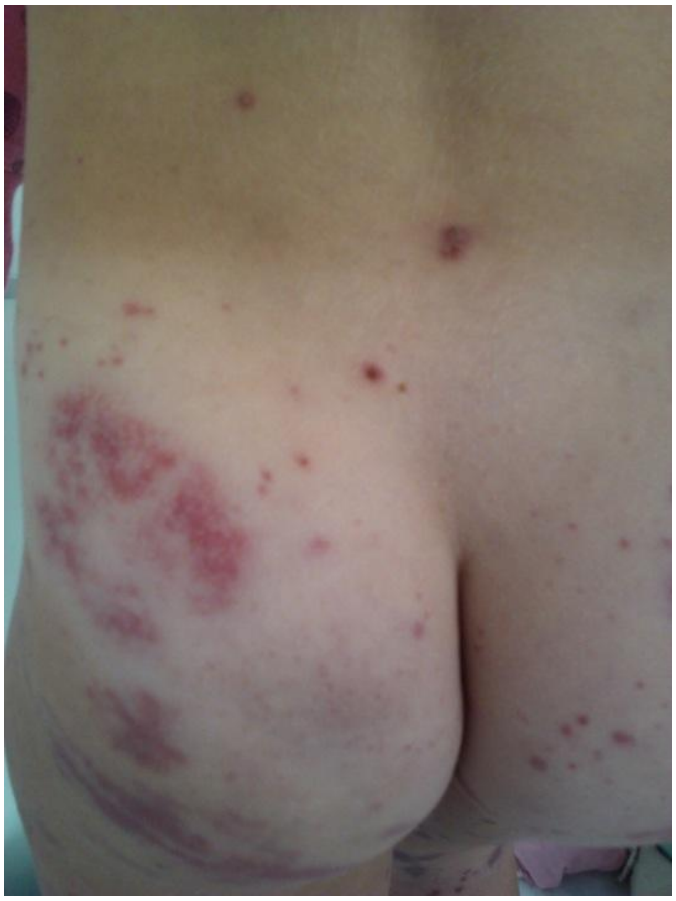
Background and aims: Henoch-Schönlein Purpura (HSP), one of the most common vasculitis in children, is characterized by a non-thrombocytopenic palpable purpura, as well as arthralgias, gastrointestinal symptoms and glomerulonephritis in some cases. HSP is caused by deposition of immune complexes in small arteries and possible inciting antigens include upper respiratory viral infections, drugs or food. In the majority of cases the etiology is unknown. Some authors describe an association with Varicella Zoster infection as a "trigger".

Clinical case: We present a case of a 6 year old girl, with palpable purpura, diagnosed as HSP. On the 2nd day of symptoms, pustules and vesicles emerged, combined with purpura (graph 1 and 2). During the clinical follow-up, the diagnosis of chickenpox and HSP was made simultaneously. Both entities had a favourable evolution, with no complications.



[skin lesions]



[skin lesions]

Conclusions: Lesions of chickenpox and HSP can present simultaneously, making the differential diagnosis a problem. At the same moment, the patient had purpura diffused in the lower extremities (buttocks and legs) and vesicular hemorrhagic lesions and pustules in the back, arms and neck. As described in the literature, we would like to suggest the role of varicella-zoster virus as a trigger, in the etiopathogenesis of HSP.

P957

PERSISTENT OXYGEN DEPENDENCY IN PRETERM NEWBORN: BEYOND BRONCHOPULMONARY DYSPLASIA

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Background and aims: There is variability in the outcome of bronchopulmonary dysplasia of comparable severity. Coexisting respiratory tract infections are expected to contribute to this variability. To identify infectious agents implicated for inducing changes similar to or prolonging morbidity due to bronchopulmonary dysplasia in preterm newborns.

Methods: Describing the clinical course of a newborn with CMV pneumonitis presenting clinically and radiologically as BPD. Literature search to identify the possible other infectious agents presenting as or prolonging the morbidity due to BPD.

Results: A 32 week preterm female weighing 1260 grams at birth. The mother had received 2 doses of antenatal steroids. During first 3 weeks of life baby was managed for multiple problems viz. E Coli sepsis requiring antimicrobials and inotropic support, congenital pneumonia requiring mechanical ventilation, anemia requiring multiple packed red cell transfusions and patent ductus arteriosus. Diagnosed as BPD due to persisting oxygen dependence after 28 days of life. Further investigations revealed positive serological markers for CMV as well as DNA PCR in urine. The baby was showed clinical improvement and resolution of reticular infiltrates on CT scan chest after 6 weeks of gancyclovir therapy.

Search of literature revealed reports of similar presentation of few other infectious agents prolonging the course of BPD: Gram negative bacilli, Gram positive cocci, Respiratory syncitial virus, Adenovirus, Ureaplasma Urealyticum.

Conclusion: Atypical presentation and persistent respiratory distress warrants ruling out coexisting respiratory tract infections like CMV as timely diagnosis and treatment can tremendously alter morbidity and cost of therapy in these babies.

P958

INTRATHECAL ANTIBODY (IGG) PRODUCTION AGAINST HHV6 IN IRANIAN PAEDIATRIC MULTIPLE SCLEROSIS (PMS)

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Background and aims: Paediatric multiple sclerosis (PMS) has long been regarded as a very rare disease, but in Iran there is emerging evidence that up to 15% of MS cases manifest in childhood and adolescence. As infectious agents may play a significant role in MS pathogenesis, we evaluated the intrathecal immune response against HHV6 (Beta-herpesvirus) in PMS.

Methods: A total of 35 paired serum and CSF samples [12 children with relapsing-remitting MS (PMS-RR), 4 children with primary-progressive MS (PMS-PP), and 19 age and sex matched children with other neurological disorders (OND)] were included in the study. Samples were tested with an ELISA method for anti-HHV6 IgG concentration, and the specific antibody index (AI) was calculated. A corrected AI greater than 1.5 was taken as evidence for intrathecal IgG production against HHV6.

Results: The seroprevalence of anti-HHV6 IgG was higher in PMS (87.5%) in contrast with OND (42.1%) (P=0.0125). HHV6 specific IgG was detected in the CSF of 37.5% of the PMS, but in only 5.26% of the OND (P=0.0318). About 37.5% of PMS patients showed an intrathecal IgG production against HHV6 versus none of the OND (P=0.0049). The HHV6 specific AIs of these patients ranged from 1.9-4.2 with a mean of 2.5.

Conclusions: PMS patients had a significantly higher intrathecal antibody against HHV6 than their OND. Our findings argue that in the majority of PMS patients with an intrathecal Ig response to HHV6, this virus is involved in the pathogenesis and disease progression might reflect reactivation of HHV6.

P959

YOUNG ADULTS ASTHMA AFTER HOSPITALIZATION FOR VIRAL BRONCHIOLITIS IN INFANCY

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Background: Wheezing in infancy increases the risk of subsequent wheezing and later asthma. The aim of the present study was to evaluate the risk of asthma in young adults after hospitalization for viral bronchiolitis in infancy.

Methods: At the median age of 16.5 years (range 15.1-18.1), a questionnaire was sent to 96 study subjects who had been hospitalized for bronchiolitis at < 24 months of age and since then prospectively followed up, and 67(70%) of them answered. RSV and rhinovirus etiology of bronchiolitis had been studied during hospitalization in infancy. The occurrence of doctor-diagnosed and self-reported asthma was compared between former bronchiolitis patients and non-selected population controls who were recruited for this study in young adulthood.

Results: Doctor-diagnosed asthma was present in 30% of the former bronchiolitis patients and 5% of the controls (OR 7.9, 95% CI 3.3-19.3). The respective figures for current self-reported asthma were 64% and 11% (OR 14.7, 95% CI 7.2-30.0). Asthma in parents was associated significantly with both current doctor-diagnosed and self-reported asthma. Current self-reported asthma was more common in the former non-RSV (73.3%; p=0.04) than in RSV patients (47.6%), but the difference between the former rhinovirus (73.3%) and non-rhinovirus patients (61.8%) was not statistical significant.

Conclusion: Hospitalization for bronchiolitis at < 24 months of age increase asthma risk in young adulthood, and asthma in parents is a strong asthma predictive factor. Both RSV and rhinovirus bronchiolitis increase the asthma risk compared with population controls but non-RSV and rhinovirus bronchiolitis seem to have a greater impact.

P960

INTRATHECAL ANTIBODY (IGG) PRODUCTION AGAINST EBV IN IRANIAN PAEDIATRIC MULTIPLE SCLEROSIS (PMS)

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Background and aims: Pediatric multiple sclerosis (PMS) has long been regarded as a very rare disease, but in Iran there is emerging evidence that up to 15% of MS cases manifest in childhood and adolescence. As infectious agents may play a significant role in MS pathogenesis, we evaluated the intrathecal immune response against EBV (Gamma-herpesvirus) in PMS.

Methods: A total of 35 paired serum and CSF samples [12 children with relapsing-remitting MS (PMS-RR), 4 children with primary-progressive MS (PMS-PP), and 19 age and sex matched children with other neurological disorders (OND)] were included in the study. Samples were tested with an ELISA method for anti-EBV IgG concentration, and the specific antibody index (AI) was calculated. A corrected AI greater than 1.5 was taken as evidence for intrathecal IgG production against EBV.

Results: The intrathecal IgG production against EBV was approximately higher in PMS (25%) in contrast with OND (10.5%) (P=0.3791). About 75% of PMS patients showed a seropositivity for anti-EBV IgG versus 47.3% in the OND (P=0.1662). EBV specific IgG was detected in the CSF of 37.5% of the PMS, but in only 10.5% of the OND (P =0.1054). The EBV specific AIs of these patients ranged from 2.9-5.6 with a mean of 3.7.

Conclusions: PMS patients had a relatively higher intrathecal antibody against EBV than their OND but it was not statically significant. Our findings argue that EBV might have not a critical role in the pathogenesis of MS in children at least in this population.

P961

HEMATOLOGICAL ADVERSE EVENTS DURING THERAPY OF CHRONIC HEPATITIS C IN CHILDREN AS A PREDICTORS OF A SUSTAINED VIRAL RESPONSE

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Background: Treatment with IFN and ribavirin is associated with adverse events, limited patient´s adherence and treatment efficacy. The aim of the study was assessing the dependences between kinetics of haematological exponents during CHC treatment and SVR.

Patients and methods: 170 children with CHC divided into two groups: 48-week course of recombinant interferon alfa-2b 3 MU 3 times a week and ribavirin 15 mg/kg/day (group 1, n=119) and children received pegylated interferon alfa-2b 1.5 µg/kg/week and ribavirin 15 mg/kg/day for 48 weeks (group 2, n=51).

Serum HCV RNA by PCR assay (COBAS® AmpliPrep/COBAS TaqMan® HCV Test , HCV genotypes using the INNOGENETICS INNO-LiPA HCV II test, hematological exponents with Sysmex 4500 were evaluated.

Results: SVR achieved 86/170 patients, 62/119 from group 1 and 24/51 from group 2.

The mean levels of serum hemoglobin, leukocytes and platelets counts were statistically significantly lower in week 12 versus baseline in responders and in non-responders from both groups ($p < 0.05$) In children treated with PEGIFN and ribavirin the serum hemoglobin levels in week 12 were lower in responders than in non-responders ($p < 0.05$).

The leukocytes counts in week 12 were statistically significantly lower in children from group 2 than in group 1 ($p < 0.05$), platelets count in week 12 was lower in responders from group 2 than in responders from group 1.

Conclusions: Mild decrease of hemoglobin levels, leukocytes and platelets counts during treatment with IFN and ribavirin of chronic hepatitis C in children may constitute the factors of achieving sustained virologic response.

P962

EPIDEMIOLOGY OF GASTROINTESTINAL INFECTIONS IN CHILDREN HOSPITALIZED IN THE DEPARTMENT OF PEDIATRICS AT WARSAW BIELANSKI HOSPITAL;2006-2010(*) *

MCPE GRANT 501-1-20-34/10

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Background and aims: Rotavirus is still the most common cause of acute gastroenteritis and principal cause of nosocomial gastrointestinal infections (NGI). Vaccination, abidance of hand-washing, individual isolation of infected patients, hygienic and room conditions of the ward, better accessibility of diagnostic methods have an impact on epidemiology of gastroenteritis in children. Defining the etiology of community acquired and NGI in hospitalized children; 2006-2010, seasonality of infections, assessment of the correlation with respect to age and gender, valuation of implemented preventive measures.

Methods: We reviewed 1722 cases with gastroenteritis symptoms-17,5% of all admissions. In those cases stool was examined for microbial culture, rotavirus, adenovirus and additionally norovirus antigen since march 2009.

Results: Etiology was found in 885 of 1722 respondents-51%. Majority of these were children 6-24 months of age-47%. Child´s gender had no effect on the incidence of gastroenteritis (51%-boys, 49%-girls). We observed shift of peak incidence in the direction of the spring months (March-2006, April-2009). The most common cause of gastroenteritis was viral infection (rotaviral-70%, noroviral-7%, adenoviral-6%). Bacterial etiology: Salmonella-12% (2010-21%), Yersinia enterocolitica-2%, Escherichia coli-EPEC-2.5%. We noted a gradual decrease of rotavirus infections (RVI)-50% in 2010, also in nosocomial RVI (63%-2006, 40%-2010). Among all respondents, NGI occurred in 20%. We observe a slight reduction of NGI (2006-23%, 2007-21%, 2008-24%, 2009-19%, 2010-17%).

Conclusions: The results indicate the gradual decrease of RVI. The epidemiology of gastroenteritis is changing constantly. In 2010, in contrast to previous years, the second most common etiology was Salmonella. We still find a high percentage of NGI.

P963

EPIDEMIOLOGY OF GASTROINTESTINAL INFECTIONS IN CHILDREN HOSPITALIZED IN THE DEPARTMENT OF PEDIATRICS AT WARSAW BIELANSKI HOSPITAL;2006-2010(*) *MCPE GRANT 501-1-20-34/10*

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Background and aims: Rotavirus is still the most common cause of acute gastroenteritis and principal cause of nosocomial gastrointestinal infections (NGI). Vaccination, abidance of hand-washing, individual isolation of infected patients, hygienic and room conditions of the ward, better accessibility of diagnostic methods have an impact on epidemiology of gastroenteritis in children. Defining the etiology of community acquired and NGI in hospitalized children; 2006-2010, seasonality of infections, assessment of the correlation with respect to age and gender, valuation of implemented preventive measures.

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Conclusions: The results indicate the gradual decrease of RVI. The epidemiology of gastroenteritis is changing constantly. In 2010, in contrast to previous years, the second most common etiology was Salmonella. We still find a high percentage of NGI.

P964

PREVALENCE OF HIV INFECTION IN THALASSEMIC PATIENTS IN FASA, IRAN, 2010

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Background: Thalassemic patients are high risk group to humanimmunodeficiency virus (HIV) infection due to repeated transfusions.

Objectives: 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, onMay 2008.

Results: No cases of HIV were found. The prevalence of HIV infection in the thalassemic patients of Fasa 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.

P965

SEROPREVALENCE OF HEPATITIS E VIRUS AMONG B-THALASSEMIC PATIENTS

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The hepatitis E virus (HEV) has a global distribution and is known to have caused large waterborne epidemics of icteric hepatitis. Transmission is generally via the fecal-oral route. Some reports have suggested parenteral transmission of HEV. There are not prevalence data of HEV among β-thalassemic patients in IRAN. The aim of this study was to determine the prevalence of anti-HEV antibodies in β-thalassemic patients in west-southern of Iran.

Methods: This descriptive and cross-sectional study was conducted in March of 2008. We tested 110 β-thalassemic patients attending the thalassemic unit in the city of Jahrom, west-southern part of Iran, for anti-HEV IgG and IgM using enzyme-linked immunosorbent assay (ELISA).

Results: The overall seroprevalence of hepatitis E was 7.4% (95% CI: 4.6%-10.6%). No significant association was found between anti-HEV positivity and age, sex, positivity for hepatitis B or C virus infection.

Conclusion: We observed high anti-HEV antibody prevalence; there was no association between HEV and blood borne infections (HBV, HCV, and HIV) in our β-thalassemic patients.

P966

CYTOKINES IN CCHF: IS THERE A CORRELATION WITH CLINICAL PHENOTYPE IN PEDIATRIC PATIENTS?

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Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic disease that can develop into a severe hemorrhagic fever in humans. It is an endemic disease in Turkey and large outbreaks have been observed since 2002. Because of the role of treatment and poor prognosis of adult patients, identification of risk groups is essential. However the clinical course and outcome of CCHF were somehow different in children but the exact mechanism for this difference and pathogenesis is still unclear. Early variations of circulating pro- and anti-inflammatory cytokines were found to be significantly associated with the severity of CCHF in adult patients. However the relation between serum inflammatory cytokine levels and disease outcome in pediatric age group isn't clear yet.

The aim of this study is to investigate levels of interleukin (IL)-6, tumor necrosis factor (TNF)-α and IL-10 in serum samples obtained from laboratory confirmed pediatric CCHF cases who were hospitalized after tick extraction with acute febril syndrome in the 2009 and 2010 outbreak in Turkey.

Totally 18 patients with CCHF were included in our study. Only one patient had positive disseminated intravascular coagulation (DIC) scores on admission and recovered with no mortality. In the first week of the disease, mean IL-6, IL-10 and TNF-α levels were found to be 42.43 pg/mL (range, 8.98-99.97 pg/mL); 21.93 pg/mL (range, 1.08-98.71 pg/mL) and 12.87 pg/mL (range, 4.03-28.53 pg/mL)

Since serum levels of IL-6 were normal in our patients, IL-6 is considered as the significant predictor of complete response, good prognosis and survival in pediatric patients.

P967

HOSPITALIZATION OF CHILDREN WITH INFLUENZA A(H1N1) VIRUS DURING THE 2009 OUTBREAK IN NORTH VIET NAM

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Objectives: To describe the clinical characteristics of children hospitalized with 2009 influenza A(H1N1) infection in North Viet Nam and the risk factors associated with this infection.

Design: Descriptive data collection for patients with confirmed infection on children hospitalized with 2009 influenza A(H1N1) infection.

Setting: Patients around North of Viet Nam from July 29, 2009, to December 31, 2009, all patients 16 years or younger hospitalized with acute respiratory or acute unspecified febrile illness were screened for 2009 influenza A(H1N1) virus by reverse transcription-polymerase chain reaction.

Main outcome measures: Clinical, laboratory characteristics of patients.

Results: The mean age of 446 patients studied was 7.11 ± 3.47years. 6/446 patients (1.35%) were admitted to the pediatric intensive care unit; 2 patients (0.45%) died. Exposed with source of infection is 21,31%. rate the most frequent clinical presentations were influenza-like illness. Risk factors group were detected in 12,33% of patients. Patients with underlying younger than 2 years of old, heart and kidney disease were at highest risk for severe complications. Laboratories: 32,07% child with mild and light anemia. 84,14% cases with white blood cell less than 10.000/mm3. Chest X-ray: pneumonia and bronchitis: 69/229. In addition, patients required mechanical ventilation are heart and kidney disease. The hospitalization mortality rate was 0.45 %.

Conclusions: The severity variables for 2009 influenza A(H1N1) were similar to the figures reported for seasonal influenza. Patients with underlying younger than 2 years of old, heart and kidney disease are at highest risk for severe complications following 2009 influenza A(H1N1) infection.

P968

COMPARISON OF PANDEMIC (H1N1) 2009 AND SEASONAL INFLUENZA A AMONG HOSPITALIZED CHILDREN IN GREECE

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Background and aim: Limited data are available on pandemic influenza A virus infection in hospitalized children. We aimed to examine the epidemiological and clinical characteristics of those children hospitalized at a large tertiary care center, in Athens and compare them with those of children with seasonal influenza A hospitalized in previous years.

Methods: We reviewed the charts of 60 children (aged>=6months) with pandemic H1N1 influenza, between November 2009 and March 2010. We compared their data with those of 156 children admitted with seasonal influenza during three consecutive years (2002/03 to 2004/05). Nasopharyngeal aspirates were taken from all patients for laboratory diagnosis of influenza with multiple reverse transcription PCR.

Results: The age distribution was similar between seasonal and pandemic influenza (53 vs 63 months, p=0.117). There were no significant differences in risk factors and clinical presentation except from fever and abdominal pain that were more common for patients with pandemic influenza (100% vs 93%, p=0.046 and 24%vs9%, p=0.02 respectively), while cervical lymphadenitis and acute otitis media were more common in seasonal influenza patients (21%vs5%, p=0.007 and 23%vs 10%, p=0.03 respectively). Only one child from each group required admission to the ICU. The proportion of patients treated with antibiotics per.os was significantly higher among those with seasonal influenza(63% versus 33%, p< 0.001). The mean length of hospitalization was greater in the seasonal influenza group (4.4 vs 2.9 days, p=0.02).

Conclusions: Clinical manifestations were similar between pandemic and seasonal influenza; pandemic influenza did not appear to cause more severe disease among hospitalized children.

P969

COMPARISON OF PANDEMIC (H1N1) 2009 AND SEASONAL INFLUENZA A AMONG HOSPITALIZED CHILDREN IN GREECE

F. Stripeli[1], I. Logotheti[1], V.-M. Vraila[1], C. Balta[1], A. Patsioura[2], V. Papaevangelou[1], G. Syridou[1], I. Papadatos[2], **M. Tsolia**[1]

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Conclusions: Clinical manifestations were similar between pandemic and seasonal influenza; pandemic influenza did not appear to cause more severe disease among hospitalized children.

P970

CLINICAL CHARACTERISTICS AND COST BURDEN OF PATIENTS WITH INFLUENZA A (H1N1) 2009 HOSPITALISED IN A TURKISH CHILDREN'S HOSPITAL

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This study aimed to describe clinical features, complications, risk factors and cost of hospitalisation of the microbiologically confirmed cases of influenza A (H1N1) infection by comparing with influenza like disease. All cases of influenza A (H1N1) 2009 infection, confirmed microbiologically by real-time reverse transcription polymerase chain reactions.

The study was performed in infection department of a children´s hospital during November 2009 and January 2010. Hundred six patients who hospitalized with influenza A (H1N1) or influenza like diseses, were included to study retrospectively.

Mean age was 53.76±4.7 months. Mean duration of hospitalisation was 5.8±0.4 days. The most frequent symptoms were fever (91,5%) and cough (74%). Thirty two (35.6%) of patients were microbiologically confirmed as H1N1 influenza A. Patients with H1N1 infection (group 1) were compared with H1N1 negative patients (group 2). Fever and malaise were significantly more common in the first group and 30% of patients presented with wheezing. Neuromuscular disorders and chronic respiratory diseases were the most common underlying diseases in the first group. It is worthy to note that 11 patients in the H1N1 positive group presented with platelet counts< 100,000. Mean cost of hospitalization was similar in both groups (350±61,8 US$). Two patients were sent to intensive care unit and one patient died in the H1N1 positive group while no deaths were observed in the second group.

Treatment with oseltamivir was well tolerated. The incidence of severe cases and lethality of influenza A (H1N1) infection were low in our setting.

P971

CLINICAL PICTURE OF HOSPITALIZED CHILDREN WITH PANDEMIC INFLUENZA H1N1 2009

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From August 2009 to February 2010, 1633 children were attended our hospital suspected influenza like illness (ILI). Of them, 628 were positive for Influenza H1N1 2009 antigen by rapid diagnostic test or PCR. 140 children admitted due to ILI, 86 children were antigen positive. Major symptoms were categorized into four groups in both antigen positive and negative groups (p/n); respiratory symptom 50/31, neurologic symptom 21/10, others 13/12, encephalopathy 2/1. Neurologic symptoms included abnormal behavior, verbal abnormality, seizure, headache, and delirium. Others included infants less than 3 months old, or dehydration due to persisting fever. Comparison of these two groups revealed older age in positive(7.4y) than negative group(3.2y), but shorter duration of hospital stay in positive group (5.6 days) than negative (7.2 days). No difference was observed on disease days of admission to hospital after the onset(2.5 versus 2.2 days).

Pneumonia was the largest number in hospitalized children. Prominent picture of this pneumonia was as follows; abrupt onset of fever as well as respiratory difficulty, and rapid progressive deterioration of respiratory state which mimics status asthmaticus with expiratory wheeze and massive secretion. Most of affected children were school-aged with or without prior history of bronchial asthma, although elevated serum IgE level was observed without history of bronchial asthma. The initial examination of antigen was sometimes negative in cases of this respiratory failure. All of these children discharged without complications after treatment for status asthmaticus with anti-viral medicine.

P972

ABSCESSING PNEUMONIA AND INFECTION ASSOCIATED HEMOPHAGOCYTIC SYNDROME (IAHS) AS SEVERE COMPLICATIONS OF H1N1 INFLUENZA IN A 5 YEAR OLD GIRL

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In 2009/2010 a previously healthy $5^{11/12}$ year old girl was admitted to our hospital with H1N1 infection and concomitant right basal pneumonia. Despite appropriate antibiotic and antiviral therapy the patient rapidly developed multiple lung abscesses and right-sided pleural effusion. After temporary improvements fever and CrP rose again after 4 weeks of treatment. Accompanied by a transient rush liver enzymes, ferritine and triglycerids rose while INR, fibrinogen, protein and albumin dropped. Further, the patient showed progressive pancytopenia and developed general edemas, hypotension, pericardial effusion, ascites, bilateral pleural effusion, hepatosplenomegaly and cholecystitis. Coinfections were excluded, we observed delayed H1N1-antibody formation. Bone marrow showed hemophagocytosis, cytokine profiles depicted elevated TNFa, sCD25, normal IL2 with diminished IL10, IL6 and perforine. According to HLH-2004 diagnosis of hemophagocytic syndrome was established.

Infection associated hemophagocytic syndrome (IAHS) is an acquired form of hemophagocytic lymphohistocytosis (HLH), a severe and possible life-threatening disorder of immune overactivity in children and adults. Due to temporary NK-cell dysfunction, termination of the inflammatory response fails, leading to cytokine storm and a hyperinflammation with hemophagocytosis within the reticuloendothelial system (causing pancytopenia, hepatosplenomegaly, lymphadenopathy and multiorgan failure). Although mainly reported in EBV infections, few cases of influenza associated IAHS are described. Early IAHS presents with non-specific clinical findings resembling those of other severe inflammations and may therefore be underdiagnosed. Hence, we want to review the features, therapy and pathogenesis of IAHS in general and Influenza-associated-IAHS in particular to raise awareness for the disease and enable diagnosis respectively immunosuppressive therapy in severe forms of IAHS.

P973

DURATION OF SHEDDING OF HUMAN PARECHOVIRUS IN FAECES OF YOUNG CHILDREN AFTER SYMPTOMATIC INFECTION

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Background and aims: Human parechoviruses (HPeV) are closely related to enteroviruses (EVs) and have recently been recognized as important cause of sepsis and CNS infection in infants. HPeV infections in children are very prevalent, mostly associated with mild gastrointestinal and respiratory disease. HPeV-specific real-time PCR is used for diagnosing HPeV infections. It is unknown for how long children are shedding HPeV in their faeces after clinical infection. Therefore, we determined the duration and amount of HPeV detection in faeces of children < 1 year in relation to clinical symptoms.

Methods: Faecessamples of 19 HPeV-positive children with symptomatic infection were collected every 2 weeks until termination of HPeV shedding. The HPeV viral load in faeces was quantified as Ct-value. Clinical symptoms were concurrently documented.

Results: Symptoms at presentation were fever, diarrhea and/or meningeal irritation. The initial Ct-value in faeces varied between 16,5 and 30. The viral load decreased gradually over time. The duration of HPeV shedding ranged from between 4 until 24 weeks. No clinical symptoms were reported after the first week except for one patient who was admitted 2,5 weeks after initial diagnosis with diarrhea and co-infection with adenovirus and two patients who had an episode of mild diarrhea respectively 3 and 15 weeks after initial diagnosis.

Conclusions: The duration of asymptomatic shedding of HPeV in faeces after clinical infection can be up to 6 months. The relative long duration of shedding can be an explanation for the high prevalence of HPeV infection in the first years of life.

P974

CARDIOMYOPATHY DUE TO HUMAN PARECHOVIRUS INFECTION IN AN INFANT AND EFFECT OF TREATMENT WITH IVIG

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Background and aims: Human parechoviruses (HPeV), like enteroviruses (EV) belong to the Picornaviridae family. HPeV-1 and-3 are the most prevalent genotypes. HPeV-3 is associated with neonatal sepsis and meningoencephalitis in young infants. HPeV-1 usually causes mild gastrointestinal and respiratory disease. In rare cases, HPeV-1 can cause more severe disease like myocarditis, paralysis and encephalitis.

No effective treatment is known or available for severe HPeV and EV infections. Since lack of type-specific antibodies in neonates is a risk factor for severe neonatal EV infection, intravenous immunglobuline (IVIG) is sometimes given as treatment, but therapeutic effects remain inconclusive. Here we present a 5 month old boy with an acute cardiomyopathy due to HPeV-1, who was treated with IVIG.

Case report: A 5-month-old boy was admitted to the PICU because of circulatory failure due to dilated cardiomyopathy. HPeV-1 was detected in blood and faeces at the time of diagnosis. No other cause for the dilated cardiomyopathy could be found. Apart from symptomatic treatment of the cardiomyopathy, treatment with IVIG (2 gram/kg) was given during 3 days. In the following weeks the patient recovered clinically and cardiac function improved a little.

It is difficult to assess whether IVIG contributed to the clinical improvement. We showed *in vitro* that IVIG contains high titers of neutralizing antibodies against HPeV-1. which indicates the therapeutic potential of IVIG in these cases.

Conclusions: This case report described an infant with an acute dilated cardiomyocardiomyopathy caused by HPeV-1. Treatment with IVIG resulted in clinical improvement with stable cardiac impairment.

P975

A PRACTICAL APPROACH TO Q FEVER IN CHILDREN

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Since 2007, the Netherlands was confronted with the largest Q fever outbreak ever. Q fever has a wide clinical spectrum ranging from asymptomatic to fatal disease. Knowledge of Q fever has greatly expanded over the last decades, but research has mainly focused on adult disease; data in children are scarce. Available data suggest that children are less severely affected than adults. The warranted approach to pediatric Q fever is often unclear to the general pediatrician. Therefore, the Working Party for Pediatric Infectious Diseases and Immunology of the Dutch Pediatric Society has composed a practical tool for the diagnosis and treatment of Q fever in children, based on best-available evidence and expert opinion. Disease transmission occurs mainly through contaminated aerosols, or by ingestion of contaminated milk. Vertical transmission has also been described. The reference method for diagnosing Q fever is serology using an indirect immunofluorescence assay. However, significant titers may take 3-4 weeks to appear. Therefore, *Coxiella burnetii*-specific PCR of serum samples can be very useful for diagnosis in the early acute phase. Self-limiting febrile illness, gastro-intestinal symptoms such as abdominal pain, nausea and diarrhea, and skin rash are the most frequently reported symptoms in pediatric Q fever. These symptoms, or a history of exposure to *C. burnetii* in a symptomatic child, should trigger the physician to investigate the possibility of Q fever. Routine serological and PCR follow-up of neonates born from Q-fever infected mothers is also recommended. Treatment regimens depend on the age of the patient and presenting symptoms.

P976

EPIDIDYMOORCHITIS AS A COMPLICATION OF BRUCELLOSIS

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Background and aims: Epididymoorchitis is one of the most problems which an urologist encountered in clinic. In addition to Neisseria gonorrhoeae and etc, some speciess of brucella must be considered as etiologic factors for epididymoorchitis. Brucellosis is a common problem in Iran especially in Hamadan.

Methods: A 14-year-old boy with no previous significant medical problems was admitted in our hospital due to left testis swelling and pain. His problem had begun as a swelling and pain in left testis from one week ago that pain had progressed gradually to the inguinal. There was no history of fever or trauma.

Results: His vital signs were: RR=20/min, PR=95/min, T=37 (Ax) and BP=110/60 mm Hg. Lymphadenopathy, erythema or fever was not detected. A complete blood count revealed 6900 WBCs/mm^3 with a differential of 50% segmented neutrophil, 48% segmented lymphocyte, 1% segmented monocyte and 1% segmented Eosinophil. Hemoglobin was 13 g/dl, ESR=50 mm/h, CRP=+, and U/C = negative. In the case of he lived in a rural district in Hamadan, a state in the west of Iran that is a hyperendemic area for brucellosis, serologic test for brucellosis was done. According to the positive serology, Wright agglutination test= 1:320, the patient received Doxycycline, Rifampicin, and Gentamicin. He recovered completely without any sequela.

Conclusions: We suggest, in endemic area serologic test for brucellosis must be routinely done for all cases of epididymoorchitis or at least for the cases that have negative urine culture or no appropriate clinical response to medical therapy for non brucella epididymoorchitis.

P977

HYDATID DISEASE IN CHILDREN

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Background: Echinococcosis is one of the most frequent parasitosis in human. The disease is endemic in Romania, with an incidence of 5.6/ 100000.

Material and methods: Between 2004 and 2010, 32 children were treaed for hydatic cysts at the Emergency Children's Hospital “Louis Turcanu” Timisoara, Romania.

Results: Age ranged between 1 and 18 years and male/ female ratio was 1.2/1. The most frequently involved site was the liver (77%) followed by the lungs (10%). In 10 case multiple cysts were found in the liver and in 3 cases there were concomitant multiple pulmonary and hepatic cysts. In the liver were 76% located in the right lobe, 17% in left and 7% in both. Uncommon locations were spleen, pancreas, choledochal duct, brain and retro uterine. The dimension was < 5 cm in 33.3%, between 5 and 10 cm in 46.6% and more than 10 cm in 20%. The surgical procedure was Lagrot partial pericystectomy. In addition to the surgical treatment, oral antihelminthic treatment was started preoperatively and was continued for 2 months after the intervention. There were no deaths. Complications occurred in two cases, a biliary fistula and hypernatremic convulsion after innactivation of the parasite with 20% chloride. Hospital stay varied from 2 days to 41 days, mean 21 days. Postoperative follow-up ranged from 6 months to 5 years, mean 3 years.

Conclusion: Echinococcosis is still an importantant source of morbidity in pediatric age patients necessitating complex approach including surgical, medical treatment and long term follow up for recurrences.

P978

SEROEPIDEMIOLOGICAL STUDY OF *BARTONELLA HENSELAE* IN CHILDREN

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Background and aims: *Bartonella henselae* is the main etiologic agent of Cat Scratch Disease (CSD), an emerging zoonotic disease with a worldwide distribution. Cats are usually asymptomatic carriers that transmit the pathogen to humans by a scratch or bite. It affects primarily children and young adults, causing regional lymphadenopathy (classical form of CSD). The clinical spectrum of the disease is ever expanding and there is an increasing scientific interest for members of the genus *Bartonella*. The aim of the study is to estimate the seroprevalence of specific *B. henselae* antibodies (IgG) in children in Greece.

Methods: Blood serum samples from children that were admitted in our department for various clinical conditions were examined by the method of indirect immunofluorescent assay (IFA). Demographic and clinical data were collected at the time of admission.

Results: Out of 400 sera, 23 were found positive (5,75%), with an antibody titer between 1/64 and 1/256.

Conclusions: Our findings are consistent with relevant studies in Europe. Since our serum samples were obtained from symptomatic children the presence of specific *B. henselae* antibodies may be caused by past or current infection.

P979

ASYMPTOMATIC CARRIAGE OF LEISHMANIA IN CHILDREN AND ADOLESCENTS

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Background and aims: Visceral leishmaniasis also known as kala azar is a zoonosis caused by intracellular protozoa of Leishmania species. Greece is amongst mediteranean countries that the disease is endemic and the main cause is the *Leishmania donovani infantum.* Many studies show that except from the clinical apparent form there is also subclinical occurance of the disease as well as asymptomatic cases. The aim of our study is to identify specific leismania antibodies in asymptomatic pediatric population.

Methods: Blood serum samples from asymptomatic children that were admitted in our department for various conditions were screened for specific Leishmania infantum antibodies using the indirect immunofluorescence assay (IFA). Demographic and clinical data were also collected at the time of admission.

Results: 5 over 600 children were tested possitive(8,3‰) with antibody titre 1/64 to 1/256.

Conclusions: It appears that the percentage of children with asymptomatic and/or subclinical leishmaniasis is extremely low in our country.

P980

DIAGNOSIS PECULIARITIES IN A CASE WITH HEPATITIS

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Background and aims: Toxocariasis is a zoonotic, helminthic infection of humans caused by the roundworms *Toxocara canis* or *Toxocara cati*. The authors emphasize the diagnosis peculiarities for a child with enlarged liver and spleen and liver function impairment.

Methods: Authors present a 2 years old boy suspected by leukemia. The patient clinical features: fatigue, fever, impaired nutritional status, skin pallor, hepatomegaly and splenomegaly.

Results: The laboratory investigations has revealed: leukocytosis (47.000/mm^3), marked eosinophilia (64%), severe iron deficiency anemia, normal platelet count, impaired liver function (high values for ASAT and ALAT). From hematological point of view: bone marrow aspirate indicated eosinophil precursors hyperplasia. Immunological evaluation of patient has shown hypergammaglobulinemia (IgM and IgG), high serum titers for *Toxocara canis* and positive serology for infectious mononucleosis. The stool sample exam was negative for parasites. The chest Xray and imagistics (abdominal ultrasonography, echocardiography) didn't show any anomalies. The ophthalmological exam was normal. In context of leukocytosis correlated with hepatomegaly and splenomegaly, the main differential diagnosis was performed with acute and chronic eosinophilic leukemia (disorders excluded based on bone marrow analysis).

Conclusions: The authors have presented a child with hematological abnormalities associated with hepatitis, enlargement of liver and spleen in context of concomitant infections (toxocariasis and infectious mononucleosis). Leukocytosis could be explained by Epstein-Barr infection and marked increase in eosinophil count. Case peculiarity: patient had 2 simultaneous infections explaining the high index of suspicion for eosinophilic leukemia.

P981

CONSIDERATIONS ON HYDATID CYST IN CHILDREN

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Background and aims. Constanta county is a region with high endemicity, there are villages where the incidence of hydatidosis exceeds 10 cases/ 100.000 inhabitants. Presence of dogs on the beach and sand contamination leads to the spreading of the disease especially among children.

Methods. We studied hydatid cyst pattern in children. The diagnosis was based on chest x-ray, abdominal ultrasonography, computed tomography and ELISA reaction.

Results. Of the 382 patients diagnosed with hydatid cyst in Constanta Infectious Diseases Clinic over a period of 5 years, 36 were children (9.4%), 22 male and 14 female, from 6 to 18 years of age. The most frequent occurrence was on the liver (18 cases), followed in frequency by the lungs (11 patients), in 2 cases both organs were involved. In one case different locations were encountered **(**kidney, spleen, peritoneal, pericardial and brain). The epidemiological conditions were positive in the majority of cases; most of the patients documented the contact with animals. There were nine familial clusters, children are diagnosed incidentally, after parents have been operated for hydatid cyst. Most patients revealed solely one cyst (25 cases); cysts dimensions between 3 and 5cm were encountered in most cases (27 cases). 28 patients with hydatid cyst with small dimensions (less than 5 cm) have received only treatment with Albendazole with good evolution, surgery was required in other cases.

Conclusions. The prevalence of hydated disease is high in our region. This disease require a particularly attention and health programs for a better management.

P982

Q FEVER IN THE NETHERLANDS IS LESS REPORTED IN CHILDREN

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Background and aims: The Q fever outbreak in the Netherlands of 2007-2009 is the largest one ever reported: 3522 notifications. *Coxiella burnetii*, that causes this zoonotic disease, is mainly transmitted to humans through aerosols. Living near contaminated farms, especially in the lambing period, is the main risk factor. In theory, the exposure risk is equal for all those living in the same area, both adults and children.

Methods: We inventoried the number of cases amongst children (0-19yr) during that period, calculated the reported incidence and compared this with adults. We reviewed the literature to inventory case reports among children.

Results: 123 children (3,6% of total notifications) were reported. The incidence in children was 0,31 per 10.000 compared to 2,65 in adults. Main reported symptoms were fever of unknown origin and gastro-intestinal symptoms. Besides 14 pneumonias, no other serious complications were reported.

We found 20 national and/or regional scientific studies reporting seroprevalences between 0-70%. In 19 articles 52 cases with a serious outcome were described. 4 children died of complications. In chronic Q fever cardiac infections were predominant.

Conclusion: With only 3,6% of notifications from 23,11% of the exposed population we conclude that infections in children are less symptomatic but also frequently overlooked. Children get infections that can present themselves with self-limiting flu-like symptoms but also as rare conditions like encephalitis, osteomyelitis, hepatitis or endocarditis. Therefore paediatricians should be aware of *Coxiella* infections in these or unexplained cases. The Dutch Society of Paediatrics (www.nvk.nl) has drafted a guideline “Advices on Q fever”.

P983

LEPTOSPIROSIS-THE NEW DISEASE OF MISTAKES

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Aim: Leptospirosis is zoonotic disease of worldwide distribution which has a broad spectrum of clinical manifestation varying from in apparent influenza like illness to fulminant fatal disease with hepatorenal dysfunction and hemorrhagic manifestation.

Method: Retrospective analysis of data of leptospirosis patients from our institution during last epidemic from May-November 2010.

Result: We had 15 children of referred to us as case of viral fever or viral hemorrhagic fever with symptoms of headache, fever, vomiting, rash and thrombocytopenia. Majority of patients were below 10 yr of age and from semi urban or rural background . All of them were within their first week of illness. The diagnosis was suspected when the labs were negative for other common illness like malaria, dengue etc All of them had generalized symptoms of flu like illness and half of them had meningitis. 25% had hemorrhagic manifestations with hepatorenal dysfunction without any mortality

Conclusion: Leptospirosis is grossly under diagnosed disease in our country due to lack of awareness and inadequate diagnostic facilities. Our data suggest that leptospirosis should be considered in differential diagnosis of acute febrile illness and prompt treatment should be initiated to prevent complications.